

Abstract 81° Congresso Nazionale della Società Italiana di Cardiologia

ARITMIE

A1: NUOVI PREDITTORI DEL RISCHIO ARITMICO NEI PAZIENTI CON PROLASSO MITRALICO: RUOLO DELLA FIBROSI MIOCARDICA E DELLA DISGIUNZIONE DELL'ANULUS MITRALICO

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Background. La disgiunzione dell'anulus mitralico (MAD) rappresenta una condizione di comune riscontro nei pazienti con prolasso valvolare mitralico (PVM), e si manifesta come una netta separazione evidente durante la sistole ventricolare a livello del complesso formato da anulus valvolare mitralico-muscolatura atriale e parete ventricolare sinistra. Esistono diversi fattori di rischio associati ad un aumentato rischio di morte cardiaca improvvisa nei pazienti con prolasso della valvola mitrale, la maggior parte dei quali può essere valutata in modo non invasivo. Tra questi, la MAD e la presenza di fibrosi in aree miocardiche specifiche rappresentano due caratteristiche cliniche oggetto di numerosi e recenti studi.

Obiettivi. Lo scopo di questo studio è di descrivere la presentazione clinica della MAD, la sua morfologia e l'associazione tra questa, la fibrosi miocardica e le aritmie ventricolari. Questo lavoro indaga il potenziale ruolo chiave della MAD e della fibrosi miocardica al fine di eseguire una corretta stratificazione del rischio aritmico nei pazienti con PVM.

Metodi. Sono stati valutati in maniera retrospettiva tutti i pazienti afferenti all'ambulatorio per le valvulopatie presso la SOD di Diagnostica Cardiovascolare dell'AOU di Careggi nel periodo compreso dal 1 gennaio 2018 al 31 luglio 2019: 35 di loro (età media 54 ± 13 anni; 18 donne), con prolasso degenerativo della valvola mitrale e con una precedente risonanza magnetica cardiaca (RMC), sono stati arruolati nello studio. A tutti i pazienti è stata effettuata una ecocardiografia transtoracica, un monitoraggio elettrocardiografico delle 24h secondo Holter e una RMC. I pazienti sono stati divisi in due gruppi in base alla presenza di MAD alla risonanza. Sono stati confrontati aspetti anamnestici, clinici e cardiaci morfologici e funzionali tra pazienti con e senza MAD. In particolare, lo studio si è focalizzato sullo studio della presenza e localizzazione della fibrosi miocardica, sull'incidenza delle aritmie nei due diversi gruppi e sulla correlazione tra gravità della MAD e la presenza di tachicardie ventricolari non sostenute (TVNS).

Risultati. MAD era presente in 18 (52%) pazienti (lunghezza media: $5,0 \pm 1,6$ mm): non c'erano differenze nell'età e nel sesso tra i due gruppi. Non c'erano differenze statisticamente significative neanche per quanto riguardava i sintomi e la classe funzionale NYHA, i volumi delle camere cardiache e la loro funzionalità, la cinetica dell'anulus mitralico e la gravità del rigurgito mitralico. Al contrario, la MAD risultava fortemente correlata alle aritmie ventricolari: i BEV/24h erano significativamente più numerosi nei pazienti con MAD (627 vs 12; $p=0,04$) e le forme complesse pure (14 vs 4; $p=0,002$). In particolare, la gravità della MAD era significativamente correlata con l'insorgenza di tachicardia ventricolare non sostenuta (TVNS) al monitoraggio Holter: un valore di MAD $>5,5$ mm ha rappresentato un forte predittore per questo tipo di aritmie (area sotto curva ROC 0,812; sensibilità 71%, specificità 73%; OR 6,7). È stata riscontrata fibrosi miocardica nella parete infero-basale e nei muscoli papillari (15 pazienti; 43%), ma non risultava correlata alla presenza di MAD (8 vs 7; $p=ns$).

Conclusioni. La disgiunzione dell'anulus mitralico è una caratteristica di comune riscontro nei pazienti con prolasso degenerativo della valvola mitralica. L'eccessiva mobilità dei lembi causata da un anomalo movimento sistolico (*curling*) determina uno stress meccanico nella parete inferobasale e nei muscoli papillari, che conduce nel tempo ad ipertrofia miocardica e fibrosi. Le aritmie ventricolari erano molto più frequenti nei pazienti con MAD, con differenze statisticamente significative rispetto a quelli senza disgiunzione. È stato evidenziato come la gravità della MAD possa rappresentare un buon predittore per l'insorgenza di NSVT. Inoltre, lo studio avanza l'ipotesi che il carico aritmico possa essere considerato da molte caratteristiche del paziente, come quelle anamnestiche, cliniche, cardiache morfologiche o funzionali, e suggerire che la MAD come entità a se stante sia sufficiente a spiegare il differente profilo aritmico nei due gruppi. Come suggerito dalla letteratura, la presenza di MAD e la sua gravità sembrano essere dei buoni fattori di rischio per valutare il profilo aritmico dei pazienti con PVM. Al contrario, la fibrosi non è risultata essere un buon predittore, forse per colpa del piccolo gruppo di pazienti, o più probabilmente perché rispetto alla MAD rappresenta un predittore con minor forza, e la sua insorgenza sia probabilmente subordinata e conseguenziale a quella della disgiunzione dell'anello

mitralico. Nel prolasso valvolare mitralico si evidenzia quindi la necessità di ricercare la MAD con forza e specificità, in quanto nessun altro parametro sembra poterci indicarne la presenza. Il riscontro della disgiunzione dell'anulus mitralico deve essere preso in considerazione nella valutazione del profilo di rischio aritmico del paziente e, unitamente ad altri fattori, deve portare alla discussione di misure avanzate per la profilassi della morte cardiaca improvvisa in casi molto selezionati.

A2: ORAL ANTICOAGULANTS IN FRAGILE PATIENTS WITH PERCUTANEOUS ENDOSCOPIC GASTROSTOMY AND ATRIAL FIBRILLATION: THE ORIGAMI STUDY

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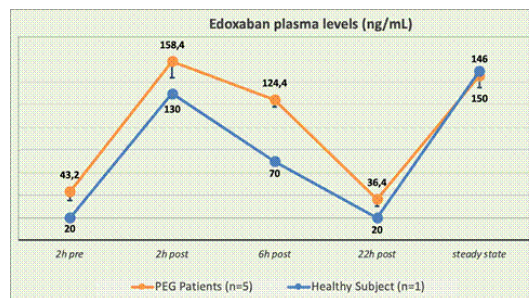
Background. Randomized trials support the safety and efficacy of direct oral anticoagulants (DOACs) versus vitamin K antagonists (VKA) in patients with nonvalvular atrial fibrillation (AF), leading to increased use of these compounds. Crushed forms of DOACs have shown to be reliable, but evidence supporting percutaneous endoscopic gastrostomy (PEG) delivery is lacking. PEG is a long-term option for enteral food and drug delivery in patients unable to maintain oral intake, bypassing the risks and disadvantages of parenteral nutrition.

Aims. We investigate the safety and efficacy of edoxaban administered via PEG in patients with atrial fibrillation and a clinical indication for a long-term anticoagulation.

Design. In this prospective, single centre observational study, 12 PEG-treated patients with indication to anticoagulation will receive edoxaban via PEG and will be followed-up to 6 months. Plasma anti-Factor Xa activity and edoxaban concentrations will be assessed. Thromboembolic (ischaemic stroke, systemic embolism, venous thromboembolism) and bleeding events (Bleeding Academic Research Consortium and Thrombolysis in Myocardial Infarction) will be recorded at 1 and 6 months.

Preliminary cases. A retrospective analysis of 5 AF cases undergoing PEG-implantation at our Institution, who received edoxaban via PEG, showed plasma anti-FXa levels at steady state of 146 ± 15 ng/ml, without major adverse event at a mean follow-up of 6 months.

Conclusion. We prospectively investigate PEG-administration of edoxaban in PEG-treated patients requiring long term anticoagulation. Our preliminary retrospective data support this route of DOAC administration.



A3: TACHICARDIA DA RIENTRO BRANCA-BRANCA DOPO IMPIANTO DI PMK HISIANO

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Maschio di 63 anni con cardiomiopatia indotta da PMK, per il riscontro di blocco intrahisiano (dissociazione AH-HV) è stato sottoposto a stimolazione hisiana permanente con cattura selettiva. Tre giorni dopo comparsa di TV sostenuta con morfologia BBS ed asse inferiore. È stato sottoposto a coronarografia con riscontro di malattia critica di IVA media sottoposta a PTCA e stenting DES. Per la persistenza di TVNS è stato eseguito SEF con stimolazione dai cateteri hisiano e VD risultava negativo. È stato infine

eseguito upgrading ad ICD in prevenzione secondaria con catetere hisiano in porta LV. Nonostante il recupero della FEVS persisteva dispnea da sforzo, per cui veniva attivata la funzione rate response, disattivata poco dopo per diversi episodi di TVS trattati con ATP. L'EGM durante TV mostrava un ciclo di 300 ms e HV 160 ms (HV spontaneo 40 ms) con innesco da parte di singolo BEV con copula di 710 ms.

Il meccanismo ipotizzato alla base dell'aritmia è il rientro branca-branca: un BEV tardivo troverebbe la branca sinistra eccitabile in senso retrogrado innescando il circuito di rientro. La refrattarietà della branca si accorcia alle frequenze più elevate e questo dimostrerebbe l'effetto pro-aritmico esercitato dalla funzione rate response. La dimostrazione di un HV costante durante TV maggiore del HV basale ed il substrato ischemico supporterebbero tale diagnosi. Un meccanismo alternativo potrebbe essere la dispersione della ripolarizzazione determinata dal cambio di stimolazione, ipotesi supportata dal miglioramento delle ARIP dopo upgrading.

Il caso dimostra che la stimolazione hisiana determina un recupero della cardiomiopatia da PMK ma potrebbe predisporre con molteplici meccanismi ad aritmie ventricolari nonostante il recupero della funzione sistolica.

A4: ABLATION OF FOCAL AND ROTATIONAL ACTIVITY DETECTED BY CARTOFINDER SOFTWARE IN PATIENTS WITH PERSISTENT AF

Leonardo Belfioretti (a, b), Umberto Falanga (a, b), Manuel Antonio Conti (a, b), Laura Cipolletta (a, b), Gino Grifoni (a, b), Alessandro Barbarossa (a, b), Giovanni Volpato (a, b), Paolo Compagnucci (a, b), Giulia Stronati (a, b), Federico Guerra (a, b), Michela Casella (a, b), Antonio Dello Russo (a, b) (a) AZIENDA OSPEDALIERO UNIVERSITARIA OSPEDALI RIUNITI ANCONA UMBERTO I - LANCISI - SALES; (b) UNIVERSITÀ POLITECNICA DELLE MARCHE **Background.** Mechanisms sustaining persistent atrial fibrillation (AF) remain poorly understood, but rotors and focal impulse sources could play an important role in maintaining arrhythmia. Cartofinder is a novel mapping software that uses the CARTO platform (Biosense Webster). It constructs an activation map through a recording of 30 seconds, referencing each electrogram relative to all the others in the LA by identifying focal and rotational activity. Currently, there is no well-defined ablation strategy to treat persistent AF and ablation of focal drivers and rotors seems to determine an improved long-term outcome.

Aim. Compare an ablation strategy guided by Cartofinder and ablation index (AI) versus ablation of the posterior wall and other trigger identified by challenge test with isoproterenol and evaluate AF recurrences in a short term follow-up.

Methods. We enrolled 16 consecutive patients with persistent AF and indication for catheter ablation. All patients underwent antral pulmonary vein isolation (PVI) guided by AI. Ablation points had an AI range of 500-550 in the anterior wall and 400 elsewhere side of PV. In 8 patients, atrial geometry was acquired using PentaRay NAV catheter (Biosense Webster) and recordings were analyzed with Cartofinder software. Stable rotational activity or focal activities were ablated follow AI targets. The other group of 8 patients underwent posterior wall homogenization and ablation of non-PV triggers identified by challenge test with intravenous isoproterenol. AF recurrences were evaluated after 3 months with 12-lead electrocardiograms.

Results. In Cartofinder group we found focal activities in left atrium (85%) and right atrium (15%). In the left atrium the majority of focal drivers were found in left atrial appendage, posterior wall and left atrium roof, while in right atrium we found focal activities in right atrial appendage, coronary sinus, superior vena cava and atrial septum. We performed an ablation index (AI) guided procedure: in left atrium mean AI value was 353, while in right atrium mean AI value was 342. Rotational activities were found only in left atrium: 30% left atrial posterior wall, 30% left atrial appendage and 30% warfarin ridge. Mean AI value in these areas was 363. During ablation of focal activities and rotors we did not observe sinus rhythm restoration. In the other group we performed posterior wall homogenization and we found non-PV triggers after challenge test with intravenous isoproterenol localized in posterior wall and atrial roof. In these areas mean AI value was 460. No complications were observed. AF recurrences were evaluated after a mean follow-up of 3 months with in-office visit. We found three symptomatic AF recurrences in both groups, all within 3 months.

Conclusions. Cartofinder software allows a reliable identification of focal activities and rotors in patients with persistent AF. We did not observe any difference between these two different ablation strategies. A larger sample of patients is needed in order to evaluate the real efficacy of ablation strategy guided by Cartofinder and ablation index.

A5: SEGMENTAL ISOLATION OF PV USING LIVEVIEW SYSTEM WITH LSI-GUIDED LESIONS: A SHORT-TERM FOLLOW-UP

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(Abbott Technologies) are well established diagnostic tools for catheter ablation of AF. The new EnSite™ LiveView Dynamic Display (Abbott Technologies) provides real-time visualization of electrical information gathered by the Advisor HD Grid catheter in order to identify the pulmonary venous breakthrough. In this way the LiveView system provides instant identification of target areas for ablation, allowing a prompt segmental PV isolation instead of performing anatomical PV encircling. Moreover, to assure a complete transmural lesion, it's important the use of lesion index (LSI), representing a novel lesion quality marker incorporating contact force, power supply and radiofrequency time. In fact, mean LSI values of 5-5,5 and 4,5-5 for anterior and posterior wall, respectively, are associated with a better acute and long-term outcomes.

Aim. To evaluate AF recurrences after segmental PV isolation using LiveView system and LSI in a short-term follow-up.

Methods. We enrolled 7 patients with paroxysmal and early-persistent AF who underwent RF ablation using Tactiath™ Quartz catheter (Abbott Technologies). The ablation procedure was conducted pursuing segmental PV isolation guided by LiveView system. Each ablation point had a target LSI value of 5-5,5 and 4,5-5 for anterior and posterior wall respectively. The complete PV isolation was validated after 30 minutes with pacing maneuvers and administration of intravenous adenosine. In case of venous reconnection, PV isolation was completed with segmental ablation identifying venous breakthrough. Then, each patient underwent loop recorder implantation. AF recurrence was evaluated 1 month after procedure with in-office visit and loop recorder interrogation.

Results. The mean procedural time was 162,5 minutes which is less than mean procedural time (212,8 minutes) for patients undergoing AF ablation with Ensite precision system using encircling PV isolation in our center. The mean ionizing radiation exposure, quantified with Dose Area Product (DAP), was 139,2 mGy*cm². Mean LSI values were 4,8 and 4,7 for LSPV respectively anterior and posterior wall; 5,1 anterior and 5 posterior for LIPV; 4,9 anterior and 4,5 posterior for RSPV; 5,3 anterior and 5,1 posterior for RIPV; 4,6 and 5,1 for left and right carena, respectively. Two patients showed PV reconnection after pacing maneuvers, while two patients showed PV reconnection after Adenosine test. No complications were observed. After a short term follow-up of 1 month, although in the blanking period, AF recurrences were detected in 2 patients. The recurrences were self-limiting, lasting respectively 27 and 120 minutes and only one patient was symptomatic. Interestingly, both of these patients showed PV reconnection after pacing maneuvers.

Conclusions. Real-time visualization of PV breakthrough and ablation LSI-guided allow a reliable and safe segmental PV isolation potentially reducing procedural time and ionizing radiation exposure. Moreover, this approach avoids additional ablative lines which are potentially arrhythmogenic. These data are preliminary and not reliable because follow-up is still in blanking period and the inflammatory process of ablation itself can be responsible of AF recurrences. We need longer follow-up to evaluate efficacy of this new approach.

A6: EVALUATION OF NEW ALGORITHM LIVEVIEW-GUIDED PULMONARY VEIN ISOLATION TECHNIQUE IN PATIENTS WITH ATRIAL FIBRILLATION

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Methods. Patients with paroxysmal and early persistent (<3 months) AF underwent segmental PVI with a CF sensing catheter (TactiCath™, Abbott) with LSI-guided ablation (LSI range 5.5 in the anterior and 4,5 elsewhere side of PV). RF lesions were created sequentially based on breakthrough activity identified by Liveview module with HD Grid mapping catheter, until the isolation of the vein was achieved. PVI was confirmed by demonstrating entry and exit block by pacing maneuvers and at least 20 minutes after electrical isolation of each PV, was performed a check with Adenosine. All patients were monitored with an implantable loop recorder.

Results. Preliminary data was collected in 7 patients. Patient characteristics are shown in Table 1. De novo and repeat ablations represented 85,7% and 14,3% of cases respectively. The mean procedure time was 164,3 minutes [120-240]. The mean time of isolation

of single vein was 12,17 minutes [0,45-28], with an average number of RF applications for single vein equal to 8 [2-28]. In 58% of cases persistent isolation of the vein guided by breakthrough activity was achieved by applying RF lesions in the anterior segments. Higher LSI values were reached in the anterior segments (median LSI = 5 [4,1-6,1]) than in the posterior wall (median LSI = 4,7 [4,1-5,4]). Persistent electrical isolation of each PV after Adenosine administration was achieved in 93% of PVs. **Conclusion.** These preliminary data on segmental PVI driven by breakthrough activity identified by Liveview module, show a positive trend towards successful electrical isolation of PVs but more data with follow-up are needed to evaluate long-term efficacy.

Age, mean ± SD [years]	58±13
Gender, male, n (%)	4 (57)
Hypertension, n (%)	4 (57%)
Diabetes mellitus, n (%)	1 (14%)
CHA ₂ DS ₂ -VASc, n	
0	1
1	1
2	2
3	3
4	0
5	0
Paroxysmal AF, n	5
Early persistent AF, n	2
Ejection fraction, mean ± SD [%]	60,7±13
Left atrial AP volume, mean ± SD [ml/m ²]	32,4±13
Ischemic cardiopathy, n (%)	0 (0)
Acute complications, n (%)	0 (0)

A7: RESTARTING ANTICOAGULATION AFTER CHRONIC SUBDURAL HEMATOMA NEUROSURGICAL EVACUATION: A PROSPECTIVE OBSERVATIONAL STUDY

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Objectives. Management of anticoagulation (AC) in patients with chronic subdural hematoma (cSDH) lacks evidences, with uncertainties regarding outcomes after neurosurgical intervention. We aimed to define safety and effectiveness of AC resumption in a single center cohort undergoing neurosurgical intervention for cSDH.

Methods. Consecutive patients undergoing neurosurgical intervention for evacuation of cSDH and taking anticoagulants due to atrial fibrillation were included and followed-up over time (3 to 30 months) to define evolution of cSDH thickness depending on AC restart. Secondary outcomes included: (i) ischemic stroke and major bleeding (including intracerebral hemorrhage, ICH), assessed at each visit, and (ii) recurrent cSDH needing neurosurgical re-intervention.

Results. Overall, we included 47 consecutive patients, mean age 82.5±7.8 years. Previous trauma emerged in 68% of cases. Patients received warfarin (n=30, 64%), low molecular weight heparin (LMWH, n=6, 13%) or direct oral anticoagulants (DOAC, n=11, 23%). Oral AC was stopped before neurosurgery (7.9±16.7 days before intervention), and 42 (89%) underwent AC reversal. Mean cSDH thickness was 2.3±0.6 cm, midline shift was detected in 94% of patients. All patients survived surgical procedure and completed a minimum of 3-month follow-up. Over a mean 8-month follow-up (range 3-29), cSDH thickness substantially decreased (baseline 2.3±0.6 cm vs follow-up 0.7±0.6 cm, p<0.001). Overall, 26 patients (55.3%) restarted AC, 15 with DOAC, 8 with warfarin, 3 with LMWH. Compared to no AC, AC resumption was not associated with changes in cSDH thickness (0.7±0.7 cm vs 0.9±0.6 cm, p=0.4) or modified Rankin scale at follow-up (2.6±1 vs 2±1.3, p=0.3). Four patients restarting AC had cSDH recurrence requiring re-intervention vs 0 in those avoiding AC (p=0.11); 3 of 4 were post-traumatic. No peri-interventional complications occurred. No ischemic stroke or major bleeding was detected during AC withdrawal.

Conclusions. The study has obviously limitations due to its preliminary nature. Even though, resumption of anticoagulation after neurosurgical intervention for cSDH seems safe, with no significant increase in recurrence rate and cSDH width over time. Longitudinal data from prospectively collected larger cohorts are needed to guide management.

A8: CAUSES, SAFETY AND OUTCOMES OF SWITCHING FROM THE INITIAL DIRECT ORAL ANTICOAGULANT TO ANOTHER IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION

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Objectives. The purpose of this study was to evaluate causes, annual rates and outcome of switching from one to another direct oral anticoagulant (DOAC) among patients with nonvalvular atrial fibrillation (NVAF).

Methods. Overall, 300 patients receiving first DOAC prescription at the Anticoagulation Center, from December 2017 to December 2019 were consecutively included and followed. Mean age was 79.3±8.5, female 46.3% (n=139). Mean follow-up was 1.6 years. Two hundred-twelve patients were received DOAC being naïve (70.7%), while 88 (29.3%) transitioned to DOAC from VKA. Baseline mean ischemic and hemorrhagic risk were both moderate (mean CHA₂DS₂-VASc 3.6, mean HAS-BLED 1.8). Most prescribed DOACs was rivaroxaban (n=107), followed by apixaban (n=82), edoxaban (n=59) and dabigatran(n=52).

Results. 39 patients (13%) switched from DOAC to DOAC. Minor bleeding led to switch in 54%, major bleeding in 100%, and non-CV events in 93% of cases. Non-CV adverse events were significantly more frequent with dabigatran vs apixaban or rivaroxaban (17.3% vs 1.2% and 0%, respectively, p<0.001). Crossover was preferentially oriented towards apixaban (43% of cases, p<0.04). After switch, 87.2% of patients had complete resolution or absence of further events. Minor bleeding annual rate was 6.9% (95% CI 4.2-9.4), while major bleeding was 0.5%/year, (95% CI 0.1-1.7). Annual rate of switch due to minor and major bleeding being was 3.6% (95% CI 2.1-5.8) and 0.7% (95% CI 0.2-1.9) respectively. Minor bleeding was less frequent after switch (1.7% vs 6.4%, p=0.09).

Conclusions. Minor bleeding and non-cardiovascular adverse events are the most common causes of switch: 15%/year. Apixaban seems, compared to other DOACs, the one with the highest persistence rate.

A9: EFFECT OF ATRIAL FIBRILLATION ON ANGIOGRAPHIC CHARACTERISTICS AND SEVERITY OF CORONARY ARTERY DISEASE IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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Background. Patients with atrial fibrillation (AF) have an increased risk of coronary artery disease (CAD) compared to patients without. Angiographic characteristics, clinical presentation and severity of CAD according to the presence of AF have been poorly described.

Methods. Retrospective study including 303 consecutive patients with and without AF undergoing percutaneous coronary intervention. Data on 1) type of CAD presentation, 2) coronary involvement and 3) number of diseased coronary vessels (≥70%/luminal narrowing), have been collected. CHA₂DS₂-VASc and 2MACE score were calculated.

Results. Mean age was 69.6±10.8 years and 23.1% were women. Presentation of CAD was STEMI in 37.6% of patients, NSTEMI-UA in 55.1%, and other in 7.3%. NSTEMI-UA was more common in AF (69.6% vs. 46.6%, p<0.001), while STEMI was more in the non-AF (22.3% vs. 46.6%, p<0.001) group. Left anterior descending artery (LAD) was the most common diseased vessel (70.6%) followed by right coronary artery (RCA, 56.4%) and obtuse marginal artery (36.6%). Patients with AF had a slightly lower LAD (64.3% vs. 74.3%, p=0.069) and a significantly lower RCA involvement (47.3% vs. 61.8%, p=0.016). At multivariable logistic regression analysis, AF remained inversely associated with RCA involvement (Odds Ratio [OR] 0.541, 95% Confidence Interval [CI] 0.335-0.874, p=0.012) and with ≥3 vessels CAD (OR 0.470, 95% CI 0.272-0.810, p=0.007). The 2 MACE score was associated with diseased LAD (OR 1.301, 95% CI 1.103-1.535, p=0.002) and with ≥3 vessels CAD (OR 1.330, 95% CI 1.330-1.140, p<0.001).

Conclusions. Patients with AF show lower RCA involvement and a general less severe CAD compared to non-AF ones. 2MACE score was higher in LAD obstruction and identified patients with severe CAD.

A10: CHA₂DS₂-VASc AS A PREDICTOR OF ATRIAL FIBRILLATION RECURRENCE AFTER CATHETER ABLATION

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Background. The identification of patients affected by atrial fibrillation (AF) who preferentially benefit from transcatheter AF ablation is a relevant

and debated issue. CHA₂DS₂-VASc score is widely utilized to stratify the thromboembolic risk in patients with non-valvular AF. A high CHA₂DS₂-VASc score has been also associated with a major grade of LA fibrosis and systemic inflammation, both representing pro-arrhythmic features.

Aim. In this study we evaluated the correlation between CHA₂DS₂-VASc score and arrhythmia recurrence after AF catheter ablation.

Methods. In a retrospective analysis we collected data from 250 patients. All patients received a strict follow-up at 3 months after the ablation and then every 3-6 months or in the case of symptoms. Primary endpoint was the incidence of AF recurrence at a mean of 23.6±2.2 month follow-up according to baseline CHA₂DS₂-VASc score.

Results. Mean age was 59.37±1.34 years and 198 patients (79.2%) were men; 104 (41.6%) had paroxysmal AF, 139 (55.6%) persistent AF and 7 (2.8%) both. All patients underwent radiofrequency ablation except 12, who received cryoablation. Class I and III antiarrhythmic drugs were used at discharge in 137 (54.8%) patients. Mean LV ejection fraction was 55.2±0.9%. CHA₂DS₂-VASc score was calculated in each patient: mean CHA₂DS₂-VASc score was 1.63±0.18; 176 (70.4%) patients had a score ≥3. AF recurrence raised progressively with parallel increase of CHA₂DS₂-VASc score. For a CHA₂DS₂-VASc of 0, the recurrence rate was 12.2%; for CHA₂DS₂-VASc 1 was 18%; for CHA₂DS₂-VASc 2 was 33.3%. For a CHA₂DS₂-VASc of 3, 4 and 5 the recurrence rates were 50, 56 and 50%, respectively. CHA₂DS₂-VASc score was 2.43±0.33 in patients with AF recurrence after the ablation vs 1.31±0.20 in those without. Multivariate analysis confirmed CHA₂DS₂-VASc as an independent predictor of AF recurrence; in particular, patients with CHA₂DS₂-VASc ≥3 had a 2.7 fold higher risk of AF recurrence after the intervention (OR 2.7; 95% CI 1.26-5.65; p=0.011).

Conclusions. A high CHA₂DS₂-VASc score is independently associated with increased risk of AF recurrence after ablation. CHA₂DS₂-VASc score could be an additive tool to conventional predictors for accurately forecasting the recurrence of AF in patients undergoing catheter ablation of the arrhythmia.

A11: UN CASO DI EMBOLIA POLMONARE BILATERALE MASSIVA DOPO PROCEDURA DI ABLAZIONE TRANSCATETERE DI TPSV

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Un paziente di 66 anni senza fattori di rischio cardiovascolare né comorbidità note veniva ricoverato per episodi di TPSV recidivanti da sottoporre a crioablazione del substrato aritmico. Previo ottenimento di accessi venosi e posizionamento di introduttore 6 e 8F in vena femorale comune destra e 7F nella vena femorale comune sinistra, veniva eseguito lo studio elettrofisiologico che documentava la presenza di una tachicardia da rientro nodale con successiva erogazione di crioenergia sul potenziale della via lenta. La durata complessiva della procedura era stata di 160 minuti. Veniva eseguita al termine emostasi compressiva manuale a livello dei siti di puntura venosa seguita da medicazione compressiva. Al monitoraggio post ablazione non si erano verificate recidive aritmiche e il paziente si era mantenuto stabile ed asintomatico. Il giorno successivo il paziente presentava un episodio pre-sincopale senza alterazioni al monitoraggio telemetrico. Veniva eseguito un elettrocardiogramma che evidenziava la presenza di ritmo sinusale normofrequente con lieve slargamento dell'onda S nelle derivazioni inferiori e laterali. Si effettuava un ecocardiogramma transtoracico che documentava una severa dilatazione delle cavità destre, precedentemente non presente, con un'insufficienza tricuspoidale moderata e pressioni polmonari sistoliche moderatamente aumentate. L'esecuzione di un'angio-TC con mezzo di contrasto iodato confermava il sospetto clinico documentando un quadro di tromboembolia polmonare bilaterale massiva. Veniva effettuato un ecocolor Doppler venoso degli arti inferiori con riscontro di trombosi della vena safena sinistra al carrefour con la vena femorale. La ricerca di mutazioni trombofiliche risultava negativa. Veniva avviata terapia anticoagulante dapprima con eparina a basso peso molecolare e quindi con DOAC (edoxaban 60 mg/die). Il paziente si manteneva emodinamicamente stabile ed euforico in assenza di supporto ventilatorio e cinque giorni dopo la procedura veniva dimesso. Sei mesi dopo l'evento veniva sottoposto a controllo ecocardiografico che documentava una normalizzazione dei segni di ipertensione polmonare con una riduzione del diametro delle sezioni cardiache destre e un decremento dei valori di Paps. L'ecocolor Doppler dei vasi venosi degli arti inferiori mostrava una ricanalizzazione del vaso interessato. Veniva quindi data indicazione a sospensione della terapia anticoagulante e a prosecuzione del follow-up clinico.

L'embolia polmonare è una complicanza delle procedure di ablazione transcattere estremamente rara; tuttavia gli studi indirizzati a valutare l'incidenza di questa complicanza sono esigui e l'incidenza di EP potrebbe essere sottostimata. Al contrario che nelle procedure dell'atrio sinistro, nelle ablazioni di tachiaritmie a origine dalle sezioni cardiache destre non è generalmente raccomandata la somministrazione di anticoagulanti prima, durante o dopo la procedura. Tuttavia l'ottenimento di accessi vascolari è intrinsecamente legato ad un aumento del rischio trombotico legato al danno di parete endoteliale, al contatto del sangue

con corpi estranei e alla successiva immobilizzazione del paziente. Non sono attualmente noti particolari fattori predisponenti allo sviluppo di EP dopo ablazione, oltre ai classici fattori individuali di rischio pro-trombotico. La durata della procedura e una prolungata immobilizzazione successiva possono aumentare tale rischio. L'identificazione di fattori predisponenti attraverso studi prospettici potrebbe aiutare a minimizzare tale complicanza e ad eventualmente giustificare la somministrazione di terapia anticoagulante nel paziente a maggiore profilo di rischio.

A12: PRELIMINARY RESULTS OF THE IDENTIFICATION OF THE OPTIMAL ABLATION INDEX TARGET VALUE IN VENTRICULAR TACHYCARDIA ABLATION (IDEA VT) STUDY

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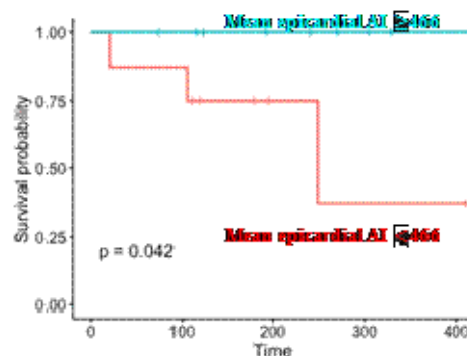
Background. Catheter ablation (CA) is a fundamental therapeutic measure for patients with ventricular tachycardia (VT) and/or electrical storm (ES), resulting in the reduction and often elimination of future ventricular arrhythmias (VAs). Conventionally, radiofrequency (RF) energy is delivered in critical areas identified by activation and/or substrate mapping, aiming to eliminate local electrograms. The optimal duration of RF delivery, as well as the role of multiparametric indexes incorporating contact force, power, and time are yet to be defined.

Objectives. To assess whether ablation index (AI) is related to risk of recurrence in patients undergoing CA for VT and/or ES.

Methods. These are the preliminary results of a multicentric prospective observational study, the IDentification of the optimal Ablation index target value in Ventricular Tachycardia ablation (IDEA VT) study, enrolling patients undergoing CA for VT and/or ES in three high volume Italian referral centers (University Hospital Ospedali Riuniti, Ancona; Monzino Heart Centre, Milan; S. Chiara Hospital, Trento). We enrolled each consecutive patient in whom CA was performed under the guidance of the CARTO electroanatomical mapping system (Biosense Webster, Diamond Bar, CA). For each procedure, mean endocardial and epicardial AI values were obtained. Patients were followed for recurrences using remote monitoring data; VT recurrence was defined as any VT episode lasting longer than 30 s. The prognostic contribution of AI for the prediction of VT recurrences was assessed in Cox proportional hazards models by the likelihood ratio (LR) test and, in case of significant association, with the Kaplan-Meier method, comparing patients reaching AI values over and under the median of mean AI with the log-rank test.

Results. We included 65 patients (mean age, 62±14 years, 89% male), undergoing endocardial (n=40, 62%), epicardial (n=4, 6%), or epicardial (n=21, 32%) CA for ES (n=46, 71%) or VT (n=19, 29%). VAs were considered idiopathic in just 4 subjects, whereas most patients had significant structural heart disease: ischemic cardiomyopathy was the most common substrate (n=32, 49%), and mean ejection fraction was 29±20%. During follow-up, 11 patients (17%) experienced recurrences; the median survival free from VT recurrence was 900 days. The median of mean endocardial AI was 452, whereas the median of mean epicardial AI was 466. Although mean endocardial AI values were not predictive of VT recurrences (LR=0.08, p=0.77), we noted a significant association between mean epicardial AI values and VT recurrences (LR=12.4, p=0.004); furthermore, patients reaching mean epicardial AI values ≥466 had significantly fewer recurrences than patients with lower values (log-rank test p=0.04, Figure).

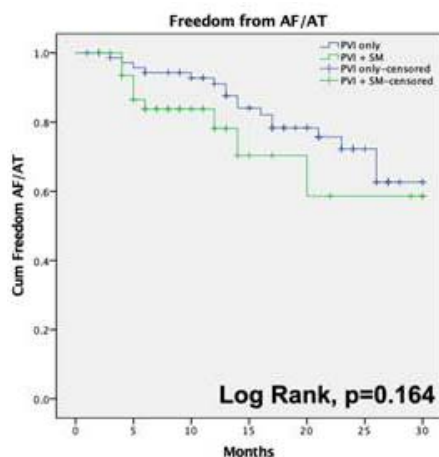
Conclusions. AI is an important parameter, which may become a procedural target in patients undergoing CA for VT. Larger data sets as well as longer follow-up are needed to confirm our preliminary observations and to define an optimal AI cutoff to maximize both safety and effectiveness.



A13: TAILORED LOW VOLTAGE ZONES ABLATION USING CONTACT FORCE SENSING TECHNOLOGY IN PATIENTS WITH PERSISTENT ATRIAL FIBRILLATION (TWEET-AF): A PILOT STUDY

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Introduction: Although pulmonary vein (PV) isolation (PVI) is very effective in paroxysmal atrial fibrillation (AF), in patients (pts) with persistent AF, PVI often is not sufficient. Many studies suggested that low voltage zones (LVZs) outside of the PV might be involved in the complex mechanisms perpetuating AF. However, ablation strategies involving substrate modification (SM) did not show additional benefits in persistent AF pts. Those studies were performed before the introduction of contact force technology, and the most likely explanation for these results could be the inability to achieve effective transmural lesions and continuous linear ablation. We hypothesized that the use of contact force technology would improve ablation efficacy. Therefore, we analyzed the long-term outcome after two different ablation strategies in pts with persistent AF depending on whether there was evidence of LVZs in the left atrium or not. **Methods:** The presence of LVZs were defined as sites of >3 adjacent low-voltage points <0.5 mV during electrophysiology study. Depending on the location of the LVZ, mainly linear ablation was performed. Catheter ablation was performed using TactiCath™ or SmartTouch™ ablation catheters aiming at contact values $\geq 10g$ <20g and FTI >400g/s. Ablation was performed in a temperature-controlled fashion with energy of 30W except at the posterior wall (20-25W). **Results:** 121 consecutive pts with persistent AF (46 female, median age 66 [59-72] years, mean duration of AF 16 [7-73] months, CT derived LA volume index 66 [56-75]ml/m²) were included: pts without LVZs underwent PVI alone (n = 74), in pts with LVZs, PVI + SM (n = 47) was performed (mitral Isthmus line in 2, supero-septal line in 39, and roof line in 47; bidirectional block was achieved in 100%, 97%, and 100%, respectively). After a median follow-up of 13 [6-21] months, 86% of pts without and 78% with substrate were in sinus rhythm, mainly without antiarrhythmic drugs (89% PVI only, 84% PVI + SM) (Figure). **Conclusions:** In patients with persistent AF without LVA, PVI alone leads to excellent 2-year freedom from AF. In pts with LVZs, additional substrate modification with CF sensing technology is associated with improved success rates compared to previous studies.



A14: LEFT CHAMBERS LONGITUDINAL STRAIN INCREASE PREDICTED SCORE OF SUDDEN CARDIAC DEATH RISK IN HYPERTROPHIC CARDIOMYOPATHY PATIENTS WITH CONCOMITANT CORONARY ATHEROSCLEROTIC DISEASE

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Background. Hypertrophic cardiomyopathy (HCM) is the most common inherited arrhythmogenic disease predisposing young adults to sudden cardiac death (SCD). It is not known yet how the coexistence of coronary atherosclerotic disease (CAD) might increase the arrhythmic burden (either brady- or tachy-arrhythmias) in patients with HCM. According to current European 2014 guidelines, the SCD risk is calculated using the HCM Risk SCD which, by means of individual risk variables, classifies HCM patients into low, intermediate or high risk, and helps clinicians in the appropriate selection of candidates to the cardioverter/defibrillator implantation (ICD) therapy in primary prevention; only for the subgroup of high-risk patients is it mandatory to implant an ICD against an increased rate of SCD /year >6%. To date, it is not clear whether the use of

echocardiographic parameters such as left atrial strain (AS) and left ventricular global longitudinal strain (LV-GLS) might predict the increased arrhythmic burden in patients with HCM. The aim of our study is to propose both AS and LV-GLS as prognostic SCD risk markers in patient with HCM and concomitant CAD.

Methods. we collected a cohort of 45 patients with HCM who came to our intensive care unit diagnosed with acute coronary syndrome (ACS). All subjects underwent standard echocardiographic in order to quantify the systolic thickness of interventricular septum (IVS) and two-dimensional strain examination (AS and LV-GLS) by 2D Speckle tracking. All patients underwent coronary angiography after which we identified two subgroups: HCM-concomitant CAD (n= 15) and HCM-no CAD (30). We excluded subjects presenting age <18 years, maximal LV outflow tract gradient >40 mmHg, bundle branch block or atrial fibrillation, previous pacemaker/cardiac surgery, including myectomy/alcohol ablation, severe aortic stenosis and other diseases associated with increased IVS thickness. During long term follow-up of 5±4 years, we monitored the onset of both brady- and tachy-arrhythmias in that two subgroups.

Results. In our 45 HCM patients (age 65 ± 14 years, 80% male), median 5-year risk of SCD at HCM Risk SCD was 4.5 ± 3%. The percentage of ICDs implanted were higher in HCM-CAD patients. HCM-CAD patients displayed a significantly higher HCM Risk-SCD Score compared to HCM-no CAD (6.3±1.8 vs. 5.2 ±1.3, p <0.05). Multivariate analysis revealed AS (p <0.05) and LV-GLS (p<0.05) to be independent predictors of appropriate ICD therapy regardless of the thickness of the SIVs (18 mm ± 3.4). Both in HCM-no CAD and HCM-CAD patients, AS and LV-GLS showed higher accuracy to predict appropriate ICD therapy, as shown by likelihood ratio test (p <0.002) and value of AS >3.8 ± 2 and LV-GLS <14± 2.2 correlate with values of HCM Risk SCD >6%. In particular, in the HCM-CAD subgroup, there is a statistically significant linear correlation (p<0.05) between AS and GLS values and HCM Risk Score >4%, allowing a sub-compartmentalization of the intermediate risk in the high risk category. No patient with both AS >40% and GLS <-14% experienced appropriate ICD therapy. The likelihood ratio test showed a significant incremental prognostic value of AS and GLS (p<0.001) as compared with a model with other standard echocardiographic risk factors (LAVi, LVOT, mitral regurgitation).

Conclusions. HCM Risk Score is the current algorithm that calculate the potential life-threatening arrhythmias and sudden death and indicates ICD implantation. Echocardiographic investigation of two novel risk markers, AS and LV-GLS, for sudden death and their add in HCM-Risk Score should be encouraged to identify high-risk patients who may benefit from a prophylactic therapy with an ICD in both HCM-concomitant CAD and HCM-no CAD.

A15: RELATION OF ECHOCARDIOGRAPHIC FINDINGS AND CARDIAC AUTONOMIC FUNCTION WITH VENTRICULAR ARRHYTHMIAS IN PATIENTS WITH MITRAL VALVE PROLAPSE

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Background and purpose. Cardiac arrhythmias are frequently detected in patients with mitral valve prolapse (MVP). The mechanisms causing ventricular arrhythmias, however, remain poorly known, although mechanical traction of prolapsing leaflets, myocardial fibrosis and sympathetic/vagal imbalance might be involved. In this study we aimed to identify whether echocardiographic parameters and cardiac autonomic function are associated with ventricular arrhythmias in patients with MVP.

Methods. We studied consecutive patients referred to our Department of Cardiology to undergo an echocardiographic examination and had evidence of MVP. Patients with acute or chronic heart disease (e.g., acute myocardial infarction, atrial fibrillation, cardiomyopathies or other significant valvular disease), previous cardiac surgery and other significant comorbidities were excluded. All patients underwent 1) a transthoracic Doppler echocardiogram (TTDE) with speckle tracking examination to assess global and regional longitudinal strain (GLS), and 2) a 24-hour ECG Holter monitoring for the evaluation of arrhythmias and heart rate variability (HRV). Patients were divided in 2 groups according to ventricular arrhythmic burden: 1) 12 patients (24.5%) with frequent premature ventricular complexes (PVCs ≥ 10 /hour); 2) 37 patients (75.5%) with no PVCs or PVCs <10/hour.

Results. Forty-nine consecutive patients (35F, mean age 49.4±15 years) with MVP were enrolled. No significant differences were found in the main clinical characteristics between the 2 groups. No complex supraventricular arrhythmias or significant ischemic ST segment changes were detected. The main echocardiographic parameters were similar between the 2 groups, except for the E/e' ratio, which was lower in patients with PVCs ≥ 10 /hour (5.8±3.2 vs 7.8±2.8; p=0.043), although it was in the normal range in both groups. Although mean GLS did not significantly differ between the 2 groups, regional longitudinal strain of the basal infero-lateral wall was significantly lower in patients with PVCs ≥ 10 /hour (17.5±3.6 vs. 20.4±4.3, p= 0.004). There were differences in some time-

domain HRV parameters [SDNNi (p=0.02) and pNN-50 (p=0.02)], which showed higher values in patients with PVCs \geq 10/hour, whereas no differences were found in frequency-domain HRV variables.

Conclusions. Our data show that in patients with MVP, subclinical abnormalities in regional left ventricle systolic function are associated with a frequent PVCs, suggesting their involvement in the genesis of ventricular arrhythmias. Conversely, the sympathetic/vagal imbalance does not seem to play a significant role in the occurrence of frequent ventricular arrhythmias in these patients.

A16: PREDITTORI CLINICI DI FIBRILLAZIONE VENTRICOLARE DURANTE PRIMO INFARTO MIocardICO E IMPORTANZA DEL TEMPO DI ISCHEMIA

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Introduzione. Pochi studi hanno valutato se esistano fattori di rischio, ereditari e non, che predispongano a fibrillazione ventricolare (FV) durante un primo infarto miocardico acuto (IMA). È noto che la familiarità per morte improvvisa (MI) sia un fattore di rischio per FV primaria tuttavia l'esistenza di una predisposizione genetica non è ad oggi dimostrata. Uno dei limiti degli studi finora condotti è che importanti parametri quali la kaliemia, la pressione arteriosa (PA) e la frequenza cardiaca (FC) alla presentazione non sono stati sempre presi in considerazione. Inoltre, le caratteristiche dei soggetti con FV primaria non sono mai state valutate in base al tempo intercorso tra esordio della sintomatologia ischemica e sviluppo dell'aritmia.

Obiettivo. Valutare i predittori di FV primaria nella popolazione PREDESTINATION (Primary vEntricular fibrillation and suDden dEath during a firST myocardial InFArcTion) e confrontare le caratteristiche di presentazione dei casi in base al tempo di ischemia.

Metodi. PREDESTINATION è uno studio caso-controllo, prospettico, multicentrico, tuttora in corso e che arruola pazienti tra i 18 e gli 80 anni con un primo IMA, complicato (casi) o non complicato (controlli) da FV prima della terapia ripercusiva e comunque entro 24 ore dall'esordio dei sintomi. I casi ed i controlli sono appaiati (1:2) per sesso ed età (± 5 anni). In accordo con la definizione di morte improvvisa, abbiamo considerato precoce una FV avvenuta ≤ 60 minuti dall'insorgenza dei sintomi e tardiva se occorsa > 60 minuti. L'inattività fisica è stata definita come meno di 30 minuti complessivi a settimana di attività fisica di intensità almeno moderata.

Risultati. L'analisi è stata condotta su 1300 pazienti (età media 59 anni, 85% maschi): 484 casi e 816 controlli. L'analisi multivariata ha individuato 5 predittori indipendenti di FV primaria: PA sistolica alla presentazione (OR 0.98, IC al 95%: 0.98-0.99 per ogni mm Hg), kaliemia ≤ 3.5 mEq/L alla presentazione (OR 2.73, IC al 95%: 1.95-3.81), familiarità per MI (OR 2.13, IC al 95%: 1.34-3.40), inattività fisica (OR 1.75, IC al 95%: 1.21-2.53) e sede anteriore dell'infarto (OR 1.56, IC al 95%: 1.19-2.10). Considerando i 354 pazienti in cui era disponibile il tempo intercorso tra i sintomi e la FV, è stato eseguito un confronto dei casi con FV precoce (n=157) e quelli con FV tardiva (n=197) da cui sono emerse differenze nei seguenti parametri: familiarità per MI (17% in FV precoce vs 9% in FV tardiva, p=0.02), terapia domiciliare con beta-bloccanti (7% vs 17%, p<0.01) e con ipoglicemizzanti orali diversi dalla metformina (1% vs 4%, p=0.04), FC di presentazione pre-FV (83 \pm 16 bpm vs 74 \pm 20 bpm, p<0.01), FC pre-VF ≤ 50 bpm (0% vs 13, p<0.01), glicemia di presentazione (193 \pm 76 mg/dl vs 144 \pm 53 mg/dl, p<0.01).

Conclusioni. La presente analisi dello studio caso-controllo PREDESTINATION ha individuato 5 predittori indipendenti di FV primaria. Inoltre, i nostri dati dimostrano una maggior prevalenza di familiarità per MI nei soggetti con FV occorsa entro 1 ora dall'insorgenza dei sintomi infartuali. Questo riscontro supporta l'ipotesi fisiopatologica che il tempo

d'ischemia sia un parametro di fondamentale importanza nello studio dei fattori predisponenti l'FV primaria durante IMA e suggerisce che la predisposizione genetica, insieme ad altri fattori quali l'iperattività adrenergica, possa avere un ruolo maggiore nelle forme di FV ad esordio precoce.

A17: CASE REPORT: MALATTIA ARITMICA ATRIALE CORRELATA A DISTROFIA MUSCOLARE DI EMERY-DREIFUSS CON ESCLUSIVO INTERESSAMENTO CARDIACO

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Caso clinico. Maschio, 23 anni, non precedenti patologie di rilievo o familiarità per cardiopatia o morte improvvisa. Precedente attività sportiva agonista, terminata 2 anni fa. Giunge a valutazione cardiologica per occasionale cardiopalmo. All'ECG a 12 derivazioni riscontro di ritmo giunzionale a 43 bpm. Veniva eseguito ecocardiogramma e routine ematologica comprendente TSH senza riscontro di reperti patologici. Il paziente veniva pertanto sottoposto a test ergometrico (cicloergometro) con incremento della frequenza cardiaca fino a 135 bpm (150 Watt) con ripristino del ritmo sinusale. Eseguiva Holter ECG 24-h con riscontro di frequenti fasi di ritmo giunzionale e pause fino a 3 secondi, episodi di TSV di breve durata. Si procedeva quindi ad eseguire RM cardiaca morfologica che documentava una moderata dilatazione dell'atrio destro, in assenza di altri reperti patologici e con normale ritorno venoso polmonare. Dopo circa 3 mesi il paziente si presentava in PS per dispnea e cardiopalmo, con documentazione di flutter atriale tipico comune. Si procedeva quindi ad ablazione transcaterete e posizionamento di Loop Recorder. Veniva contestualmente eseguito prelievo ematico per test genetico con tecnica Next Generation Sequencing (NGS). Dopo alcuni mesi l'interrogazione del loop recorder documentava brevi episodi di fibrillazione atriale ed arresti sinusali di durata fino a 7 secondi. La valutazione NGS risultava diagnostica per mutazione patogena (Classe C5) in emizigiosi del gene EMD sul cromosoma X, indicativo di distrofia muscolare di Emery-Dreifuss. Il paziente veniva quindi sottoposto ad impianto di PMK bicamerale e indirizzato ad un programma di valutazione neuropsicologica.

Commento. La distrofia muscolare X-linked EMD (incidenza 1:100 000) è caratterizzata da un decorso benigno relativamente alla disfunzione muscolare ma da frequente interessamento cardiaco. L'assenza di sintomi clinici legati alla tipica disfunzione scapolo-omerale-peroneale ha reso difficile l'identificazione di una distrofia muscolare. La tecnica NGS con pannello cardiovascolare completo, permette di avere una visione completa delle possibili alterazioni in ambito cardiovascolare e favorire un corretto orientamento diagnostico.

A18: UNEXPLAINED SUDDEN CARDIAC ARREST IN CHILDREN: CLINICAL AND GENETIC CHARACTERISTICS OF SURVIVORS

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Sudden cardiac arrest (SCA) is defined as the sudden cessation of cardiac activity with hemodynamic collapse, with restores of circulation by an intervention (e.g., defibrillator) or spontaneously. The aim of this study was to evaluate prevalence, clinical and genetic characteristics of survivors that experienced an unexplained SCA as disease onset in a consecutive cohort of pediatric patient.

Of 4025 consecutive pediatric patients, we investigated 9 consecutive survivor patients that experienced an unexplained SCA with documented ventricular tachycardia or ventricular fibrillation requiring direct current cardioversion or defibrillation (unexplained SCA group). All patients underwent a comprehensive clinical-instrumental-genetic evaluation. Patient with known cause for SCA were excluded.

Moreover, we investigated 3 consecutive patients that experienced transient loss of consciousness (TLOC) due to arrhythmogenic syncope (arrhythmogenic syncope group).

Of the 9 patients of unexplained SCA group, 7 (78%) showed a primary electrical disease (6 (67%) with long QT syndrome, LQTS, and 1 (11%) with catecholaminergic polymorphic ventricular tachycardia, CPVT) and 2 (22%) a structural heart disease (1 (11%) with myopericarditis and 1

(11%) with hypertrophic cardiomyopathy, HCM). A disease-causing mutation was identified in all the genetically analyzed patients. All patients belonging to the arrhythmogenic syncope group showed Brugada syndrome, and no pathogenic mutation was identified in these patients. In conclusion, primary electrical disease can explain the largest part of survived pediatric patients who experienced an unexplained SCA as disease onset.

A19: METODOLOGIE DI DIDATTICA ASINCRONA PER LA FORMAZIONE DEI FUTURI INFERMIERI SULLE COMPETENZE SPECIFICHE NELL'ASSISTENZA ALLA PERSONA CON ALTERAZIONE DEL TRACCIATO ELETTROCARDIOGRAFICO

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La formazione in ambito accademico deve prevedere metodologie di apprendimento in grado di sviluppare le Competenze dei futuri Infermieri per favorire quel "sapere agito", fondamentale nei contesti di cura, che richiedono capacità di Problem Solving e di Decision Making.

L'utilizzo di Scenari di Simulazione nella formazione dei professionisti della salute è riconosciuto come strumento in grado di soddisfare le necessità di apprendimento, sviluppare e consolidare le conoscenze orientate alla risoluzione di problemi clinici assistenziali nei diversi ambiti di cura.

Le competenze in ambito Cardiologico richiedono specifiche conoscenze teorico-pratiche per poter tempestivamente riconoscere le situazioni di emergenza e urgenza; situazioni riprodotte attraverso l'utilizzo dei simulatori a media/alta fedeltà in "ambienti protetti" dove lo studente infermiere può apprendere dai propri errori senza ripercussioni sulla persona assistita.

L'emergenza Covid-19 ha accelerato non solo i tempi della Formazione (Sessioni di Laurea Anticipate) ma anche quelli dell'inserimento in contesti "critici" degli stessi neolaureati in setting specialistici, limitando, oltretutto la possibilità di affiancamento per i professionisti neofiti. Fornire in maniera efficace ed efficiente in modalità asincrona, ovvero utilizzando piattaforme digitali in grado di rispettare i tempi di apprendimento del discente e cercando di sostenere lo sviluppo di competenze pratiche, è stata una sfida per i formatori rivolta non esclusivamente agli studenti ma anche ai neo inseriti nei contesti di cura critici.

Gli ambiti formativi su cui ci si è concentrati, hanno permesso di selezionare le cosiddette "core competence" fondamentali per garantire agli studenti le abilità necessarie per affrontare le esperienze in ambito cardiologico. Tra queste è risultata fondamentale la lettura del tracciato elettrocardiografico, come prima "procedura" indispensabile per sostenere un algoritmo decisionale in grado di orientare correttamente la presa in carico della persona.

Le restrizioni dettate dalla fase prolungata di lockdown, hanno costretto i formatori a ricercare nuove modalità didattiche, strumenti innovativi, di utilizzo immediato e senza oneri economici per consolidare e sviluppare le competenze nella gestione dell'assistito con problematiche cardiache.

Il lavoro di ricerca ha fatto emergere due strumenti adatti allo scopo, ovvero una sorta di piattaforma skilltrainer destinata all'esercizio di lettura dei tracciati elettrocardiografici (<https://www.skillstat.com/tools/ecg-simulator/#/HOME>) e l'utilizzo della Piattaforma Kahoot per impostare Scenari Problem Based Learning, basati, appunto, sulle principali patologie cardiovascolari.

Gli studenti e i neo laureati hanno utilizzato questi strumenti di autoapprendimento in modalità asincrona, riportando un netto miglioramento delle loro conoscenze come in una sorta di "gara", nel riconoscimento del tracciato fisiopatologico.

A20: IL TRATTAMENTO DELLA FIBRILLAZIONE ATRIALE IN PRONTO SOCCORSO: L'ESPERIENZA DI UN SINGOLO CENTRO CON AMBULATORIO ARITMOLOGICO DEDICATO

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Background. La fibrillazione atriale (FA) è l'aritmia di più frequente diagnosi ed è causa di circa il 2% degli accessi in pronto soccorso (PS). Analizzare i dati provenienti dai registri clinici aiuta a delineare alcuni elementi che possono migliorare la gestione della FA in PS riducendo i ricoveri impropri, soprattutto quando il quadro clinico ed il contesto gestionale lo consentono.

Scopo. L'obiettivo principale dello studio è valutare l'impatto di un ambulatorio aritmologico dedicato in termini di riduzione delle ospedalizzazioni e dei tempi di degenza in PS per i pazienti con diagnosi principale di FA. L'obiettivo secondario è analizzare la gestione terapeutica (antiaritmica e anticoagulante) della FA in PS in due periodi storici differenti (pre e post istituzione dell'ambulatorio).

Metodi. È stato effettuato uno studio retrospettivo valutando tutti gli

accessi in PS con diagnosi principale di FA da novembre 2016 a settembre 2017 (gruppo A – periodo senza ambulatorio dedicato) e da dicembre 2018 a novembre 2019 (gruppo B – periodo con ambulatorio dedicato). Per tutti i pazienti sono state analizzate variabili cliniche, laboratoristiche e strumentali, sono stati raccolti e analizzati i dati inerenti le terapie effettuate e, infine, è stato analizzato il tempo medio di permanenza in PS nonché l'esito dell'accesso (dimissione a domicilio, dimissione a struttura ambulatoriale, ospedalizzazione).

Risultati. Sono stati analizzati in tutto 858 pazienti, 410 per il gruppo A e 448 per il gruppo B. La popolazione del gruppo B rispetto a quella del gruppo A presentava differenze significative in termini di comorbidità: diabete [106 vs 36, p<0,0001], ipertensione [304 vs 229, p<0,0003], pregressi eventi cerebrovascolari [69 vs 24, p<0,0001] e aveva più pazienti con CHA₂DS₂-VASc >3 (2073 vs 205, p<0,0015). Nonostante questo, la percentuale di ospedalizzazione nel gruppo B rispetto al gruppo A risulta ridotta del 13% [193 vs 152, p<0,0001]. Dall'analisi univariata risulta che la presenza di un ambulatorio aritmologico dedicato e l'utilizzo degli anticoagulanti orali diretti (DOACs) sono fattori associati alla dimissione da PS (rispettivamente P=0,0001 e P<0,0001). Il ruolo dell'ambulatorio viene inoltre enfatizzato anche dall'analisi multivariata come fattore indipendente associato alla dimissione da PS (OR 0,3, CI 0,2-0,43; p<0,0001). Nel gruppo A, la mediana del tempo di degenza PS era di 26,5 ore (IQR 12,6-49,5), mentre nel gruppo B il tempo di degenza era notevolmente ridotto, con una mediana di 12,6 ore (IQR 5,6-26,8) (p<0,0001). Nel gruppo A vi erano più pazienti con FA di recente insorgenza (338 vs 228, p<0,0001) e veniva intrapresa più spesso una terapia di controllo del ritmo (264 vs 175, p<0,0001) che risultava efficace; nonostante questo, i pazienti erano più ospedalizzati. Infine, nel gruppo A veniva più spesso utilizzata l'eparina come terapia anticoagulante (279 vs 85, p<0,000), mentre nel gruppo B prevaleva l'utilizzo dei con DOACs (197 vs 37, p<0,0001).

Conclusioni. Il nostro studio ha dimostrato come negli ultimi anni è stato attuato un notevole cambiamento gestionale della FA in PS. Si dimostra che l'ambulatorio cardiologico dedicato di tipo "open access" e l'utilizzo dei DOACs facilitano la gestione del paziente con FA e sono positivamente associati ad una riduzione dei tempi di degenza in PS e alla dimissione dallo stesso.

A21: ABLAZIONE TRANSCATETERE E CONTESTUALE IMPIANTO DI CRT-D "NEAR-ZERO FLUOROSCOPY": NUOVE APPLICAZIONI DEL MAPPAGGIO ELETTROANATOMICO

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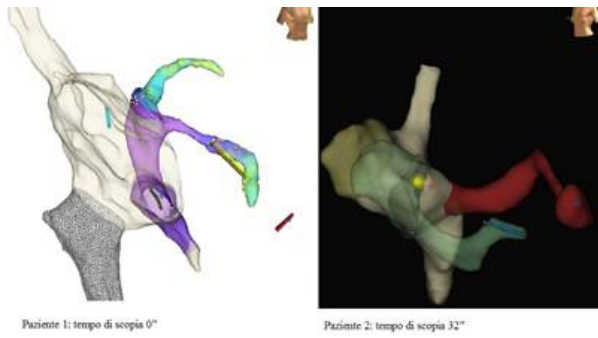
Contesto. L'impianto di dispositivi di resincronizzazione cardiaca (CRT) è gravato dall'utilizzo di radiazioni e dal rischio di nefrotossicità da mezzo di contrasto (mdc) che possono essere ridotti o eliminati impiegando sistemi di mappaggio elettroanatomico (ElectroAnatomical Mapping System, EAMS). La mappa di attivazione elettrica del seno coronarico, inoltre, può guidare il posizionamento dell'elettrocatteretere (EC) ventricolare sinistro per identificare la zona ad attivazione più tardiva. L'esecuzione di procedure di ablazione con EAMS associate ad impianto di device permette di ottenere in un'unica procedura l'abolizione del substrato aritmico e la CRT, il tutto a raggi zero (o quasi).

Caso 1. Uomo di 78 anni con cardiomiopatia ipocinetica postischemica con frazione di eiezione (FEVS) 22% e blocco di branca sinistra. Ricoverato per scompenso cardiaco a ridotta FEVS (HFREF) associato a flutter atriale ad elevata penetranza ventricolare, con quadro coronarografico stabile; veniva sottoposto ad ablazione dell'istmo cavotricuspidale e ad impianto di CRT-D "near-zero fluoroscopy" EAMS-guidato (EnSite NavX). Dopo mappaggio elettroanatomico è stata eseguita l'ablazione del flutter. Dopo aver posizionato sotto guida elettroanatomica i due EC nelle sezioni destre, mediante una guida angiografica collegata al sistema di mappaggio sono state ricostruite l'anatomia e la mappa di attivazione dei rami del CS. È stato quindi posizionato un EC nel ramo posterolaterale del CS, ove l'attivazione risultava più tardiva.

Caso 2. Donna di 78 anni con cardiomiopatia ipocinetica non ischemica (FEVS 25%) con plurimi ricoveri per HFREF. In seguito a recidiva di scompenso in corso di fibrillazione atriale non regredita né con cardioversione farmacologica né elettrica e scarsamente responsiva a terapia dromotropica negativa, veniva posta indicazione ad ablazione del nodo atrioventricolare e a contestuale impianto di CRT-D. Dopo aver ricostruito l'anatomia cardiaca mediante EAMS, un EC è stato posizionato nell'apice ventricolare destro senza l'utilizzo di fluoroscopia. Successivamente il CS è stato incannulato con una guida VisionWire con la quale è stato eseguito il mappaggio dei rami e dei ritardi di attivazione del CS. Un EC quadripolare è stato quindi posizionato in un ramo posterolaterale. A seguire, con guida EAMS, è stata eseguita ablazione del NAV.

Conclusioni. L'esecuzione di procedure di ablazione associate ad impianto di CRT con guida elettroanatomica, permette di ottenere in una singola procedura la risoluzione del substrato aritmico e l'impianto del

dispositivo, ottimizzato in base alle caratteristiche elettriche del paziente, senza mdc e con utilizzo quasi inesistente di fluoroscopia. Tutti questi vantaggi rappresentano pertanto allettanti motivazioni per implementare queste tecniche nella comune pratica interventistica.



A22: SUBMAMMARY IMPLANTABLE CARADIOVERTER DEFIBRILLATOR WITH PERIAREOLAR APPROACH: TECHNIQUE AND FOLLOW-UP

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Aims. Given the increased indications for implantable cardioverter defibrillator (ICD), different new devices and implant techniques to limit patient's discomfort are emerging. Conventional ICD implantation in the infraclavicular region usually leads to scarring and prominence of the device generator, with young women often experiencing aesthetic concerns, psychological distress and physical discomfort. Submammary device implantation (SMI) could represent a valid alternative to the conventional infraclavicular site of implant. We present our experience with periareolar technique of SMI implantation.

Methods. We implanted submammary ICD in five young women. Veins for the lead passage were identified with an infraclavicular incision; a second incision was made along the areola to access the subglandular area. The leads were connected to the generator via a tunnel from the subglandular pocket to the infraclavicular region. A regular follow-up was performed every 3-6 months.

Results. Mean follow-up was 50 ± 37 months. No device complication was observed. One patient experienced an electrical storm and received appropriate ICD therapy; one had inappropriate antitachycardia pacing (ATP) therapy while on atrial fibrillation. One patient underwent successful generator replacement. All patients were pleased with the aesthetic results. No patient reported pain or any discomfort related to the device.

Conclusions. Submammary ICD implantation in women appears to be a valid alternative to standard infraclavicular implants, offering superior cosmetic results and causing less patient's discomfort. The periareolar technique, although more complex, is effective, safe and may warrant further aesthetic advantages and lesser discomfort.



Figure Aesthetic result at the time of implantation (A), after two years (B) and five years (C) of follow-up

A23: HYPERTROPHIC CARDIOMYOPATHY: WHEN TO CHOOSE S-ICD

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A 56-year-old woman was admitted to the Cardiology Department of our Hospital after the finding of various episodes of non-sustained ventricular tachycardia (NSVT) at a routine Holter ECG exam. She had a history of non-obstructive hypertrophic cardiomyopathy (HCM), diagnosed 12 years before, and no further known cardiovascular risk factors. At that time, as she complained palpitations, in the absence of chest pain, dyspnoea or syncope, an EKG was performed, showing signs of severe left ventricular hypertrophy with secondary T-wave abnormalities, and the patient was referred to another hospital. A transthoracic echocardiogram was

performed, showing a picture of HCM. Moreover, a cardiac MRI showed late enhancement signs. In addition, she reported that her father had died at the age of 46 for sudden death in end staged not specified cardiomyopathy. The patient was therefore discharged on beta-blocker therapy, with benefit on the palpitations symptoms. A dedicated follow-up was carried out: from 2014 on, she was followed by the Outpatient clinic of our Centre. In 2018, an echocardiogram showed asymmetric hypertrophy of septum and anterolateral wall with papillary hypertrophy; the interventricular septum was 24 mm thick, with normal left ventricular function and dimensions, impaired relaxation with high filling pressures, and moderate left atrium dilation. She was asymptomatic. In April 2018 the patient underwent a routine Holter ECG exam that showed various episodes of NSVT during the night sleep. Therefore, a bicycle stress echocardiogram was carried out, reaching 81% of the predicted maximal HR, in course of metoprolol therapy; no SAM was present, and no arrhythmias were reported. Therefore, given the intermediate risk of sudden cardiac death because of the family history, the RMI findings and the documented NSVT episodes, she was then admitted to the hospital in order to be submitted to the implantation of an ICD in primary prevention. As she fulfilled the correct criteria, she was offered the opportunity to an S-ICD that she accepted. The implantation of S-ICD was then performed, in the thoracic subcutaneous site at the level of the left middle axillary line. An induction test was performed, which proved effective with restoration of sinus rhythm following shock at 65J. No complications were found. The patient is now carrying out her routine follow-up, with regular controls of S-ICD. This case suggests that S-ICD may be a good option for HCM patients, given the young age, the risk of transvenous ICD lead failure related to age and activity level and specific lead, if the centre experience can provide this option.



A24: ELECTROGRAM CHARACTERIZATION OF VENTRICULAR TACHYCARDIA REENTRANT CIRCUITS IN POST-MYOCARDIAL INFARCTION PATIENTS

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Objectives. To explore EGM characteristics along the diastolic pathway of VT reentrant circuits with the three most common 3D mapping systems in post-myocardial infarction patients undergoing ablation of ventricular tachycardia (VT) in order to identify specific signatures of those EGMs.

Background. Ventricular tachycardia (VT), in the context of ischemic structural heart disease, is related to patchy or incomplete scar, usually arising from re-entrant circuits which are dependent on surviving channels of activation through scar tissue. These protected isthmuses are critical for the maintenance of VT. An improved understanding of the characteristics of the diastolic pathway of VT is key in guiding VT ablation strategies.

Methods. 29 consecutive patients who underwent VT ablation guided by high-density mapping were enrolled. Patients were consecutively enrolled in the study when activation mapping was performed and the full diastolic pathway was recorded. 12 patients underwent endocardial electroanatomical mapping with Rhythmia (Boston Scientific), 10 patients with Ensite Precision (Abbott Medical) and 7 patients with Carto V3 (Biosense). Only patients with ischemic cardiomyopathy (ICM) were included in the study. The EGMs were analyzed in terms of amplitude and duration and distinguished as belonging to the entrance, isthmus or exit. Bystander EGMs were collected and compared to EGMs belonging to the diastolic circuit.

Results. 29 patients were included. Complete recording of the diastolic pathway was achieved in all patients. Entrance and exit sites were characterized by long duration and low amplitude EGMs (entrance mean $109.29 \text{ msec} \pm 37$ and $0.15 \text{ mV} \pm 0.20$; exit mean $103.8 \text{ msec} \pm 27$ and $0.18 \text{ mV} \pm 0.17$) while isthmus sites demonstrated high amplitude and shorter duration EGMs (isthmus mean $56 \text{ msec} \pm 17$ and $0.60 \text{ mV} \pm 0.55$, $p < 0.0001$). Only in the Rhythmia group we recorded the bystander EGMs that presented distinct features, higher amplitude and shorter duration, (mean $71.3 \text{ msec} \pm 39.9$ and $1.44 \text{ mV} \pm 1.5$) as compared to EGMs belonging to the diastolic pathway of VT circuit ($100.9 \text{ msec} \pm 44$ and $0.21 \text{ mV} \pm 0.43$), $p < 0.0001$

Conclusions. Entrance and exit sites demonstrate EGMs with longer duration and lower amplitude reflecting their slower conduction while isthmus sites have higher amplitude and shorter duration EGMs reflecting faster conduction. Bystander EGMs present distinct features (higher amplitude, short duration) which make these easily distinguishable from EGMs belonging to the VT circuit.

A25: CATHETER ABLATION OF LEFT-SIDED MACRO-REENTRANT ATRIAL TACHYCARDIAS AFTER MITRAL VALVE SURGERY: A SINGLE CENTER EXPERIENCE

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Background. Data regarding catheter ablation (CA) of atrial tachycardias (AT) occurring after mitral valve surgery (MVS) are scarce. Considering the high prevalence of complex AT in this setting and the potential issues occurring during CA in patients with MV prostheses, aim of this study was to assess safety and efficacy of CA of left-sided post-surgical AT occurring in a patient population with prior history of MVS.

Methods. A patient population undergoing CA of left-sided AT occurring after MVS was retrospectively considered at our centre from April 2005 to May 2018. Before ablation, a thorough point-by-point mapping of the arrhythmogenic substrate was performed using a 3D-electroanatomic mapping system (CARTO®) by means of a dedicated setting of the window of interest, as previously described elsewhere. Radiofrequency CA was performed at the mid-diastolic isthmus and was considered successful after validation of the CA lines of block using dedicated pacing manoeuvres. Periprocedural efficacy and safety together with mid and long-term maintenance of sinus rhythm on/off antiarrhythmic drugs were evaluated. Electrophysiologic features and anatomic locations of the investigated AT were furtherly assessed.

Results. Twenty-two consecutive patients (65±10-year-old; F:M 13:9) with prior MVS (19 mitral valve replacements, 3 mitral valve valvuloplasty) underwent 27 CA procedures (1.2 procedure/patient). No periprocedural complication requiring interventions were recorded. Thirty-five left-sided macro-reentrant AT were identified (1.6±0.8 per patient) and 27 (77%) were mapped and ablated. Twenty-five (93%) out of the 27 mapped AT (15 single loop AT; 12 double loop AT) were successfully ablated achieving the periprocedural success in 19 (86%) patients. The average procedure time, fluoroscopy time, and radiological exposure were 233±50 min, 33±20 min, and 27±23 mSv, respectively. Mid-diastolic isthmus was commonly located at the left atrial roof (33%), followed by interatrial septum (30%), left atrial posterior wall and mitral isthmus (22%), and, finally, pulmonary vein ostia (15%). Maintenance of sinus rhythm on/off antiarrhythmic drugs at mid and long-term follow-up (range from 2 to 11 years) was 74% and 90% after single and repeat procedures, respectively.

Conclusions. CA of left-sided macro-reentrant AT occurring after MVS is highly safe and effective. Before ablation, proper setting of the window of interest and mapping of the arrhythmic substrate with the aid of 3D electro-anatomic mapping systems could have played a key role to achieve the observed high success rate even at a mid and long-term follow-up. Moreover, the anatomic location of the ablated AT was closely located to the site of prior surgical scar, providing useful information for the proper strategical planning of CA in this setting.

A26: SPORADIC HIGH PACING IMPEDANCE AT REMOTE MONITORING IN HYBRID CIED SYSTEMS: A MULTICENTER RETROSPECTIVE EXPERIENCE

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Background. Cardiac implantable electronic devices (CIEDs), as pacemakers and implantable cardioverter defibrillators (ICDs), are used worldwide for the treatment of rhythm disorders. Pulse generator and lead integrity are necessary for the right functioning of CIEDs and are usually assessed by periodic controls of sensing, capture thresholds and lead impedance measurements. Impedance represents the ratio of voltage to current in an electrical circuit and provides important diagnostics in CIED systems. Small studies have reported transient high lead impedance on remote evaluation, without sensing and pacing anomalies, as consequence of header-lead pin mismatch in hybrid CIED systems with pulse generator and leads from different manufacturers. We report our retrospective, multicenter experience with hybrid ICD systems, the associated anomalies and related management.

Methods. We collected data about patients with transient high lead impedance alert on remote monitoring and an hybrid ICD system with pulse generator implanted between January 2015 and December 2019. Following data were retrieved: patient age, generator position, generator model, leads model, date of generator implantation and replacement, date of lead implantation and revision and extraction (when available), and indication for CIED implantation. Impedance values, sensing and pacing thresholds were collected at generator implantation or last generator substitution and at last in-office visit. Furthermore, the ranges of impedance, sensing and pacing thresholds by remote monitoring and at in-office controls were collected. Pace impedance and shock impedance trends from Boston Scientific remote monitoring Latitude™ were retrieved for each patient.

Results. Among 150 patients with hybrid CIED system, 14 presented with high impedance value at remote monitoring (7 dual-chamber ICD, 3 single-chamber ICD and 4 biventricular ICD). All had Boston Scientific ICD paired with Medtronic or Biotronik leads. The median age at first high

impedance recording was 69.5 years (64.5; 81.2 years). Ten patients were male (71%), and in all but one patient the CIED system was implanted for primary prevention of arrhythmic death. The most frequent cardiomyopathy leading to CIED implantation was post-ischemic dilated cardiomyopathy (n = 7, 50%), whereas other etiologies were valvular cardiomyopathy (n = 2, 14%), idiopathic dilated cardiomyopathy (n = 4, 29%) and Brugada syndrome (n = 1, 7%). By remote monitoring, 3 patients presented high atrial lead impedance, 6 patients high right ventricular lead impedance, 1 patient left ventricular impedance and 2 patients high shock impedance values. In all patients but one, all lead measures were in normal range at initial evaluation and during different maneuvers, and in none of the cases was detected oversensing phenomenon during device interrogation. In the remaining patient with right ventricular pacing impedance increase, lead fracture was diagnosed leading to lead extraction and new lead implantation. In two patients jumpy high shock impedance values were found at remote monitoring, without any other associated anomaly at chest radiograph or fluoroscopy. In one patient, after two months from the first high shock impedance recording at remote monitoring, the CIED system correctly recognized and treated a sustained ventricular tachycardia. In one patient with a CRT-D INOGEN G141 and Biotronik leads, 41 months after generator replacement a first episode of high pacing impedance in the left ventricular lead (Biotronik Corox implanted in 2007) was found, with peak values as high as >3000 ohm, returning at baseline value of 550 ohm after 1 month.

Conclusions. Sporadic high pacing and shock impedance values at remote monitoring are detected in almost 10% of patients with hybrid CIED system and seem to be associated with a normal functioning of the device. For the first time we describe this phenomenon for shock impedance and for coronary sinus lead impedance in biventricular ICD. Follow-up is needed to diagnose possible lead fractures. However, the clinical importance of underscoring this phenomenon, especially for shock impedance and coronary sinus lead impedance, is that lead extraction or system revision should be avoided in the setting of hybrid system.

A27: IMPACT OF PERCUTANEOUS MITRAL VALVE REPAIR ON VENTRICULAR ARRHYTHMIA BURDEN IN PATIENTS WITH CRT-D

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Background. Functional mitral regurgitation (MR) is a common valvular disorder in patient with heart failure (HF), associated with poor prognosis and an increase of ventricular arrhythmias. In selected patients who are not eligible for mitral valve surgery, percutaneous valve repair with MitraClip (MC) device may improve clinical outcomes. Cardiac resynchronization therapy with implantable defibrillator (CRT-D) is for HF patients, with depressed ejection fraction (EF), left ventricular dyssynchrony and functional mitral regurgitation. Our aim was to evaluate the impact of percutaneous mitral valve repair using MC system on ventricular arrhythmic burden in patients with CRT-D.

Methods. We enrolled in our study 24 patients with CRT-D and functional MR treated with MC. We collected clinical and remote monitoring data before procedure and at a follow-up of 1 and 12 months. In particular, we analysed ventricular arrhythmias burden recorded by CRT-D home monitoring transmissions.

Results. Mean age of patients was 67.6 ± 8.5 years. Twenty patients (83%) were men. Mean of EF was 21.8 ± 3.8%. Before percutaneous repair, 33% of patients had premature ventricular complex (PVC) burden >5%, at a follow-up of 1 month it decreased to 3% (P=0.06), while at a follow-up of 12 months it decreased to <1% (P=0.04). Non-sustained ventricular tachycardia (NSVT) occurred in 66% of patients before MC and reduced to 33% 1-month after procedure (P=0.11), and to 16% at 12 months (P=0.01).

Conclusions. From our analysis, patients undergoing percutaneous mitral valve repair showed some interesting data on arrhythmic burden reduction. These preliminary data may be related to changes in the cardiac chamber remodelling process due to preload variation leading to changes in regional wall stress. We suppose that the reduction of ventricular arrhythmic load is related to this mechanism, but further studies are needed to better understand this relationship.

A28: ASSOCIATION BETWEEN ANTIARRHYTHMIC THERAPY AND RISK OF VENTRICULAR LIFE-THREATENING ARRHYTHMIAS IN ARVC

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Aims. Antiarrhythmic drugs (AAD) are prescribed in arrhythmogenic right ventricular cardiomyopathy (ARVC) to prevent ventricular arrhythmias and

control symptoms. However, there are no controlled clinical trials and knowledges regarding the efficacy of AAD in ARVC are lacking. The aim of our study was to investigate the benefit of AAD (beta-blockers, sotalol, amiodarone) in a cohort of ARVC patients with long-term longitudinal follow-up.

Methods. The study population included 123 patients with definite diagnosis of ARVC and ≥ 2 clinical evaluations. The primary outcome was a composite of sudden cardiac death (SCD) or major ventricular arrhythmias (MVA): sudden cardiac arrest, sustained ventricular tachycardia (VT) and appropriate ICD interventions, including recurrent events in patients with >1 MVA. Time to first event (SCD or MVA) was considered as secondary composite endpoint.

Results. Sixteen patients were taking AAD at baseline and 75 started at least one AAD during a median follow-up of 132 months [61-255]. A total of 37 patients experienced ≥ 1 MVA with a total count of 83 recurrent MVA. After adoption of a propensity score analysis, no AAD were associated with lower risk of recurrent MVA. However, if dosage of AAD was considered, beta-blockers at $>50\%$ target dose were associated with a significant reduction in the risk of MVA (HR 0.10, 95% CI 0.02-0.46, $p=0.004$).

Conclusions. In a large cohort of ARVC patients with a long-term follow-up, only beta-blockers administrated at $>50\%$ target dose were associated with lower risk of recurrent MVA.

A29: A RARE CASE OF CALMODULIN-RELATED LONG QT SYNDROME

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Background. Long QT syndromes (LQTS) are arrhythmic diseases in structurally normal heart, characterized by mutations of different ion channels and proteins. If a specific trigger is present (adrenergic stimuli, bradycardia, swimming, auditory stimuli and other) ventricular tachycardias, typically torsade de pointes, may occur and degenerate in ventricular fibrillation. Among the spectrum of these syndromes, there are some rare forms characterized by mutations of calmodulin genes that encode for an ubiquitously protein, a modulator of different ion channels expressed in the heart.

Case report. Here we present a case of a newborn girl, born from a caesarian section because of heart rate deceleration during cardiocardiography. The electrocardiogram showed a sinus rhythm with a very prolonged QTc (almost 600 ms). During the hospital stay the newborn developed two episodes of torsade de pointes that required treatment with intravenous magnesium sulphate. Propranolol and mexiletine were started to short the QT interval and inhibit adrenergic stimuli. Genetic analysis showed a heterozygous, pathogenic mutation of Calmodulin Gene 3 (CALM3), encoding for calmodulin, and an heterozygous mutation, with uncertain significance, of Solute Carrier Family 4 Member 3 (SCL4A3), encoding for a solute carrier expressed in different sites of the organism. The little patient was dismissed in home-monitoring, in therapy with propranolol and mexiletine; parents was properly trained at p-BLS. ICD implantation will be considered when the newborn weighs 8-10 kg.

Discussion. Calmodulinopathies are a very rare cluster of early-onset arrhythmic diseases, characterized by poor prognosis; only 74 cases are documented in the world. LQTS and catecholaminergic polymorphic ventricular tachycardia (CPVT) are the more frequent conditions, but idiopathic ventricular fibrillation (IVF), sudden unexplained death (SUD), sudden cardiac death (SCD) and aborted cardiac arrest (ACA) are encountered among the clinical presentations. Some patients may develop neurological features, due to post-anoxic sequelae or unrelated to cardiac arrest. There is a need for new studies to better understand the underlying mechanisms and improve prognosis.

A30: PREVALENCE AND PREDICTORS OF PERSISTENT SINUS RHYTHM IN A COHORT OF PATIENTS UNDERGOING ELECTRICAL CARディオVERSION FOR ATRIAL FIBRILLATION. A REAL-LIFE EXPERIENCE

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Aims. Electrical cardioversion (EC) for atrial fibrillation (AF) is a common procedure performed in an attempt to restore normal sinus rhythm (NSR). However, recent data on long-term effectiveness of EC and on possible predictors of persistent restoration of NSR are lacking. The aim of this study was to evaluate the prevalence and predictors of persistent NSR in a recent cohort of unselected patients undergoing to EC for AF.

Methods. We analyzed the data of all consecutive patients undergoing elective EC for AF at our institution between January 2017 to December

2018. We analyzed clinical and echocardiographic data as well as pharmacological antiarrhythmic therapy at baseline and at 12-month follow-up. Primary endpoint was the maintenance of NSR at 12-month.

Results. Of the 300 patients enrolled, 270 (90%) had successful EC and among them 201 patients (i.e. study population) have follow-up data (mean age 70 ± 10 years; 74% male; 47,8% with hypertensive cardiomyopathy). After 12 months, only 45,7% were in NSR. Whereas patients without persistent NSR at 12 months had a lower left ventricle ejection fraction (LVEF) at the baseline ($49,1 \pm 16$ vs $59,7 \pm 9$, $p=0.02$), no significant differences in the baseline other clinical variables have been found. Regarding pharmacological antiarrhythmic therapy, patients without persistent NSR at 12 months were less prescribed to flecainide (21 (23,1%) vs 11 (10,8%); $p=0.018$) and sotalol (13 (14,3%) vs 5 (4,9%); $p=0.045$), whereas there were no differences in the use of amiodarone at baseline and during follow-up. At the multivariate analysis only the duration of the disease beyond 12 months (OR 0.269, 95% CI: 0.078-0.932, $p=0.038$), an higher LVEF (OR 1.065, 95% CI 1.011-1.122, $p=0.018$) and the presence of RS at 1 month follow-up (OR 17.789 95% CI 3.2-99.9, $p=0.002$) were associated with the probability to maintaining NSR.

Conclusion. In a cohort of unselected patients with AF undergoing elective EC, only 45,7% were in NSR at 12 months follow-up. Only the duration of the disease beyond 12 months, an higher LVEF and the presence of RS at 1-month follow-up emerged as independent predictors of maintenance of NSR. This highlights that early re-evaluation of these patients appears useful for assessing longer-term outcome. Further larger studies are needed to confirm these results also in the perspective of possible selective approach to ablation strategies.

A31: MODIFICHE MORFO-FUNZIONALI DEL CUORE DESTRO NEI PAZIENTI AFFETTI DA FIBRILLAZIONE ATRIALE PERMANENTE

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Background. La fibrillazione atriale (FA) è l'aritmia più comune al mondo, di cui si stima sia affetto tra il 2 e il 4% della popolazione adulta, con maggiore prevalenza tra gli anziani e pazienti con policomorbidità. È da chiarire se e attraverso quali meccanismi l'FA determini peggioramento clinico nei pazienti che ne sviluppano la forma permanente.

Obiettivo. Valutare a quali modifiche morfo-funzionali vadano incontro il ventricolo destro (VD) e l'atrio destro (AD) nei pazienti affetti da FA permanente, ponendo particolare attenzione sulla correlazione con l'epoca di insorgenza dell'aritmia.

Materiali e metodi. Studio prospettico osservazionale per cui sono stati arruolati 193 pazienti dal 1 gennaio 2018 al 1 dicembre 2019, secondo i criteri di inclusione previsti nel disegno iniziale: pazienti tra 18 e 90 anni in ritmo sinusale (RS) o FA permanente non valvolare sottoposti ad ecocardiografia trans-toracica per qualsiasi motivo. Sul totale degli arruolati, 123 (63,7%) erano in RS e 70 (36,3%) in FA permanente con una media di durata della FA di 3 anni (2-10). Sono stati valutati i parametri di funzione del VD, le dimensioni del VD e dell'AD, la presenza ed il grado di insufficienza tricuspide, il gradiente transvalvolare ventricolo-atriale e la vena cava inferiore, facendo riferimento alle raccomandazioni sulla valutazione del VD della Società Americana di Ecocardiografia [Rudski LG et al J Am Soc Echocardiogr 2010;23:685-713].

Endpoints. Primario: prevalenza di disfunzione ventricolare destra nei pazienti con FA permanente rispetto a quelli con RS. Secondari: valutazione del rapporto che intercorre tra la durata della FA in termini di anni e indici di funzione del VD; valutazione delle modifiche morfo-funzionali che sviluppano i pazienti con FA rispetto a quelli con RS.

Risultati. Nel gruppo FA rispetto al gruppo RS sono stati registrati valori maggiori di: disfunzione diastolica del ventricolo sinistro (VS) (II grado 27,1% vs 7,3%; III grado 7,1% vs 1,6%), insufficienza mitralica per presenza (48% vs 14,3%) e grado (II 38,6% vs 10,6%), area dell'AD (15 ± 4 vs 23 ± 6 ; $p<0,001$), dilatazione del VD (52,5% vs 13,2%; $p<0,001$), insufficienza tricuspide di ogni grado, maggiormente per i gradi II e III (grado II 40,6% vs 13%; grado III 17,3% vs 0,8%), pressione arteriosa sistolica (32 ± 8 vs 26 ± 13 ; $p=0,020$); nel gruppo RS rispetto al gruppo FA sono stati registrati valori maggiori per: TAPSE (24 ± 4 vs 20 ± 2 ; $p<0,001$), onda S (14 ± 3 vs 11 ± 2 ; $p<0,001$), FAC % (47 ± 7 vs 40 ± 9 ; $p<0,001$). La percentuale di disfunzione del VD, valutata sulla base di tutti i parametri illustrati, è significativamente più elevata nel gruppo FA rispetto al gruppo RS (60,3% vs 16,5%; $p<0,001$). Utilizzando la ROC curve è stato possibile individuare tre anni di permanenza in FA come cut-off riferibile alla relazione con la comparsa di dilatazione e disfunzione ventricolare destra (sensibilità del 64% e specificità del 60%).

Limiti dello studio. Una popolazione più ampia consentirebbe di valutare in maniera più precisa l'andamento della correlazione evidenziata dai risultati ottenuti dalla nostra analisi e ottenere valori più significativi di sensibilità e specificità (AUC $0,64 \pm 0,30$).

Conclusioni. In pazienti con FA permanente le sezioni destre del cuore vanno incontro ad una dilatazione a cui è associato un peggioramento della funzione sistolica del VD che è indipendente dai fattori di rischio, dal grado di compromissione diastolica del VS e dalla presenza di insufficienza mitralica.

A32: CONCOMITANT THORACOSCOPIC LEFT CARDIAC SYMPATHECTOMY AND RIGHT EPICARDIAL ABLATION OF THE ARRHYTHMOGENIC SUBSTRATE IN A PATIENT WITH LONG QT AND BRUGADA SYNDROMES RELATED TO UNCOMMON SODIUM CHANNEL BETA-SUBUNIT MUTATION

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Introduction. Long QT syndrome and BrS may present as overlap syndrome. We describe the case of a patient with both BrS and likely LQTS and the BrS-associated mutation in the SCN2B gene, which has never been linked to LQTS before.

Case report. A 24-year-old man with a family history of sudden cardiac death was scheduled for screening in our Center after syncope. The 12-lead ECG showed intermittent long QTc. The patient also tested positive for a Brugada type 1 pattern Syndrome following an Ajmaline test resulted. The genetic analysis revealed a heterozygous variant (KL3) of the SCN2B gene, encoding for the β -subunit domain-2 of the sodium channel, known to be associated with BrS. Short VTs were documented on a implantable loop recording. Considering the clinical findings and the patient history we proposed a video assisted thoracic sympathectomy with epicardial right ventricle (RV) arrhythmogenic substrate ablation for Brugada syndrome and ICD implantation. The procedure was performed under general anesthesia guided both by the EnSite Precision™ 3D electroanatomical mapping system (Abbott, Chicago, Illinois, USA) and the noninvasive CardioInsight™ mapping vest (Medtronic, Minneapolis, Minnesota, USA). A minimal-invasive left thoracoscopic access was obtained. Bipolar voltage mapping of the RV epicardium was performed, showing a small area of abnormal electrograms (AEMs) in the RVOT, close to the pulmonary valve. A protocol of ajmaline infusion was then started with appearance of complete RBBB. Epicardial mapping of the RVOT/RV anterior wall at peak ajmaline was repeated pre ablation to identify the full extension of the arrhythmogenic substrate, revealing an increased area of AEMs if compared to baseline. A video assisted thoracoscopic left cardiac sympathectomy (from distal C8 to T5) was performed. A second infusion of ajmaline was started. At peak ajmaline, complete RBBB appeared once again. Invasive epicardial mapping of the RVOT and anterior RV wall revealed the same area of AEMs, but late fragmented potentials had longer duration and double potentials appeared, indicating a likely increase in the conduction delay in this area as compared with pre sympathectomy. A Coolrail™ linear ablator (Atricure, Mason, Ohio, USA) was then advanced on the area of AEMs and erogation of radiofrequency (RF) energy was performed on a surface of approximately 15 cm² of the anterolateral RVOT and anterior RV wall. The last ajmaline infusion after the RF epicardial ablation revealed no more fragmented potentials in this area at the contact and non invasive mapping. At a follow-up of 4 months, the patient had no symptoms and no episodes of VT/VF.

Conclusion. Noninvasive mapping (ECGi) provides useful information on the arrhythmogenic substrate of BrS and can help to identify areas of activation delay. The inferolateral region of the right ventricle, in proximity to the tricuspid valve, may harbor the same arrhythmogenic substrate of the RVOT. This area may be more sensitive to the effect of the autonomous nervous system, showing appearance of the BrS pattern upon parasympathetic stimulation. This phenomenon may explain the parasympathetic dependence of the BrS pattern previously described in some patients.

A33: MECHANICAL DISPERSION AS A PREDICTOR OF ARRHYTHMIC DEATH

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Sudden cardiac death (SCD) is defined as a non-traumatic, unexpected fatal event occurring within 1 hour of the onset of symptoms in an apparently healthy subject, due to a cardiac cause. SCD represents the cause of 25-50% of deaths from cardiovascular disease. In 88% of cases SCD is due to an arrhythmic mechanism. The guidelines of the European Society of Cardiology (ESC) for primary prevention of SCD use the reduction of left ventricular ejection fraction (LVEF) <35% as the main indicator to decide if a patient needs an implantable cardioverter defibrillator (ICD). However, several trials have demonstrated that LVEF lacks sensitivity and specificity. In our study we focused on the role of global longitudinal strain (GLS) and mechanical dispersion (MD) assessed by speckle tracking echocardiography (STE), in the prediction of arrhythmic events.

Methods. In our study 71 patients (62 men and 9 women) with ICD or CRT-D were enrolled; 49 for primary prevention and 22 for secondary prevention. All patients underwent an ICD/CRT-D control, a 12 leads ECG before implantation and during the follow-up, and a transthoracic echocardiogram with color Doppler.

Results. During the follow-up 39 patients had no arrhythmic event (group

A), 32 patients had arrhythmic events (group B), 11 ventricular fibrillation and 22 ventricular tachycardia. All events were treated successfully by ICD/CRT-D intervention. Before device implantation all patients had LVEF markedly depressed. We found no significant differences in age, gender, cardiovascular risk factors, and underlying heart disease etiology between patients with and without arrhythmic events. No significant difference was found for EF before implantation or during follow-up (EF before 39% \pm 17.5% vs 35.9% \pm 12.7%, p=0.28 and during follow-up EF 43.7% \pm 16.3% vs 39.9% \pm 13.7%, p=0.42) and for GLS (9.3 vs 9.7; p=0.72). We found a significant linear correlation between the mechanical dispersion value and the presence of ventricular arrhythmic events (r = - 0.53, p=0,0001) and the MD was significantly higher in patients with arrhythmic events in when comparing patients of group A (80,9 \pm 36,1 ms vs 129 \pm 38,4 ms; p=0,0001). The correlation between mechanical dispersion and arrhythmic events is confirmed both in patients with EF \geq 35% (r = 0.51, p=0,007) and in patients with severely impaired systolic function (EF <35%, r = 0.58, p<0,001). From the analysis of ROC curves, a MD value \geq 104.5 ms was the best predictor of arrhythmic events (area under the curve = 0.81, p=0,0001 sensitivity 75%, specificity 80%). Analysis of the Kaplan-Meier curve shows that patients with a MD \geq 104.5 ms had a significantly higher incidence of events at the follow-up (75% vs 25%, p=0,0001) compared to patients with a lower mechanical dispersion (log-rank p=0,03, chi square 4.42). At multivariate analysis only a MD value \geq 104.5 ms (HR 3.1, 95% CI 1.27-7.54, p=0,012) and age were found to be independent predictors of arrhythmic events (HR 1.04, 95% CI 1.01-1.07, p=0,017).

Conclusions. Mechanical dispersion measured by STE improve arrhythmic risk stratification regardless LVEF. Using a more specific MD cut-off could allow for a better selection of high-arrhythmic risk patients eligible to ICD/CRT-D implantation, however further studies are needed.

A34: ADDITIVE PREDICTIVE POWER OF THE CHA₂DS₂-VASc AND HAS-BLED SCORES FOR MORTALITY IN PATIENTS WITH ATRIAL FIBRILLATION

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Background and objectives. Atrial fibrillation (AF) associates with increased mortality, predictors of which are poorly characterized. We investigated the predictive power of the CHA₂DS₂-VASc and the HAS-BLED score, commonly used to assess the risk of stroke and bleeding, for mortality in AF patients.

Methods. PREFER-in-AF was a large, prospective, real-world registry including AF patients across 7 European countries. We used logistic regression to analyze the relationship between the CHA₂DS₂-VASc and HAS-BLED scores and outcome events, including mortality, at one year. The performance the logistic regression models was evaluated by discrimination measures (c-index and DeLong test for statistical difference) and calibration measures (quantified by the Hosmer and Lemeshow goodness of fit test, integrated discrimination improvement). In addition, the integrated discrimination improvement (IDI) were evaluated.

Results. 5,209 AF patients had complete information on both scores. Mean age was 71.8 \pm 10.5 years; 3145 subjects (60.4%) were male. Stroke risk was high (mean CHA₂DS₂-VASc total score of 3.4 \pm 1.8), with a total score ranging between 2 to 5 in the majority of patients (>70%). Bleeding risk had a total score ranging from 1 to 3 in >80% of cases, and a mean HAS-BLED total score of 2.0 \pm 1.1. The majority of the non-study sample (N=2034, excluded when no risk scores were available) had similar baseline characteristics as those included in the study sample. Average 1-year mortality was 3.1%. We found strong gradients between examined outcomes (stroke and systemic embolic events (SSE), major bleeding and mortality) for both the CHA₂DS₂-VASc and the HAS-BLED risk scores. Both scores had similar c-statistics for models predicting stroke/SSE, major bleeding and mortality. When including the individual components of both scores separately, c-statistics increased to 0.715, 0.694 and 0.636 with CHA₂DS₂-VASc, and to 0.681, 0.697 and 0.680 with HAS-BLED. The improvement of the models with the CHA₂DS₂-VASc and HAS-BLED combined components over the HAS-BLED individual component models alone was significant for models predicting mortality and stroke in terms of c-statistics (c-statistics: 0.73, 0.70, and 0.74, respectively) and IDI. For prediction of major bleeding, the increase in c-statistic was non-significant (0.680 vs 0.705, p=0.112). Moreover, a very small but significant improvement in sensitivity was found (IDI: 0.88%, p<0.001).

Conclusion. Both the CHA₂DS₂-VASc and the HAS-BLED score predict mortality similarly in patients with AF, and a combination of all their components increases prediction significantly. Such combination may be clinically useful.

A35: INTRACRANIAL HAEMORRHAGE IN ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW OF CURRENT LITERATURE

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Background. Evidence-based medicine (EBM) establishes a hierarchy of evidence based on the study design with randomized controlled trials (RCTs) considered superior to observational studies. A well conducted Systematic reviews (SR) of the RCTs is essential to empower the results of the RCTs. The present study aims to conduct a systematic review of randomized controlled trials on NOAC compared to warfarin to evaluate intracranial hemorrhage in patients with atrial fibrillation.

Methods. We retrieved all published papers that compared NOAC with warfarin in patients with non-valvular atrial fibrillation. Three clinician-researchers independently reviewed and abstracted a total of 110 articles that meet our inclusion criteria. A total of 9 randomized controlled trials (RCT) published between 2010 and 2020 were analyzed by random-effects meta-analysis.

Results. A total of 54 877 patients, randomly allocated to a direct oral anticoagulant (n=23940) or warfarin (n=23901), were included in our analyses. No significant differences were observed between patients who received NOACs and those who received warfarin in terms of total bleeding, major bleeding, non-major clinically relevant bleeding. The risk of fatal bleeding (HR 0,53), intracranial hemorrhage (HR 0,51), hemorrhagic stroke (HR 0,58) and all-cause mortality (HR 0,91) was lower in patients who received NOACs compared to the patients who received warfarin.

Conclusions. This was the first systematic review in the published literature, comparing NOACs vs warfarin, that evaluates the risk of ICH. Our results clearly confirm that NOACs significantly reduce the onset of intracranial hemorrhage and bleeding-related death. Systematic reviews (SR) of RCTs are essential to empower the results and minimizes the bias weight of the single publications.

A36: LONG-TERM FOLLOW-UP OF HIGHLY CHARACTERIZED MYOCARDIAL SUBSTRATE IN COMPLEX VENTRICULAR ARRHYTHMIC PHENOTYPE: MYOCARDITIS, MYOCARDIAL FIBROSIS, ARRHYTHMOGENIC CARDIOMYOPATHY

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Introduction. Ventricular tachyarrhythmias (VA) are closely related to the risk of sudden cardiac death (SCD). Risk assessment should be based not only on left ventricular ejection fraction but also on additional parameters, as late gadolinium enhancement (LGE) detected by cardiac magnetic resonance imaging (MRI), scar by three-dimensional electroanatomic mapping (3D-EAM), genetic third-level screening. Therefore, the evaluation of different predictors of life-threatening VA in different clinical settings represents a crucial step in the arrhythmic risk stratification.

Aim. To identify the electroanatomic and histological substrate in three well-defined populations with SCD-related cardiomyopathies in order to define independent predictors of life threatening VAs.

Methods. This population-based risk prospective single-center observational study enrolled consecutive patients with unexplained complex VAs, defined as sustained VT and/or VF, or Non sustained VT +high burden of premature ventricular contractions (PVCs) >25% recorded by 24h-Holter ECG. All patients underwent cardiac MRI, coronary angiography and electrophysiological study with 3D- EAM and Endomyocardial biopsy (EMB) guided by 3D-EAM.

A follow-up scheduled at 6 months interval, including a recording of 24h-ECG Holter and device (ICD/Loop Recorder) interrogation in patients with implanted device, was performed.

Results. We enrolled 99 patients, 63 males (63.6%), with mean age was 39.11 ± 15.00. Sixty-seven patients (67.7%) presented PVCs/Non sustained VT, 26 patients (26.3%) presented VT or VF, and 8 patients (8.1%) presented aborted SCD. Histological diagnosis divided all patients in 4 defined groups: 50 patients (50%) with myocarditis (M group); 26 patients (26.3%) with focal replacement myocardial fibrosis (FRMF group); 10 patients (10%) with arrhythmogenic cardiomyopathy (ACM group) histological diagnosis; 13 patients (13%) with no histological myocardial alterations. Significant differences in cardiac MRI and in 3D-

EAM among the four groups were observed: in occurrence of RV alternations, in terms of LDE or wall motion abnormalities or bulging or hyperintensity in T1 (p= 0.02) and in terms of mean bipolar scar area (p= 0.01). After a median follow-up of 79± 53 months, the primary outcome of sustained VT/VF or death occurred in 20/99 patients (20%): 14 in M group (28%), 1 in FRMF group (3.8%), 1 in control group (7.7%) and 4 in ACM group (40%) (p= 0.02). Regression analysis demonstrated that sustained VT/VF at admission, catheter ablation, histological diagnosis of myocarditis or arrhythmogenic cardiomyopathy and bipolar and unipolar total scar areas were independent predictors of sustain VT/VF or death. After 170 months of follow-up, freedom from sustained VT/VF or death is significantly different among the four groups (survival rate 60% ACM; 72% M; 96.2% FRMF; 92.3% control group; log rank p= 0.02).

Conclusion. Patients with unexplained VAs should be evaluated with an extensive diagnostic work-up including 3D-EAM and tissue cardiac characterization by EMB. Personalizing population-based risk stratification for SCD could be very helpful for primary prevention ICD implantation and future perspectives should include multivariable risk score for different clinical settings.

A37: VENTRICULAR ECTOPIC BEATS AS A PREDICTOR FOR CLINICAL OUTCOMES IN A COHORT OF YOUNG PATIENTS WITH MAJOR CARDIAC EVENTS AND EARLY REPOLARIZATION PATTERN

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Introduction. The early repolarization pattern (ERP) on the electrocardiogram (ECG) is widely diffused in the general population, representing a benign variant; however, it has been associated with arrhythmic death in a minority of cases. ERP can be diagnosed in the presence of J-point elevation ≥ 1 mm in ≥2 contiguous inferior and/or lateral leads of a standard 12-lead ECG. To date, electrophysiological determinants of major ventricular arrhythmias (VTach) in this condition are not clarified yet, and the real impact of ERP "per se" is poorly defined in the ventricular arrhythmogenicity.

Purpose. We sought to investigate the link between ST-segment elevation and ventricular ectopic beats (VEBs), and to find ECG markers of major cardiac events.

Methods. We investigated a cohort of thirty-four consecutive patients (28 males, 40±15 years, median 40 years) referred to our outpatient clinics for the presence of J-point elevation 2.0 ± 0.7 mm in 3 ± 1 contiguous inferior and/or lateral leads of a standard ECG. Clinical history (asymptomatic, N=9; palpitations, N=13; syncope, N=9; and cardiac arrest/sudden cardiac death, CA/SCD N=3) were collected. Twelve lead 24-hour Holter ECG monitoring (12L-Holter) was performed in all subjects, while echocardiography, effort test, HUTT, and coronary angiography were performed according to clinical judgement and to current recommendations. Univariate and multivariate logistic regression analysis were performed to assess predictors of syncope. P-value <0.05 was considered statistically significant. All data were processed using the Statistical Package for Social Sciences, version 25 (SPSS, Chicago, IL, USA).

Results. ERP was located in lateral ECG leads in 7 cases; in inferior leads in 12 cases; in inferolateral site in the remaining 15 subjects. The majority of cardiac events was observed in patients with inferior and inferolateral site patterns. We then evaluated VEBs count (861±3206 counts/24hour), which was aggravated by progressive shortening of the coupling interval (according to symptoms). In group 1 (asymptomatic) VEBs count was 7,8 ± 9,1; in group 2 (palpitations) it was 2112,31 ± 4868,02; in group 3 (syncope) it was 1,13 ± 1,12; finally, in group 4 (CA/SCD group) VEBs count was 8,00 ± 13,856. Therefore, we did not observe correlation between symptoms and number of ventricular extrasystoles. In fact, CI count in group 1 was 338,60 ± 51,81 ms, in group 2 was 455,36 ± 229,44 ms, in group 3 was 362,14 ± 270,46 ms, and in group 4 was 400 ± 10,0 ms. Interestingly, in multivariate logistic regression analysis, a strong correlation was observed between syncope occurrence and VEB with short CI, irrespective of age and number of VEBs (95% CI -0,002-0,001; p <0,05). In our cohort, ERP was associated with cardiac arrest in 8.8% cases and syncope was detected in those patients with the shortest VEBs CI, irrespective of number of VEBs.

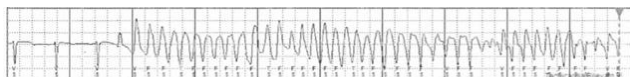
Conclusions. These findings suggest that CI of VEBs may be considered as an independent predictor of cardiac events in ERP patients and aggressive treatment might be indicated in patients with coexistence of ERP and short CI for preventing major cardiac events.

A38: SHORT-COUPLED POLYMORPHIC VENTRICULAR TACHYCARDIA: LA SFIDA DIAGNOSTICA DI UNA RARA PATOLOGIA ARITMICA

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Caso clinico. Donna di 47 anni, non precedenti cardiovascolari né familiarità per cardiopatia o morte improvvisa. Nel dicembre 2018 giungeva per episodio sincope dopo pranzo ed assunzione di ortostatismo, non preceduto da prodromi. Gli esami strumentali effettuati (ECG, ecocardiogramma, massaggio del seno carotideo, TC, RM encefalo ed EEG) risultavano nella norma; il test da sforzo, negativo per ischemia inducibile, evidenziava battiti ectopici ventricolari isolati (BEV), monomorfi, con morfologia a blocco di branca destra (durata del QRS 130 ms) e deviazione assiale sinistra, insorti sul tratto discendente terminale dell'onda T. All'Holter 24 h si documentava un breve tratto di tachicardia parossistica a QRS stretto ed alcuni BEV isolati monomorfi. Considerata la presenza di sincope ad eziologia indeterminata, la paziente veniva sottoposta ad impianto di loop recorder. Dopo circa tre mesi, si verificava nuovo episodio sincope, insorto dopo assunzione di ortostatismo, in occasione del quale si documentava tachicardia ventricolare polimorfa indotta da un'extrasistole ventricolare con intervallo di accoppiamento breve (360 ms; Figura).



La coronarografia e la cine RM cardiaca non mostravano reperti patologici. Posta diagnosi di short-coupled polymorphic ventricular tachycardia, si impiantava ICD sottocutaneo in prevenzione secondaria. Veniva inoltre eseguito studio genetico con tecnica Next Generation Sequencing che rivela una variante di significato incerto (VUS) sul gene della rianodina (RyR2) con genotipo eterozigote (c.2203+2_2203+insAC). **Commento.** La short-coupled polymorphic ventricular tachycardia è una patologia rara descritta prevalentemente come case report e case series, caratterizzata da eventi clinici non indotti dallo sforzo a differenza della più nota tachicardia ventricolare polimorfa catecolaminergica (CPVT). Il caso in esame evidenzia la difficoltà diagnostica di tale affezione, in quanto l'assenza di alterazioni morfo-funzionali e di un chiaro stimolo adrenergico rende complesso il work-up diagnostico. Infatti, l'insorgenza della sincope in ortostatismo e l'età della paziente potrebbero orientare verso una genesi neuromediata; tuttavia la presenza di extrasistole ventricolari precoci e monomorfe con morfologia tipica di un'origine dal sistema di conduzione, deve far sospettare una possibile genesi aritmica. Inoltre, appare di particolare interesse la documentazione di VUS di RyR2: altre varianti sono state rilevate nel 2% della popolazione generale e fino al 70% dei pazienti con CPVT, nella quale mutazioni missenso causano un guadagno di funzione del gene; d'altra parte, sono state descritte alcune varianti determinanti perdita di funzione genica associate a short-coupled polymorphic ventricular tachycardia. La ricerca nei familiari delle varianti geniche potrebbe essere importante per una stretta vigilanza di eventi clinici.

A39: THE PREDICTOR ROLE OF WORSENING RENAL FUNCTION IN PATIENTS WITH NEW ONSET ATRIAL FIBRILLATION ON DIRECT ORAL ANTICOAGULANT

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Background. Chronic kidney disease (CKD) is an important outcome predictor in patients with atrial fibrillation (AF). Moreover, renal function at baseline is used to guide oral anticoagulant (OA) selection and dosing. The prognostic role of worsening renal function (WRF) during treatment with direct oral anticoagulants (DOACs) has been poorly explored.

Purpose. To estimate the prognostic role of WRF in terms of major adverse cardiovascular events (MACEs) and bleedings in a series of patients with newly diagnosed non-valvular AF (NVAF) treated with DOACs.

Methods. Between January 2017 and March 2019, we enrolled 866 patients with newly diagnosed NVAF treated with DOACs. Renal function (creatinine levels and estimated glomerular filtration rate - eGFR) was assessed at baseline and at follow-up. eGFR was calculated using Cockcroft-Gault (CG), Modification of Diet in Renal Disease (MDRD) and

Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulas and as the mean value (MV) of the three. At baseline, hemorrhagic risk was estimated with the main available scores (HAS-BLED, ATRIA and ORBIT). WRF was defined as an increase in creatinine levels or a decrease in eGFR of at least 20%. Bleedings were identified according to the ISTH definition.

Results. Patients were followed for a median time of 21.7 ± 8.3 months. WRF was observed in 159 (18.3%), 139 (16.1%), 170 (19.6%), 153 (17.7%) and 153 (17.7%) patients using creatinine, CKD-EPI, CG, MDRD and MV, respectively. Patients with WRF had significant higher rates of acute heart failure (AHF) and major bleedings (MB), while acute coronary syndrome (ACS) episodes were more frequently observed only in WRF detected by creatinine levels or CKD-EPI formula. Mortality was higher exclusively in patients with WRF using CKD-EPI. Conversely, the incidence of total bleeding events and stroke was not affected by WRF. Different type of DOAC did not significantly impact the observed renal impairment and had no effect on the occurrence of MACEs in patients showing WRF. The baseline predictors of WRF were found to be age, female sex, lower hemoglobin and creatinine levels, and higher CKD-EPI and MDRD eGFRs. At multivariate analysis, WRF was identified as an independent predictor of MB (OR 2.04, 95% CI 1.06-3.94, $p=0.034$), regardless of the bleeding risk.

Conclusions. This is the first prospective study to evaluate the impact of WRF on cardiovascular events in patients with NVAF treated with DOACs. In this population, WRF resulted a frequent event, was associated with higher rates of MB, death, and MACEs, and emerged as an independent predictor of MB. CKD-EPI showed the best accuracy in predicting MACEs among patients with WRF. The specific DOAC did not affect either the entity of worsening renal function or the incidence of cardiovascular events.

A40: ADMISSION BLOOD GLUCOSE LEVEL AS AN ISCHEMIC STROKE MODIFIER IN PATIENTS WITH NEW ONSET ATRIAL FIBRILLATION

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Background. Several scores have been proposed to assess the stroke risk in patients with non-valvular atrial fibrillation (NVAF). However, type 2 diabetes mellitus (T2DM) is considered a major stroke risk factor regardless of glycemic control. Whether blood glucose level at baseline modifies the risk of stroke in NVAF is still unclear.

Purpose. To evaluate the risk of ischemic stroke according to the presence of T2DM and admission blood glucose (ABG) level in patients with new-onset NVAF starting direct oral anticoagulants (DOACs).

Methods. We analyzed all consecutive patients with NVAF at our outpatient clinic from January to December 2018. The study population was constituted by 1014 patients with new-onset NVAF starting new anticoagulant therapy. Baseline characteristics were evaluated in the overall cohort whereas outcomes were assessed for 915 patients. The median follow-up time was 19.6 ± 12.9 months.

Results. Overall, 50.3% were male with a mean age of 73.9 ± 12.5 years. Diabetic NVAF patients were more frequently male ($p=0.04$) with higher prevalence of dyslipidemia ($p<0.001$), hypertension ($p<0.001$), severe renal impairment ($p=0.02$), peripheral vasculopathy ($p=0.007$) and history of myocardial infarction ($p<0.001$) compared to non-diabetic NVAF. Conversely, no differences were observed between subgroups in terms of age ($p=0.8$). Baseline blood glucose level was significantly higher in the diabetic NVAF population (160 ± 67 mg/dL vs 119 ± 39 mg/dL; $p<0.001$). As expected, the mean CHA₂DS₂-VASC score was significantly higher in diabetic NVAF compared to non-diabetic groups (4.7 ± 1.4 vs 3.2 ± 1.5 ; $p<0.001$). During a 2 year follow-up period, we collected 27 (3.0%) ischemic stroke. As expected, the rates of stroke were significantly higher in diabetic NVAF (7.6% vs 2.3%, $p<0.001$). Also, the ABG was significantly greater in NVAF who had an ischemic stroke compared to others (160 ± 68 mg/dL vs 119 ± 39 mg/dL, $p=0.005$). The incidence of stroke was almost five-time greater in NVAF with ABG level major than 150 mg/dl (9.8% vs 1.9%, $p<0.001$). At multivariate Cox-regression model adjusted for age, sex and presence of T2DM, blood glucose level at admission was the only independent predictor of ischemic stroke at follow-up (HR 1.01, 95% CI 1.001 - 1.02; $p=0.03$). Finally, another multivariate Cox-regression model, adjusted for the mean CHA₂DS₂-VASC score, showed that the ABG still remained a strong independent predictor of ischemic stroke at follow-up (HR 1.012, 95% CI 1.003 - 1.02; $p=0.01$).

Conclusions. Diabetic NVAF had a worse baseline profile and higher stroke risk compared to non-diabetic NVAF. Baseline blood glucose level was an independent predictor of stroke regardless of the presence of diabetes mellitus or stroke risk profile. These findings underline the role of basal blood glucose level as a potential stroke risk modifier and therefore emphasize the importance of its routine determination to better stratify the stroke risk in NVAF starting DOACs.

A41: EPICARDIAL OR ENDO-EPICARDIAL VS ENDOCARDIAL ONLY APPROACH IN CATHETER ABLATION OF ELECTRICAL STORM AND VENTRICULAR TACHYCARDIA

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(a) OSPEDALI RIUNITI ANCONA

Background. Few studies have suggested that a strategy of combined endo- and epicardial access for mapping and transcatheter ablation (CA) of ventricular tachycardia (VT) may provide superior efficacy to an endocardial-only approach in selected patients.

Objective. We sought to evaluate the number of VT recurrences in patients undergoing CA for ventricular tachycardia or electrical storm (ES), comparing endocardial approach to epicardial or endo-epicardial approach.

Methods. We conducted a retrospective, single center, observational study, enrolling patients who underwent CA for treatment of VT or ES. The ablation strategy (endocardial vs. endo-epicardial or epicardial approach) was chosen by the operators according to their personal evaluation of the characteristics of patients, preferring the epicardial approach for patients with non-ischemic cardiomyopathy and ECG criteria suggesting an epicardial origin of the VT. Patients were divided into two groups (endocardial approach vs. epicardial or endo-epicardial approach), and the primary outcome was sustained VT recurrence at short- middle term follow-up, as assessed by implantable cardioverter-defibrillator (ICD), remote monitoring and clinical evaluation.

Results. We included 43 patients, with a total of 44 procedures (27 endocardial ones and 17 endo-epicardial or epicardial ones). Most common indication for CA was ES (61.5%). Ischemic cardiomyopathy was the most common disease in patients that underwent endocardial approach (66.7%), while non-ischemic cardiomyopathy was the underlying disease of the 17 patients that underwent epicardial or endo-epicardial CA. In our short-middle term follow-up (median follow-up: 4 months), we found six VT recurrences (3 in the endocardial approach group, 3 in the epicardial or endo-epicardial approach group). In particular, among the 3 recurrences occurred using the epicardial approach, a premature in-hospital recurrence took place in a patient with severe ventricular dysfunction and several comorbidities.

Conclusions. In our experience, we found the same number of VT recurrences between the two approaches. Further data on a larger number of patients with longer follow-up are needed to assess the comparative efficacy of endocardial and epicardial or epi-endocardial approaches. In the future, further analysis focusing on patients' underlying cardiomyopathy or electrophysiological characteristics could show interesting perspectives.

A42: INSIGHTS INTO CEREBRAL HEMODYNAMICS DURING ATRIAL FIBRILLATION: A NON-INVASIVE NEAR-INFRARED SPECTROSCOPY APPROACH

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Background. Atrial fibrillation (AFib) is the most common cardiac arrhythmia, currently affecting about 3% of the general population. Recently, it has been observed that AFib is associated with cognitive decline/dementia, independently from clinical strokes. Several mechanisms have been proposed to explain this association. Among these, the hypothesis of an altered cerebral blood flow dynamics during AFib has been the least investigated, most likely due to the evident concerns related to the direct sampling in the cerebral circulatory system. In particular, it is unknown how abnormal heart rhythm influences hemodynamic parameters of the distal cerebral circulation. The aim of this study was to use non-invasive cerebral near-infrared spectroscopy (NIRS) to investigate: (a) the behaviour of hemodynamic signals in the deep cerebral circle, (b) how these signals are affected by different rhythm status (AFib, atrial flutter – AFL, restoration of sinus rhythm – SR).

Methods. From January to August 2019, we enrolled 53 consecutive patients, who underwent a hemodynamic and cerebral monitoring before and after an effective electrical cardioversion (ECV) (39 in AFib, 14 in AFL). We analyzed the Tissue Oxygenation Index (TOI), a spatially-resolved NIRS signal known to effectively reflect tissue blood flow. A statistical paired t-test was used to compare pre and post-ECV signals.

Results. ECV was successful in maintaining SR in 51 out of 53 (96%). Mean (μ) TOI did not differ pre and post-ECV both in AFib and in AFL patients (AFib: 64.72 ± 6.61 vs 65.59 ± 7.22 , $p=0.26$; AFL: 64.35 ± 7.37 vs 63.64 ± 7.43 , $p=0.32$; Overall: 64.61 ± 6.75 vs 65.02 ± 7.25 , $p=0.48$), while standard deviation (σ) of TOI showed a trend towards significant decrease in the totality of the sample (1.313 ± 0.671 vs 1.139 ± 0.715 , $p=0.01$). When we compared the coefficient of variation (CoV) of TOI, calculated as the ratio between σ and μ (σ/μ) and representing a measure of signal variability, normalized for the CoV of arterial blood pressure (ABP), we found a significant decrease of normalized CoV of TOI in AFib and in the

totality of the sample, but not in AFL (AFib: 0.124 ± 0.055 vs 0.103 ± 0.066 , $p=0.03$; AFL: 0.108 ± 0.050 vs 0.090 ± 0.052 , $p=0.10$; Overall: 0.119 ± 0.054 vs 0.099 ± 0.062 , $p=0.01$). Of note, the cv of ABP did not differ between pre and post-ECV (AFib: 0.183 ± 0.055 vs 0.194 ± 0.058 , $p=0.26$; AFL: 0.187 ± 0.055 vs 0.189 ± 0.050 , $p=0.87$; Overall: 0.184 ± 0.054 vs 0.193 ± 0.055 , $p=0.27$).

Conclusions. NIRS non-invasive analysis of deep cerebral hemodynamics suggest that, even though baroreceptor reflexes adequately dampen central blood pressure oscillations in AF, the deep cerebral circle suffers from an increased variability of hemodynamic signals, which are restored with the return to the SR. These data support previous computational studies which claimed that during AFib transient hyperperfusion or hypertensive events occur deeply in the brain, plausibly related to cognitive decline.

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A43: QUANDO IL PROTAGONISTA DEL TEST DA SFORZO È SOLO L'ST

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Introduzione. L'indicazione più frequente all'esecuzione di un test ergometrico riguarda ancora oggi la cardiopatia ischemica, sebbene da nuove linee guida sia rimasta un'indagine ormai sovrastata da test di imaging più specifici. Nei soggetti giovani può fornire informazioni riguardo all'insorgenza di aritmie e/o la loro potenziale benignità o malignità. È pertanto di fondamentale importanza analizzare ogni singolo dato fornito dal test ergometrico in quanto, come nel nostro caso, una mancata visione d'insieme può condurci a diagnosi errate.

Caso clinico. Giunge alla nostra attenzione atleta di sesso maschile, di anni 48, in merito al rilascio dell'idoneità agonistica per tennis. Anamnesi familiare negativa; nessuna terapia farmacologica riferita. Il paziente era asintomatico per angor, riferiva soltanto sporadici episodi di cardiopalmo prolungato in concomitanza dell'attività sportiva sproporzionato all'intensità dell'esercizio, ai quali non aveva dato particolare importanza. L'esame obiettivo e l'elettrocardiogramma di base non mostravano anomalie di rilievo. L'ecocardiogramma transtoracico effettuato ambulatorialmente non evidenziava cardiopatie strutturali. Durante prova da sforzo al cicloergometro all'acme dello sforzo veniva evidenziato un sottoslivellamento del tratto ST orizzontale profondo e diffuso, più evidente in sede laterale che permaneva anche durante il recupero con associato sovra-ST in aVR. In considerazione della franca positività dell'esame si richiedeva coronarografia che mostrava aterosmasia coronarica diffusa in assenza di lesioni significative, non anomalie di origine e decorso delle coronarie. Valutando più attentamente il caso con il collega aritmologo, emergeva un accorciamento dell'intervallo P-R agli alti carichi di lavoro con l'insorgenza di onda delta e slargamento del QRS. Nel sospetto di sindrome di Wolff-Parkinson-White, il paziente veniva sottoposto a studio elettrofisiologico endocavitario che evidenziava comparsa di fibrillazione atriale pre-ecitata con R-R minimo <210 msec durante sforzo e, durante infusione di isoproterenolo, l'emergenza di una via di conduzione anterograda accessoria con R-R <220 msec. Il paziente veniva pertanto sottoposto ad ablazione di via accessoria con concessione dell'idoneità agonistica dopo 6 mesi, previa esecuzione di test ergometrico che documentava buon esito della procedura.

Discussione e Conclusioni. La sindrome di Wolff-Parkinson-White può spesso trarre in inganno poiché nelle forme intermittenti, può mimare diverse condizioni cliniche, tra cui una genesi infartuale. È importante distinguere le caratteristiche delle sindromi da pre-ecitazione come la Wolff-Parkinson-White poiché i pazienti possono necessitare di terapia con farmaci antiaritmici specifici e/o ablazione con radiofrequenza. Inoltre la morte cardiaca improvvisa rappresenta la prima manifestazione della sindrome di WPW in circa la metà dei pazienti affetti da tale patologia che muoiono improvvisamente durante attività fisica o in seguito a intensi stress emozionali. Il nostro caso clinico è finalizzato inoltre a sensibilizzare la diffusione e la corretta interpretazione del test ergometrico classico o di altre tipologie di ECG-stress test per la concessione di idoneità sportive, essendo in grado di identificare patologie potenzialmente letali, indirizzando il corretto work-up diagnostico e terapeutico.

A44: SOPRAVVIVENZA DOPO ARRESTO CARDIACO EXTRA-OSPEDALIERO: L'IMPORTANZA DI UN FOLLOW-UP A LUNGO TERMINE

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Introduzione. La sopravvivenza dopo un arresto cardiaco extra-ospedaliero rappresenta una sfida in tutto il mondo. Negli ultimi 10 anni

sono stati creati numerosi registri di arresti cardiaci extra-ospedalieri secondo le raccomandazioni Utstein ma la maggior parte riporta un follow-up limitato ad un mese dall'evento. Pochi sono dati disponibili in merito alla sopravvivenza a lungo termine ed in nessun caso i risultati vengono forniti suddividendo i pazienti nelle diverse categorie di pazienti Utstein, tra le quali potrebbero esserci importanti differenze in termini di sopravvivenza. Nel 2015 è stato istituito il Registro degli Arresti Cardiaci Extra-ospedalieri della Regione Lombardia (Lombardia CARE), che coglie questa sfida e, attraverso un follow-up fino a 5 anni, permette di studiare come possa variare la sopravvivenza nel tempo al fine di migliorare il trattamento.

Obiettivi. Fornire la prima analisi relativa alla sopravvivenza a lungo termine dei pazienti con arresto cardiaco extra-ospedaliero, divisi secondo le categorie Utstein.

Materiali e metodi. Tutti gli arresti cardiaci extra-ospedalieri che si sono verificati nella provincia di Pavia dal 01/01/2015 al 31/12/2018 e nelle province di Pavia, Lodi, Cremona e Mantova dal 01/01/2019 al 31/12/2019 sono stati arruolati prospetticamente nel registro Lombardia CARE. Per ciascun paziente, abbiamo valutato il trattamento pre-ospedaliero, la sopravvivenza e la categoria di performance cerebrale (CPC) a 1 mese, 6 mesi, 12 mesi e poi ogni anno fino a 5 anni dopo l'evento.

Risultati. In cinque anni, il nostro registro ha raccolto i dati di 5094 arresti cardiaci extra-ospedalieri per i quali sia stato allertato il sistema di emergenza. Le manovre di rianimazione cardiopolmonare (RCP) sono state tentate in 3346 casi e solo questi sono stati inclusi nell'analisi, in linea con le raccomandazioni Utstein. L'età mediana era 78 anni [IQR, 68-88], il nel 59% dei casi era di sesso maschile, l'eziologia dell'ACC è stata medica nel 92%, e il domicilio è stato il luogo dell'ACC per il 78% dei pazienti. L'evento è stato testimoniato nel 55% dei casi da astanti, che hanno eseguito RCP nel 36.3% dei casi, mentre il 15% è stato testimoniato dal 118. Per quanto riguarda i ritmi di presentazione, quello defibrillabile rappresentava il 17%. Nella popolazione generale la sopravvivenza all'arrivo in ospedale è stata del 18.6% (n=624), alla dimissione è stata del 7.8% (n=261). La sopravvivenza è stata significativamente superiore (Log Rank test) per le categorie Utstein con ritmo defibrillabile rispetto a quella con ritmo non defibrillabile, sia considerando la sopravvivenza dall'evento (22% vs 1.5% a 5 anni), sia limitando l'analisi ai pazienti dimessi vivi (76% vs 60% a 5 anni). Le curve di Kaplan-Meier per la sopravvivenza dalla dimissione (mediana del follow-up 398 giorni) mostrano una progressiva riduzione della sopravvivenza anche per i soggetti con ritmo defibrillabile alla presentazione, da circa il 95% a 30 giorni fino al 75% a 5 anni. Un simile trend di sopravvivenza si osserva anche categorizzando i pazienti dimessi secondo l'outcome neurologico (buono se CPC≤2).

Conclusioni. I risultati delle nostre analisi mostrano quanto sia importante monitorare la sopravvivenza a lungo termine dopo arresto cardiaco extra-ospedaliero, considerata la differenza osservata nelle varie categorie Utstein. A nostro parere, la prossima revisione Utstein dovrebbe raccomandare un follow-up più lungo rispetto agli attuali 30 giorni.

A45: IN-HOSPITAL MORTALITY IN COVID-19 PATIENTS ACCORDING TO THE PRESENCE OF ATRIAL FIBRILLATION

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Background. Since the outbreak of coronavirus infective disease (COVID-19) by the end of 2019, it was found that patients with cardiovascular (CV) diseases show greater susceptibility to the infection than the general population. Atrial fibrillation (AF) shares with COVID-19 various prevalent co-morbidities and risk factors. The impact of AF on adverse outcomes, rather historical AF and new onset of AF, in patients with COVID-19 has not been evaluated yet.

Methods. Six hundred thirty-seven patients hospitalized for COVID-19 in three large Italian hospitals were enrolled in the study. Main clinical characteristics, past medical history, and clinical course were collected. In-hospital mortality, according to the presence of AF, both historical and new-onset, was then investigated. Estimated survival rates were investigated in the three subgroups. Mortality odds ratios adjusted for demographic, baseline characteristics and treatment were calculated.

Results. 134 (21.0%) patients had overall AF (79 with historical and 55 with new-onset AF). Patients with new-onset AF were younger than those with historical AF but older than those without AF. Patients with a history of AF showed a higher prevalence of co-morbidities (cardiomyopathy, peripheral artery disease, chronic obstructive pulmonary disease, renal failure, cancer, and liver disease) than patients with new-onset AF. The in-hospital mortality rate was significantly higher in patients with new-

onset of AF and in patients with historical AF than patients with sinus rhythm (n=27, 49.1%; n=29, 36.7%; n=107, 21.3%; p<0.001). The estimated survival rates at 30 days were 30.8% (CI 17.4%-45.2%) in those with new onset AF (log-rank p<0.001 vs no AF) and 44.3% (CI 27.7%-59.6%) in patients with historical AF (log-rank p=0.007 vs no AF). The adjusted odds ratio for mortality were 1.26 (0.58-2.74, p=0.55) and 3.34 (1.54-7.25, p=0.002).

Conclusions. The presence of AF in patients with COVID-19 seems to be associated with increased risk of in-hospital mortality, especially among patients with new-onset arrhythmia.

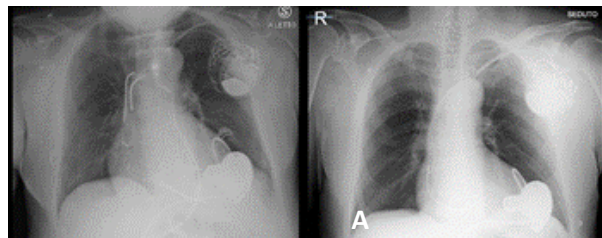
A46: TWO DUAL-COIL ICD LEAD TRANSVENOUS EXTRACTION IN A PATIENT WITH LEFT VENTRICULAR ASSIST DEVICE: A CASE REPORT

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Background. Implantable intracardiac device can require complete extraction due to lead failures or infection; this procedure is deemed at high-risk and appears very challenging in patients with left ventricular assist device (LVAD), due to patient's frailty, risk of systemic infections and the need of uninterrupted oral anticoagulation therapy (OAC, target INR 2-3). We present here the case of complete 2 right ventricular (RV) lead extraction in a patient with LVAD.

Case presentation. A 68-year-old man with esotoxic dilated cardiomyopathy (DCM) with ejection fraction (EF) 10% received a CRT-D device in 2009; in 2010 the right ventricular (RV) coil (Medtronic Sprint Fidelis Active Fixation Dual coil) showed signs of rupture, so it was abandoned, and a new coil (Medtronic Sprint 4 Active Fixation Dual coil) was implanted. In 2013 he received a LVAD (HeartWare, Medtronic). In 2020 the patient was admitted for inappropriate ICD shock delivery due to noise sensing and increased impedance of RV lead suggesting lead fracture was documented (pre-operative chest XR, panel A). Considering the residual risk of malignant arrhythmias, complete extraction of both the RV leads and implantation of a new RV lead was planned, maintaining warfarin with a INR of 2.11 the day of the procedure. After opening the pocket and freeing the proximal portion of the leads, the lead connectors were cut and two locking stylets (Liberator Beacon Tip Locking Stylet, Cook Medical), secured with compression coils, were inserted into the central core of each of the malfunctioning RV leads to prevent disruption. The mechanical rotational extractor (one short 11 French and one long 13 French Evolution RL, Cook Medical) with tissue stabilization sheath (SteadySheath Evolution, Cook Medical) were then advanced gradually lysing vascular adhesions until we gained access of the whole RV lead and were able to extract the leads without complications. After completing the extraction, a new RV single-coil lead was implanted (post-operative chest XR, panel B). In the days after the procedure, a pocket hematoma required treatment with ice and a tight medication. Empirical antibiotic therapy was then administered for 10 days (patients was chronically colonized by S. epidermidis on LVAD wiring). The patient was discharged after two weeks.

Conclusions. Complete transvenous lead extraction is a high-risk procedure associated with important complications, especially in patients with OAC and with higher risk of infection. The procedure should be performed by a well-trained staff in a complete full-safe setting with a close clinical monitoring after the procedure, to prevent all the possible complications.



A47: IMPACT OF EMERGENCY MEDICAL SERVICE ARRIVAL TIME AND INITIAL ARREST RHYTHM ON RETURN OF SPONTANEOUS CIRCULATION (ROSC) AFTER OUT-OF-HOSPITAL CARDIAC ARREST: THE EXPERIENCE OF THE PROVINCE OF LECCE, ITALY

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(a) SEUS 118

Introduction. Out-of-hospital cardiac arrest (OHCA) is a major cause of death and disability worldwide. In 2013, the Territorial Emergency Medical Service (EMS) of Lecce, a public service operating in an Italian province of 814,495 inhabitants, developed an OHCA registry. The present study aims to evaluate the relationship between EMS arrival time, shockable rhythms and return of spontaneous circulation (ROSC).

Materials and methods. All OHCA cases from 1st January 2013 and 31st December 2017 in Lecce OHCA registry were assessed. Data were collected chronologically by the ambulance crew and included patient characteristics (age and sex), arrest features, EMS response times, treatment and patient outcomes (ROSC or death).

Results. 4203 OHCA cases of EMS treated cardiac arrests were recorded in the study period (103 per 100,000 of resident population per year), with a survival rate at hospital transfer of 4.5%. Asystole was the most common cardiac arrest rhythm (87.2%), while ventricular fibrillation or tachycardia (VF/VT) and pulseless electrical activity (PEA) were observed for 9.4% and 3.4% of cases, respectively. Relative to ROSC cases, the percentage of shockable rhythms raised to 54.1%. mean EMS response times (mm:ss) were 11:37 for shockable rhythms with ROSC, 13:31 for shockable rhythms with death, 12:58 for non-shockable rhythms with ROSC and 16:12 for non-shockable rhythms with death. ROSC cases with VF/VT were assisted in less time than the others.

Conclusion. According to Lecce OHCA registry, survival rate after OHCA is low. Initial arrest rhythm can influence the outcome, since most ROSC cases are represented by shockable rhythms. ROSC cases after VF/VT were associated with the shorter EMS arrival time, thus suggesting that an early assistance could increase the possibility to find a shockable rhythm and to improve survival rate.

A48: VALUTAZIONE DELLA T-WAVE VARIABILITY (TWV) IN SOGGETTI SANI

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(a) CARDIOLOGO LIBERO PROFESSIONISTA

Introduzione. Diversi studi hanno dimostrato come la variabilità dell'intervallo QT possa essere associata alla comparsa di aritmie ventricolari e di morte cardiaca improvvisa. Peraltro, i dati disponibili sulla variabilità della morfologia dell'onda T e il suo valore prognostico non sembrano essere ancora conclusivi. In questo lavoro, abbiamo valutato un nuovo approccio per la misurazione della variabilità delle onde T (TWV) che riflette i cambiamenti nella morfologia delle onde T [1].

Materiali e metodi. La popolazione di studio era composta da 24 pazienti sani (età 44,17 ± 16,86 anni, 11 donne:13 uomini, frequenza cardiaca media 76,62 ± 12,99 battiti/minuto) senza precedenti cardiologici clinicamente di rilievo e senza terapie farmacologiche in atto, nei quali avevamo escluso la presenza di anomalie della conduzione intraventricolari o di fibrillazione atriale. Il parametro TWV è stato misurato in base alla varianza dell'ampiezza delle onde T.

Risultati. Nei nostri pazienti il valore di TWV si attestava a 27.804 ± 8.835 microV (cluster esaminati 11,21 ± 9,13) con la seguente distribuzione temporale:

CLUSTER.TAV	TAV INDEX	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
MEDIA	11.2083333	27.8045167	25.96675	30.8476127	37.6871836	38.5702227	31.4186366	27.4918182	29.1333636	27.7871926	28.3491026
DEV. ST.	9.13179472	8.83470403	8.40727689	8.96632769	11.5013942	13.59522671	9.52402222	9.21439182	11.0488926	11.2500951	11.16631053

Conclusion. Questi valori sono ben al di sotto di quelli ritrovati nella popolazione dello studio MADIT II come predittivi per eventi aritmici (59 microV). Questo metodo per la valutazione della variabilità della ripolarizzazione ventricolare nelle registrazioni elettrocardiografiche dinamiche ambulatoriali secondo Holter ha quindi mostrato di poter rilevare, in soggetti sani senza terapia in atto, l'assenza di una variabilità transitoria della morfologia delle onde T che, nel caso fosse stata presente, avrebbe potuto essere predittiva per episodi di tachiaritmia ventricolare.

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A49: T-WAVE VARIABILITY IN SOGGETTI SANI: DIFFERENZA TRA SOGGETTI FUMATORI E NON FUMATORI

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Introduzione. Diversi studi hanno dimostrato come la variabilità dell'intervallo QT possa essere associata alla comparsa di aritmie ventricolari e di morte cardiaca improvvisa. Peraltro, i dati disponibili sulla variabilità della morfologia dell'onda T e il suo valore prognostico non sembrano essere ancora conclusivi. In questo lavoro, abbiamo valutato le possibili differenze tra soggetti fumatori e non fumatori di un nuovo approccio per la misurazione della variabilità delle onde T (TWV) che riflette i cambiamenti nella morfologia delle onde T [1].

Materiali e metodi. La popolazione di studio era composta da 24 pazienti sani [8 soggetti: 16 non fumatori, età media 38,25 ± 10,9 anni e 47,13 ± 18,77 anni (p=0,116)] senza precedenti cardiologici clinicamente di rilievo e senza terapie farmacologiche in atto, nei quali avevamo escluso la presenza di anomalie della conduzione intraventricolari o di fibrillazione atriale. Il parametro TWV è stato misurato in base alla varianza dell'ampiezza delle onde T.

Risultati. Nei due gruppi di pazienti non sono state trovate differenze nei valori di frequenza cardiaca massima [115 ± 21,9 bpm versus 119 ± 30,07

bpm (p=0,356)], mentre vi era una differenza nei valori medi [85,63 ± 13,49 bpm versus 72,13 ± 10,45 bpm (p=0,006)] e minimi [63,25 ± 14,14 bpm versus 52,71 ± 10,69 bpm (p=0,027)] della frequenza cardiaca. Non è stata trovata alcuna differenza significativa nei valori dell'SDNN [134,01 ± 38,46 ms versus 129,91 ± 29,304 ms (p=0,387)], del rapporto LF/HF [6,48 ± 3,78 versus 4,43 ± 3,357 (p=0,094)] e nei valori medi di TWV [26,796 ± 8,669 microV versus 28,907 ± 9,154 microV (p=0,351)].

Conclusion. I valori nella nostra popolazione sono ben al di sotto di quelli predittivi nella popolazione dello studio MADIT II per eventi aritmici (59 microV) e non differiscono significativamente in base all'abitudine al fumo. Questa analisi ha quindi mostrato l'assenza di significative differenze tra soggetti fumatori e non fumatori nella variabilità transitoria della morfologia delle onde T, variabilità che se presente potrebbe essere predittiva per episodi di tachiaritmia ventricolare.

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A50: DIFFERENZE UOMO-DONNA NELLA T-WAVE VARIABILITY (TWV) IN SOGGETTI SANI

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Introduzione. Diversi studi hanno dimostrato come la variabilità dell'intervallo QT possa essere associata alla comparsa di aritmie ventricolari e di morte cardiaca improvvisa. Peraltro, i dati disponibili sulla variabilità della morfologia dell'onda T e il suo valore prognostico non sembrano essere ancora conclusivi. In questo lavoro, abbiamo valutato le possibili differenze uomo-donna di un nuovo approccio per la misurazione della variabilità delle onde T (TWV) che riflette i cambiamenti nella morfologia delle onde T [1].

Materiali e metodi. La popolazione di studio era composta da 24 pazienti sani [11 donne, 13 uomini, età media 45,54 ± 20,36 anni e 43 ± 13,99 anni (p=0,36)] senza precedenti cardiologici clinicamente di rilievo e senza terapie farmacologiche in atto, nei quali avevamo escluso la presenza di anomalie della conduzione intraventricolari o di fibrillazione atriale. Il parametro TWV è stato misurato in base alla varianza dell'ampiezza delle onde T.

Risultati. Nei due gruppi di pazienti non sono state trovate differenze nei valori di frequenza cardiaca massima [122,8 ± 35,6 bpm versus 113,9 ± 18,1 bpm (p=0,218)], mentre vi era una differenza nei valori medi [69,9 ± 7,5 bpm versus 82,3 ± 14,1 bpm (p=0,008)] e minimi [51,3 ± 4,98 bpm versus 60,5 ± 15,7 bpm (p=0,038)] della frequenza cardiaca. Non vi era differenza nei valori dell'SDNN [130,49 ± 27,1 ms versus 131,98 ± 36,477 ms (p=0,456)] mentre vi era nei valori del rapporto LF/HF [3,482 ± 2,242 versus 6,495 ± 3,946 (p=0,018)]. Non sono state trovate significative variazioni nei valori medi di TWV [29,553 ± 10,172 microV versus 26,323 ± 7,629 microV (p=0,192)].

Conclusion. I valori nella nostra popolazione sono ben al di sotto di quelli predittivi nella popolazione dello studio MADIT II per eventi aritmici (59 microV) e non differiscono significativamente in base al gender. Questa analisi ha quindi mostrato l'assenza di significative differenze uomo/donna nella variabilità transitoria della morfologia delle onde T, variabilità che se presente potrebbe essere predittiva per episodi di tachiaritmia ventricolare.

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A51: DIFFERENTE INCIDENZA UOMO-DONNA NEL RISCONTRO AMBULATORIALE DI FIBRILLAZIONE ATRIALE MEDIANTE ELETTROCARDIOGRAMMA DI BASE: ANALISI SU 369 PAZIENTI CONSECUTIVI

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Introduzione. In questo studio abbiamo valutato la diversa incidenza tra maschi e femmine della fibrillazione atriale (di qualsiasi natura e forma) in soggetti che si presentavano per una visita cardiologica ambulatoriale di controllo.

Materiali e metodi. Abbiamo analizzato i dati di 369 pazienti ambulatoriali (155 maschi e 214 femmine) giunti consecutivamente alla nostra osservazione per una visita cardiologica di controllo. L'età media dei pazienti era di 64,73±14,26 anni (maschi 63,61±14,01 anni, femmine 65,54±14,45 anni; p=0,0996).

Risultati. Nella popolazione generale oggetto della nostra analisi, si è evidenziata una lieve differenza statistica tra maschi e femmine per quanto riguarda la presenza di un ritmo sinusale stabile (maschi 93.5±24.6% vs femmine 97.6±15.1%; p=0.0484) mentre non si è notata alcuna differenza statisticamente significative tra maschi e femmine per quanto riguarda la fibrillazione atriale, quale che fosse la causa e la durata dell'evento aritmico (maschi 5.3±22.2% vs femmine 2.3±15.1%; p=0.0673).

Discussione. I risultati della nostra analisi evidenziano come sia presente una lieve differenza maschio-femmina nell'incidenza di fibrillazione atriale nella popolazione generale, che si riflette consequenzialmente sulla

numerosità dei pazienti in ritmo sinusale. Tali differenze però non raggiungono, se prese complessivamente, la piena significatività statistica. Ulteriori analisi su campioni più ampi e su popolazioni maggiormente selezionate potrebbero aiutarci a convalidare questo dato sulla differente incidenza della fibrillazione atriale nella porzione maschile della nostra popolazione rispetto a quella femminile oppure a non confermarlo affatto.

A52: ELECTROCARDIOGRAPHIC SIGNS RELATED TO WORST PROGNOSIS IN BRUGADA SYNDROME

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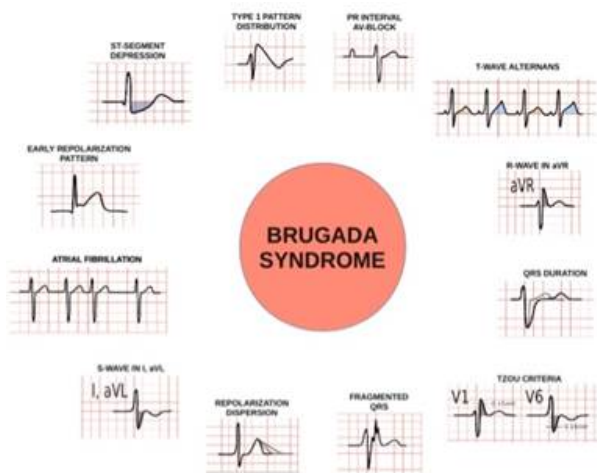
Background. The 12-lead electrocardiogram (ECG) has played an essential role for the diagnosis of Brugada Syndrome (BrS) since its first description. Different ECG signs other than spontaneous type 1 ECG pattern were linked to arrhythmic risk with conflicting results.

Purpose. To evaluate the prognostic value of different ECG signs in BrS patients.

Methods. We retrospectively analyzed 46 patients with BrS and spontaneous type 1 ECG pattern. Patients were categorized in three groups: asymptomatic, with previous syncope and with previous cardiac arrest (CA) / documented ventricular arrhythmias (VTA) / appropriate ICD interventions. Signs collected from each ECG were: presentation rhythm, heart rate, atrial depolarization duration and axis, PR interval (ms), QRS complex morphology, QRS duration in V2 and DII (ms), QRS fragmentation, Tzou criteria (V1R >0.15 mV, V6S >0.15 mV, V6S/R >0.2 mV), duration and voltage of S wave in lateral leads (≥40 ms and ≥0.1 mV), aVR sign (R' ≥0.3 mV), QT and QTc (Bazett) duration in DII and repolarization dispersion (T peak - T end in V2 and V6).

Results. In our BrS patients with spontaneous type 1 ECG pattern PR interval >200 ms (p=0,017), QRS duration >120 ms in DII (p=0,001) and >140 ms in V2 (p=0,02), presence of aVR sign (p=0,006), wide and or large S wave in DI-aVL (p= 0,02), fQRS (p= 0,012) and Tzou Criteria (p=0,039) were associated with CA and VTA.

Conclusions. In our population, prolonged PR interval, wide QRS in DII and V2, fragment QRS, wide and large S wave in lateral leads, wide R' wave in aVR and presence of Tzou Criteria were associated with worst clinical outcome.



A53: PERIPROCEDURAL ANTIBIOTIC PROPHYLAXIS FOR CARDIAC IMPLANTABLE ELECTRONIC DEVICES TAILORED ON PATIENT INFECTION RISK

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Background. Cardiovascular implantable electronic devices (CIEDs), such as pacemakers (PMs), implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy (CRT) devices, have an estimated incidence of infections between 1 to 7%. A pre-implant evaluation of the potential risk factors for device infection is important to the implementation of prophylactic strategies to prevent the infective event.

Purpose. Peri-operative antibiotic prophylaxis tailored on patient infection risk could reduce infective complications.

Methods. We analyzed prospectively 872 patients undergoing CIED implantation enrolled in the "PRACTICE" study. Patients undergoing leadless PM or subcutaneous ICD implantation were excluded. The Shariff score was used for patient infection risk quantification. One point was given for each item: diabetes, heart failure, chronic kidney disease

(eGFR <60 ml/min), oral anticoagulant therapy, corticosteroid use, previous CIED infection, generator replacement, device upgrade, presence of more than two leads, epicardial leads and temporary pacemaker. If the Shariff score was <3 only two intravenous (IV) administrations of antibiotic were given, one before the index procedure and one six hours thereafter. If the score was ≥3, antibiotics were given IV after the procedure (every 8 hours for two days) and then orally thereafter (for 7 days).

Results. Mean Shariff score was 1,5±1,3, 685 patients were in the low infective risk group (score<3) and 187 were in the high infective risk group (≥3). The protocol was not applicable for 68 patients. At 30 days no difference in CIED infection rate (7 vs 4 patients; p=0,17) and in all cause death (72 vs 51 patients; p=0,1) was noted between the two groups. We reported only one case of infective endocarditis, in a patient with low baseline infective risk.

Conclusions. Without new prophylactic antibiotic regimen the rate of CIED infections at 30 days was low (1.6%), and not statistically different between risk groups.

A54: COMBINATION OF A LEADLESS PACEMAKER AND SUBCUTANEOUS DEFIBRILLATOR IN A SEVERELY OBESE PATIENT

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Case report. We present the case of a 68-year-old male patient with severe obesity (BMI 58.8 kg/m²), diabetes, permanent slow atrial fibrillation, idiopathic dilated cardiomyopathy with severe biventricular dysfunction emerged in 2008 with sustained ventricular tachycardias. The patient had a transvenous bicameral cardioverter defibrillator (ventricular pacing 99%) with an additional atrial lead abandoned due to an insulation defect; the ICD generator was replaced in June 2018 for natural battery depletion. The patient came to our attention in June 2019 for swelling of the ICD pocket after an accidental trauma. He was asymptomatic and persistently afebrile, with normal blood tests, despite this he was given Amoxicillin thrice daily for two weeks. In October 2019 the patient came to the emergency department for pulmonary edema and suppurative at the level of the ICD pocket. At that time, blood cultures and pocket cultures were still negative thus empirical antibiotic therapy was started. Transesophageal echocardiogram was performed, highlighting the presence of vegetations attached to the ICD leads and small aortic endocarditic lesions (3 mm x 2 mm); left ventricular ejection fraction was 25%. A F-FDG PET/CT showed F-FDG activity in the region of the pocket generator, leads and at the left clavicular level. The patient underwent lead extraction and surgical removal of the generator. The culture of the leads was positive for multisensitive Staphylococcus capitis and therapy with oxacillin was started, as per antibiogram. During hospitalization the patient had slow atrial fibrillation phases with significant pauses and multiple episodes of hemodynamically stable sustained ventricular tachycardia. Given the need for ventricular pacing, titration of antiarrhythmic therapy and defibrillation, leadless pacemaker implantation (Micra - Medtronic) was performed at first. The procedure was complicated by multiple device thrombosis during anchoring, despite effective periprocedural anticoagulation. After 7 days, subcutaneous defibrillator implantation (Emblem S-ICD, Boston) was performed in conscious sedation thanks to anesthesiological blockage of the serratus muscle. The patient was discharged after few days, still receiving antibiotic therapy with optimal pacemaker and subcutaneous defibrillator parameters.

A55: EFFICACY OF ACTIVATION MAP DURING VENTRICULAR TACHYCARDIA ABLATION

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Background. Catheter ablation (CA) of ventricular tachycardias (VT) represents a challenge, due to the complexity of the underlying substrate and to the difficulty in characterizing the arrhythmia mechanisms and circuitry.

Methods. We conducted a prospective cohort study, aimed at investigating whether VT interruption during radiofrequency (RF) delivery can be regarded as a marker indicating a lower risk VT recurrence during follow-up. From November 2018 to September 2020, 43 patients with VTs underwent CA using RF energy. Six patients were not included in the study due to the shortness of follow-up (<2 months). In patients in whom activation mapping could be performed, we first attempted VT interruption, followed by substrate modification (fragmented/late potential elimination and/or dechanneling of the entire pathologic zone). In 14 patients, activation mapping was not feasible due to the poor hemodynamic VT

tolerance and/or to the absence of VT inducibility with programmed ventricular stimulation. In these cases, substrate CA was performed, aimed at eliminating fragmented and/or late potentials, which could act as presumed arrhythmia mediators. Recurrences were assessed via ICD in office interrogations and remote monitoring for a median of 6 (IQR 3-9) months of follow-up.

Results. Thirty-seven patients were included in the study. The median age at baseline was 62±14 years. Fifteen patients underwent endoepicardial CA due to the presumed epicardial VT origin and/or to the non-ischemic etiology of the underlying cardiomyopathy. In 22 patients, the indication for the procedure was electrical storm refractory to pharmacological therapies. Among the 17 patients in which it was possible to interrupt the arrhythmia through RF delivery, we observed only 1 sustained VT recurrence at follow-up. Among the 20 patients in which VT was not interrupted with RF delivery or the VT had poor hemodynamic tolerance, there were 5 sustained VT recurrences at follow-up. Risk of recurrence at follow-up was numerically lower in patients in which VT was interrupted with RF delivery during the procedure (OR 0.187, CI 0.02-1.8; p=0.13).

Conclusions. In patients undergoing CA for VTs, activation mapping is a useful tool to enhance the understanding of the arrhythmia circuitry. Our preliminary results seem to suggest that VT interruption during RF delivery may represent a positive prognostic factor, pointing to better outcomes and lower recurrence rates, even if the results were not statistically significant. Further investigations with a larger cohort of patients is required to confirm these findings.

ASSISTENZA CARDIACA IN ACUTO

A56: DELAYED ONSET OF VENTRICULAR FIBRILLATION AFTER ELECTRICAL INJURY IN A YOUNG PATIENT WITH ASYMPTOMATIC MITRAL VALVE PROLAPSE

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Background. The most frequent cardiovascular effects induced by electrical injury (EI) are arrhythmias, which occur mostly early after the electrical shock. A few cases of delayed malignant arrhythmias have been described, raising doubts about the helpfulness of heart monitoring after an EI.

Case report. A 46-year-old man experienced an out-of-hospital cardiac arrest four hours after receiving an electrical shock with an alternating voltage of 380 volts from high-pressure water jet cleaner. The out-of-hospital ECG displayed ventricular fibrillation, eight DC shocks were delivered, and return of spontaneous circulation was obtained after 15 minutes. ECG on admission showed bradycardia, HR 55 bpm, no clear P waves and prominent T waves in the precordial leads (Figure A). No coronary lesions were detected at the urgent PCI. An ABG on admission revealed lactic acidosis (LAC 18 mmol/L), mild hyperkalemia (5,19 mmol/L) and mild renal dysfunction (serum creatinine 1,71 mg/dL). Toxicology screen was negative. During the hospital stay, the patient developed a voluminous hematoma and swelling on the right arm, site of the EI. In the following days, blood tests revealed an increase in serum creatinine (peak 4,99 mg/dL), creatine kinase (peak 46186 U/L), liver enzymes (AST peak 2859 U/L and ALT peak 1365 U/L), LDH (peak 2718 U/L) and troponin T (peak 2757 ng/L); these alterations were probably linked to rhabdomyolysis provoked by EI and acute kidney injury was secondary to myoglobinuria. The patient received fluid therapy and furosemide bolus injections. On echocardiography a myxomatous mitral valve with prolapse of both leaflets, mitral annular disjunction and severe mitral regurgitation were displayed (Figure B). Left ventricle was severely dilated with ejection fraction 69%. After improvement in renal function, a cardiac MRI was performed, which ruled out myocardial edema and displayed subendocardial LGE at the base of the posteromedial papillary muscle (Figure C). The Heart Team opted for mitral valve surgery with P2 resection and mitral valve annuloplasty with 36 mm Carpentier-Edwards Physio II Ring. An ICD was not implanted because the electrical shock and the alteration in electrolytes were considered the primary reasons for cardiac arrest. The patient underwent a cycle of rehabilitation after the intervention and now he does not report any relevant symptom.

Conclusion. Our patient had bileaflet mitral valve prolapse, mitral annular disjunction and myocardial fibrosis of the papillary muscles, all of which are associated with higher risk of sudden cardiac death. This case highlights that patients with an underlying heart condition predisposing to arrhythmias should promptly seek medical care even after a mild EI for appropriate management.



A57: UNO STRANO CASO DI SHOCK: ESORDIO ACUTO DI UNA FISTOLA ARTERO-VENOSA

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Le fistole artero-venose (FAV) occorrono in <1% degli aneurismi dell'aorta addominale. Sono di origine primitiva nella maggioranza dei casi, tuttavia circa il 20% è attribuibile a causa traumatica o iatrogena, spesso come complicanza di procedure endovascolari. In circa un terzo dei casi possono esordire clinicamente come scompenso cardiaco ad alta gittata; risulta invece quasi aneddottico l'esordio acuto con shock distributivo e/o con arresto cardiocircolatorio.

Il paziente di questo caso era un maschio di 73 anni, senza precedenti cardiologici, che aveva allertato i soccorsi per dolore epigastrico irradiato alla spalla e all'emitorace destri. In pronto soccorso, alla luce di un quadro clinico-strumentale suggestivo per ischemia miocardica acuta con scadimento moderato della funzione contrattile del ventricolo sinistro, si decise di ricoverare in Cardiologia come sospetto NSTEMI. Nelle successive ore di ricovero, tuttavia, si assisteva ad un rapido scadimento delle condizioni del paziente, fino all'instaurarsi di uno stato di shock non responsivo a riempimento volemico né a supporto inotropo e vasopressorio con dobutamina e noradrenalina. La mancanza di modificazioni ecg ed ecocardiografiche faceva propendere per un'origine distributiva dello shock, tuttavia di non chiara origine.

Per un caso fortuito, durante l'esecuzione di escopia dell'addome inferiore per anuria, si riscontrava la presenza di una voluminosa formazione aneurismatica a livello aorto-iliaco destro. All'angioTC eseguita in urgenza si documentava una fistola artero-venosa iliaca destra. Tale reperto giustificava vari reperti clinici a cui fino a quel momento non si era dato rilievo: il dolore epigastrico, il soffio addominale e la tachicardia sinusale.

D'accordo con i colleghi chirurghi vascolari, si procedeva a studio coronarografico con riscontro di malattia critica trivale. Come da decisione dell'Heart Team, si decideva di procedere in primis ad impianto di endoprotesi (EVAR) per escludere la fistola e stabilizzare il paziente in vista di una futura rivascularizzazione miocardica chirurgica. In seconda giornata dopo intervento di esclusione della fistola, a seguito di peggioramento del quadro di ischemia miocardica, si procedeva in urgenza a triplice bypass aorto-coronario. Il successivo post-operatorio era complicato da leak periprotetico di tipo IIb ed arresto cardiaco in assistenza secondaria ad insufficienza respiratoria. Il paziente decedeva dopo alcuni mesi in seguito a scadimento delle condizioni generali.

Questo caso dimostra la difficoltà di giungere ad una diagnosi e ad un trattamento tempestivi delle FAV condizionanti instabilità emodinamica. Proprio perché estremamente rara e legata ad un contesto di urgenza, infatti, questa modalità di presentazione è da considerarsi particolarmente subdola, con il rischio di ritardi diagnostici che possono compromettere la già delicata prognosi di questi pazienti.



A58: ECMELLA, QUANDO IL POTERE DELL'ECMO SI UNISCE ALL'UNLOADING VENTRICOLARE

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Uomo di 67 anni, giunge alla nostra osservazione per STEMI anterolaterale. All'arrivo dei soccorsi al domicilio si evidenziava quadro di shock cardiogeno con paziente marcatamente ipoteso (PAS 60 mmHg) e ipoperfuso (diaforetico e con tendenza ad assopirsi). All'ingresso in UCIC: PAO 65/35 mmHg, Fc 110 bpm, Sat O₂ 83% in O₂ terapia con maschera facciale 12 L/min. Si procedeva a riempimento volemico e ad infusione di dobutamina. Una valutazione ecocardiografica bedside evidenziava assenza di complicanze meccaniche, assenza di versamento, FE pari a 35-40%. Trasportato in sala di Emodinamica, dopo posizionamento di Impella CP, si eseguiva studio coronarografico con riscontro di:

- occlusione totale del tronco comune in assenza di circoli collaterali;
- coronaria destra dominante con diffusa aterosclerosi calcifica, multiple stenosi moderate al I e II tratto, flusso TIMI 3.

Eseguita ricanalizzazione del vaso con PTCA e stenting medicato su TC-DA. Ripristino di flusso TIMI 2-3 su DA e CX. In ragione dell'evidenza di quadro di acidosi mista ed ipotensione si incrementava supporto inotropo con noradrenalina ed adrenalina. Per il persistere del quadro di shock refrattario si procedeva a intubazione OT e posizionamento di ECMO VA. L'emodinamica veniva quindi supportata con dobutamina 7 μ g/kg/min, Adrenalina 0.1 μ g/kg/min, Noradrenalina 0.2 μ g/kg/min, Impella CP 3 L/min, ECMO 4 L/min. Un ecocardiogramma in seconda giornata mostrava ventricolo sinistro lievemente dilatato e severa riduzione della funzione di pompa (FE 10%). In quarta giornata il paziente, in supporto con dobutamina 7 μ g/kg/min, Adrenalina 0.05 μ g/kg/min, Noradrenalina 0.1 μ g/kg/min, ed ECMO 3 L/min, veniva progressivamente svezzato dal supporto con Impella fino alla rimozione dello stesso, in assenza di complicanze e con mantenimento di buoni parametri emodinamici ed emogasanalitici. Il giorno seguente la valutazione ecografica mostrava un ventricolo sinistro di normali dimensioni, con funzione di pompa severamente ridotta (FE 24%). Sei giorni dopo la rimozione dell'Impella si procedeva a rimozione dell'ECMO e mantenimento del supporto emodinamico con dobutamina 7 μ g/kg/min, adrenalina 0.05 μ g/kg/min, noradrenalina 0.02 μ g/kg/min.

Conclusioni. Il caso mostra l'efficacia dell'associazione di Impella ed ECMO nel trattamento dello shock cardiogeno. L'unloading ventricolare con Impella, associato alla capacità di supporto emodinamico con ECMO (pur in presenza di aumento del postcarico), contribuisce a determinare un miglioramento della performance cardiaca e della perfusione sistemica.

A59: LO SHOCK CARDIOGENO NEI REPARTI DI CARDIOLOGIA DELLA LIGURIA: RISULTATI DI UN REGISTRO MULTICENTRICO

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Background. Lo shock cardiogeno (SC) rappresenta una patologia ad elevata mortalità, la cui gestione risulta ancora complessa e controversa nonostante lo sviluppo di nuove opzioni terapeutiche.

Obiettivo del nostro studio è stato esaminare le caratteristiche dei pazienti con SC nei reparti di Cardiologia della Liguria nell'anno 2018, analizzando la sua gestione e la mortalità associata.

Metodi. Il nostro registro multicentrico ha incluso tutti i pazienti ospedalizzati nei reparti di Cardiologia della Liguria con diagnosi di SC all'ingresso o durante il ricovero dal 1 Gennaio al 31 Dicembre 2018. Sono stati valutati l'eziologia dello SC, i dati clinici, laboratoristici e strumentali dei pazienti, la gestione terapeutica (farmaci e dispositivi di assistenza al circolo) e la mortalità intraricovero ed a 6 mesi.

Risultati. Negli 8 principali ospedali della Liguria sono stati inclusi 90 pazienti con SC, 55 (61.1%) erano uomini, l'età media era 73.4 \pm 14.2 anni; la principale causa di SC è stata la sindrome coronarica acuta (65, 72.2%) seguita dalla riattivazione di scompenso cardiaco (15, 16.7%). La coronaria più frequentemente coinvolta è stata la discendente anteriore (45/65, 69.2%), il tronco comune è stato interessato in 15/65 (23.1%) pazienti, mentre 30/65 (46.2%) presentavano coronaropatia trivasale. All'ingresso la frazione di eiezione del ventricolo sinistro era 31.4 \pm 12.3%. Abbiamo registrato 37/90 (41.1%) morti intraospedaliere e 5/53 (9.4%) morti a 6 mesi, con nessuna differenza legata all'eziologia dello SC in entrambi i casi. Gli inotropi/vasopressori maggiormente utilizzati sia da soli (52/90, 57.8%) che in combinazione (33/90, 36.75%) sono stati: dopamina (33, 36.7%), dobutamina (27, 30.0%), noradrenalina (28, 31.1%), adrenalina (17, 18.9%), levosimendan (7, 7.8%). I dispositivi meccanici di assistenza al circolo sono stati utilizzati in 44/90 (48.9%) pazienti con predominanza del contropulsatore aortico (41/90, 45.6%). Alla regressione di Cox multivariata aggiustata per l'età, il sesso e gli altri predittori univariati significativi (arresto cardiaco all'esordio, uso di adrenalina, creatininemia all'ingresso), la malattia renale cronica (HR: 3.88, 95% CI: 1.02-14.77, p=0.046) ed i livelli di lattati nel sangue all'ingresso >2 mmol/L (HR: 1.21, 95% CI: 1.08-1.35, p<0.001) sono risultati indipendentemente associati ad un'augmentata mortalità intraospedaliere. Al contrario, l'uso del contropulsatore aortico (HR: 0.33, 95% CI: 0.12-0.93, p=0.033) era associato ad una riduzione della mortalità intraospedaliere. Il modello di Cox multivariato per la mortalità a 6 mesi, aggiustato per l'età, il sesso e gli altri predittori univariati significativi (creatininemia all'ingresso, arresto cardiaco all'esordio e livelli di lattati nel sangue all'ingresso >2 mmol/L) ha mostrato esclusivamente la malattia renale cronica (HR: 2.15, 95% CI: 1.09-10.12, p=0.036) come predittore indipendente di mortalità a 6 mesi.

Conclusioni. Da questo registro emerge come la mortalità intraricovero e quella a breve termine per SC sono ancora molto elevate nei reparti di

Cardiologia della Liguria, nonostante il progressivo incremento dell'intensità di cura. Se da un lato risulta abbastanza frequente il ricorso a farmaci inotropi/vasopressori, l'utilizzo di dispositivi di supporto meccanico al circolo, diversi dal contropulsatore aortico, è ancora molto ridotto.

A60: DISULFIRAM-ETHANOL REACTION MIMICKING CARDIOGENIC, ANAPHYLACTIC AND SEPTIC SHOCK

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Un signore di 53 anni si presentava autonomamente presso il pronto soccorso (PS) in stato di shock con quadro confusionale, riferendo insorgenza di dolore toracico a seguito di assunzione di 500 cc di alcol etilico. In anamnesi presentava una pregressa (2016 presso altra sede) angioplastica (PTCA) e stenting (DES) di arteria circonflessa (CX), con coronaria destra (CDx) cronicamente occlusa e stenosi borderline su arteria discendente anteriore (DA); presentava inoltre un disturbo affettivo di personalità con dipendenza da alcol in terapia di disassuefazione con disulfiram. In UTIC si presentava in shock con quadro di confusione, arrossamento eritematoso diffuso su tutto il tronco e con reiterati episodi di vomito. All'ECG si aveva marcato sopraslivellamento del tratto ST in aVR con sottoslivellamento in più di otto derivazioni. Agli ematochimici la troponina al primo punto e a tre ore risultava negativa, mentre si aveva un quadro di insufficienza renale acuta e negatività degli indici di flogosi. All'EGA acidosi metabolica (pH 7,27) da consumo di bicarbonati (HCO₃-18.8 mmol/l) a gap anionico aumentato (AG 16) con incremento dei lattati (lac 3.8 mmol/l) compatibile con uno stato di bassa portata. Veniva eseguito ecocardiogramma che descriveva ventricolo sinistro ipertrofico senza anomalie della cinetica segmentaria e con funzione sistolica conservata, vena cava di piccole dimensioni, non flap a livello della radice aortica, assenza di versamento pericardico e sezioni destre nei limiti. Veniva dunque impostato un "fluid challenge" e terapia vasopressiva con noradrenalina 0,03 μ g/kg/min e correzione di bicarbonati con rapido ripristino di ottimi valori di pH arterioso. Dopo tre ore si aveva risoluzione completa delle alterazioni elettrocardiografiche, in assenza di segni ischemici, con paziente asintomatico, in compenso emodinamico con possibilità di sospendere prontamente terapia vasopressiva. Il giorno successivo veniva eseguita coronarografia che documentava una restenosi intrastent su CX trattata con PTCA e DES, CDx occlusa con parziale ricircolo da CX e stabile la stenosi borderline di DA, che presentava FFR positiva (0,80) per cui veniva eseguita PTCA + DES. Il quadro coronarico e clinico deponevano per un infarto miocardico tipo 2 con discrepanza legata allo stato di importante vasodilatazione causata dall'accumulo di acetaldeide. Il disulfiram è un farmaco utilizzato nel contesto della dipendenza alcolica, poiché inibendo l'aldeide deidrogenasi, all'assunzione combinata di alcol etilico provoca accumulo di acetaldeide, causando sintomi sgradevoli, quali cefalea, nausea, malessere e vomito. L'acetaldeide è un potente agente vasodilatatore, presenta tossicità mitocondriale causando rialzo dei lattati e ha effetto cardiotossico; il disulfiram invece ha un'inibizione diretta della dopamina β -idrossilasi, riducendo la produzione di noradrenalina e conseguentemente il tono vasomotorio. Nel presente caso l'assenza di anomalie di cinetica segmentaria, la normale funzione sistolica ventricolare sinistra all'ecocardiogramma e la negatività degli enzimi di miocardiocitolisi, stante la presentazione elettrocardiografica "STEMI-like" e il sintomo anginoso, portavano ad escludere una genesi cardiogeno dello shock, quanto uno stato di discrepanza, consentendo di diffirere lo studio coronarografico. Una coronarografia in emergenza avrebbe posto di fronte al rischio di un'angioplastica senza chiaro target, e pertanto non risolutiva lo stato di shock, con verosimile necessità di supporto meccanico di circolo, e di ricorrere a duplice terapia antiaggregante ed eparinica in un paziente ad elevato rischio di sanguinamenti gastrointestinali, data la storia di potus.

A61: EJECTION FRACTION TO GUIDE VA-ECMO WEANING PROCEDURE, TO TRUST OR NOT TO TRUST?

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Introduction. The decision whether a patient can tolerate veno-arterial extracorporeal membrane oxygenation (VA ECMO) removal (waning procedure) depends on several parameters: cardiac output, ejection fraction (EF), mean arterial pressure and oxygen saturation. Despite these factors, a high proportion of patients experiences a new episode of cardiogenic shock in a short period of time after ECMO removal. This means that all these parameters are insufficient to assess the tolerability of VA ECMO removal in some patients.

Purpose. To evaluate whether EF is a reliable parameter during a VA ECMO procedure.

Methods. Stroke volume (SV) assessed by the difference between end diastolic (EDV) and end systolic volume (ESV) (SV_{EF}) and the SV calculated on the basis of the multiplication of aortic valve area by pulse wave Doppler velocity time integral (SV_{VTI}) have been recorded in 16 VA ECMO weaned patients at different flow of VA ECMO support during a

transesophageal echocardiogram (TOE)-guided VA ECMO weaning procedure. The results have been divided into 2 groups according to the method of SV calculation (Table).

Results. The distribution of the results was not normal, so the groups have been compared by Wilcoxon rank signed test. No patients had significant valve abnormalities. SV_{EF} median value was significantly lower than SV_{VTI} value (33.9mL v.s 48.5 mL).

	SV_{EF} group	SV_{VTI} group	p-Value
Median (IQR)	33.9 mL (21,3 -52,2)	48.5 mL (37,5-60,3)	<0.0001

SV_{EF} is the numerator of EF equation, so the reliability of EF parameter depends on correct volume quantification and SV_{EF} calculation. Normally SV_{EF} and SV_{VTI} should be equal (at least similar) in every condition but relevant valve abnormalities/shunts. In case of mitral valve regurgitation SV_{EF} should be higher than SV_{VTI} . No relevant shunts or valve abnormalities have been found in our group of patients. The divergence between SV_{EF} and SV_{VTI} is consequence of an inaccurate quantification of left ventricle volumes. This is due to both the foreshortening of the image by TOE and the instability of VA ECMO weaning procedure, when VA ECMO flows change and the volume quantification must be fast.

Conclusions. EF can be a misleading parameter to be used to guide VA ECMO procedure. Further parameters must be found, to help in identifying patients who can tolerate VA ECMO weaning procedure.

A62: IL RUOLO DELLA TROMBOLISI NELL'EMBOLIA POLMONARE, UN DEDALO DI DUBBI E CERTEZZE

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L'embolia polmonare (EP) rappresenta una emergenza cardiovascolare che può indurre grave scompenso acuto del ventricolo destro (VD), anche se potenzialmente reversibile. Sebbene la terapia anticoagulante sia lo standard nel trattamento, la trombolisi, con la sua abilità nel produrre una rapida lisi del coagulo, è stata a lungo considerata una attraente alternativa anche nei pazienti emodinamicamente stabili con disfunzione ventricolare destra.

Noi presentiamo un caso di embolia polmonare di una donna di 79 anni, emodinamicamente stabile, con severa dispnea ed evidente disfunzione del ventricolo destro, trattato con terapia trombolitica.

Un ventricolo destro dilatato e un rigurgito tricuspidalico (TR) moderato-severo, dovuti all'embolia polmonare massiva, sono stati identificati con l'ecocardiogramma transtoracico 2D (ETT).

Dopo 72 ore dalla terapia trombolitica, l'ETT ha mostrato un notevole miglioramento delle dimensioni del ventricolo destro e dell'insufficienza tricuspidalica, con una quasi completa risoluzione del quadro di embolia polmonare.



A63: UN CASO DI SINDROME TAKOTSUBO: FEOCROMOCITOMA, IPERTIROIDISMO O ENTRAMBI?

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Introduzione. La sindrome takotsubo (STT) è caratterizzata da transitoria disfunzione del ventricolo sinistro e da sintomi e segni tipici di ischemica miocardica acuta. I fattori predisponenti includono stress e malattie endocrine come il feocromocitoma e alcune tireopatie.

Descrizione del caso. Un uomo di 69 anni con recente diagnosi di ipertensione arteriosa e ipertiroidismo in terapia da qualche giorno con olmesartan, bisoprololo e metimazolo veniva ricoverato per dolore precordiale persistente, crisi ipertensiva, tachicardia, dispnea e diaforesi. Veniva posta diagnosi di NSTEMI ad alto rischio in base al quadro elettrocardiografico (T invertita in V4-V6) e al significativo rialzo della hstropoina I. La coronarografia risultava tuttavia negativa per lesioni coronariche ostruttive. L'angio-TC, eseguita per escludere dissezione aortica data la persistenza dei sintomi, rilevava una massa surrenalica sinistra compatibile con feocromocitoma e una tiroide aumentata di volume con aspetto disomogeneo. L'ecocardiogramma mostrava acinesia apicale con funzione ventricolare sinistra severamente ridotta; pertanto veniva posta diagnosi di STT. Il paziente veniva stabilizzato con nitrati, urapidil, esmololo iv e metimazolo ad alte dosi. Successivamente il paziente venne sottoposto a surrenectomia. Nei giorni seguenti l'intervento si è assistito a regressione completa di tutti i sintomi, normalizzazione della funzione ventricolare sinistra, della pressione

arteriosa e della frequenza cardiaca. Il dosaggio delle metanefrine urinarie ed l'esame istologico hanno confermato la diagnosi di feocromocitoma. È stata esclusa contestualmente una Neoplasia Endocrina Multipla di tipo 2 (condizione che associa carcinoma midollare della tiroide, feocromocitoma e iperplasia/neoplasia delle paratiroidi) e posta diagnosi di morbo di Basedow.

Discussione. L'increzione delle catecolamine plasmatiche può determinare uno squilibrio immunologico con predominanza della risposta Th2-mediata risultante in un'aumentata risposta umorale. Le catecolamine prodotte dal feocromocitoma infatti agendo sul recettore β_2 presente sulle cellule presentanti l'antigene e sui linfociti Th1 determinano l'inibizione della risposta immune cellulare ed attivazione di quella umorale mediata dai linfociti Th2. Nel nostro paziente la tiroide è stata l'organo bersaglio di tale squilibrio immunologico. Gli esami ematici e l'ecografia tiroidea documentavano infatti un quadro conclamato di tireotossicosi e un'intensa vascolarizzazione ghiandolare interessante l'intero parenchima ("inferno vascolare") che hanno consentito di fare diagnosi di morbo di Basedow, patologia della tiroide notoriamente associata ad un pattern immunologico prevalentemente di tipo Th2.

Conclusioni. Un'alterazione della funzione tiroidea che può manifestarsi come crisi tireotossica e che si sviluppa su base immunologica può associarsi alla presenza di un feocromocitoma. Pertanto la disfunzione ventricolare sinistra in questo caso potrebbe essere stata innescata da entrambi i disordini endocrini che determinando di fatto un'iperattivazione simpatica massiva hanno peggiorato sinergicamente l'assetto emodinamico complessivo del paziente. Al trattamento della problematica cardiaca deve quindi necessariamente associarsi quello del disturbo endocrino legato al feocromocitoma e alla tiroide.

A64: RISULTATI DEL SUPPORTO MECCANICO AL CIRCOLO MEDIANTE ECMO VENO-ARTERIOSO NELLO SHOCK CARDIOGENO REFRAATTARIO

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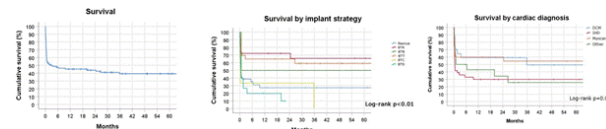
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Introduzione. Presentiamo la nostra esperienza con l'utilizzo dell'ECMO veno-arterioso (VA) in casi di shock cardiogeno refrattario.

Metodi. Dal 2008 al 2020, sono stati eseguiti 176 impianti di ECMO-VA presso il nostro Centro. Abbiamo escluso: 45 post-cardiotomy, 18 primary-graft-dysfunction dopo trapianto cardiaco, 10 durante trapianto di fegato, 5 disfunzioni di LVAD, 4 insufficienze respiratorie, 1 shock emorragico iatrogeno, 1 donatore d'organo. La popolazione in studio constava, pertanto, di 92 casi. Gli outcomes principali erano mortalità ospedaliera e svezzamento dal supporto. Gli eventi avversi sono stati classificati secondo il registro IMACS.

Risultati. L'età media era di 43 ± 17 anni. La diagnosi era cardiopatia ischemica in 36 (39%) casi, cardiomiopatia dilatativa primitiva in 20 (21%), miocardite acuta in 20 (21%) e 18 (19%) "altro". La strategia d'impianto era: rescue 31 (34%), bridge-to-recovery 18 (20%), bridge-to-bridge 2 (2%), bridge-to-transplant 23 (25%), bridge-to-candidacy 3 (3%) e bridge-to-decision 15 (16%). In totale, abbiamo registrato 48 (52%) decessi ospedalieri. La sopravvivenza stimata a 1 e 5 anni è risultata 45% (IQR 35-55%) e 39% (IQR 29-49%), rispettivamente. Le curve di K-M stratificate per strategia d'impianto erano divergenti (log-rank $p=0,01$). L'analisi multi-variabile della mortalità ospedaliera ha identificato insufficienza renale acuta come fattore di rischio indipendente (OR 10,3; CI 2,6-40,1). Insufficienza renale acuta (OR 10,5; CI 1,59-69,61), picco di bilirubina (OR 1,62; CI 1,07-2,45) e tempo di contropulsazione aortica (OR 0,87; CI 0,77-0,97) sono risultati indipendentemente predittivi di fallito svezzamento dal supporto.

Conclusioni. Lo shock cardiogeno refrattario con necessità di supporto ECMO-VA è associato ad una significativa mortalità ospedaliera.



A65: SUPPORTO MECCANICO AL CIRCOLO MEDIANTE ECMO VENO-ARTERIOSO NELLA MIOCARDITE ACUTA IN ETÀ PEDIATRICA: ESPERIENZA IN SINGOLO CENTRO

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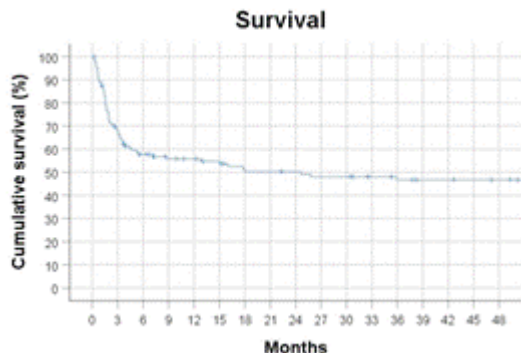
Introduzione. Abbiamo valutato l'outcome dell'utilizzo dell'ECMO veno-arterioso (VA) in casi di shock cardiogeno per miocardite acuta in età pediatrica, presso la nostra Istituzione.

Metodi. Dal 2008 al 2020, 27 pazienti pediatrici (<18 anni) sono stati

impiantati con ECMO-VA. Di questi, abbiamo incluso nello studio tutti i casi con diagnosi di miocardite acuta. Tutti i dati della cartella clinica sono stati revisionati, il follow-up è stato ottenuto dall'ultima visita ambulatoriale ed è stato completo ed aggiornato in tutti i casi.

Risultati. Abbiamo incluso nove pazienti. L'età media era di 15,3 anni (IQR 0,2-17,6 anni). Quattro pazienti (44%) erano stati sottoposti a rianimazione cardio-polmonare pre-impianto. In 5 (56%) casi la cannulazione è stata centrale, in 4 (44%) periferica: 3 femoro-femorale, 1 arteria carotide e vena femorale. La diagnosi istologica è risultata miocardite virale in 8 ed a cellule giganti in 1. Complicanza post-operatoria più comune è stata insufficienza renale acuta (56%). La durata mediana della degenza ospedaliera è stata 26 giorni (IQR 8-33 giorni). Il tempo di supporto mediano è risultato 5 giorni (IQR 2-9 giorni). In 5 (56%) casi si è ottenuto lo svezzamento dal supporto, un paziente è stato trapiantato. La mortalità ospedaliera è stata 33%, la causa di morte è stata insufficienza multi-organo in 2 e danno cerebrale anossico in 1. La sopravvivenza stimata a 1 anno è risultata del 50% (95% CI: 41-59%).

Conclusioni. Nella nostra serie, la miocardite acuta in età pediatrica con necessità di supporto ECMO-VA si è associata ad una significativa mortalità ospedaliera.



A66: SAFETY OF LEVOSIMENDAN THERAPY IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE AND SEVERE OR END-STAGE RENAL DISEASE: TWO CASE REPORTS

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Background. In patients with acute decompensated heart failure (ADHF) levosimendan has a favourable, rapid and sustained effect on haemodynamics, neurohormone levels and symptoms. Despite not yet conclusive data on efficacy when used on top of usual catecholamines, there have not been reports of worsened survival in contrast to conventional inotropes. Although this remarkable safety profile, an important limit to levosimendan use in clinical practice is the concomitant presence of severe renal impairment (eGFR <30 ml/min). Limited data on this clinical setting are available but concerns regarding a more pronounced and prolonged haemodynamic effect in these patients exist.

Patients and methods. We sought to evaluate the safety of levosimendan, administered as "extrema ratio", in two male patients, admitted for ADHF with concomitant severe renal impairment, who did not benefit from initial standard medical treatment. Levosimendan was administered at a rate of 0.05 mg/Kg/min without a loading dose, on top of standard drugs. Both patients were diagnosed with idiopathic dilated cardiomyopathy and implanted with CRT-D. They had a history of permanent atrial fibrillation and were on optimal medical therapy at home. Patient No.1 was 71 years-old and exhibited severe renal impairment (eGFR 20 ml/min). Patient No.2 was 41 and presented with end-stage renal disease (ESRD) requiring renal replacement therapy. They both signed an informed-consent before levosimendan therapy.

Results. Levosimendan was well tolerated. No clinically significant changes in mean arterial blood pressure were observed compared to pre-treatment measurements. Previous rate control of atrial fibrillation was maintained. Patient No.1 experienced only short episodes of non-sustained ventricular tachycardia. No significant hypokalaemia was detected. Moreover, subtle improvement in renal function was registered in both patients and a significant left ventricular ejection fraction increase was observed in patient No. 2. Late adverse reactions were not reported after 1-month follow-up.

Discussion and Conclusions. Levosimendan has a remarkable safety profile but its use in patients with severe renal impairment is contraindicated. Concerns emerged only from pharmacokinetic findings of prolonged and higher exposure to its metabolites. Conversely, there is mounting evidence supporting a renal-protective effect of levosimendan, making this drug the inotrope of choice in the case of worsening cardio-

renal syndrome. Kidney dysfunction is encountered in a substantial proportion of patients with heart failure and has been identified as one of the most adverse prognostic indicators. Therefore, further evidence of levosimendan safety in these patients may significantly improve clinical practice. Our group designed a prospective study to investigate Levosimendan safety in patients with severe or ESRD admitted for ADHF. Here we reported some preliminary data from our series. First two included patients didn't experience significant hypotension, sustained arrhythmia or hypokalaemia during the hospitalization and at 1-month follow-up.

ASSISTENZA INFERMIERISTICA E TECNICA IN CARDIOLOGIA

A67: RIMOZIONE DI DEVICE CARDIACO IMPIANTABILE: LE COMPETENZE AVANZATE INFERMIERISTICHE

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Introduzione. In Italia, secondo il registro AIAC, già nel 2017 venivano eseguiti 24.457 impianti di pacemaker e questo numero è in crescita a causa di un aumento delle indicazioni all'impianto, di una durata maggiore della vita media delle persone portatrici di PM e di una complessità clinica più elevata di queste persone, la quale porta alla necessità di frequenti up-grade di sistemi già impiantati.

Nonostante lo sviluppo di device sempre più biocompatibili è possibile che questi sviluppino complicanze, con una frequenza compresa tra 1% e il 6%. Quelle a breve termine sono soprattutto correlate alla procedura di impianto, come emotorace, pneumotorace, formazione di ematoma della tasca, pericardite o tamponamento cardiaco. Nel medio termine tra le complicanze sono da sottolineare l'infezione, la formazione di cicatrice ipertrofica, disfunzione della valvola tricuspide, embolia, dolorabilità alla tasca. Per il lungo termine invece è da ricordare la possibile rottura dei cateteri a causa di stress meccanici. Nella nostra revisione ci siamo maggiormente concentrati sull'infezione del device e dei cateteri in quanto è l'indicazione principale alla rimozione di dispositivo ed elettrocatereteri. Nei pazienti dipendenti da PM, quando esso viene rimosso e non è possibile un immediato reimpianto a causa di sepsi o di altre problematiche, viene posizionato un PM temporaneo che implica assistenza infermieristica avanzata.

Materiali e metodi. È stata effettuata una revisione della letteratura di studi primari e secondari per rispondere al quesito di ricerca formulato con metodo PIOM: Persone adulte ricoverate per rimozione CIED, Presenza di device cardiaco temporaneo, Assistenza infermieristica, Revisione della letteratura.

Sono state consultate principalmente le banche dati PubMed e CINHAL, con l'aggiunta di alcune informazioni reperite sul sito dell'Associazione Italiana di Aritmologia e cardiostimolazione, dell'European Society of Cardiology e di Centers for Disease Control and Prevention. Le key words maggiormente utilizzate sono state: Clinical trial, cardiac implantable electrical devices, cardiac implantable electrical AND infection, pacemaker AND type of infection, temporary pacemaker AND CIED extraction, temporary pacemaker AND nursing care.

Risultati e Conclusioni. Per quanto le moderne tecnologie abbiano permesso la creazione di dispositivi sempre più biocompatibili ed avanzati, essi non sono scevri da complicanze. In un paziente PM dipendente che viene sottoposto ad estrazione, in attesa di un nuovo reimpianto, può essere posizionato un PM temporaneo con generatore esterno. In tale situazione l'infermiere è responsabile del monitoraggio, della prevenzione e della gestione delle possibili complicanze di questi device. L'infermiere dovrà essere in grado di riconoscere tempestivamente il fallimento di pacing, sensing e cattura. In merito a ciò è stato creato un algoritmo utilizzabile per il riconoscimento e l'individuazione del miglior intervento da attuare.

A68: IL PAZIENTE SOTTOPOSTO A CONTROPULSAZIONE AORTICA: ANALISI DELL'ASSISTENZA INFERMIERISTICA

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Lo studio intrapreso per stendere la mia tesi di laurea si basa sulla revisione della letteratura. Per la ricerca di documenti ed articoli inerenti al mio studio mi sono concentrata su specifiche "keyword" come, in particolare, anatomia del cuore, contropulsatore aortico, paziente cardiopatico, indicazioni/controindicazioni IABP, tecnica seldinger e gestione infermieristica/ruolo dell'infermiere.

La contropulsazione aortica è una tecnica di assistenza meccanica cardiocircolatoria temporanea che si è sviluppata a partire dagli anni '60 (del 1900). Questa tecnica consiste nel posizionamento di un palloncino che si gonfia (diastole) e sgonfia (sistole) in aorta toracica discendente ed ha come obiettivo l'incremento della perfusione coronarica durante la diastole e la riduzione del post-carico del ventricolo sinistro. Questo dispositivo è ampiamente utilizzato, soprattutto nell'ultimo decennio, per

la sua economicità, facilità di utilizzo e basso tasso di complicanze. La contropulsazione aortica è raccomandata ai pazienti con determinate condizioni: in attesa di trapianto, infarto miocardico acuto esteso, shock cardiogeno, supporto emodinamico in pazienti ad alto rischio da sottoporre ad interventi di chirurgia generale. Normalmente l'assistenza tramite contropulsazione aortica ha una durata di 48-72 ore, ma in alcuni casi (paziente in attesa di trapianto cardiaco) può durare anche settimane. Molto importante è l'assistenza infermieristica al paziente per prevenire eventuali complicanze che potrebbero portare ad un prolungamento della degenza o, nel peggiore dei casi, alla morte. Per una buona assistenza infermieristica l'infermiere deve conoscere ed essere in grado di utilizzare la console e i comandi del contropulsatore aortico, deve mantenere un monitoraggio continuo diretto del paziente per quanto riguarda la temperatura della cute e dei polsi periferici dell'arto che presenta il punto d'inserzione del catetere per prevenire l'occlusione arteriosa, inoltre deve notare preventivamente la presenza di segni e sintomi di infezione e sanguinamento. Importante compito dell'infermiere è educare il paziente a mantenere la testata del letto sollevata non più di 20° e a non girarsi sul fianco per prevenire la dislocazione e/o rottura del catetere. Un altro compito non meno importante dell'infermiere è il supporto psicologico al paziente durante tutta la durata della degenza.

A69: EFFICACIA DEL COLLOQUIO MOTIVAZIONALE PER MIGLIORARE IL SELF-CARE NEI PAZIENTI CON SCOMPENSO CARDIACO: RISULTATI DEL TRIAL MOTIVATE-HF

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Introduzione. Il self-care è una componente fondamentale nei pazienti affetti da scompenso cardiaco (SC) e nella maggior parte dei pazienti risulta carente.

Obiettivi. Valutare se il Colloquio Motivazionale (CM): (i) migliora il self-care maintenance del paziente (endpoint primario; ad esempio l'assunzione di farmaci), il self-care management (ad esempio la risposta ai sintomi) e il self-care confidence (o self-efficacy) a 3 mesi dopo l'arruolamento; (ii) modifica il self-care nell'arco di 1 anno e (iii) aumenta il self-care dei pazienti se c'è il coinvolgimento di un caregiver.

Metodi. Trial clinico randomizzato controllato, multicentrico con tre bracci paralleli (1:1:1). Il campione era composto da 510 pazienti (età mediana 74 anni, 58% maschi) e caregivers (età mediana 55 anni, 75% femmine). Pazienti e caregiver sono stati randomizzati nel Braccio 1 (CM solo per i pazienti), nel Braccio 2 (CM per pazienti e caregiver), o nel Braccio 3 (cure standard). L'intervento, eseguito nei Bracci 1 e 2, consisteva in una sessione di CM faccia a faccia e successivamente, era seguito da tre contatti telefonici. Il self-care è stato valutato con la versione italiana del Self-Care of HF Index v.6.2 (SCHFI V.6.2) che misura il self-care maintenance, management e confidence. I punteggi su ciascuna scala vanno da 0 a 100; un punteggio ≥ 70 è considerato adeguato.

Risultati. A 3 mesi, il self-care maintenance è migliorato di 6,99, 7,42 e 2,58 punti rispettivamente nei Bracci 1, 2 e 3 ($p=0,028$). Il self-care maintenance era adeguato nel 18,4%, 19,4% e 9,2% dei pazienti rispettivamente nei Bracci 1, 2 e 3 ($p=0,016$). A un anno, i punteggi di self-care maintenance, management e confidence, nei Bracci 1 e 2, erano significativamente più alti rispetto al Braccio 3, in diversi follow-up. A 1 anno, nel Braccio 2, il self-care management ha ottenuto un punteggio migliore.

Conclusioni. Il CM migliora significativamente il self-care dei pazienti con SC. Il coinvolgimento dei caregiver può potenziarne l'effetto, specialmente nella dimensione del self-care management.

A70: L'ASSISTENZA INFERMIERISTICA AL PAZIENTE CON EPA CARDIOGENO

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Obiettivi. I pazienti con edema polmonare acuto cardiogeno necessitano di un rapido intervento terapeutico-assistenziale, di cui l'infermiere fa attivamente parte, poiché contribuisce alla realizzazione di procedure volte a correggere tutte le condizioni che sono causa e conseguenza della patologia. Le conoscenze basate sull'applicazione delle evidenze scientifiche più recenti permettono una crescita della professione infermieristica in termini di responsabilità, autonomia e competenze, che portano alla consapevolezza dell'importante ruolo che l'infermiere ha nel processo d'assistenza. Lo scopo del lavoro è di sottolineare come la corretta gestione della terapia farmacologica del paziente con edema polmonare acuto cardiogeno, l'utilizzo appropriato dei devices di supporto (NIV, CVVH) nei tempi e nelle modalità raccomandati dalla letteratura e la stesura di un piano educativo efficace e personalizzato possano incidere positivamente sulla guarigione e sul mantenimento dello stato di salute del paziente cardiogeno.

Metodi. Per la ricerca degli articoli utilizzati per la stesura del progetto, è stata effettuata una revisione della letteratura primaria e secondaria nelle

banche dati Pubmed, Cochrane Database of Systematic Reviews e Cinhal. La ricerca bibliografica si è concentrata sulla lettura critica degli studi degli ultimi dieci anni e sono stati selezionati dieci articoli che corrispondevano ai criteri di selezione. Le parole chiave individuate sono: *acute cardiogenic pulmonary edema, non invasive ventilation, CPAP, continuous veno-venous hemofiltration in heart failure, educational intervention, self-care*.

Risultati. Dagli studi è emerso che, nella gestione del paziente con EPA cardiogeno, la tempestività del trattamento con ventilazione non invasiva attraverso l'utilizzo della pressione positiva continua (CPAP), associato alla terapia medica, è cruciale e produce nella maggior parte dei casi un rapido miglioramento del quadro clinico, riducendo la necessità di intubazione del paziente e il rischio di exitus. La scelta del device e dei sistemi di antidecubito facciale costituiscono una parte importante della presa in carico del paziente e dell'efficacia del trattamento. Anche i sistemi di assistenza della funzione renale (nel nostro caso la CVVH) rappresentano un trattamento efficace per il trattamento del paziente cardiogeno acuto, poiché possono correggere gli squilibri acido-base e sottrarre i volumi necessari con pochi effetti collaterali.

Conclusioni. La cura dei pazienti con edema polmonare acuto cardiogeno risulta un processo dinamico, nel quale l'infermiere esercita una funzione essenziale, per la guarigione e per il mantenimento della condizione di salute dell'assistito, sia dal punto di vista fisico che psicologico. È altrettanto importante una revisione sistematica della letteratura e delle evidenze scientifiche, al fine di garantire una presa in carico globale dell'assistito e una cura personalizzata, fondata sulle competenze e sulle migliori pratiche di gestione infermieristica.

A71: L'INSORGENZA DI NUOVE ANOMALIE DELLA CONDUZIONE E L'IMPIANTO DI PACEMAKER DOPO PROCEDURA TAVI

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Introduzione. L'impianto transcateretere di valvola aortica (TAVI) è divenuto col tempo una valida alternativa alla terapia chirurgica standard per il trattamento delle stenosi aortiche severe in pazienti ad elevato rischio chirurgico. Sebbene il numero di TAVI stia crescendo, con la conseguente riduzione dei rischi legati alle procedure chirurgiche, l'incidenza di anomalie della conduzione necessitanti l'impianto di pacemaker (PM) post-TAVI rimane un importante elemento di discussione. Lo scopo di questo studio è stato quello di valutare l'incidenza di variazioni elettrocardiografiche e di impianti di PM post-TAVI in pazienti sottoposti a tale procedura.

Materiali e metodi. È stato condotto uno studio osservazionale retrospettivo su pazienti sottoposti a TAVI nel periodo 2010-2018 su dati registrati su documentazione clinica. Tutte le procedure di TAVI sono state condotte in sala ibrida per il trattamento di stenosi aortica severa usando protesi Edward Sapien, Sapien 3 e Sapien XT con approccio vascolare valutato dall'Heart Team. Sono stati raccolti dati riguardo esame ecocardiografico, ECG, EuroSCORE, fragilità, comorbidità e classe NYHA.

Risultati. Sono stati presi in considerazione 278 casi che rispettassero i criteri di inclusione ed esclusione imposti dal protocollo di ricerca. I pazienti avevano un'età media di 82 anni ed il 56,1% di essi era di sesso femminile, mentre l'87,8% è stato definito clinicamente in classe NYHA III. Il 20,9% dei pazienti ($n=58$) ha sviluppato l'insorgenza di una nuova anomalia della conduzione, mentre il 3,6% ($n=10$) ha dovuto subire l'impianto di PM. Predittori dell'insorgenza di una nuova anomalia della conduzione sono stati: la presenza di un blocco di branca dx o sx pre-TAVI, l'assenza di fibrillazione atriale pre-TAVI e l'approccio vascolare transaortico durante la procedura TAVI ($R^2=0,14$). Predittori della necessità di impianto di PM sono stati: il punteggio EuroSCORE e l'assenza di fibrillazione atriale pre-TAVI ($R^2=0,05$).

Discussione. L'insorgenza di nuove anomalie della conduzione, specie se queste portano alla necessità dell'impianto di PM, rimane la problematica principale post-esecuzione di procedura TAVI. Conoscere possibili predittori di questi potenziali sviluppi clinici rappresenta elemento fondamentale nella valutazione clinica dei pazienti da sottoporre a TAVI. Questo studio ha fatto emergere come anomalie del ritmo ECG pre-TAVI e un approccio vascolare transaortico possano portare allo sviluppo di nuove anomalie della conduzione, mentre un punteggio EuroSCORE elevato e l'assenza di fibrillazione atriale possono influenzare la possibilità di ricorrere al posizionamento di un PM post-TAVI.

A72: CONTRIBUTO AL SELF-CARE, CARICO ASSISTENZIALE ED ISOLAMENTO SOCIALE DEI CAREGIVERS DI PAZIENTI CON SCOMPENSO CARDIACO E DEFICIT COGNITIVO SEVERO

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Introduzione. L'associazione fra scompenso cardiaco (HF) e deficit cognitivo (CI) è confermata da numerosi studi, arrivando a interessare il 50% della popolazione totale con scompenso cardiaco. In caso di CI severo, ossia sfociante verso la demenza o l'Alzheimer, i pazienti potrebbero avere un'assoluta inconsapevolezza riguardo lo HF, con un

conseguente ed ulteriore carico assistenziale verso i relativi caregivers. Lo scopo di questo studio è stato quello di valutare il contributo al self-care dei caregivers di pazienti con HF e CI severo, nonché il carico assistenziale e l'isolamento sociale da loro percepito.

Materiali e metodi. Si tratta di uno studio osservazionale trasversale su un campione di convenienza tratto da caregivers di pazienti affetti da HF e CI severo in regime di ricovero. Rispettando i criteri di inclusione ed esclusione, sono stati reclutati 40 caregivers, ai quali è stata somministrata una batteria di test self-reported riguardo: contributo del caregiver al self-care del paziente con HF (CC-SCHF1), carico assistenziale (CBI), isolamento sociale (JGLS), livello di conoscenza riguardo il self-care nello HF (Dutch HF Knowledge Scale) e qualità di vita (SF-36).

Risultati. Il campione è stato composto principalmente da caregivers donne (60%) con un'età inferiore ai 60 anni (60%). Questi caregivers si prendevano cura di pazienti con un punteggio medio al MMSE di 4.5 ed un livello di comorbidità di 4.7 al CCI. Alla CC-SCHF1 si sono registrati punteggi medi nei domini della maintenance, confidence e management, rispettivamente di: 64.9, 53.7 e 55.9. Il carico assistenziale dei caregiver (CBI), ha raggiunto nel punteggio totale un valore medio di circa 31.3. Il punteggio medio complessivo ottenuto attraverso la Jong Gierveld Loneliness Scale è stato di 5.1. I risultati sono comparabili con studi simili presenti in letteratura, ma rispecchiano punteggi peggiori se comparati con studi relativi a pazienti con HF in assenza di CI severo.

Discussione. Secondo i dati analizzati è possibile affermare che le capacità assistenziali dei caregivers presi in esame e la loro conoscenza relativa la patologia dello scompenso cardiaco, nonostante siano in linea con le evidenze presenti in letteratura, non raggiungono un livello sufficientemente elevato. In linea generale il caregiver risente dell'assistenza e la sua vita è parzialmente compromessa. Tale condizione non gli impedisce di svolgere quelle che sono le principali attività di vita, ma non gli consente di godere di un buono stato di benessere fisico, mentale e sociale. I caregivers di pazienti con HF e CI severo, necessitano quindi di attenta valutazione e supporto da parte del personale sanitario, al fine di garantire anche una migliore qualità del caregiving.

A73: IL VISSUTO ESPERIENZIALE DEI PROFESSIONISTI SANITARI IN CARDIOLOGIA DURANTE LA PANDEMIA DA SARS-CoV-2

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Introduzione. La pandemia da SARS-CoV-2 ha rappresentato per il nostro Paese una sfida per il Sistema Sanitario Nazionale. La riorganizzazione del sostegno sanitario ospedaliero e territoriale ha necessariamente coinvolto anche l'ambito cardiologico con una forte rimodulazione di protocolli e percorsi diagnostici e terapeutici. Scopo di questo studio è stato quello di valutare il vissuto esperienziale di infermieri, TSRM e TFCPC durante la pandemia, cercando di esplorare l'effetto di questi cambiamenti nel proprio setting lavorativo e nella gestione dei pazienti cardiologici.

Materiali e metodi. È stato condotto uno studio fenomenologico qualitativo con intervista strutturata attraverso contatti multimediali e telefonici rivolto a infermieri, TSRM e TFCPC provenienti da differenti città, setting e ruoli nell'ambito della cardiologia. Lo studio è stato promosso attraverso l'operato del Gruppo di Studio di Assistenza Infermieristica e Tecnica della SIC, ed è stato condotto nel periodo maggio-settembre 2020. Dopo trascrizione delle interviste, il testo è stato analizzato in cieco da due sperimentatori, ed eventuali divergenze nel coding sono state risolte in condivisione. Per l'analisi è stato impiegato il software Atlas.ti.

Risultati. Dall'analisi delle interviste sono emersi dei temi principali, fondamentalmente riconducibili ai seguenti ambiti: riorganizzazione della struttura sanitaria e dei protocolli di gestione dei pazienti, ridotto afflusso di pazienti cardiologici in emergenza o per follow-up per timore del contagio, soddisfazione ed orgoglio per la propria professione, difficoltà nel rapporto tra paziente e familiari durante le fasi di ricovero, proposte per una rivisitazione proattiva dell'organizzazione ospedaliera e territoriale.

Discussione. I dati quantitativi espressi dalla letteratura riguardo il peggioramento degli outcome clinici nei pazienti cardiologici durante la pandemia da SARS-CoV-2 necessitavano di un'analisi introspettiva della percezione diretta degli operatori sanitari coinvolti. Questo studio qualitativo ha permesso di far emergere testimonianze esperienziali chiave, capaci di spiegare dinamiche assistenziali "nuove", che necessiteranno inevitabilmente di un'attenzione futura, al fine di rivedere i percorsi diagnostici e terapeutici.

A74: ASSISTENZA INFERMIERISTICA AL PAZIENTE CON CONTROPULSATORE AORTICO O CON IMPELLA

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Introduzione. Alcune condizioni di urgenza emodinamica, primo fra tutti lo shock cardiogeno, ma anche l'esecuzione di procedure coronariche

percutanee (PCI) ad alto rischio, richiedono l'impiego di dispositivi di supporto cardiocircolatorio di tipo temporaneo. Questi permettono di migliorare la prestazione cardiaca o si sostituiscono in parte ad essa, talvolta fungendo da "ponte" per l'impianto di dispositivi a lunga durata o per il trapianto cardiaco.

In un contesto così complesso la figura dell'infermiere svolge un ruolo importante non soltanto nelle sale di emodinamica, ma anche in tutto il periodo che segue la fase di impianto dei dispositivi, fino alla loro rimozione. Nello specifico, il presente studio è incentrato su due dispositivi di assistenza cardiocircolatoria (e sulla relativa assistenza infermieristica): il contropulsatore aortico e la pompa assiale Impella.

Metodi. È stata condotta una revisione della letteratura consultando la banca dati multimediali PubMed, le linee guida dell'ACC (American College of Cardiology), nonché i dati statistici elaborati dalla Società Italiana di Cardiologia Interventistica- GISE. I risultati sono stati altresì corredati dall'esperienza diretta svolta presso l'Unità di Emodinamica dell'Ospedale Santa Maria Goretti di Latina.

Risultati. Dalle ricerche emerge che l'impiego del contropulsatore aortico, prima di effettuare una PCI ad alto rischio, permette di ridurre del 34% la mortalità dovuta a complicanze legate alla procedura stessa, specialmente nel lungo termine. Risultati ancora migliori si stanno ottenendo con la pompa Impella, che si dimostra più efficace nella riduzione di complicanze periprocedurali. Anche nel trattamento dello shock cardiogeno l'Impella sembra offrire un supporto migliore rispetto alla contropulsazione aortica, sebbene l'uso sistematico di entrambi i dispositivi sia comunque sconsigliato, infatti il loro impiego deve essere accuratamente ponderato sulla base del singolo paziente. In ogni caso, gli esiti positivi che derivano dall'impiego di questi dispositivi sarebbero vanificati se non fosse presente una corretta gestione infermieristica dei pazienti in cui sono stati impiantati. L'attenzione è rivolta principalmente: al monitoraggio costante dei parametri vitali, al controllo della coagulazione, alla cura del sito di inserzione, ad un adeguato posizionamento del paziente a letto e ad una mirata movimentazione.

Conclusioni. Il management di questi dispositivi, fornisce un chiaro esempio di nursing avanzato: conoscerne i lineamenti teorici e le abilità pratiche permette una loro corretta gestione, affinando anche le attività di nursing a favore dei pazienti coinvolti, e migliorandone potenzialmente gli outcome.

A75: TIROCINIO VIRTUALE INTERATTIVO PER ACQUISIRE COMPETENZE ASSISTENZIALI RIVOLTE AL PAZIENTE CON SCA

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Introduzione. Il *flip teaching* è una metodologia didattica innovativa, che ha tempi di studio invertiti rispetto a quella tradizionale, e si basa sull'apprendimento tra pari. Il primo momento di conoscenza avviene in maniera autonoma; gli studenti, per imparare, sono chiamati a ideare continue soluzioni ai problemi, attivando le conoscenze pregresse e avvalendosi dell'ausilio di materiali multimediali. Gli elementi caratterizzanti questa metodologia didattica sono il *team working* e il *debate*.

Obiettivo. Misurare il gradimento, l'incremento delle conoscenze e il cambiamento del metodo di studio degli studenti che hanno partecipato al tirocinio virtuale immersivo.

Materiali e metodi. Studio pilota di tipo descrittivo osservazionale su 40 studenti del II anno iscritti all'a.a. 2019/2020. L'analisi della ricaduta del corso FAD, erogato attraverso la piattaforma Moodle, è avvenuta nei mesi di Aprile/Maggio 2020. I dati sono stati raccolti attraverso test di valutazione pre - post e interviste attraverso questionari autocompilabili on line.

Risultati e Discussione. I campi di analisi hanno fatto riferimento a tre dei quattro livelli gerarchici descritti da Kirkpatrick. I dati hanno evidenziato un buon gradimento attraverso una forte preponderanza degli aspetti positivi e un buon consenso alla riproposta dell'esperienza ai colleghi. Anche l'incremento delle conoscenze è stato elevato e molte di queste hanno generato buone competenze nel *decision making*. La ricaduta sulla prassi di studio si è evidenziata in modo particolare sulla modalità di studiare/lavorare in gruppo attraverso una maggiore consapevolezza delle competenze che la professione richiede.

Conclusioni. La *Flipped classroom*, applicata a una esperienza di tirocinio virtuale rivolta a studenti infermieri, potrebbe permettere di avvicinare la teoria alla pratica, costituendo un ottimo spazio propedeutico al tirocinio in un futuro Covid free.

A76: LA CURA INFORMALE NELLO SCOMPENSO CARDIACO: UNA QUESTIONE DI TEMPO. I RISULTATI DI UNO STUDIO INTERNAZIONALE

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Background. I caregiver informali svolgono un ruolo fondamentale nella gestione dei pazienti con scompenso cardiaco (SC), molti dei quali fanno

affidamento sul sostegno non retribuito di partner, familiari, amici o vicini nella gestione della cronicità. La letteratura su altre popolazioni di caregiver riporta un'esperienza peggiore all'aumentare della richiesta di tempo da dedicare all'assistenza del paziente. Ad oggi non ci sono dati circa la gestione del tempo da parte dei caregiver di pazienti con SC quando non sono occupati dall'assistenza.

Obiettivo. Descrivere l'esperienza della gestione del tempo dei caregiver informali di pazienti con SC quando non occupati dal caregiving.

Metodo. È stata condotta un'intervista semi-strutturata con 52 caregiver di pazienti con SC arruolati, con un campionamento di convenienza, in tre paesi europei: Italia, Spagna e Paesi Bassi. Le interviste sono state trascritte integralmente ed analizzate con il metodo della content analysis secondo Mayring. I dati sono stati analizzati con i software NVivo 12 e SPSS v.26.

Risultati. Il campione era prevalentemente di sesso femminile (82,6%) con età media di 69 anni (SD 8,57). La content analysis ha mostrato esperienze differenti nella gestione del tempo in base al sesso. I caregiver donne erano prevalentemente occupati in attività di tipo domestico che permettevano loro anche di restare in contatto con l'attività di caregiving. I caregiver uomini prediligevano, invece, attività all'aria aperta e solitamente riguardanti l'attività fisica (es. passeggiate). Entrambi sperimentavano rinunce nella gestione del tempo causate dal caregiving quali le uscite in compagnia, le gite fuori porta e le vacanze. L'allontanamento fisico dalla persona assistita veniva percepito come necessario per mantenere un'adeguata qualità nel caregiving, anche se era frequentemente associato a sentimenti di frustrazione, insoddisfazione e difficoltà nello svolgere anche semplici attività di relax (es. difficoltà di concentrazione durante la lettura). Inoltre, i caregiver esperivano sentimenti di limitazione correlato allo spazio in cui viveva il paziente ed al suo grado di dipendenza che vincolava la presenza del caregiver.

Conclusioni. Sebbene i caregiver riuscivano a ricavare del tempo libero dal caregiving, questo era disfunzionale in quanto non realmente percepito ed esperito come tale. Nella pratica clinica è necessario riflettere circa i supporti sociali di cui i caregiver dispongono. Per cristallizzazione si potrebbe ipotizzare che la qualità del tempo libero potrebbe incidere negativamente sulla qualità del contributo del caregiver al caregiving e di conseguenza sulla salute della diade paziente-caregiver. Sono necessari studi quantitativi longitudinali per capire meglio come la gestione del tempo libero del caregiver possa avere un impatto economico e sul sistema sanitario.

A77: LA PREVENZIONE DELLE INFEZIONI DA DISPOSITIVI CARDIACI ELETTRONICI IMPIANTABILI (CIED) E LA TECNOLOGIA HYDROFIBER: ESPERIENZA DEL LABORATORIO DI ELETTROSTIMOLAZIONE DEL POLICLINICO TOR VERGATA

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Introduzione. I progressi tecnologici raggiunti nel campo dell'elettrostimolazione cardiaca hanno permesso la realizzazione di moderni dispositivi elettronici cardiaci impiantabili (CIED) utili nella prevenzione primaria e secondaria della morte improvvisa e dello scompenso cardiaco. Purtroppo, all'evoluzione tecnica è seguito un aumento delle complicanze settiche post-impianto. La più comune e temibile è l'infezione della tasca del generatore con un notevole impatto sulla qualità di vita del paziente, oltre che sull'aumento dei costi sanitari. Le infezioni dei CIED, rappresentano circa lo 0,6%-2,2% del totale delle infezioni ospedaliere mondiali, ma se non adeguatamente trattate, sono responsabili del 34% del totale della mortalità per infezione ospedaliere. Obiettivo del lavoro è quello di proporre l'utilizzo della tecnologia *Hydrofiber*® combinata con ioni argento su ferita chirurgica a chiusura primaria come ulteriore misura preventiva delle infezioni delle tasche dei CIED.

Materiali e metodi. Attraverso le riprese video, durante un impianto di CIED nel Laboratorio di Elettrostimolazione, direttamente al tavolo operatorio con tecnica asettica, si vuole mostrare la corretta applicazione della medicazione che incorpora la tecnologia *Hydrofiber*® combinata con ioni argento su ferita chirurgica a chiusura primaria. La medicazione è costituita da tre strati: tampone interno in tessuto non tessuto contenente la tecnologia *Hydrofiber*® combinata con ioni argento, che in presenza di essudato, gelifica, assorbe e trattiene l'essudato prodotto, garantendo attività antimicrobica a largo spettro ed ambiente ideale per la riparazione tissutale; componente idrocolloidale in doppia lamina, per consentire una sostenuta adesione alla cute perilesionale; strato di rivestimento esterno, costituito da un film di poliuretano per proteggere la ferita dalle contaminazioni e consentire la gestione della trasmissione di vapore acqueo.

Risultati. Nel biennio 2019-2020 la tecnologia *Hydrofiber*® combinata con ioni argento è stata utilizzata come medicazione primaria su 500 pazienti sottoposti a impiantato o sostituzione di CIED. Applicata direttamente al tavolo operatorio con tecnica asettica e rimossa al 1° controllo post dimissione. Inizialmente la valutazione è stata fatta mantenendo la

medicazione in sede di incisione per 2 giorni, successivamente si è arrivati a 8 giorni, senza evidenti segni clinici che indicassero la necessità di eseguire il cambio anticipatamente. L'essudato, dove presente, è stato gestito in modo eccellente, la cute è risultata essere in condizioni ottimali, non sottoposta ad arrossamenti dovuti a frizione o macerazione e senza segni di infezione superficiale. La diminuzione del numero di cambi di medicazione ha ridotto il rischio di contaminazione del sito. I pazienti hanno riportato un buon comfort legato alla medicazione, che ha permesso di eseguire l'igiene giornaliera senza alterarla o bagnarla, e di conseguenza la necessità di sostituirla. La medicazione permette una normale mobilità senza percepire trazioni perché la parte adesiva è elastica.

Discussione. Il sinergismo tra adeguata profilassi antibatterica, migliore condizione interventistica ed attenta gestione della ferita chirurgica, è di fondamentale importanza per ridurre al minimo le complicanze che possono generare un ritardo nella guarigione della ferita CIED. Non avendo in letteratura studi che riguardano l'impiego di tecnologia *Hydrofiber*® combinata con ioni argento per la prevenzione delle infezioni del sito chirurgico in caso di impianti CIED, sarebbe interessante effettuare un confronto con l'utilizzo di altre medicazioni per valutarne le performance in termini di gestione delle complicanze della ferita chirurgica.

A78: SVILUPPO E VALIDAZIONE PSICOMETRICA DI UNO STRUMENTO PER MISURARE IL SUPPORTO DEL CAREGIVER AL SELF-CARE NELLO SCOMPENSO CARDIACO

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Background. Gli outcome dei pazienti con scompenso cardiaco (SC) possono essere migliorati attraverso comportamenti di self-care (ad esempio, aderenza alla terapia farmacologica e risposta ai sintomi di riacutizzazione) che possono essere misurati con l'European Heart Failure Self-Care Behaviour Scale (EHFScBS). Come già ampiamente dimostrato dalla letteratura il ruolo dei caregiver informali (per esempio, i membri della famiglia) è importante nel supporto ai comportamenti di self-care dei pazienti con SC. Risulta quindi necessario disporre di uno strumento valido ed affidabile per misurare questo supporto. Pertanto, lo scopo di questo studio è stato di sviluppare e testare l'European Heart Failure Self-Care Behaviour Scale-Caregiver version (EHFScBS-C).

Metodi. L'EHFScBS-C è stata creata modificando in versione caregiver gli item della EHFScBS sviluppata per i pazienti. È stato utilizzato un disegno osservazionale con pazienti affetti da SC arruolati in tre paesi europei: Italia, Spagna e Paesi Bassi. L'EHFScBS-C è stata testata con l'analisi fattoriale esplorativa e la validità relativa a criterio. L'affidabilità è stata testata con l'alfa di Cronbach, il composite reliability ed il factor score determinacy.

Risultati. Sono stati arruolati 193 pazienti (età media 74 anni, SD \pm 14,1, 72,5% donne, classe NYHA II 53%). L'analisi fattoriale esplorativa ha evidenziato la presenza di due fattori denominati: "Contributo del caregiver al self-care in relazione a problemi di natura clinica" e "Contributo del caregiver al self-care in relazione ad un corretto stile di vita". Gli indici di adattamento di questa analisi sono risultati eccellenti (CFI = 0,990; RMSEA = 0,048). La validità relativa a criterio ha evidenziato correlazioni significative ($p=0,001$) con la Caregiver Preparedness Scale. L'affidabilità è risultata egualmente eccellente con un alfa di Cronbach = 0,80-0,93, un composite reliability = 0,80-0,95 ed un factor score determinacy = 0,92-0,98).

Conclusioni. L'EHFScBS-C ha mostrato ottime caratteristiche di validità e affidabilità e può essere utilizzata nella pratica clinica e nella ricerca per valutare la misura in cui i caregiver informali supportano il paziente con SC nelle pratiche di self-care. È raccomandato l'uso dell'EHFScBS-C in combinazione con l'EHFScBS per un approccio diadico alla valutazione del self-care.

A79: GESTIONE AMBULATORIO PMK DURANTE IL LOCKDOWN

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Il nostro centro è stato uno dei pochi a proseguire l'attività di follow-up ambulatoriale di controllo PMK nel Lazio durante l'epidemia COVID 19 che ci ha colpiti tutti. Siamo andati avanti quotidianamente cercando di fornire supporto ed assistenza ai pazienti portatori di device impiantabili. La nostra équipe della U.O.S. di Elettrofisiologia ed Elettrostimolazione coordinata dal Dott. Filippo Lambertini è formata da quattro Cardiologi, due infermieri e un Tecnico di Fisiopatologia Cardiocircolatoria e Perfusione Cardiovascolare mettendo appunto il modo migliore per poter accogliere i pazienti che facevano accesso in ambulatorio PMK, proteggendoci con gli appositi DPI (maschera facciale, mascherina chirurgica e guanti monouso). Infermieri e Tecnico ci siamo occupati di contattare i pazienti e valutare insieme a loro, o ai loro familiari, se fossero in condizioni per poter fare accesso in ambulatorio o programmare insieme una data successiva. L'infermiere si occupava di accogliere il paziente, verificare che indossasse correttamente la mascherina e i guanti, prima di entrare in

ambulatorio invitava alla corretta igienizzazione delle mani ed in fine che fosse in possesso dell'impegnativa, correttamente registrata al CUP. Il paziente, veniva quindi, fatto accomodare in ambulatorio e distendere sul lettino, preventivamente igienizzato e allestito con lenzuolino monouso. Veniva effettuato il controllo del device dal Tecnico di Fisiopatologia Cardiocircolatoria e Perfusioni Cardiovascolari, la testina di telemetria veniva igienizzata ad ogni paziente e ricoperta da custodia monouso. Al termine del controllo veniva effettuata la sanificazione dell'ambiente. Quest'organizzazione ci ha permesso di poter fornire supporto ai pazienti che necessitavano di follow-up programmati o in urgenza, evitando inutili accessi in Pronto Soccorso Nei 69 giorni della fase 1 e fase 2 di 840 prestazioni previste, escluse le prestazioni extra ci ha permesso di effettuare il 65% delle prestazioni, garantendo sicurezza ai pazienti. Durante questo periodo, abbiamo potuto continuare a ricoverare pazienti in regime di Day Hospital o ricovero ordinario per la sostituzione dei device in fase di esaurimento. I pazienti in possesso di monitoraggio remoto, venivano valutate, insieme al Cardiologo le trasmissioni e nei casi di pazienti maggiormente compromessi si è evitato di esporli ad ulteriori rischi e si è programmato un nuovo controllo ambulatoriale.

A80: GESTIONE DELL'ACCESSO ARTERIOSO FEMORALE NEL LABORATORIO DI EMODINAMICA DELL'OSPEDALE MAGGIORE – UN PROGETTO DI MIGLIORAMENTO

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Background. Presso il laboratorio dell'ospedale Maggiore di Bologna circa il 15% dei casi necessita ancora di essere svolto mediante accesso femorale e il 50% circa richiede una compressione manuale. Nei primi mesi del 2017 vi è stata la percezione di un aumento delle complicanze emorragiche tra i pazienti con accesso arterioso femorale: per questo motivo abbiamo deciso di raccogliere i dati e avere una idea più oggettiva della situazione presso il nostro laboratorio.

Scopo. Abbiamo intrapreso uno studio con scopo di fotografare il modello organizzativo della gestione degli accessi arteriosi femorali, presso il laboratorio di emodinamica ed elettrofisiologia dell'ospedale Maggiore di Bologna. Oltre a confrontare l'incidenza di complicanze emorragiche maggiori abbiamo valutato quanto l'introduzione dell'approccio eco guidato e di sistemi di chiusura siano stati efficaci nel prevenire la comparsa di tali complicanze.

Metodo. Mediante una scheda di raccolta dati a partire dal 1 luglio 2017 abbiamo analizzato diversi aspetti di tutti gli accessi femorali reperiti presso il nostro centro. La raccolta ha riguardato la tecnica di puntura, la terapia in corso, la modalità di chiusura dell'accesso oltre agli operatori coinvolti. Il monitoraggio continua nei giorni seguenti per valutare insorgenza e decorso delle eventuali complicanze. Dallo studio sono stati esclusi i pazienti che, dopo l'esecuzione della procedura, venivano trasferiti presso i reparti di rianimazione.

Risultati. Dopo 10 mesi abbiamo analizzato 322 casi di accesso femorale. *Metodica di puntura:* 38.5% di puntura Rx guidata, 28% puntura eco guidata, 33.5% puntura con la sola palpazione del polso femorale ("alla cieca"). *Modalità di compressione:* 55% compressive manuali, 36.5% Proglide, 8.5% Angioseal. *Complicanze:* 0.7% di fistole arterovenose, 1.5% ematoma maggiore/pseudoaneurisma (>5 cm o calo emoglobina >2 g/dl). Tra gli ematomi maggiori rilevati 1 ha richiesto la chiusura chirurgica e 5 una ulteriore compressione manuale soltanto; 2 hanno richiesto trasfusione. L'approccio eco guidato ha annullato le complicanze di fistola arterovenosa, ma non gli ematomi (14.6% durante tutto il periodo analizzato). I sistemi di chiusura quando applicati con successo (no ematoma nei primi minuti) hanno ridotto le complicanze emorragiche (1 ematoma >5 su 91 device applicati).

Conclusioni. La scheda di monitoraggio è uno strumento utile per mantenere un'adeguata attenzione sulle possibili complicanze dell'accesso arterioso femorale. Oltre ha poter misurare l'incidenza di complicanze ha permesso di analizzare l'efficacia dei diversi approcci (eco guidato e Rx guidato), dei diversi sistemi di chiusura nonché l'intero processo organizzativo. Riteniamo che la formazione dei vari operatori coinvolti sia la chiave per ridurre le complicanze e la scheda di monitoraggio sarà ancora un valido strumento anche per misurare l'efficacia della formazione.

A81: CLUSTER DI CAREGIVING NELLO SCOMPENSO CARDIACO: STUDIO IN SPAGNA, ITALIA E PAESI BASSI

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Background. Essere un caregiver informale di pazienti con scompenso cardiaco (SC) è complesso e stressante e può avere un impatto importante sulla loro qualità di vita. Poiché i bisogni e problemi dei

caregiver sono diversi e multidimensionali, è possibile ipotizzare l'esistenza di cluster di caregiver accomunati da caratteristiche simili. L'identificazione di questi cluster permetterebbe interventi personalizzati per migliorare le condizioni di vita dei caregiver.

Obiettivi. L'obiettivo di questo studio è stato di identificare cluster di caregiver di persone con SC e di associare i cluster identificati alle caratteristiche sociodemografiche dei caregiver stessi.

Metodi. È stato condotto uno studio qualitativo con interviste semi-strutturate in tre paesi europei: Italia, Spagna e Paesi Bassi. Le interviste sono state trascritte integralmente ed analizzate con analisi esplorativa multidimensionale (EMDA) di Fraire. Il software utilizzato per l'analisi è stato IRaMuTeQ.

Risultati. Sono stati arruolati ed intervistati 52 caregiver (20 in Italia, 21 in Spagna e 11 nei Paesi Bassi). I caregiver erano principalmente di sesso femminile (tra 81% e 85% nei tre paesi) ed avevano un'età media di 64 Anni (SD 11,4). I pazienti erano prevalentemente di sesso maschile in Italia e Paesi Bassi (63,7% e 65% rispettivamente) mentre di prevalenza femminile in quello spagnolo (33%). Dall'analisi delle interviste sono emersi tre cluster di caregiver in ciascun Paese: coniugi, figli adulti e membri non familiari (es. amici, volontari o parenti indiretti). Questi tre cluster erano caratterizzati da omogeneità interna ma eterogeneità esterna per diverse tipologie di bisogni e problemi relativi al caregiving.

Conclusioni. I risultati di questo studio mostrano per la prima volta cluster di soggetti simili nei tre paesi europei analizzati in termini di bisogni e problemi. Le caratteristiche dei cluster potrebbero essere utilizzate per disegnare futuri interventi anche di dimensioni internazionali a sostegno dei caregiver di persone con SC.

A82: GESTIONE INFERMIERISTICA DEGLI ACCESSI VENOSI IN CARDIOLOGIA E COMPLICANZE FLEBITICHE PERIPROCEDURALI

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Introduzione. La flebite individua un danno infiammatorio della parete interna venosa che può scaturire da eventi di tipo chimico, biologico, infettivo o meccanico. Generalmente ha prognosi favorevole, ma caratterizza negativamente il decorso clinico dei pazienti aumentando il periodo di ospedalizzazione ed i costi per la gestione delle complicanze. Nella nostra U.O. si è registrata un'elevata incidenza di flebiti, negli accessi venosi periferici, in un arco temporale di 6 mesi, in concomitanza alla sostituzione dei vecchi ago-cannula con i nuovi in utilizzo.

Obiettivi. In questo studio prospettico in aperto abbiamo valutato l'utilizzo di due differenti tipi di ago-cannula ai fini di individuare eventuali differenze nelle complicanze periprocedurali durante il ricovero.

Materiali e metodi. Da Giugno ad Agosto 2020 si è avviata una sistematica survey dei pazienti ai fini del riconoscimento precoce delle flebiti. È stata elaborata e compilata, per ciascuno dei pazienti individuati, una scheda in cui sono stati annotati: dati anagrafici-data di ricovero-data e zona di posizionamento accesso venoso-controlli quotidiani stato dell'accesso venoso-eventuali sostituzioni in base allo score di flebite. L'accesso era effettuato da 5 infermieri, di riconosciuta esperienza, (un operatore per ogni turno di guardia). La rilevazione dell'accesso e delle eventuali complicanze era obiettivamente da una documentazione fotografica, valutata indipendentemente da 2 cardiologi e da 2 infermieri, non impegnati in prima persona nel posizionamento dei presidi.

Risultati. Sono stati individuati e monitorati 120 pazienti ricoverati nel Reparto di Cardiologia, di età tra i 37 e gli 80 anni (media 62 anni), affetti da Sindromi Coronariche Acute (SCA), nella fase post-intensiva, suddivisi in due gruppi (A e B) paragonabili per età, sesso e fattori di rischio per le patologie cardiovascolari. Al gruppo A erano stati applicati ago-cannula di vario calibro, sterile, monouso, in etilene propilene fluorato (FEP) con rastrematura a doppia conicità ed affilatura tipo Back Level. Al gruppo B erano stati applicati ago-cannula di vario calibro, sterile, monouso in poliuretano e teflon con punta dell'ago a triplice affilatura. I pazienti non avevano in terapia soluzioni urticanti o irritanti per accessi periferici, ma NaCl in infusione continua o farmaci a bassa osmolarità o addirittura non necessitavano di infusione. I casi di flebiti osservati nel gruppo A sono stati pari a più del 40% (indipendentemente dall'età, dal sesso dei pazienti e dal tipo di SCA), nonostante le sostituzioni preventive ai primi accenni di eritema cutaneo. La flebite si manifestava, talora, anche entro 24-48 ore dall'applicazione dell'ago-cannula e senza alcuna infusione. I casi di flebiti osservati nel gruppo B sono stati complessivamente meno del 10% del campione esaminato. Non si registrava alcuna differenza dell'incidenza delle flebiti negli accessi venosi posizionati dai diversi infermieri impegnati nello studio, nell'ambito dei 2 gruppi di paziente arruolati.

Conclusioni. Esistono potenziali fattori esogeni che determinano l'insorgenza delle flebiti, quali la negligenza in campo assistenziale e l'osmolarità del farmaco in infusione, che è di fondamentale importanza negli accessi periferici. Tale studio *pilota*, elaborato su un campione di piccole dimensioni, ha evidenziato che il tipo di ago-cannula, utilizzato da

operatori sanitari con riconosciuta pluriennale esperienza, potrebbe favorire la comparsa delle flebiti, nella zona di accesso venoso, indipendentemente dall'età del paziente, dal sesso e dai fattori di rischio per le patologie cardiovascolari. Tale risultato dovrà essere confermato, in ambito del dipartimento Cardiologico, su una popolazione più ampia, eliminando per quanto possibile gli eventuali elementi confondenti.

A83: HUB DI EMODINAMICA DURANTE COVID-19: L'ESPERIENZA DEL TEAM INFERMIERISTICO DEL PAPA GIOVANNI XXIII DI BERGAMO

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Introduzione. La provincia di Bergamo è stata una delle aree maggiormente colpite dall'infezione da SARS COVID in Italia, con un totale di 14679 casi segnalati dall'inizio dell'epidemia al 14 luglio 2020 (ISS, 2020). Per fronteggiare l'emergenza sanitaria, Regione Lombardia ha identificato ospedali Macro-HUB in cui centralizzare e trattare le urgenze delle patologie cardiovascolari tempo-dipendenti in modo da garantire una migliore allocazione e relativo trattamento dei pazienti. L'ASST Papa Giovanni XXIII è stata identificata come centro HUB provinciale (DGR XI 2906-2020) per il trattamento di STEMI e NSTEMI, con l'individuazione di percorsi fast-track con accesso diretto del paziente al servizio di emodinamica senza transitare dal centro di Emergenza ad Alta Specializzazione.

Obiettivo. Descrivere l'esperienza del team infermieristico dell'Emodinamica dell'ASST HPGXXIII di Bergamo durante l'emergenza COVID-19.

Metodi. Studio cross sectional mixed-method. I dati relativi al periodo 13/03 - 06/05/2020 sono stati estratti dal sistema informatizzato di refertazione delle procedure, unito ad una raccolta dati effettuata sui pazienti emergenti. Oltre all'osservazione partecipante, agli infermieri è stato chiesto di riflettere su aspetti positivi e negativi dell'esperienza.

Risultati. Nel periodo in esame sono stati trattati 60 casi di STEMI (di cui 24 COVID+) e 32 casi di NSTEMI (di cui 6 COVID+). I cambiamenti organizzativi e la presentazione clinica dei pazienti trattati hanno richiesto l'introduzione di nuove procedure: presenza degli infermieri in guardia attiva h24 per garantire il percorso fast track; attuazione delle misure indicate dal servizio prevenzione e protezione con relativa modifica di spazi e percorsi e creazione di aree di decontaminazione e smaltimento dei presidi; allestimento di zone dedicate alla valutazione ed accettazione del paziente in fast track; inquadramento diagnostico comprensivo di ecocardiogramma fast e prelievi ematici sia di routine sia di valutazione completa dell'assetto coagulativo del paziente; raccolta dati mirata alla ricerca di segni e sintomi riconducibili a COVID con successiva archiviazione in banca dati; identificazione di spazi protetti per l'esecuzione pre-procedura di RX torace allo scopo di identificare precocemente eventuali interstiziopatie polmonari; collaborazione multidisciplinare con il personale della sala operatoria di cardiocirurgia mobilitato in supporto all'emodinamica per garantire un'assistenza continuativa al paziente e una migliore gestione delle zone sporche-pulite. Gli snodi critici legati a fattori organizzativi e clinico assistenziali sono stati: difficile allocazione dei pazienti post procedura a causa della carenza di posti letto in aree intensive e nelle degenze; permanenza prolungata dei pazienti nelle sale di emodinamica con conseguente difficoltà nella gestione di urgenze contemporanee e confinamento dei pazienti; gestione complessa dei casi di IMA associato a insufficienza respiratoria severa da COVID (rapporto PaO₂/FIO₂ <100) per instabilità clinica e presenza di NIV-CPAP; necessità di una formazione rapida all'utilizzo di sistemi informatici per l'accettazione e l'inquadramento diagnostico dei pazienti ad accesso diretto dal territorio. Gli aspetti positivi: una grande coesione all'interno del team infermieristico, con una partecipazione attiva e propositiva nei repentini cambiamenti dell'unità operativa; un forte spirito di gruppo teso al supporto reciproco e al continuo perfezionamento degli spazi e delle modalità operative; la collaborazione con il gruppo della sala operatoria di cardiocirurgia, che ha portato al confronto su vari aspetti lavorativi aumentando così le differenti competenze professionali dei due team; la valorizzazione dei differenti background clinico assistenziali degli infermieri per far fronte all'elevata complessità dei pazienti trattati.

Discussione. La creazione di nuovi percorsi clinico assistenziali è risultata essere un elemento fondamentale per la gestione dell'emergenza COVID. Nel servizio di emodinamica dell'ASST Papa Giovanni XXIII tutte le procedure, i comportamenti e i percorsi attuati nel periodo di massima crisi sono diventati i precursori di una gestione più articolata e definita messa in atto nei mesi successivi al periodo di osservazione. L'analisi dell'esperienza professionale degli infermieri merita di essere approfondita per creare nuovi protocolli e procedure, condivisi a livello nazionale ed internazionale, da attuare in caso di situazioni estreme come quella vissuta durante la pandemia da COVID-19. Anche le raccolte dati effettuate all'accettazione dei pazienti uniti ai dati clinici e strumentali stanno diventando la base di studi e approfondimenti utili a comprendere e trattare efficacemente questa patologia.

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A84: DIFFERENZE DI GENERE NELLE PATOLOGIE CARDIOVASCOLARI: UNA REVISIONE DELLA LETTERATURA

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Introduzione. La medicina di genere è una nuova branca della medicina che mira a studiare le patologie comuni fra uomini e donne, quali ad esempio le patologie cardiovascolari, che presentano differenze nella presentazione, sintomatologia, diagnostica e cura. Il concetto di base della medicina di genere è che tali differenze non sono esclusivamente legate alle diversità biologiche dell'individuo e del suo apparato riproduttivo. Il termine "genere" intende infatti coinvolgere tutti i fattori ambientali, culturali e relazionali appartenenti al soggetto. L'obiettivo dello studio è andare a descrivere, attraverso una revisione della letteratura, le differenze esistenti fra uomini e donne in ambito cardiologico al fine di analizzarle ed individuare eventuali criticità.

Materiali e metodi. È stata condotta una revisione della letteratura sulle banche dati biomediche PubMed, Cinhal e Cochrane. I siti inoltre consultati sono stati: Ministero della Salute, Istituto Superiore di Sanità, European Society of Gender Health and Medicine. Le parole chiavi utilizzate sono state: Sex Characteristics, Gender, Cardiovascular diseases, Risk factors, Sign and symptoms, Diagnosis, Treatment, Evidence-Based Practice. I criteri di inclusione sono stati tutti gli articoli inerenti al tema trattato. I criteri di esclusione sono stati gli articoli con data di pubblicazione più vecchia del 2010, articoli non inerenti alle patologie cardiovascolari, articoli con un campione di riferimento molto limitato.

Risultati. Le malattie cardiovascolari rappresentano ad oggi la principale causa di morte nella popolazione dei Paesi industrializzati. Queste patologie sono sempre state ritenute appartenenti al solo campo maschile portando così ad un insufficiente studio e preparazione del personale sanitario nell'assistere le donne per tali problematiche. L'insorgenza delle patologie cardiovascolari è differente, si prende come esempio la cardiopatia ischemica in cui negli uomini inizia a manifestarsi nella quarta decade di vita, mentre nelle donne questa incidenza è bassa prima della menopausa ed aumenta drasticamente successivamente. I fattori di rischio cardiovascolari tradizionali sono gli stessi per entrambi i sessi, ma hanno un impatto differente. Inoltre, sono stati individuati nuovi fattori di rischio genere-specifici non presi prima in considerazione per la donna, quali ad esempio la menopausa precoce, il diabete gestazionale, storia di pre-eclampsia. Clinicamente molti studi dimostrano come i sintomi associati a tali patologie possano essere diversi avendo manifestazioni atipiche e questo maggiormente accade nelle donne. Sono state individuate inoltre differenze nell'affidabilità di alcuni esami diagnostici tipicamente utilizzati; ad esempio l'elettrocardiogramma da sforzo è un test utilizzato a scopo diagnostico a seguito di un sospetto di cardiopatia ischemica ed ha una minore accuratezza diagnostica nella donna. Un altro campo in cui si possono notare delle differenze è quello farmacologico, ma le donne sono state scarsamente arruolate negli studi clinici necessari per l'immissione in commercio dei farmaci. Differenze infatti si possono notare nell'assorbimento, nelle vie di somministrazione, nella distribuzione, nel metabolismo e nell'eliminazione dei farmaci.

Conclusioni. La speranza è che la medicina di genere in ambito cardiologico possa promuovere un approccio differenziato e mirato optando per una medicina genere-specifica, incrementando nuovi trial clinici con l'inserimento fondamentale di tale variabile nella pratica clinica.

A85: RIANIMAZIONE CARDIOPOLMONARE IN EMERGENZA SARS-CoV-2

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Scopo. Diffondere capillarmente le modifiche apportate alle linee guida internazionali di rianimazione cardiopolmonare per garantire la sicurezza degli operatori durante le manovre di rianimazione ed altresì garantire una rianimazione adeguata di qualità per la vittima di arresto cardiocircolatorio.

Razionale. Le linee guida per la rianimazione cardiopolmonare, che vengono sistematicamente riviste ogni 5 anni, hanno la caratteristica peculiare di porre l'attenzione non solo sull'atto della rianimazione cardiopolmonare vero e proprio, ma viene presa particolarmente in considerazione la sicurezza del soccorritore e della vittima. Nel periodo di emergenza SARS-CoV-2 l'aspetto della sicurezza, per il potenziale elevato rischio infettivo, ha portato a modificare le linee guida che sono state ritoccate con l'obiettivo di garantire la massima sicurezza per gli operatori impegnati nella rianimazione cardiopolmonare.

Vengono descritti i singoli passaggi per una attività di rianimazione cardiopolmonare efficace e sicura, dall'utilizzo dei Dispositivi di Protezione Individuale, sia in ambito ospedaliero che extraospedaliero, alla corretta gestione delle protezioni per la vittima, dalle valutazioni del respiro e della coscienza che sono state modificate per garantire un minor rischio di contagio, alle attività di rianimazione con le modalità differenti di ventilazione, da eseguirsi soltanto se si hanno a disposizione i presidi corretti quali pallone auto-espandibile con filtri e in due operatori.

Questo documento sintetizza le integrazioni apportate confrontandole con

le attività previste precedentemente ed evidenziando nei singoli passaggi le attività che si differenziano ed il motivo per le quali tali attività sono state modificate.

A86: COMPRESSIONI TORACICHE MANUALI VERSO COMPRESSIONI TORACICHE MECCANICHE: QUALI GLI OUTCOMES NEUROLOGICI? REVISIONE DELLA LETTERATURA

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Introduzione. La percentuale di sopravvivenza, in seguito ad un arresto cardiaco, può variare dal 5% al 50%: i danni neurologici si presentano diversamente in più della metà dei sopravvissuti; altri pazienti entrano in coma dopo arresto cardiaco e altri ancora possono sperimentare situazioni che vanno dalla morte a una parziale o completa ripresa (Brooks et al., 2014). L'obiettivo del trattamento nei pazienti con arresto cardiaco è il mantenimento della circolazione spontanea, della perfusione d'organo e della normale funzione neurologica, in tempi rapidi, riducendo al minimo il danno e la disfunzione degli organi terminali (Brooks et al., 2014). Le compressioni manuali sono operatore dipendente, in quanto effettuare un massaggio cardiaco comporta un grande dispendio di energie e a lungo andare può diventare estenuante, fino a determinare una diminuzione della qualità delle compressioni manuali (Gyory et al., 2017). Le ragioni per cui spesso una RCP ha alti tassi di insuccesso sono molteplici, ma due delle più studiate riguardano la qualità delle compressioni manuali e la quantità di pause effettuate durante le manovre. Ogni qual volta che durante il ciclo di RCP vengono effettuate delle pause, il cuore e il cervello sono ipo-perfusi: è fondamentale pertanto ridurre al minimo le interruzioni (Gyory et al., 2017).

Sono stati pertanto sviluppati dispositivi meccanici di compressione toracica (LUCAS e Autopulse) per migliorare la RCP che garantiscono compressioni toraciche continue ed efficaci, che hanno mostrato maggiore pressione di perfusione d'organo, un aumento del flusso sanguigno al cervello e un valore più elevato di CO₂ rispetto alla RCP manuale (Rubertsson et al., 2014).

Materiali e metodi. È stata effettuata una ricerca sistematica utilizzando banche dati quali PUBMED, CINAHL, SCOPUS e WEB OF KNOWLEDGE. I criteri di inclusione stabiliti, affinché un articolo potesse essere utilizzato, era l'attinenza all'argomento.

Risultati e Discussione. Da tutti gli studi analizzati per l'elaborazione della revisione, si evince che non vi sono differenze di esiti neurologici (CPC = 1 o 2) nei pazienti sottoposti a compressioni toraciche manuali e a compressioni toraciche meccaniche.

Conclusioni. Dall'analisi degli articoli ricercati, nella pratica clinica la RCP con dispositivi meccanici può essere utilizzata senza complicazioni maggiori ma, essa non determina risultati migliori dal punto di vista neurologico rispetto alle compressioni manuali.

A87: L'IMPATTO DEL COVID-19 SUGLI ARRESTI CARDIACI EXTRA-OSPEDALIERI (OHCA): CAUSE ED OUTCOMES. REVISIONE DELLA LETTERATURA

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Introduzione. La malattia da sindrome respiratoria acuta grave (SARS-CoV-2) o meglio conosciuta come COVID-19, rappresenta la pandemia del secolo, con 33.206.004 casi confermati nel mondo e 999.239 morti dall'inizio della pandemia. All'interno di questi dati, vi sono le morti per arresto cardiaco extra-ospedaliero (OHCA), che ad oggi rappresentano la terza causa di morte in Europa. Un aumento dell'incidenza di OHCA è stato segnalato nella fase precoce dell'epidemia, ma manca una chiara dimostrazione della correlazione tra l'aumento dell'incidenza di OHCA e di COVID-19. Alcuni studi, hanno cercato quindi di verificare l'esistenza di un'associazione tra la differenza di OHCA rispetto al 2019 e la curva epidemica del COVID-19.

Obiettivo. Determinare l'impatto del COVID-19 sugli arresti cardiaci extraospedalieri, individuandone le cause e gli outcomes.

Materiali e metodi. È stata condotta una revisione della letteratura consultando banche dati, quali PubMed, Scopus ed Embase. Sono state utilizzati termini MeSH e key-word combinati tra loro attraverso gli operatori booleani. Sono stati fissati i seguenti criteri: tra i criteri di inclusione vi erano l'OHCA nel 2020 rispetto al 2019 e i soggetti con età >18 anni; tra i criteri di esclusione vi erano i soggetti con età <18 anni e l'arresto cardiaco in ambiente intra-ospedaliero.

Risultati e Discussione. Dagli studi analizzati si evince che il COVID-19 ha comportato un tasso di mortalità per OHCA che oscilla tra il 77-90%, percentuale che maggiormente viene attribuita ai casi sospetti o conclamati di COVID-19. Durante la pandemia i pazienti avevano una probabilità più alta (89,4% vs 74,8%; P <0,001) di non veder portate a termine le manovre di RCP rispetto al 2019, riflettendo così l'impossibilità di ottenere un ritorno alla circolazione spontanea (ROSC) o sostenuta dopo 20 minuti di RCP (41% in meno di probabilità di raggiungere il ROSC e il 47% in meno di probabilità di raggiungere ROSC sostenuto durante la pandemia), con conseguente diminuzione del 50% della sopravvivenza. Dagli studi inoltre, si evince che l'OHCA durante il periodo

COVID-19 è stato determinato da cause multifattoriale; sono state infatti individuate cause cardiache e non, meccanismi fisiopatologici e tossicità cardiaca da farmaco. Altre cause sono da attribuire ad un ritardo di chiamata dei soccorsi e/o alla non attivazione del Sistema di Emergenza, ad un ritardo nell'invio dei mezzi a causa della necessità di porre domande sullo stato di COVID-19 ed ai tempi di partenza e di arrivo del mezzo sul luogo di intervento.

Conclusioni. Durante la pandemia COVID-19, la mortalità per OHCA è aumentata significativamente, con una riduzione dei tassi di RCP da parte degli astanti e dei ritmi defibrillabili, insieme a una riduzione importante della sopravvivenza. L'aumento della mortalità per OHCA è da attribuire a cause multifattoriali. Per affrontare la pandemia, sono stati introdotti approcci innovativi che sfruttano le moderne tecnologie e che includono la telemedicina, la diffusione di materiale educativo sui social media, le app per smartphone per il monitoraggio dei casi e l'intelligenza artificiale.

A88: FARMACI CARDIOVASCOLARI IN UTIC: INCOMPATIBILITÀ CHIMICO-FISICA E DISPOSITIVO VENOSO APPROPRIATO

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Il tema dell'incompatibilità chimico-fisica dei farmaci somministrati per via endovenosa è tema sottovalutato da parte del personale sanitario, sia medico che infermieristico, durante la quotidiana pratica clinica. Questo accade nonostante esista un'ampia e fondata letteratura scientifica che ha portato a conoscenze chiare in merito. Tale campo è in continua scoperta sia per lo sviluppo di strumenti scientifici di indagine che per l'immissione di nuovi farmaci sul mercato.

Dobbiamo innanzitutto distinguere tra interazione e incompatibilità. Per interazione tra farmaci si intendono le reazioni, di qualsiasi genere (chimico-fisiche, farmacocinetiche, farmacodinamiche o di tossicità) dovute al contatto tra due o più sostanze chimiche, sia all'esterno che all'interno dell'organismo umano. Questa è materia inerente alla Farmacologia e richiede la competenza di ogni operatore sanitario nell'atto della cura e della somministrazione dei farmaci. Quindi l'incompatibilità chimico-fisica è parte integrante del tema più ampio dell'interazione.

Perché avviene l'interazione chimico-fisica? Quando avviene la reazione di incompatibilità? Come si manifesta? Quali le principali complicanze e danni potenziali da incompatibilità? Quali sono i fattori determinanti l'incompatibilità? Nelle Unità di Terapia Intensiva Coronarica accadono inconsapevolmente episodi di incompatibilità infusoriale dei farmaci a causa di tre motivazioni principali:

- la scarsa conoscenza delle incompatibilità chimico-fisiche
- la necessità di infondere contemporaneamente più farmaci per esigenze terapeutiche
- l'inadeguatezza di accessi venosi appropriati per la terapia articolata che riceve il paziente di UTIC.

La risposta alle precedenti domande e il contenimento degli effetti dannosi potenziali che l'incompatibilità chimico-fisica dei farmaci porta al patrimonio venoso e alla salute dei pazienti, il miglioramento dell'efficacia terapeutica, l'indicazione del dispositivo venoso più appropriato al farmaco utilizzato e la sua gestione migliore sono oggetto e scopo di questo contributo sintetico e essenziale, strumento utile per tutto il personale infermieristico e medico che opera in Cardiologia e Terapia Intensiva Coronarica.

A89: LA RETE DELL'INFARTO A LATINA

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Introduzione. Il soccorso extraospedaliero dell'infarto STEMI è una tipologia di soccorso tempo dipendente per una buona riuscita della riperfusione miocardica. La terapia riperfusiva è la componente principale dell'approccio terapeutico nell'infarto miocardico acuto con soprallivellamento del tratto ST (STEMI). Il trattamento riperfusivo più efficace è l'angioplastica primaria (pPCI) che viene considerata la terapia riperfusiva di scelta quando eseguita entro i 90 minuti e da operatori esperti, ma nonostante queste evidenze, la pPCI non è utilizzata in tutti i pazienti con STEMI. Le varie centrali operative in Italia stanno attuando diversi protocolli che mirano a ridurre i tempi di soccorso extraospedalieri, quindi i tempi di diagnosi e trasporto del paziente nel centro HUB più idoneo, e i tempi morti intraospedalieri rappresentati dai tempi di attesa al pronto soccorso e la diagnosi nello stesso. A tal proposito si sono sviluppate le reti Hub & Spoke, tale sistema, nella sua applicazione ottimale, prevede l'attivazione del 118 da parte del paziente, la teletrasmissione al centro Hub del tracciato ECG registrato sul territorio, l'accesso diretto del paziente in emodinamica senza transito nel Pronto Soccorso (PS).

Tale organizzazione rappresenta il requisito fondamentale per lo sviluppo di percorsi "veloci" e per il corretto funzionamento della rete.

Scopo. Lo studio è stato effettuato per valutare la performance della rete di emergenza-urgenza nell'ambito del trattamento dei pazienti con STEMI nella provincia di Latina

Materiale e metodi. Sono stati raccolti dati dal 2014 al 2019 per verificare il tasso di successi a Latina di questa organizzazione; i dati sono stati analizzati e messi a confronto con i risultati di tutta Italia.

Risultati. Latina è risultata una delle eccellenze italiane, un modello da perseguire, un sistema dove, grazie alla rete dell'infarto, le strutture ospedaliere sono perfettamente integrate con il Territorio della Provincia mediante il servizio del 118. Grazie alla realizzazione di questo progetto la ASL Latina è tra le più efficaci in Italia per la cura dell'infarto. Ad oggi L'Ospedale Santa Maria Goretti è primo in Italia nel settore, con 509 interventi di angioplastica primaria durante l'infarto acuto del miocardio, grazie alla rapidità di intervento ed un'equipe esperta.

Discussione. Lo studio condotto ha permesso di poter constatare l'efficacia dell'assistenza erogata nella rete di emergenza-urgenza per il trattamento dell'infarto miocardico acuto nella provincia di Latina. Si è verificato un buon funzionamento della rete dell'infarto miocardico per l'utilizzo della terapia ripercussiva angioplastica primaria (pPCI) grazie alla corretta applicazione di questa organizzazione che ha permesso di salvare numerose vite.

A90: IL RUOLO DELL'INFERMIERE NELLE DIVERSE FASI CHE COSTITUISCONO LA RETE DELL'INFARTO DEL MIOCARDIO

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Introduzione. L'infarto miocardico acuto è la prima causa di morte della popolazione adulta nei paesi europei con circa il 30% di decessi, oltre la metà dei quali prima dell'ospedalizzazione. La terapia ripercussiva è la componente principale dell'approccio terapeutico nell'infarto miocardico acuto con soprassollamento del tratto ST (STEMI). Il trattamento ripercussivo più efficace è l'angioplastica primaria (pPCI) che viene considerata la terapia ripercussiva di scelta quando eseguita entro i 90 minuti e da operatori esperti, ma nonostante queste evidenze, la pPCI non è utilizzata in tutti i pazienti con STEMI. Per ovviare a questo limite si sono sviluppate le reti Hub & Spoke, tale sistema, nella sua applicazione ottimale, prevede l'attivazione del 118 da parte del paziente, la teletrasmissione al centro Hub del tracciato ECG registrato sul territorio, l'accesso diretto del paziente in emodinamica senza transito nel Pronto Soccorso (PS). Tale organizzazione rappresenta il requisito fondamentale per lo sviluppo di percorsi "veloci" e per il corretto funzionamento della rete.

Scopo. Lo studio è stato effettuato per individuare il ruolo dell'infermiere nelle diverse fasi che risultano essere importanti per il raggiungimento del benessere del paziente.

Materiale e metodi. Sono state eseguite ricerche inerenti al ruolo dell'infermiere nelle diverse fasi che costituiscono questa "rete" soffermandoci sul corretto protocollo da seguire per far sì che sia erogata un'assistenza efficace. Sono state utilizzate anche dati professionali come PubMed, EBN.

Risultati. Lo studio ha permesso di dimostrare che il ruolo dell'infermiere, nelle diverse fasi, è sufficientemente codificato e messo in atto con successo, permettendo l'apporto efficace di tale figura professionale nella realizzazione della performance.

Discussione. Lo studio condotto ha permesso di poter verificare, grazie a procedure e protocolli, l'efficacia dell'assistenza erogata da un'equipe multiprofessionale per il trattamento dell'infarto miocardico acuto. Inoltre risulta evidente l'apporto, nel trattamento dell'infarto del miocardio, della figura dell'infermiere sin della chiamata al 118, allorché è necessario e fondamentale effettuare un corretto triage.

A91: STUDIO DELLA TC DEL TORACE ALL'INTERNO DI UN PERCORSO ROSSO

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Introduzione. Il 30 gennaio 2020 l'OMS ha dichiarato l'epidemia covid-19 un'emergenza globale che il 21 febbraio 2020 ha raggiunto e colpito l'Italia. La pandemia di coronavirus 2019 (COVID-19) sta mettendo a dura prova i sistemi sanitari di tutto il mondo, mettendo sotto stress la maggior parte degli ospedali. Poiché la polmonite virale da coronavirus-2 (SARS-CoV-2) è trasmessa da persona a persona per via aerea, tutti gli operatori di imaging, che sono in stretto contatto con i pazienti, sono esposti a un rischio elevato di contagio. Anche tutte le apparecchiature mediche sono potenziali veicoli di contagio. Per ridurre al minimo il rischio di un'ulteriore diffusione della malattia è, infatti, molto importante che ogni test di imaging cardiaco sia eseguito in modo appropriato. Anche nei pazienti senza sintomi o segni di COVID-19. Nel nostro lavoro prendiamo in esame il percorso in sicurezza dell'indagine diagnostica tac per lo studio del torace. Con la raccomandazione che tutte le indagini diagnostiche devono essere eseguite in modo sicuro, per ridurre al minimo il rischio di esposizione a pazienti e personale.

Materiale e metodi. Nella ricerca di correlazione dati abbiamo preso di riferimento il mese di marzo. Sono stati inseriti al Monzino due percorsi distinti, dedicando uno scanner ai pazienti asintomatici e l'altro ai pazienti con sospetta o confermata infezione da COVID-19. La differenziazione del percorso del paziente all'interno dell'attività ospedaliera segue una diagnosi precoce dei soggetti portatori del virus SARS-CoV-2 tramite l'esecuzione di un tampone orofaringeo e un esame di imaging radiologico. Al CCM ci siamo occupati di una differenziazione del percorso già dai primi giorni di marzo al fine di rispondere con

tempestività all'emergenza insorgente. Sono stati svolti un numero complessivo di 422 TC, così distinte in 210 eseguite nella TC "verde" e 212 nella CT "rosso". Di queste, 76 di quelle svolte nella tac del percorso dedicato ai pazienti sospetti sono poi risultate positive al virus SARS-CoV-2. Di questi 76 pazienti presi in considerazione per la CT che evidenziava il caratteristico "ground glass" circa il 10% è risultato negativo al tampone. L'età media dei pazienti in esame è pari a 65anni. Il 44% (33 pazienti) di sesso femminile e il 56% (42 pazienti) maschile. Nella tac del percorso sospetto è stato da noi introdotto un protocollo con kV e mA e filtri ottimizzati volto evidenziare le caratteristiche della polmonite interstiziale da Covid-19.

Obiettivi. La differenziazione dei percorsi dei pazienti caso non sospetto e caso sospetto ha permesso di canalizzare questi ultimi nella TC del percorso rosso. Andando ad adottare, all'interno di tale percorso, un protocollo con parametri e tecnica di esecuzione ottimizzati ad hoc nel rispetto del principio di giustificazione. La manifestazione clinica nell'immagine radiologica di tutti i pazienti è stata poi correlata con gli esiti dei tamponi.

A92: EFFICACIA DEL TELEMONITORAGGIO DELLA PRESSIONE ARTERIOSA

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Introduzione. Nonostante il telemonitoraggio della pressione arteriosa (TMPA) abbia alcuni vantaggi rispetto ai tradizionali metodi di monitoraggio, vi sono dubbi sui suoi benefici nella pratica clinica.

Obiettivo. Valutare l'efficacia del TMPA sui valori pressori rispetto al monitoraggio effettuato presso lo studio medico.

Metodi. Nel luglio 2017 è stata implementata una strategia di ricerca sui seguenti database: The Cochrane Library, Medline, Embase, CINAHL. I record restituiti sono stati analizzati e quelli che rispettavano i criteri di inclusione sono stati reperiti in versione integrale. Sono state incluse solo revisioni sistematiche con o senza meta-analisi di RCT che confrontassero il TMPA con il monitoraggio effettuato presso lo studio medico. Per la valutazione di qualità è stata impiegata la AMSTAR checklist; per il confronto fra meta-analisi sono stati valutati i risultati del test di inconsistenza I².

Risultati. Sette revisioni sistematiche hanno rispettato i criteri di inclusione, cinque disponibili in full text, quattro con meta-analisi. Il test I² ha presentato valori fra 40 e 85% (eterogeneità fra RCT moderata-elevata). Il TMPA, a confronto con il monitoraggio effettuato presso lo studio medico, è associato ad una modesta ma statisticamente significativa riduzione della pressione arteriosa sistolica (-3.90/-5.64 mmHg) e diastolica (-1.99/-2.68 mmHg).

Discussione. L'effetto ridotto del TMPA produce un modesto beneficio nella pratica clinica. I potenziali vantaggi dipendono dall'interesse dei soggetti verso l'intervento, dalle caratteristiche del dispositivo utilizzato e dei programmi di TMPA, dal rapporto costo-efficacia.

Conclusioni. Il TMPA è più efficace per ridurre la pressione sistolica e diastolica rispetto al monitoraggio presso lo studio medico ma la rilevanza clinica del beneficio è modesta.

A93: PROGETTO "HEARTS-IN-DYADS": VALUTAZIONE DEL SELF-CARE NELLA DIADE DEI PAZIENTI AFFETTI DA CORONAROPATIA ISCHEMICA

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Introduzione. Le indagini scientifiche riguardanti il Self Care (SC) dei pazienti cardiologici italiani si sono focalizzate maggiormente nell'inclusione di individui con diagnosi di insufficienza cardiaca congestizia. In tale popolazione è stato descritto un basso livello di SC e sono state registrate le caratteristiche, socio-demografiche e cliniche, determinanti lo scarso SC. I recenti studi riguardanti il SC dei pazienti italiani hanno coinvolto la cosiddetta diade cardiovascolare (CV), composta da paziente CV e dal proprio caregiver, delineando il SC come un fenomeno diadico, dove, il SC del paziente, ed il contributo al SC del caregiver, sono relazionati in termini di predittori ed esiti. Il questionario Self care of Coronary Heart Disease Inventory (SC-CHDI) è riconosciuto come strumento designato all'accertamento dei livelli di SC nei pazienti con coronaropatia ischemica (CHD). Purtroppo, il SC-CHDI non è ancora stato sottoposto alla validazione sulla popolazione italiana, d'altro canto, in Letteratura non sono disponibili degli strumenti atti alla misurazione del contributo dei caregivers al SC dei pazienti con CHD.

Scopo. L'obiettivo primario del presente studio sarà quello di: a) validare il questionario SC-CHDI nella versione italiana. Gli obiettivi secondari saranno: b) costruire e validare il questionario Caregiver Contribution to Self Care of Coronary Heart Disease Inventory (CC-SC-CHDI); c) descrivere le variabili, sociodemografiche e cliniche, associate al SC dei pazienti ed al contributo dei caregivers al SC.

Metodi. *Disegno dello studio.* Studio osservazionale-correlazionale di tipologia longitudinale e multicentrica, non profit. *Contesto, arruolamento e follow-up, dimensione campionaria.* Questo studio sarà svolto nel contesto di diversi Centri Ospedalieri. L'arruolamento (TO) dei pazienti avverrà nel corso del loro ricovero nel reparto di Cardiologia. Successivamente, gli stessi soggetti inclusi nello studio saranno ricontattati telefonicamente per svolgere i due follow-up programmati, rispettivamente a tre (T1) e sei (T2) mesi dopo l'arruolamento. Se esistenti, verranno arruolati anche i caregivers informali principali dei pazienti. Si prevede di includere 310 pazienti con i potenziali caregivers. *Variabili e strumenti di raccolta dati.* Verranno registrate le caratteristiche sociodemografiche e cliniche delle diadi partecipanti. Gli strumenti che verranno impiegati saranno i seguenti: SC-CHDI, Self Care Confidence of Chronic Illness Scale (Versione Paziente e Caregiver), Generalized Anxiety Disorder Screener, 9-item Patient Health Questionnaire, Mutuality Scale (Versione Paziente e Caregiver), Dyadic care types scale (Versione Paziente e Caregiver), Caregiver Preparedness Scale, CC-SC-CHDI. *Durata dello studio.* La raccolta dati partirà da settembre 2020 previo parere positivo dei Comitati Scientifici ed Etici dei Centri aderenti allo studio.

Implicazioni dei risultati di studio. A livello clinico, i risultati raggiungibili potrebbero ricavare gli strumenti utili alla valutazione dei pazienti affetti da CHD e dei loro caregivers. Per di più, tali dati rappresenterebbero un orientamento sui possibili predittori di scarso SC, o di contributo dei caregivers ad esso.

A94: VIVERE CON LO SCOMPENSO CARDIACO DURANTE LA PANDEMIA DI COVID-19: UNA INTERPRETATIVE PHENOMENOLOGICAL ANALYSIS

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Introduzione. La pandemia di COVID-19 rappresenta un'importante sfida per i servizi sanitari, chiamati a modificare la propria organizzazione per garantire l'accesso alle cure e limitare la diffusione della malattia. Questi cambiamenti hanno avuto un impatto considerevole non solo sui pazienti con COVID-19 ma anche su coloro che convivono con patologie croniche, come lo scompenso cardiaco. Nonostante ciò, l'impatto della pandemia sulla vita di questi individui non è ancora stato indagato.

Obiettivo. Esplorare il vissuto delle persone con scompenso cardiaco durante la pandemia di COVID-19.

Metodi. È stata condotta un'indagine qualitativa con la metodologia della interpretative phenomenological analysis. Un campione propositivo di persone con scompenso cardiaco ha partecipato a video-interviste in profondità semi-strutturate. L'analisi è stata effettuata in accordo con la metodologia della interpretative phenomenological analysis, e per assicurare il rigore sono stati utilizzati la triangolazione, il diario riflessivo, e il member checking.

Risultati. 14 partecipanti (12 uomini e 2 donne, con età mediana 68 anni) hanno preso parte allo studio. Sono stati individuati 3 temi in grado di descrivere il vissuto delle persone con scompenso cardiaco durante la pandemia di COVID-19: "Vulnerabilità", "Essere in bilico", e "Strategie di coping". I partecipanti si sono sentiti particolarmente vulnerabili al nuovo coronavirus, sperimentando sentimenti di angoscia e paura. I cambiamenti nell'assetto organizzativo dei servizi sanitari hanno determinato un senso di incertezza che si è tradotto nel sentirsi "in bilico", senza punti di riferimento. Tuttavia, nonostante considerevoli difficoltà, i partecipanti sono riusciti a fronteggiare la situazione attuando specifiche strategie di coping.

Conclusioni. La pandemia di COVID-19 ha influenzato significativamente la vita delle persone con scompenso cardiaco, e i risultati dello studio mettono in luce le considerevoli difficoltà da loro sperimentate, evidenziando la necessità di interventi mirati che potrebbero essere sviluppati sulla base delle strategie di coping emerse.

A95: PREVENZIONE DELLA NEFROPATIA DA MEZZO DI CONTRASTO IN PAZIENTI SOTTOPOSTI A CORONAROGRAFIA: IL RENALGUARD

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(a) OSPEDALE SANTA MARIA GORETTI DI LATINA U.O.C. UTIC-EMODINAMICA
La nefropatia da mezzo di contrasto (CIN) è tra le maggiori cause di insufficienza renale acuta, oltre ad essere una nota complicanza delle procedure interventistiche coronariche, le quali, a loro volta, aumentano il rischio di sviluppare questa patologia fino al 50%; essa può influire

negativamente sull'outcome clinico, inoltre può determinare un allungamento del periodo di degenza con conseguente incremento dei costi. La nefropatia da mezzo di contrasto si manifesta con un aumento della creatinina sierica del 25% rispetto ai valori basali ed un aumento della stessa >0,5 mg/dl entro le prime 48/72 ore dopo l'esposizione del paziente al mezzo di contrasto. Numerose strategie farmacologiche sono state valutate nel tentativo di ridurre il rischio di CIN, soprattutto in pazienti con insufficienza renale cronica ma, a parte una terapia idropinica e l'impiego di agenti antiossidanti, ben poche di queste terapie hanno mostrato un chiaro e consistente beneficio.

Il Renalguard è un nuovo sistema di bilanciamento dei fluidi che sta riscuotendo risultati positivi nel trattamento dei pazienti a rischio CIN. Questo device è in grado di controllare il flusso idrico in entrata e in uscita attraverso un circuito chiuso che somministra soluzione fisiologica per via endovenosa e drena urina attraverso un catetere Foley, permettendo così un controllo e un bilanciamento idrico istantaneo, monitorizzando altresì la capacità glomerulare di produrre urina prima, durante e dopo la procedura con mezzo di contrasto, di fatto prevenendo il rischio CIN.

Presso la U.O. di Cardiologia e UTIC - Emodinamica dell'Ospedale Santa Maria Goretti di Latina, il personale infermieristico ha messo a confronto due campioni di pazienti con un quadro d'insufficienza renale moderata o severa sottoposti a coronarografia, trattati con due tipologie di protocolli:

A. Protocollo che prevede idratazione con sodio bicarbonato, soluzione fisiologica e N-acetilcisteina.

B. Protocollo che prevede l'impiego del sistema Renalguard su pazienti sottoposti a PCI.

Il controllo della creatinina e dell'azotemia eseguito dopo 24 e 72 ore ha evidenziato una maggiore efficacia del trattamento eseguito con Renalguard; l'incidenza di nefropatia da mezzo di contrasto passa dal 18% evidenziato dal trattamento tradizionale (protocollo A) al 5% riscontrato sui pazienti sottoposti a trattamento con Renalguard (protocollo B). Un ulteriore vantaggio dell'impiego del Renalguard è la gestione autonoma da parte del personale infermieristico dei pazienti a rischio di nefropatia da mezzo di contrasto. Attraverso l'utilizzo di un protocollo standard, l'infermiere attua la connessione e l'avviamento del device e, in base alle informazioni cliniche da questo ricavate, procederà alla somministrazione di furosemide per via endovenosa, stimolando in questo modo la diuresi con lo scopo di eliminare il mezzo di contrasto con più efficacia.

Alla luce dello studio effettuato si può concludere, quindi, che il sistema Renalguard, rispetto ai protocolli tradizionali, presenta notevoli vantaggi sia in termini di miglioramento della funzione renale che di gestione del paziente a rischio CIN grazie all'utilizzo di protocolli standardizzati che l'impiego del device prevede, riducendo così in alcuni casi anche i tempi di degenza grazie al repentino rientro nei range dei valori di creatinina.

A96: RAGIONAMENTO CLINICO E APPRENDIMENTO COOPERATIVO: UN'ESPERIENZA DI TIROCINIO VIRTUALE

Simone Zamarian (a), Barbara Banchio (b)
(a) CITTÀ DELLA SALUTE E DELLA SCIENZA DI TORINO; (b) CORSO DI LAUREA IN INFERMIERISTICA - UNIVERSITÀ DEGLI STUDI DI TORINO

Introduzione. L'attuale spaccato sanitario richiede professionisti infermieri in grado di saper rispondere e pianificare l'assistenza rispetto ai bisogni articolati e complessi. Per fare ciò l'infermiere deve saper applicare correttamente il ragionamento clinico il quale deve essere insegnato già durante la formazione di base, la quale si caratterizza però per un'eterogeneità sia tra gli insegnamenti che tra gli ambienti formativi.

Obiettivo. Al fine di comprendere come ottimizzare l'insegnamento del ragionamento clinico, è stata realizzata una ricerca avente come obiettivo quello di descrivere le modalità di ragionamento clinico e gli elementi collaborativi ed interazionali in gruppi di lavoro di studenti.

Metodi. La ricerca si è svolta parallelamente allo svolgimento di un percorso formativo e-learning per gli studenti infermieri del II° e III° anno finalizzato all'acquisizione di conoscenze e competenze da spendere nell'assistenza a pazienti con Sindrome Coronarica Acuta (SCA).

È stato seguito un approccio esplorativo in profondità per lo studio qualitativo del fenomeno in analisi, ricercando e descrivendo gli elementi di ragionamento clinico, le connessioni mentali (intese come i collegamenti clinico-assistenziali) effettuate e le modalità-caratteristiche-dinamiche di gruppo. Rispettivamente ai primi due elementi, sono stati revisionati ed esaminati gli elaborati di pianificazione attraverso indicatori costruiti ad hoc e associati ai dati provenienti dalle osservazioni dei momenti di discussione-confronto, svolti durante i momenti di didattica e-learning. Rispettivamente all'elemento relativo alle dinamiche di gruppo, alle interazioni e alle modalità operative dei gruppi di lavoro è stata svolta un'osservazione neutrale e trasparente associata alla raccolta di note di campo.

Risultati. Hanno partecipato in totale 72 studenti e sono state analizzate 6 pianificazioni assistenziali infermieristiche. Tutti i gruppi di lavoro hanno identificato in modo corretto molti degli aspetti correlati all'assistenza dei pazienti con SCA, svolgendo ragionamenti e correlazioni mentali idonee. Alcune delle aree individuate, rispetto al quadro clinico, non sono state esplorate, ricollegate o connesse correttamente. A livello di ragionamento clinico sul piano gruppale è emersa come modalità comune quella analitica (caratterizzata da un andamento ste-by-step), ma un minor "tempo mentale" in termini di ragionamento e brain-storming mentale nei

gruppi del terzo anno. Le conoscenze teoriche ed esperienziali hanno svolto un ruolo cruciale nello sviluppo dei ragionamenti e delle connessioni mentali, in un quadro di circolazione della conoscenza e andamento addizionale del sapere nel confronto tra pari. L'impianto cooperativo tra studenti si è dimostrato essere elemento cardine sia sotto il punto di vista operativo dei gruppi di lavoro sia elemento favorente l'apprendimento, predisponendo un setting *cooperative learning based*. **Conclusioni.** La ricerca svolta ha permesso di conoscere come ragiona lo studente infermiere qualora si trovi di fronte ad un caso clinico. La gestione puntuale degli aspetti cognitivi, meta-cognitivi e interazionali interconnessi al ragionamento clinico, diventano fondamentali per l'azione tutoriale atta allo sviluppo di tale competenza. Ulteriori studi, svolti su outcomes e setting differenti, permetterebbero l'approfondimento del fenomeno in analisi. Una conoscenza approfondita e ad ampio raggio di tali aspetti si connoterebbe strategica ai fini della pianificazione e programmazione didattica nell'ottica del miglioramento della formazione al ragionamento clinico.

A97: UTILITÀ DEL MONITORAGGIO REMOTO DEI DEVICE IMPIANTABILI DURANTE PANDEMIA COVID-19

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(a) U.O. CARDIOLOGIA - OSPEDALE G. DA SALICETO AUSL PIACENZA

Background. Durante la pandemia COVID-19, molti degli ospedali italiani hanno sospeso tutte le attività elettive non urgenti, al fine di ridurre la diffusione del virus. Anche nella nostra U.O. di Cardiologia tutte le procedure interventistiche e le attività ambulatoriali elettive sono state annullate provvisoriamente. In particolare, l'attività di controllo ambulatoriale dei device cardiologici impiantabili è stata sospesa, solo per gli esami differibili, mentre quella di monitoraggio remoto è stata mantenuta e in alcuni casi selezionati implementata. È noto che il monitoraggio remoto (MR) sia sicuro nel controllo a distanza dell'integrità del sistema, nel rilevare precocemente aritmie cardiache e indici clinici attraverso l'invio di alerts, riducendo il numero di follow-up ambulatoriali oltre che, numero e durata delle ospedalizzazioni.

Metodi. Nel nostro studio abbiamo considerato tutti i pazienti (pz) con dispositivo Implantable Cardiac Defibrillators (ICD) seguiti presso il nostro ambulatorio di Elettrostimolazione che avevano già in programma un follow-up ambulatoriale nel periodo compreso fra il 23 Febbraio 2020 e il 18 Maggio 2020.

Risultati. I controlli in office pianificati coinvolgevano 216 pz, di cui l'85% era seguito anche con MR; dopo aver provveduto a rinviare l'appuntamento, il personale tecnico dedicato ha programmato per ognuno di loro una trasmissione di controllo. In totale sono pervenute 450 trasmissioni, in parte programmate e in parte con allarmi. Di quelle con alert, 7 erano per ERI (elective replacement indicator) ed è stato necessario programmare la sostituzione del device; 2 erano per rumore, in cui abbiamo programmato l'impianto di un nuovo elettrocattetero ventricolare ed infine 12 alert per aritmia ventricolare trattata. È stato indispensabile effettuare il controllo ambulatoriale nei pz sprovvisti di MR secondo i protocolli di sicurezza stabiliti a livello aziendale, 3 dei quali hanno dovuto eseguire il controllo in office ogni 2 mesi, a uno dei quali è stata programmata la sostituzione. Durante la pandemia abbiamo adottato una nuova procedura per l'accesso ambulatoriale: il paziente veniva contattato telefonicamente entro 24/48h dall'appuntamento e veniva eseguito il triage telefonico: se il triage era negativo, al paziente era confermato l'appuntamento. Al momento dell'accesso, attraverso check point posti all'ingresso dell'ospedale, veniva misurata la temperatura e ripetuto il questionario. Per garantire una maggiore sicurezza, sono stati aumentati i tempi fra un appuntamento e il seguente, sia per offrire una sanificazione adeguata, sia per ridurre il numero di persone in sala d'attesa.

Conclusioni. Il monitoraggio remoto dei device impiantabili, per tutto il periodo dell'emergenza COVID-19, è stato estremamente utile durante tutte le fasi della pandemia, sia per ridurre i controlli ambulatoriali, in una fase in cui l'esigenza della riorganizzazione ambulatoriale mostrava numerose criticità, sia per l'identificazione dei problemi tecnici e clinici.

ATEROTROMBOSI

A98: INTERPLAY BETWEEN COVID-19, POLLUTION, AND WEATHER FEATURES ON CHANGES IN THE INCIDENCE OF ACUTE CORONARY SYNDROMES IN EARLY 2020

Simone Ferrito (a), Achille Gasparone (b), Alessandro Danesi (c), Fabio Ferranti (f), Enrica Mariano (e), Francesco Rotolo (g), Carmine Musto (h), Alessandro Di Giosa (i), Giada Marchegiani (i), Giuseppe Biondi Zoccai (d), Francesco Versaci (a)

(a) OSPEDALE SANTA MARIA GORETTI; (b) OSPEDALE SANTEUGENIO; (c) OSPEDALE SANTO SPIRITO; (d) SAPIENZA UNIVERSITÀ DI ROMA; (e) UNIVERSITÀ TOR VERGATA; (f) OSPEDALE G. B. GRASSI; (g) OSPEDALE SAN PIETRO-FATEBENEFRATELLI; (h) OSPEDALE SAN CAMILLO; (i) ARPA LAZIO

Background. Coronavirus disease 2019 (COVID-19) has caused an unprecedented change in the apparent epidemiology of acute coronary

syndromes (ACS). However, the interplay between this disease, changes in pollution, climate, and aversion to activation of emergency medical services represents a challenging conundrum. We aimed at appraising the impact of COVID-19, weather, and environment features on the occurrence of ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) in a large Italian region and metropolitan area.

Methods. Italy was hit early on by COVID-19, such that state of emergency was declared on January 31, 2020, and national lockdown implemented on March 9, 2020, mainly because the accrual of cases in Northern Italy. In order to appraise the independent contribution on changes in STEMI and NSTEMI daily rates of COVID-19, climate and pollution, we collected data on these clinical events from tertiary care cardiovascular centers in the Lazio region and Rome metropolitan area. Multilevel Poisson modeling was used to appraise unadjusted and adjusted effect estimates for the daily incidence of STEMI and NSTEMI.

Results. The sample included 1448 STEMI and 2040 NSTEMI, with a total of 2882 PCI spanning 6 months. Significant reductions in STEMI and NSTEMI were evident already in early February 2020 (all $p < 0.05$), concomitantly with COVID-19 spread and institution of national countermeasures. Changes in STEMI and NSTEMI were inversely associated with daily COVID-19 tests, cases, and/or death ($p < 0.05$). In addition, STEMI and NSTEMI incidences were associated with daily NO_2 , PM_{10} , and O_3 concentrations, as well as temperature ($p < 0.05$). Multi-stage and multiply adjusted models highlighted that reductions in STEMI were significantly associated with COVID-19 data ($p < 0.001$), whereas changes in NSTEMI were significantly associated with both NO_2 and COVID-19 data (both $p < 0.001$).

Conclusions. Reductions in STEMI and NSTEMI in the COVID-19 pandemic may depend on different concomitant epidemiologic and pathophysiologic mechanisms. In particular, recent changes in STEMI may depend on COVID-19 scare, leading to excess all-cause mortality, or effective reduced incidence, whereas reductions in NSTEMI may also be due to beneficial reductions in NO_2 emissions in the lockdown phase.

A99: MOTHER AND DAUGHTER: TWO SIDES OF THE SAME COIN

Francesco Ceravolo (a), Antonella Romaniello (b), Camillo Autore (b), Massimo Volpe (b)

(a) UNIVERSITÀ SAPIENZA DI ROMA; (b) AZIENDA OSPEDALIERA UNIVERSITARIA SANT'ANDREA

Most of the coronary events are due to atherosclerosis and its complications, though about the 20% of coronary heart disease in young adults is related to other pathologies such as coronary abnormalities, autoimmune diseases and connective tissue disorders. The last two of these conditions are also associated to an increased risk of thromboembolic events.

We report a case of a 41-year-old woman, with two unexplained miscarriages and no cardiovascular risk factors, who had an ST-elevation myocardial infarction complicated by several episodes of ventricular fibrillations, and of her daughter, a 20-year-old-woman, previously healthy, who had, a few days later her mother's admission, a massive pulmonary embolism with syncope at presentation. Laboratory tests demonstrated the presence of anticardiolipins antibodies of IgG isotype in both patients' serum.

With this case report we want to focus on the importance of considering acute myocardial infarction caused by an unexplained intracoronary thrombosis or pulmonary embolism such as first manifestations of prothrombotic states, especially in young patients. Early diagnosis of these conditions, in fact, is crucial because it might entail therapeutic implications not only on the short-term (i.e., rapid diagnosis and treatment of catastrophic antiphospholipid syndrome) but also on the long-term patient management.

A100: VITAMIN D INHIBITS TISSUE FACTOR IN IL-6 TREATED ENDOTHELIAL CELLS BY MODULATING NFKB PATHWAY

Mariarosaria Morello (a), Grazia Pellegrino (a), Stefano Conte (b), Laura Marra (d), Andrea Morello (c), Paolo Golino (b), Plinio Cirillo (a), Giovanni Cimmino (a)

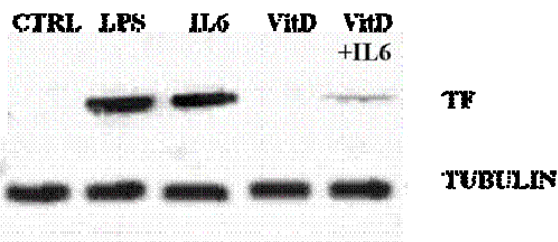
(a) DEPARTMENT OF ADVANCED BIOMEDICAL SCIENCES, UNIVERSITY OF NAPLES FEDERICO II, NAPLES; (b) DEPARTMENT OF TRANSLATIONAL MEDICAL SCIENCES, UNIVERSITY OF CAMPANIA LUIGI VANVITELLI, NAPLES; (c) BIOCHEMICAL LABORATORY, CARDARELLI HOSPITAL, CAMPOBASSO; (d) RESEARCH DEPARTMENT, CELLULAR BIOLOGY AND BIOTHERAPY UNIT, PASCALE FOUNDATION, NAPLES

Background. Inflammation plays an important role in the pathophysiology of athero-thrombosis. Many evidences have clearly indicated that endothelial cells stimulated with inflammatory mediators show an athero-thrombotic phenotype, since they express adhesion molecules and tissue factor (TF) on their surface. IL-6 seems to have a central role in modulating these phenomena. Patients with elevated plasma levels of IL-6 have a higher risk to develop acute cardiovascular events (ACS). Epidemiologic studies have demonstrated that Vitamin D (VitD) deficiency is associated with the increased risk of ACS. Here, we have investigated whether VitD might modulate TF expression in IL-6 treated endothelial cells.

Methods. HUVEC cultivated in medium enriched with VitD (10 nM) were stimulated with IL-6 (0,5ng/mL). TF gene (RT-PCR), protein (western blot), surface expression (FACS) and procoagulant activity (FXa generation assay) were measured. NF-κB translocation was also investigated.

Results. VitD significantly reduced TF gene as well protein expression and procoagulant activity in oxLDL-treated HUVEC. These effects were associated with VitD modulation of NF-κB pathway.

Conclusions. This study, although in vitro, shows that VitD prevents the pro-thrombotic effects of IL-6 on endothelial cells by inhibiting TF expression. Thus, we might speculate that this is one of the mechanisms by which VitD exerts its protective cardiovascular effects.



A101: ANTICOAGULATION IN ATRIAL FIBRILLATION: NOT ONLY THE RISK OF STROKE. A CASE REPORT

Gaetana Ferro (a), Neril Kola (a), Agnese Bevilacqua (a), Lorenzo Iuliano (a), Claudia Vicidomini (a), Luigi Tedesco (a)
(a) UO CARDIOLOGIA UTIC, OSPEDALE "SANTA MARIA DELLA SPERANZA", BATTIPAGLIA (SA)

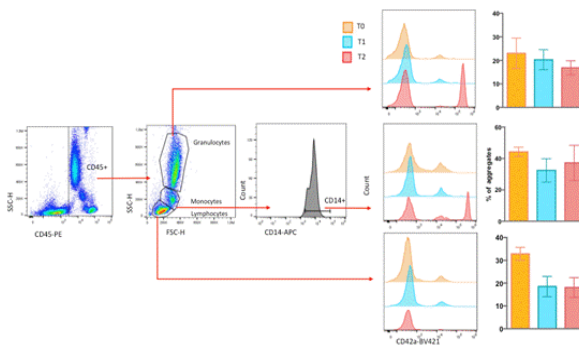
A.C., a 74-year-old female patient with history of hypertension in treatment with ramipril 10 mg/die, reports dyspnea for some time, exacerbated by mild physical exertion. No palpitation, chest pain or syncope is reported. An electrocardiogram is immediately performed which shows atrial fibrillation, not reported in her clinical history and not present in an electrocardiogram of two months before, brought into view by the patient. When questioned again, the patient reports that she has never experienced palpitations in the previous two months or in the past. The only significant anamnestic data is a recurrent abdominal pain, for which she had recently performed abdominal ultrasound, gastroscopy and colonoscopy which had not highlighted any significant pathologies.

Considering the poor tolerance to arrhythmia despite a good heart rate control with b-blockers, an electrical cardioversion of atrial fibrillation is indicated and therefore a transesophageal echocardiogram is performed to search for any cardiac thrombotic formation. The exam highlights a large jelly-like thrombus at the level of the left appendage. The patient starts an anticoagulant therapy with NOAC for 3 weeks. In parallel, the presence of the thrombus associated to abdominal pain suggests a likely ischemic origin of the symptoms so the patient undergoes an abdominal angio-CT scan that, surprisingly, does not highlights a thrombotic disease of the mesenteric arteries. After the treatment with oral anticoagulant the patient undergoes an electrical cardioversion of AF which is effective. Questioned before the cardioversion, she reports a marked improvement in abdominal pain symptoms since the start of NAO therapy and, 1 month later she reports the complete resolution of the abdominal symptoms. This outcome associated to the lack of evidence about a mesenteric ischemia at the CT scan made us postulate the responsibility for microemboli, originating from left appendage and reaching intestinal smallest vessels in determining the symptomatology without CT detectable lesions. Atrial fibrillation is the most frequent sustained arrhythmia with a general prevalence of 5-1%. The prevalence is relatively low among young people, but increases with age reaching 8.8% among 80 to 89 years old. This clinical case, in its simplicity, wants to highlight the need to consider in addition to the well-known stroke risk linked to this arrhythmia, also the not negligible effect that systemic embolism may have on other organs and systems. For that reason it is mandatory to have a multidisciplinary approach to the most common pathologies, especially in elderly population.

A102: PHOSPHORYLCHOLINE-COATED CIRCUIT PREVENTS THE FORMATION OF PLATELET-LEUKOCYTE AGGREGATES

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Extracorporeal circulation (ECC) involves the contact of blood cells with artificial surfaces, which could lead to adverse effects, such as hemostasis disorders. During ECC, platelets (PLT) and leukocytes can be activated causing their aggregation. This study aimed to evaluate the thrombogenic potential associated with a blood-recirculating device by identifying the changes over time of the platelet-leukocytes aggregates.

Thus, we quantified the percentage of PLT-granulocytes (P-G), -monocytes (P-M), and -lymphocytes (P-L) aggregates during procedures that required a phosphorylcholine-coated (PC) mechanical pump for ECC. Our preliminary analyses are referred to three patients (two females and one male) who underwent a procedure of aortic valve replacement. We collected 1 mL of arterial blood at three times directly from the mechanical pump (INSPIRE 6F, Livanova, Sorin Group Italia Srl, Italy): before initiating the extracorporeal perfusion (T0, before the heparin injection), after 70±23 min (T1), and at the end of ECC (T2; 138±81 min). Two hundred uL were stained immediately with CD45-PE, CD14-APC, CD42a-BV421 (from R&D System, BioLegend, and Beckman Coulter, respectively), washed with BD FACS Lysing Solution and, then, acquired with an Attune NxT (Thermo Fisher Scientific). Granulocytes, monocytes, and lymphocytes were identified among CD45+ cells, based on their physical parameters. Monocytes were further identified as CD14+ cells. Among the three leukocytes populations, the percentage of aggregates was identified using the PLT marker CD42a. The Figure below shows the representative dot plots for the gating strategy and the representative histograms of the aggregate count at different times of collection. As reported on the right side of the Figure, the percentage of aggregates remains similar during the surgical procedures (p<0.05; Two-way ANOVA for repeated measures). Our study confirms that a PC-coated circuit not only improves PLT preservation (Schulze et al. J Card Surg 2009) but also prevents aggregates formation.



A103: A CURIOUS CASE OF MASSIVE RIGHT HEART THROMBOSIS

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Background. Intraventricular masses are a relatively rare condition ranging from asymptomatic to potentially life-threatening situations.

Case summary. Herein, we report a case of a 49 years old woman under investigation for a massive right ventricular mass who underwent complete investigation for possible differential diagnosis, in the suspect of right ventricular tumour. Surgical removal of the mass showed a large area of stratified thrombosis with an underlying area of endocardial fibrosis. The patient has been then discharged in good clinical condition and with lifetime oral anticoagulation.

Discussion. Massive right ventricular (RV) thrombosis is a rare yet potentially fatal condition. Invasive management is preferable and lifetime anticoagulation is required to reduce possible downstream thrombotic complications.

A104: ACT E NUOVI ANTICOAGULANTI ORALI

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L'activated clotting time (ACT) è il test di monitoraggio della coagulazione di scelta durante il periodo periprocedurale poiché che presenta numerosi vantaggi.

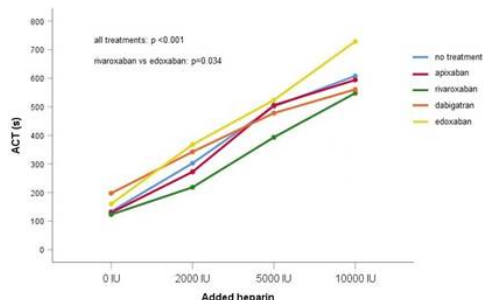
Una recente meta-analisi ha evidenziato come non esista ancora una chiara relazione tra l'incidenza di eventi cardiovascolari o sanguinamenti maggiori e i valori di ACT; inoltre non esiste un valore target dell'ACT universalmente riconosciuto come efficace in termini di prevenzione degli eventi tromboembolici e sicuro in termini di rischio di sanguinamento.

In un recente studio si è visto che i pazienti che assumevano dabigatran o apixaban era necessario tempo maggiore per il raggiungimento di un ACT superiore a 300 secondi rispetto ai gruppi che assumevano rivaroxaban o warfarin; inoltre si è riscontrata una percentuale inferiore di pazienti con ACT superiore a 300 s dopo la somministrazione del primo bolo di eparina nei primi due gruppi rispetto agli altri due.

In un altro studio in pazienti che dovevano effettuare ablazione per fibrillazione atriale il gruppo che assumeva edoxaban presentava un ACT inferiore al baseline rispetto al gruppo di controllo che assumeva warfarin

e inoltre era richiesta una dose maggiore di eparina in bolo per raggiungere lo stesso valore dell'ACT a 15 minuti.

Dalla Letteratura emerge quindi come i NAO interferiscano in maniera non bene definita con l'attività anticoagulante dell'eparina non frazionata. Lo scopo dello studio è valutare la variazione dei valori di ACT rispetto al basale, aggiungendo diversi dosaggi di eparina non frazionata (2000 UI, 5000 UI, 10,000 UI) in pazienti che assumono i quattro diversi tipi di NAO e in un gruppo di controllo che non assume nessun anticoagulante. Dai risultati si evidenzia l'esistenza di una differenza statisticamente significativa nell'aumento dei valori di ACT in presenza di concentrazioni crescenti di eparina tra i vari tipi di NAO; in particolare nei pazienti che assumono rivaroxaban l'aumento dei valori di ACT è meno importante rispetto ai pazienti che assumono edoxaban; inoltre i pazienti che assumono apixaban o dabigatran presentano variazioni di ACT più simili al gruppo di pazienti che non assumono anticoagulanti.



ATTIVITÀ FISICA E CARDIOLOGIA DELLO SPORT

A105: IS PICKELHAUBE SIGN REALLY THE HALLMARK OF ARRHYTHMOGENIC MVP IN ATHLETES? AND DOES MVP REALLY CAUSE SUDDEN DEATH? A CASE REPORT

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The Pickelhaube Sign is today recognized as a novel Echocardiographic Risk Marker for Malignant Mitral Valve Prolapse Syndrome. Mitral Valve Prolapse (MVP) has long been recognized to be a relatively common valve abnormality in the general population. Patients with relatively non-specific symptoms and asymptomatic athletes who have MVP still represent an important clinical conundrum for any physician involved in preventive medicine and sports screening. Although cardiac arrhythmias and/or cardiac death are an undesirable problem in MVP patients, when these subjects were studied with Holter Electrocardiogram (ECG) monitoring a prevalence of ventricular arrhythmias up to 34% was observed, with premature ventricular contractions as the most common pattern (66% of cases). At this regard a paper by Anders et al. described a series of cases that suggest that even clinically considered benign cases of MVP in young adults may cause sudden and unexpected death. However, cardiac arrest and Sudden Arrhythmic Cardiac Death (SCD) resulted in rare events only in patients with MVP based on data from a community study. A middle-aged athletic male who has been practicing competitive cycling for about 20 years came to our Sports Medicine Centre to undergo screening of sports preparation for competitive cycling and the related renewal of certification for participation in sports competitions. This athlete was always considered suitable in previous competitive fitness assessments performed in other sports medicine centers. His family history was unremarkable, as well as his recent and remote pathological anamnesis. The physical examination revealed a 3/6 regurgitation heart murmur with a click in the mid late systole. Previous echocardiographic examinations revealed a MVP which was considered benign with mild not relevant mitral regurgitation. He did not complain of symptoms such as dyspnea or heart palpitations during physical activity. The resting ECG showed negative T waves in the inferior limb leads, and the stress test showed sporadic premature ventricular beats (a couple) with right bundle branch block morphology. An echocardiogram confirmed the presence of a classic mitral valve prolapse with billowing of both mitral leaflets, associated with a mild to moderate valve regurgitation. The TDI exam at the level of the lateral mitral annulus showed a high-velocity mid-systolic spike like a Pickelhaube sign, i.e. spiked German military helmet morphology. Consequently, an in-depth diagnostic imaging with cardiac magnetic resonance imaging was proposed, but the athlete refused it, both because he was totally asymptomatic and above all because he would be forced to pay a considerable amount of money as the examination is not guaranteed by the Italian National Health Service. In conclusion, the athlete remained sub judice as for competitive suitability. Finally, the question is: does MVP really cause sudden death? Is it enough to detect the Pickelhaube signal by echocardiography to stop this athlete? Let us bear in mind that this athlete was asymptomatic, and he

had not had any trouble during exercise and maximal effort for many years. Why must we declare him unsuitable to do competitive sports?

A106: LA CAPACITÀ FUNZIONALE NELLA CARDIOMIOPATIA IPERTROFICA: IL RUOLO DELL'ALLENAMENTO E L'IMPORTANZA DEL TEST CARDIOPOLMONARE

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Introduzione. Nonostante la cardiomiopatia ipertrofica (HCM) sia considerata come ad alto rischio di causare morte cardiaca improvvisa (SCD) durante l'esercizio fisico, recenti evidenze suggeriscono che l'attività fisica moderata abbia un effetto favorevole sul rimodellamento cardiovascolare anche in pazienti con HCM senza compromettere la loro sicurezza. Pertanto, abbiamo effettuato questo studio con l'obiettivo di valutare, mediante test cardiopolmonare (CPET), la capacità funzionale dei pazienti HCM che svolgevano regolare attività fisica confrontandola con pazienti HCM sedentari.

Metodi. Sono stati valutati 17 pazienti con HCM, suddivisi in due gruppi in base alla quantità di attività fisica praticata. In entrambi i gruppi è stato eseguito un ECG a 12 derivazioni, un ecocardiogramma transtoracico e un CPET.

Risultati. I dati CPET hanno mostrato che il gruppo che svolgeva attività fisica ha raggiunto un carico di lavoro maggiore ($p < 0,05$) con una percezione dello sforzo inferiore ($p < 0,05$) e ha raggiunto un picco di consumo di ossigeno (VO_2) superiore ($p < 0,05$) rispetto al gruppo dei sedentari. Inoltre, la seconda soglia anaerobica si assestava a livelli di frequenza cardiaca superiori ($p < 0,05$) nei pazienti attivi, che peraltro mostravano un range più ampio tra la prima soglia aerobica e la seconda anaerobica ($p < 0,05$). Non sono state registrate differenze in termini di aritmie nei due gruppi.

Conclusioni. Nei pazienti con HCM, il gruppo di pazienti che svolgeva attività fisica ha mostrato una capacità funzionale migliore rispetto al gruppo dei pazienti completamente sedentari. Questi risultati supportano l'ipotesi secondo cui la pratica di un esercizio fisico moderato regolare possa migliorare la capacità funzionale dei pazienti HCM, in relativa sicurezza.

A107: L'IMPORTANZA DELLA PRIMA E DELLA SECONDA SOGLIA VENTILATORIA PER DEFINIRE L'INTENSITÀ DELL'ESERCIZIO AEROBICO IN PAZIENTI CARDIOPATICI E IN SOGGETTI SANI: CIÒ CHE È ESSENZIALE PUÒ ESSERE VISIBILE AGLI OCCHI!

Francesca Anselmi (a), Luna Cavigli (a), Antonio Pagliaro (b), Francesca Valentini (a), Matteo Cameli (a), Marta Focardi (a), Nicola Mochi (c), Sergio Mondillo (a), Marco Bonifazi (d), Serafina Valente (b), Flavio D'Ascenzi (a)

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Introduzione. Sebbene l'attività fisica sia fortemente raccomandata nei pazienti cardiopatici, esistono ancora incertezze sui metodi per determinare l'intensità dell'esercizio (EI) e la loro corrispondenza con l'EI efficace ottenuta dalle soglie ventilatorie. Lo scopo di questo studio è stato determinare la prima (VT1) e la seconda soglia ventilatoria (VT2) in pazienti cardiopatici e in soggetti sani sedentari e di confrontare le risposte individuali con l'EI definita dalle raccomandazioni.

Metodi e risultati. Abbiamo arruolato prospettivamente 350 soggetti (167 pazienti cardiopatici, 150 soggetti sani sedentari, 33 atleti agonisti). Ogni soggetto è stato sottoposto a ECG, ecocardiografia e test da sforzo cardiopolmonare. Le percentuali di VO_2 di picco e frequenza cardiaca (FC) di picco sono state ottenute a VT1 e VT2 e confrontate con la definizione di EI proposta dalle raccomandazioni. I pazienti cardiopatici avevano un picco di VO_2 inferiore alle corrispondenti VT1 e VT2 e inferiore FC di picco, rispetto agli altri gruppi ($p < 0,0001$); il 67,1% e il 79,6% dei pazienti cardiopatici aveva VO_2 alla VT1 corrispondente a una EI alta piuttosto che moderata applicando i cut-off proposti dalle precedenti raccomandazioni e dalle linee guida del 2020, rispettivamente. La maggior parte dei pazienti cardiopatici aveva valori di VO_2 alla VT2 corrispondenti a EI molto alta piuttosto che ad una EI alta (59,9% e 50,3%, rispettivamente secondo le raccomandazioni precedenti e le linee guida del 2020).

Conclusioni. La definizione di EI basata su percentuali di picco di FC e VO_2 può classificare erroneamente l'EI efficace. I domini di EI suggeriti dalle linee guida 2020 presentano una migliore corrispondenza con VT1 e VT2, rispetto alle raccomandazioni precedenti. Tuttavia, è consigliabile un approccio basato su soglie piuttosto che su uno basato sugli intervalli percentuali per definire un livello appropriato di EI, in particolare nei pazienti con malattia cardiaca.

A108: DIAGNOSI, GESTIONE CLINICA E FOLLOW-UP DI GIOVANI ATLETI AGONISTI CON BATTITI PREMATURE VENTRICOLARI: UNO STUDIO PROSPETTICO DI COORTE

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Premessa. I battiti prematuri ventricolari (BPV) sono un reperto di comune riscontro ed in certi casi la loro interpretazione è complessa. Purtroppo, abbiamo ad oggi a disposizione pochi dati che mettano in correlazione le caratteristiche dei BPV con il rischio che essi sottendano una malattia cardiaca negli atleti. Lo scopo di questo studio prospettico è stato quello di indagare il valore diagnostico e prognostico delle caratteristiche dei BPV negli atleti agonisti.

Metodi. Da una coorte di 1.751 atleti valutati al nostro centro di Cardiologia dello sport, abbiamo reclutato 112 atleti agonisti di età <40 anni (età media 21 ± 10 anni), senza cardiopatia nota, inviati a causa del riscontro di BPV. Tutti gli atleti sono stati sottoposti ad esame obiettivo, ECG, Holter ECG a 12 derivazioni, test ergometrico ed ecocardiogramma. Ulteriori esami, inclusa la risonanza magnetica cardiaca, sono stati effettuati in caso di risultati anomali agli esami di primo livello o in caso di specifiche caratteristiche dei BPV.

Risultati. La maggior parte (79%) degli atleti ha mostrato BPV monomorfi con *pattern* infundibolare o fascicolare (morfologie comuni). Una diagnosi definitiva di cardiopatia è stata raggiunta in 26 atleti (23% dell'intera popolazione) ed era correlata a BPV con morfologia non comune ($p < 0.001$) e aritmie complesse ($p < 0.001$). Il numero di BPV nelle 24 ore è risultato più basso negli atleti con cardiopatia che in quelli con cuore sano ($p < 0.05$). Durante il follow-up è stata osservata una riduzione spontanea dei BPV e non si è verificato nessun evento avverso.

Conclusioni. Tra gli atleti con aritmie ventricolari, i BPV più comunemente osservati presentano una morfologia infundibolare e fascicolare. La morfologia e la complessità dei BPV sono risultati predittivi della probabilità di malattia sottostante ma non il loro numero. Gli atleti con BPV ma in assenza di cardiopatia strutturale hanno mostrato una buona prognosi, ad indicare che la prognosi è dettata dalla presenza o meno di cardiopatia strutturale e non è influenzata dalla pratica sportiva.

A109: I DETERMINANTI DELLA POSITIVIZZAZIONE DELLE ONDE T NEGATIVE ANTERIORI NEI BAMBINI

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Introduzione. Sebbene le onde T negative anteriori (TNA) siano manifestazioni elettrocardiografiche di comune riscontro nelle cardiomiopatie, nei bambini tale pattern di ripolarizzazione è solitamente una caratteristica benigna e tende a positivizzarsi con l'età. Ancora poco si conosce sui determinanti dell'età di positivizzazione nei soggetti sani. Lo scopo di questo studio longitudinale è quello di identificare l'età e i determinanti della positivizzazione delle TNA nei bambini sani.

Metodi. Su una popolazione totale di 2.227 bambini, in 331 soggetti sani sono state osservate TNA. I bambini sono stati sottoposti a follow-up (massimo: 4 anni). La positivizzazione è stata osservata in 312 soggetti e questa nuova coorte è stata selezionata per le finalità di questo studio. Sono state acquisite le informazioni riguardanti la durata della gravidanza, il peso e la lunghezza alla nascita e i rispettivi percentili. Inoltre, sono stati raccolti i dati riguardante il peso e l'altezza al momento della positivizzazione ed i rispettivi percentili.

Risultati. La positivizzazione delle TNA è stata osservata ad una età media di 13 ± 2.0 anni. Al momento della positivizzazione la maggior parte dei bambini aveva un peso oltre il 75° percentile e tra 51° e 75° percentile. La percentuale di bambini nati pretermine, così come il peso e la lunghezza alla nascita, non mostravano variazioni significative tra i bambini con positivizzazione <13 e quelli >13 anni (rispettivamente $p=0.39$, $p=0.87$ e $p=0.70$). Il percentile medio del peso al momento della positivizzazione non differiva fra i due gruppi ($p=0.17$), mentre il percentile medio dell'altezza era maggiore nel gruppo con età <13 anni.

Conclusioni. Le caratteristiche antropometriche al momento della positivizzazione sono i più forti predittori indipendenti della positivizzazione delle TNA, mentre non è stata osservata una correlazione tra prematurità, caratteristiche antropometriche alla nascita ed età di positivizzazione.

A110: LA RISPOSTA ACUTA BIVENTRICOLARE ED ELETTRICA ALL'ULTRAMARATONA NEGLI ATLETI MASTER NON PROFESSIONISTI

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Introduzione. La partecipazione alle attività fisiche di "endurance" è esponenzialmente aumentata negli ultimi anni, con un numero crescente di atleti "master". Sebbene i benefici di una regolare attività fisica di intensità moderata siano ben conosciuti, i danni cardiaci indotti da un esercizio fisico estremo di "endurance" sono attualmente oggetto di discussione, specialmente in questa popolazione. L'obiettivo dello studio è stato quello di analizzare gli effetti acuti di una ultramaratona in termini di funzione biventricolare ed aritmie in una popolazione di atleti master non professionisti.

Metodi. Abbiamo reclutato un gruppo di atleti master non professionisti partecipanti alla gara "Terre di Siena Ultramarathon" (50 km). Tutti i partecipanti sono stati sottoposti ad ECG il giorno prima della gara e al termine di essa. In tutti gli atleti è stato effettuato un monitoraggio continuo elettrocardiografico il giorno prima della manifestazione e per l'intera durata della gara. L'ecocardiogramma è stato effettuato prima e dopo la fine della gara ed ha incluso un'analisi dei dati "speckle tracking" (STE) effettuata successivamente offline.

Risultati. Nella popolazione finale, composta da 68 master atleti (età media 47.2 ± 8.8) non si sono registrate aritmie ventricolari significative. A livello elettrocardiografico, è stata osservata un aumento significativo dell'ampiezza dell'onda R in V1 e della durata del QTc rispetto ai valori di partenza ($p < 0.01$). La funzione ventricolare sinistra, stimata dalla frazione di eiezione, s' TDI e dallo strain longitudinale, non ha subito variazioni significative rispetto ai valori registrati prima della gara. Dopo l'ultramaratona, non sono state riscontrate differenze significative a carico delle dimensioni ventricolari destre né della funzione ventricolare destra valutata tramite RVFAC, TAPSE e s' TDI. Analogamente, lo strain longitudinale del ventricolo destro e la PAPs sono rimasti sostanzialmente invariati.

Conclusioni. In una popolazione di atleti master non professionisti, abbiamo osservato che l'esercizio fisico di ultra-endurance (ultramaratona) non ha avuto un significativo impatto acuto sulla funzione biventricolare e sulle aritmie ventricolari.

A111: GENDER AND BMI DIFFERENCES IN CARDIOPULMONARY RESPONSE IN A GENERAL UNSELECTED POPULATION WITH ACUTE EXPOSURE TO HIGH ALTITUDE: A SCREENING STUDY ON A LARGE COHORT OF SUBJECTS

Benedetta Nusca (a, b), Carlo Vignati (a, b), Massimo Mapelli (a, b), Elisabetta Salvioni (a), Anna Apostolo (a), Piergiuseppe Agostoni (a, b)
(a) CENTRO CARDIOLOGICO MONZINO; (b) UNIVERSITÀ DEGLI STUDI DI MILANO

Background. Every year, thousands of people approach high altitude for sport or tourism. At high altitude, oxygen pressure decreases and so human body increases cardiac and respiratory work to compensate it. Furthermore, also the capability to use oxygen from the muscle is reduced. These cardiovascular changes, which most of the times occur without any complication, carry an increased risk of myocardial infarction, stroke and pulmonary edema, particularly in subjects with previous cardiovascular disease. The availability of modern lifts allows more people to reach high altitude in little time and without efforts. While some data about mountaineers are available, little is known about the cardiopulmonary effects of acute high altitude in general population, especially in large cohorts of subjects.

Aim. The aim of this preliminary, descriptive, observational study is to describe the cardiovascular features of people with acute exposure to high altitude.

Methods. In December 2019 we installed at the third station of Skyway Monte Bianco station (Punta Helbronner, 3466 meters, Fig.1) an automatic station for measuring peripheral oxygen saturation (SpO₂), heart rate (HR), blood pressure (BP), height, weight and BMI.

Results. A total number of 2750 consecutive subjects were enrolled between January and February 2020 (age 39.4 ± 14.5 years, male 55.3%). Overall average arterial systolic and diastolic BP values are 124.6 ± 17.8 and 73.3 ± 7.4 mmHg respectively. There was no significant gender difference in systolic BP while diastolic BP was slightly higher in male vs female. Heart rate was lower in male vs female (overall population 87.8 ± 15.8 bpm). Overall average SpO₂ showed low oxygen values ($86.5 \pm 7.2\%$) with lower values in males. Overweight subjects (BMI >25 kg/m²) were older, showed slightly lower SpO₂, higher systolic BP and diastolic BP. Among subjects with lower SpO₂ values (an arbitrary cutoff of <80% was used), we observed higher ages and BMI values.

Conclusion. In this large population acutely exposed to high altitude male

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subjects showed higher diastolic (but not systolic) BP values, lower SpO₂ and heart rate values compared to females. Overweight subjects are more prone to develop low SpO₂ values and higher BP values. BMI and age are both predictors of significant desaturation.

	Male	Female	p	BMI >25	BMI ≤25	p	SpO ₂ ≥80%	SpO ₂ <80%	p
Age (years)	38.5 ± 14.8	38.4 ± 14.3	0.852	44.6 ± 14.15	35.2 ± 13.9	<0.001	38.4 ± 14.6	41.8 ± 16.2	<0.001
HR (bpm)	86.8 ± 15.7	89.0 ± 16.0	0.002	87.1 ± 15.5	87.8 ± 16.1	0.276	87.6 ± 15.9	89.6 ± 15.5	0.059
SBP (mmHg)	124.8 ± 18.2	123.6 ± 17.4	0.139	129.1 ± 17.8	121.9 ± 17.6	<0.001	124.5 ± 17.8	125.1 ± 17.9	0.624
DBP (mmHg)	75.5 ± 7.2	70.2 ± 6.6	<0.001	77.1 ± 7.1	70.8 ± 6.7	<0.001	73.2 ± 7.5	73.8 ± 6.8	0.181
SpO ₂ (%)	85.9 ± 6.9	87.3 ± 7.3	<0.001	85.7 ± 6.9	87.1 ± 7.0	<0.001	-	-	-
BMI (kg/m ²)	25.5 ± 3.7	22.7 ± 3.4	<0.001	-	-	-	24.3 ± 3.9	24.9 ± 4.2	0.019



A112: LA PRESCRIZIONE DELL'ESERCIZIO FISICO ADATTATO COME STRUMENTO DI PREVENZIONE E TERAPIA

Elisa Lodi (a, b), Gustavo Savino (b), Letizia Reggianini (a), Giulio Toni (b), Laura Bernaroli (b), Maria Grazia Modena (a) (a) CENTRO P.A.S.C.I.A. (PROGRAMMA ASSISTENZIALE SCOMPENSO CARDIACO, CARDIOPATIE DELL'INFANZIA E A RISCHIO), AOU POLICLINICO DI MODENA; (b) SERVIZIO DI MEDICINA DELLO SPORT, AZIENDA USL DI MODENA. Le malattie croniche non trasmissibili (MCNT) rappresentano il principale problema di sanità pubblica, essendo la prima causa di morbilità, invalidità e mortalità e provocando danni umani, sociali ed economici elevatissimi. Secondo l'OMS sono 4 le più importanti MCNT (malattie cardiovascolari (MCV), cancro, malattie polmonari cronico ostruttive e diabete), collettivamente responsabili di quasi il 70% dei decessi in tutto il Mondo e del 70-80% del budget che i Paesi europei spendono per la salute. Questi dati sono destinati a peggiorare, vista la maggiore sopravvivenza agli eventi acuti e l'innalzamento dell'aspettativa di vita. A tal proposito, dato fondamentale, allo stesso tempo preoccupante e confortante, è che almeno l'80% di tutti i casi di MCV, ictus e diabete di tipo 2 e almeno il 30% dei casi di cancro, si potrebbero prevenire, agendo sui fattori di rischio modificabili, tra i quali l'inattività fisica. Sono ormai inconfutabili le evidenze scientifiche che dimostrano che l'attività fisica è necessaria a tutte le età per mantenere lo stato di buona salute e la completa efficienza fisica e mentale; recenti studi hanno documentato che l'inattività fisica produce più danni alla salute del fumo di tabacco. In conformità a tali considerazioni, l'AUSL di Modena ha istituito il progetto "La prescrizione dell'attività fisica come strumento di prevenzione e terapia", che la prescrizione di programmi personalizzati di attività fisica, come fosse un vero e proprio farmaco, a soggetti con MCV (prevenzione secondaria) o a rischio di svilupparle (prevenzione primaria), da parte di medici specialisti in Cardiologia e Medicina dello Sport in collaborazione con i Laureati in Scienze Motorie. Gli effetti attesi sono un miglioramento della funzionalità cardiovascolare, della qualità di vita e del profilo glicometabolico. A lungo termine è atteso anche un calo dei costi medici, diretti e indiretti, e della mortalità. Da gennaio 2018 a maggio 2019 sono stati arruolati 72 soggetti, tra i 18-79 anni (età media 53 anni), con almeno uno dei seguenti criteri di inclusione: esiti stabilizzati di MCV (51,4%), diabete tipo 2 (12,5%), sindrome metabolica (52,8%). I soggetti sono stati valutati al tempo di arruolamento ed a intervalli di 2, 6 e 12 mesi, con l'obiettivo di andare a valutare il grado di gradimento e aderenza al programma, ed alcuni parametri clinici. Dalla nostra esperienza, il progetto si è dimostrato sostenibile sul piano organizzativo ed è stato molto apprezzato dai pazienti. Il confronto tra le rilevazioni effettuate all'inizio dell'arruolamento e dopo 2 mesi ha mostrato miglioramenti per determinati indici di salute psicofisica, alcuni dei quali a valenza potenzialmente prognostica per patologie croniche cardiovascolari e dismetaboliche: velocità media e frequenza cardiaca al test del km, tempo di alzata/seduta, test dell'equilibrio e punteggi della scala VAS motoria e rachidea. Non sono stati registrati eventi avversi nonostante l'inclusione di pazienti con elevato grado di compromissione cardiovascolare (criterio esclusione EF <25%). In conclusione, stando ai dati dell'esperienza modenese, l'esercizio fisico si conferma essere uno strumento preventivo e terapeutico ideale, in quanto fisiologico, economico, sicuro ed efficace in numerose condizioni cliniche ad elevato impatto socio-assistenziale.

A113: LA CARDIOLOGIA E LO SPORT: UN BINOMIO CHE FUNZIONA

Elisa Lodi (a, b), Lucia Tardini (c), Gustavo Savino (b), Stefano Cappelli (c), Maria Grazia Modena (a), Giampiero Patrizi (c) (a) CENTRO P.A.S.C.I.A. (PROGRAMMA ASSISTENZIALE SCOMPENSO CARDIACO, CARDIOPATIA DELL'INFANZIA E A RISCHIO), UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA, A.O.U. POLICLINICO DI MODENA; (b) SERVIZIO MEDICINA DELLO SPORT AZIENDA USL DI MODENA; (c) U.O. CARDIOLOGIA OSPEDALE RAMAZZINI CARPI. Negli ultimi anni si è sempre più consolidato il binomio tra Cardiologia e Medicina dello Sport. Da questa associazione è nata la branca della Cardiologia dello Sport, che ha l'obiettivo di valutare gli adattamenti cardiovascolari all'esercizio fisico ed i possibili rischi e benefici ad esso associati. La Cardiologia dello Sport conosce due realtà di applicazione differenti: dal punto di vista Cardiologico si occupa della prescrizione dell'esercizio fisico come se fosse un vero e proprio farmaco ai pazienti con storia di malattia cardiovascolare o a rischio di esserlo; dal punto di vista Medico Sportivo si occupa della tutela degli atleti. L'esercizio fisico, infatti, può trasformarsi in un trigger di eventi avversi fino alla morte improvvisa (MI), in soggetti affetti da condizioni patologiche predisponenti, spesso misconosciute. In Italia, esiste una lunga tradizione di medicina preventiva dedicata agli atleti, che è iniziata nel 1950 per poi arrivare al D.M. Balduzzi del 1982, che impone a chiunque pratici attività sportiva agonistica di sottoporsi a visita Medico Sportiva, che ne certifichi l'assenza di controindicazioni. Attualmente, le condizioni che portano alla richiesta di esami aggiuntivi o alla formulazione di giudizi di non idoneità, riguardano per la grande maggioranza dei casi (80% circa) l'apparato cardiovascolare. In quest'ottica, è nato all'interno dell'U.O. di Cardiologia dell'Ospedale di Carpi un ambulatorio dedicato, con la finalità di eseguire valutazioni e fornire consulenza sulla concessione di idoneità sportiva agonistica ed individuare precocemente cardiopatie misconosciute. Nel biennio 2018-2019 sono stati valutati in suddetto Ambulatorio 308 atleti, di età compresa tra 7 e 70 anni. Le principali motivazioni di accesso sono state: disturbi del ritmo, alterazioni elettrocardiografiche a riposo o da sforzo, alterazioni morfo-funzionali alle indagini di imaging, disturbi di conduzione. Ad un quarto di questi atleti (77) è stata diagnosticata una qualche forma di cardiopatia. 28 atleti (9,1%) hanno ricevuto diagnosi di cardiopatia a rischio di MI (aterosclerosi coronarica, cicatrice non ischemica alla CardioRM, origine anomala delle coronarie ed decorso intramiocardico di ramo coronarico) ed è stato di conseguenza formulato un giudizio di non idoneità alla pratica sportiva agonistica; 49 atleti (15,9%) sono invece risultati essere affetti da cardiopatie potenzialmente evolutive (valvulopatie, ectasia dell'aorta toracica, dilatazione ventricolare, ipertrofia ventricolare, genotipo positivo per cardiopatie, ...) e hanno quindi ricevuto un giudizio di idoneità alla pratica sportiva agonistica subordinata a stretto e specifico follow-up cardiologico. Dei 308 atleti valutati in 2 anni di attività, al 25% è stata fatta una diagnosi di cardiopatia di cui il 9,1% a rischio di MI. Tale dato rende lampante l'utilità del protocollo italiano di tutela degli atleti. I numeri parlano chiaro: il sistema italiano funziona, e la disponibilità di un Ambulatorio di Cardiologia dello Sport con l'attiva collaborazione tra Cardiologo e Medico Sportivo può sicuramente contribuire a potenziarne l'efficienza. I numeri parlano chiaro: il sistema italiano funziona, e la disponibilità di un Ambulatorio di Cardiologia dello Sport con l'attiva collaborazione tra Cardiologo e Medico Sportivo può sicuramente contribuire a potenziarne l'efficienza.

A114: ANALISI DEI CASI E DEI MOTIVI DI NON IDONEITÀ ALL'ATTIVITÀ SPORTIVA A MODENA E PROVINCIA NELL'ULTIMO VENTENNIO

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l'ipertensione arteriosa seguita dalle condizioni aritmogene. L'ipertensione è stata largamente diagnosticata negli Over 35 e in un terzo dei casi era già presente un danno d'organo. Altri dati rilevati sono stati l'introduzione degli esami di terzo livello cardiologici come risonanza magnetica cardiaca e coro-TC a partire dal 2010 che potranno sempre più contribuire nell'individuazione di patologie con scarsa espressione fenotipica. Tra le cause di non idoneità di origine non cardiovascolare sono emerse le cause ortopediche. La commissione regionale ha accolto 25 ricorsi sui 34 richiesti. In conclusione è stato analizzato il ruolo dello specialista nella Medicina dello Sport e si spera in studi futuri di tipo prospettico per poter confermare le tendenze emerse da questo studio.

A115: DETRAINING IN UN GRUPPO DI GIOVANI ATLETI, RUOLO PROTETTIVO O FAVORENTE LE ARITMIE VENTRICOLARI?

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Il lockdown legato alla pandemia da COVID 19 ha imposto per oltre 3 mesi uno stop agli allenamenti e le attività sportive agonistiche in generale, fornendo idealmente un lungo periodo di "detraining" generalizzato. Il detraining è una delle modalità attraverso la quale nei casi dubbi si valuta se siamo di fronte a un cuore d'atleta oppure a una Cardiomiopatia Ipertrofica, inoltre si è dimostrato efficace per ridurre il burden aritmico in alcune forme di Fibrillazione Atriale Parossistica, mentre è stato scarsamente indagato l'effetto di questa strategia sulle aritmie ventricolari. In riferimento all'ECG secondo Holter delle 24 ore uno studio pubblicato nel 2018 da Zorzi e coll. sul JACC su 440 soggetti sia sportivi che non, riportava una prevalenza di almeno 1 battito ectopico ventricolare nella registrazione delle 24 ore nel 59% dei soggetti, senza variazioni significative tra sportivi e sedentari. Facendo riferimento invece al test da sforzo massimale un recentissimo studio pubblicato sull'European Journal of Preventive Cardiology dimostra come analizzando un campione di quasi 11000 soggetti, l'aggiunta di Test da sforzo monitorato mostrava la presenza di aritmie ventricolari nel 5% dei soggetti con anamnesi, storia familiare, esame obiettivo e ECG a riposo silenti.

Lo scopo dello studio è di ricercare eventuali discrepanze statisticamente significative in complessità e numero assoluto di aritmie ventricolari tra sedentari e fisicamente attivi nel periodo di stop dell'attività agonistica servendosi della diagnostica cardiologica di secondo livello. Questa consiste in test massimale al cicloergometro con registrazione della traccia ECG e, soprattutto, ECG secondo Holter delle 24 ore prescritti nel periodo compreso tra inizio giugno e fine settembre alla Medicina dello Sport delle sedi di Modena e Carpi.

Oltre al confronto con la letteratura esistente questo studio potrebbe fornire ulteriori informazioni sul comportamento delle aritmie ventricolari in giovani atleti mettendolo in relazione con l'attività fisica svolta prima della valutazione.

Lo studio viene condotto in un campione di giovani agonisti di età compresa tra 10 e 18 anni suddivisi in due gruppi sulla base di questa semplice intervista (previa esclusione di infezione da COVID 19 certa o fortemente sospetta nei mesi antecedenti la visita): 1.L'attività svolta nel periodo di stop dell'attività agonistica è stata meno o più intensa rispetto al periodo precedente? 2.In media, quante ore settimanali ha dedicato all'allenamento? (considerando sedute di almeno 20 minuti continuativi). Basandosi in particolare sul secondo quesito, i soggetti con un allenamento compreso tra 0 e 2 ore settimanali vengono inclusi nel gruppo dei sedentari, al contrario dalle 3 ore in su i soggetti vengono inseriti nel gruppo degli attivi. Sarà dunque possibile confrontare i due gruppi, con l'obiettivo di identificare eventuali differenze statisticamente significative (non emerse nei pochi studi a riguardo presenti in letteratura). Verranno studiati i battiti ectopici ventricolari definendone sia la prevalenza sul totale del campione, che la numerosità, che la complessità (dato quest'ultimo più clinicamente rilevante). Se i dati emersi da questo studio saranno statisticamente significativi oppure fortemente suggestivi per una riduzione del burden aritmico nel gruppo con detraining completo, potrebbero essere teorizzati nuovi studi con maggior numerosità per confermare questa ipotesi. La conferma ulteriore porterebbe a prendere in considerazione il detraining in forme aritmiche benigne (senza causa organica sottostante) ma persistenti.

A116: LE ARITMIE VENTRICOLARI NEGLI ATLETI: UN CAMPANELLO D'ALLARME?

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Il riscontro di extrasistolia ventricolare (BEV) è un evento frequente nella popolazione generale e negli sportivi. Seppur tale riscontro sia aspecifico nella maggioranza dei casi, può talora essere spia di una cardiopatia sottostante potenzialmente minacciosa per la salute dell'atleta.

La distinzione tra BEV innocui e BEV potenzialmente pericolosi non è sempre immediata, e richiede l'esecuzione di accertamenti di secondo livello (ecocardiogramma, Holter ECG, test da sforzo massimale). Tuttavia, alcune cardiopatie possono sfuggire a suddette indagini e necessitano di valutazioni di terzo livello, inclusive, tra le altre, della risonanza magnetica cardiaca (RMC). Essendo tale metodica costosa oltre che poco disponibili, è fondamentale disporre di strumenti che permettano di selezionare quella popolazione di atleti con riscontro di BEV con maggiori probabilità di cardiopatia associata. A tale scopo, anche alla luce delle raccomandazioni C.O.C.I.S. 2017, il gruppo padovano del Prof. Corrado ha proposto un algoritmo diagnostico che aiuti in tale intento. Tale protocollo include la valutazione di diverse caratteristiche dei BEV: morfologia, prevalenza, numerosità e complessità, comportamento durante sforzo ed in risposta al disallenamento.

Da alcuni anni all'interno della U.O.C. Di Cardiologia dell'Ospedale di Carpi è nato un ambulatorio specialistico di Cardiologia dello Sport dedicato agli atleti che in seguito alla visita medico-sportiva necessitano di un approfondimento cardiologico. Anche nella popolazione di atleti valutati da suddetto ambulatorio nel biennio 2018-2019, le aritmie ventricolari (semplici o complesse) hanno rappresentato la principale causa di accesso. In particolare, nel biennio 2018-2019 il riscontro di BEV ha comportato la definizione e l'organizzazione di un iter diagnostico per 95 atleti.

Seguendo i Protocolli C.O.C.I.S. e l'applicazione dell'algoritmo suggerito dal gruppo del Prof. Corrado, è stato possibile identificare 18 cardiopatie a rischio di morte improvvisa e 6 cardiopatie potenzialmente evolutive. Questi traguardi non si sarebbero potuti raggiungere senza due tappe fondamentali di questo percorso. Innanzitutto, la competenza specifica e la costante collaborazione delle diverse figure professionali che partecipano all'attività dell'Ambulatorio specialistico in un terreno in continua evoluzione. Inoltre, la disponibilità della RMC, che si è dimostrata essere una metodica essenziale e sempre più necessaria nella corretta identificazione di condizioni a rischio.

In definitiva, anche dalla nostra esperienza il riscontro di BEV si è dimostrato frequente nella popolazione praticante attività sportiva, tuttavia, le conoscenze sviluppate sull'argomento, unitamente alla disponibilità di nuovi strumenti diagnostici, possono fornire un contributo concreto nella corretta gestione di tale reperto, al fine di poterne sfruttare il possibile ruolo predittivo di sottostanti condizioni minacciose per la salute.

A117: STRATIFICAZIONE DEL RISCHIO CARDIOVASCOLARE MEDIANTE VALUTAZIONE FUNZIONALE CARDIORESPIRATORIA IN PAZIENTI CON ARTRITE PSORIASICA

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Introduzione. L'artrite psoriasica (AP) è un'artropatia debilitante che si caratterizza per un'importante varietà di manifestazioni cliniche e radiografiche. Come le altre malattie infiammatorie sistemiche, anche l'AP si associa ad un aumento della morbilità e della mortalità per cause cardiovascolari (CV). L'obiettivo del presente studio è quello di studiare il grado di disfunzione diastolica misurata mediante ecocardiogramma trans-toracico e la limitazione funzionale ricavata attraverso il test da sforzo cardiopolmonare (CPET).

Materiali e metodi. Sono stati valutati 12 soggetti affetti da AP (età media 61±5 anni, 58% donne) nel periodo di tempo compreso tra settembre 2019 e febbraio 2020 afferenti presso l'ambulatorio di Reumatologia dell'Azienda Ospedaliera Santa Maria di Terni, Università di Perugia. Come gruppo controllo sono stati considerati i dati derivati da una coorte di pazienti sani precedentemente pubblicati in letteratura. I criteri di esclusione riflettono quelli adottati per l'esecuzione del classico test ergometrico. Per ogni paziente è stata effettuata una valutazione globale comprensiva di anamnesi, esame obiettivo, BMI, ECG standard a 12 derivazioni, esami ematochimici, ecocardiografia, CPET.

Risultati. Tra i pazienti con AP, il 66% è risultato iperteso. L'area dell'atrio sinistro, valutato in proiezione apicale 4 camere (media 19,4±2,6), risultava più elevata nei pazienti con AP rispetto al gruppo controllo (media 13,7± 3,4). Il 42% dei pazienti con AP presentava disfunzione di primo grado, il 58% disfunzione di secondo grado. Nei soggetti con AP vi era una relazione statisticamente significativa tra il valore di VO₂ di picco e le pressioni di riempimento del ventricolo sinistro (E/E') (R² =0,40, p<0,01). Era inoltre evidente una correlazione diretta fra RQ (quoziente respiratorio, ossia il rapporto tra ossigeno consumato e anidride carbonica prodotta) ed E/E' laterale (R²=0,53, p<0,001).

Conclusioni. I risultati del presente studio suggeriscono che, nei pazienti con AP, la disfunzione diastolica del ventricolo sinistro è di frequente riscontro. Inoltre, il grado di disfunzione diastolica correla con il livello di limitazione funzionale e di tolleranza all'esercizio fisico valutati mediante CPET che potrebbero essere attribuiti anche ad un decondizionamento fisico legato alla sedentarietà e alla patologia di base e ad una eccessiva rigidità ventricolare che determina incremento delle pressioni di riempimento polmonare e precoce shift verso il metabolismo anaerobico a livello periferico con incremento della lattacidemia e "senso di fatica

muscolare". Tali risultati, sebbene preliminari, suggeriscono l'utilità di una valutazione diagnostica integrata (ecocardiogramma, CPET) ai fini della prescrizione individualizzata della prescrizione dell'esercizio fisico, con ripercussioni favorevoli nei confronti della riduzione del rischio cardiovascolare nei pazienti con artrite sieronegativa.

CARDIOLOGIA INTERVENTISTICA CORONARICA E STRUTTURALE

A118: THE ROLE OF PREPROCEDURAL ASSESSMENT OF AORTIC VALVE CALCIUM VOLUME FOR THE OPTIMIZATION OF PERCUTANEOUS AORTIC BIOPROSTHESIS IMPLANTATION (TAVI)

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Background. Paravalvular leaks (PVL) and conduction disorders requiring permanent pacemaker implantation (PPI) in patients with severe Aortic Valvular Stenosis (SA) undergoing percutaneous aortic valve prosthesis (TAVI) still have a significant and unacceptable incidence for patients at medium and low surgical risk, who represent, with increasing scientific evidence, the prevalent population. The appearance of these complications seems to be related to clinical, anatomical and procedural factors, which influence the decision-making process of the type and size of bioprosthesis to be implanted. Particular attention has been paid to the role of the volume of calcium present at the native aortic valve (VCA) as a predictor of these complications, in order to optimize the percutaneous procedure. The VCA can be quantified using algorithms derived from Multilayer Computed Computed Axial Tomography (MSCT), an examination that has become a pivotal element in the evaluation of the patient's eligibility for TAVI. The aim of our study was to document the pre-procedural added value of VCA in terms of possible containment of adverse events and how much it may affect the choice of the type of bioprosthesis to be implanted.

Methods. 111 patients underwent TAVIs at the Interventional Cardiology Unit of the AOU S. Giovanni di Dio and Ruggi D'Aragona, between 2017 and 2020, subsequently divided into 2 groups: group A (self-expandable bioprosthesis, Medtronic Evolut R or Evolut Pro) and group B (balloon expandable bioprosthesis, Edward Sapien 3). The clinical, electrocardiographic, echocardiographic and anatomical parameters of the enrolled patients were analyzed, and the VCA in the preprocedural phase was quantified for each of them, using an algorithm extracted from the MSCT reading software, OsiriX (OsiriX-MD v.2.8.2 64-bit).

Results. A univariate logistic regression analysis was performed for the risk of developing the composite event of significant PVL and IPP. In Group B, no significant variables were found, while in Group A, the VCA (OR: 1.001; 95% CI, 1.000-1.002; p < 0.043) and incomplete left branch block (OR: 5.781; 95% CI, 0.013-32.988; p < 0.048) were significant. Subsequently, these two variables were tested in a multivariate regression model according to which only the VCA emerged as an independent predictor for the composite event (OR: 1.001; 95% CI, 1.000-1.002; p < 0.039).

Conclusions. VCA is significantly associated with the risk of moderate to severe PVL and rhythm disturbances requiring PPI, in the group of patients in whom a self-expandable bioprosthesis was implanted, unlike patients who received a balloon-expandable bioprosthesis where this association is not significant.

A119: HIGH-RISK PERCUTANEOUS CORONARY INTERVENTION IN THREE-VESSEL CORONARY ARTERY DISEASE AND AORTIC STENOSIS WITH IMPELLA SUPPORT

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A 73-year-old male patient with hypertension, type 2 diabetes mellitus, and smoking habit was admitted to our institution complaining of new-onset typical chest pain and exertional dyspnea (New York Heart Association functional class II). He had a history of positive stress test without evidence of severe coronary artery disease (CAD) at coronary angiography ten years before. Moreover, he was affected by severe chronic obstructive pulmonary emphysema with pulmonary hypertension. His physical examination revealed a systolic ejection murmur and the electrocardiogram showed a right bundle branch block with non-specific repolarization disorders. High sensitivity cardiac troponin I was 250 ng/L. Transthoracic basal echocardiography revealed normal left ventricular ejection fraction and end-diastolic volume (EF 60%, EDV 50 ml/m²) with normal kinetics, right ventricular chamber dilation and dysfunction, systolic pulmonary pressure of 54 mmHg and moderate aortic valve stenosis with a mean gradient of 20 mmHg and a valve area of 1.4 cm². Coronary

angiography showed a three-vessel coronary artery disease with severe stenosis (70%) of distal left main coronary artery (LM) involving left anterior descending (LAD) and circumflex (LCx) coronary ostia, severe stenosis (85%) at the mid tract of the LAD, chronic total occlusion (100%) of a small diagonal branch, severe stenosis (90%) of the first tract of the obtuse marginal branch (OM) and tandem severe stenosis (70% and 90%) of the posterolateral branch of the right coronary artery (RCA). Left and right heart catheterization confirmed the presence of a moderate aortic valve stenosis (with a peak to peak gradient of 25 mmHg and a valve area of 1.4 cm²) with normal wedge pressure and mild pulmonary hypertension (with a mean pulmonary artery pressure of 28 mmHg). During the Heart Team discussion, percutaneous myocardial revascularization with Impella support was planned considering the patient comorbidities and the diffuse coronary artery disease. Although aortic stenosis is considered a contraindication to Impella implantation, the assist device acts as a bypass of the stenotic valve increasing cardiac output and reducing left ventricular end-diastolic pressure, thus improving coronary perfusion. After Impella CP insertion across the aortic valve into the left ventricle, through a femoral artery access, the patient underwent a high-risk PCI. T and protrusion double stenting technique on LM bifurcation was performed and two overlapping stents on the first tract of LCx-OM and the first tract of LAD were implanted. Final kissing balloon dilation and proximal optimization technique of the LM stent was done without complications. During the procedure with multiple long stents implantation in coronary bifurcation, hemodynamic parameters were stable.

The post-procedural phase was uneventful, and the patient was discharge on day three. Dual antiplatelet therapy (DAPT) with aspirin and ticagrelor was prescribed for 12 months as indicated in acute coronary syndromes. After 12 months of DAPT without bleeding complications and considering the diffuse coronary artery disease, a long DAPT with aspirin and ticagrelor 60 mg was considered. Currently, the patient has been continuing DAPT for 18 months without complications.

A120: DURATION OF DUAL ANTIPLATELET THERAPY AND SUBSEQUENT MONOTHERAPY TYPE IN PATIENTS UNDERGOING DRUG-ELUTING STENT IMPLANTATION: A NETWORK META-ANALYSIS

Stefano Benenati (a), Gabriele Crimi (b), Claudia Canale (a), Fabio Pescetelli (a), Vincenzo De Marzo (a), Rocco Vergallo (c), Mattia Galli (c), Roberta Della Bona (b), Marco Canepa (a), Pietro Ameri (a), Filippo Crea (c), Italo Porto (a)

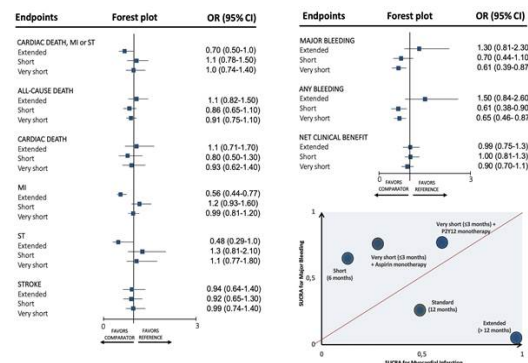
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Aims. To compare safety and efficacy of very short (≤3 months), short (6 months), standard (12 months) and extended (>12 months) DAPT, and subsequent monotherapies, after DES.

Methods. Twenty-two RCT (n=110059 patients/year) were selected and included in a network meta-analysis, conducted according to both the Bayesian and Frequentist approaches. The primary efficacy endpoint was a composite of cardiac death, myocardial infarction (MI) and stent thrombosis (ST), the primary safety endpoint was major bleeding. Odds ratios (OR) and 95% confidence intervals (CI) were estimated.

Results. Compared to standard, we found lower rate of MI (OR 0.56, 95% CI 0.44-0.77) and, only in the frequentist analysis, ST (OR 0.42, 95% CI 0.28-0.64) in extended DAPT; lower rate of major bleeding (OR 0.61, 95% CI 0.39-0.87) in very short and lower rate of any bleeding (OR 0.61, 95% CI 0.38-0.90) in short DAPT. All DAPT durations were comparable regarding the secondary efficacy endpoints. Very short followed by P2Y₁₂ inhibition was the treatment of choice to reduce both major bleeding and myocardial infarction. In the ACS subgroup, extended (as compared to standard DAPT) reduced PEP and ST (but not MI).

Conclusion. The efficacy of short and very short is comparable with that of standard DAPT after DES implantation, whereas extended DAPT reduces MI and ST rates. Very short DAPT reduces haemorrhagic events and, followed by a P2Y₁₂ inhibitor monotherapy, may be preferred in order to pursue a trade-off in between major bleeding and ischemia.



A121: PREDICTORS OF PACEMAKER IMPLANTATION AFTER TAVI ACCORDING TO KIND OF PROSTHESES AND RISK PROFILE: A CONTEMPORARY META-ANALYSIS

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Introduction. Permanent pacemaker implantation (PPI) may be required after transcatheter aortic valve implantation (TAVI). Evidence on PPI prediction has largely been gathered from high risk patients receiving first generation valve implants, but there is lack of data regarding low/intermediate risk patients and last generation devices. Accordingly, we undertook a meta-analysis of the existing literature to examine the incidence and predictors of PPI after TAVI according to surgical risk, generation of valve and valve type.

Methods. We made a systematic literature search for studies with ≥ 100 patients reporting the incidence and adjusted predictors of PPI after TAVI. Subgroup analyses examined these features according to surgical risk, generation of valve and specific valve type.

Results. We obtained data from 43 studies, encompassing 29, 113 patients. PPI rate ranged from 6.7%-39.2% in individual studies with a pool incidence of 19% (95% CI 16-21). Independent predictors for PPI were age (OR: 1.05; 95% CI: 1.01-1.09), left bundle branch block (LBBB) (OR: 1.45; 95% CI: 1.12-1.77), right bundle branch block (RBBB) (OR: 4.15; 95% CI: 3.23-4.88), implantation depth (OR: 1.18; 95% CI: 1.11-1.26) and self-expanding valve prosthesis (OR: 2.99; 95% CI: 1.39-4.59). Among subgroups analyzed according to valve type, valve generation and surgical risk, independent predictors were RBBB, self-expanding valve type, first degree atrioventricular block and implantation depth.

Conclusions. Patient's characteristics (age), baseline ECG (RBBB, LBBB), procedural factors (valve implantation depth) and type of valve implanted (self-expanding valve type) are the main independent predictors of PPI following TAVI and they should be taken into account to evaluate pre-operative risk of conduction disorders, in order to reduce PPI and improve clinical outcomes after TAVI.

A122: AORTIC VALVE REPLACEMENT VS BALLOON-EXPANDABLE AND SELF-EXPANDABLE TRANSCATHETER IMPLANTATION: A NETWORK META-ANALYSIS

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Introduction. While clinical equipoise has been demonstrated for surgery and transcatheter aortic valve interventions (TAVI) in appropriate candidates with severe aortic stenosis, observational data have raised concerns about safety of self-expandable (SE) compared to balloon-expandable (BE) valves in TAVI, although potentially limited by patient selection bias.

Methods. All randomized controlled trials (RCTs) comparing BE vs. SE TAVI or/and vs. aortic valve replacement (AVR) were included and compared through Network Meta Analysis (NMA). All-cause and cardiovascular (CV) mortality during follow-up were the primary endpoints, while stroke, rates of permanent pacemaker implantation (PPI), moderate/severe paravalvular leak (PVL) and re-intervention were the secondary endpoints.

Results. We obtained data from 11 RCTs, encompassing 9752 patients (3 with patients at low, 3 with patients at intermediate and 5 with patients at high surgical risk). After one and two years, no significant differences were noted for all-cause and CV mortality between BE, SE and surgical bioprosthetic valves. Compared to surgical bioprostheses, both BE and SE TAVI reduced the risk of acute kidney injury (OR 0.42; CI 95% 0.30-0.60 and OR 0.44; CI 95% 0.32-0.60), new-onset atrial fibrillation (OR 0.24; CI 95% 0.14-0.42 and OR 0.21; CI 95% 0.13-0.34) and major bleedings (OR 0.32; CI 95% 0.16-0.65 and OR 0.47; CI 95% 0.25-0.89) but were associated with increased risk of vascular complications (OR 2.29; CI 95% 1.37-3.85 for BE and OR 2.76; CI 95% 1.66-4.61 for SE). The BE prostheses reduced the risk of moderate/severe PVL at 30-day (OR 0.31; CI 95% 0.17-0.55) and of PPI both at 30-day (OR 0.51; CI 95% 0.33-0.79) and 1 year (OR 0.40; CI 95% 0.30-0.55) as compared to SE TAVI. Aortic valve reintervention was increased in SE prostheses compared to surgery (OR 3.13; CI 95% 1.47-6.64), while in BE prostheses were not (OR 2.26; CI 95% 0.93-5.47).

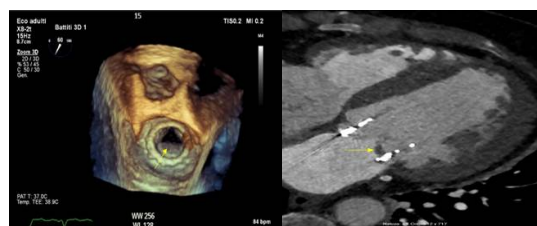
Conclusions. A TAVI strategy, independently from BE or SE prostheses,

offers a survival benefits comparable to AVR. The BE prostheses are associated with a reduction of PPI and PVL compared to SE prostheses without any differences in all-cause and CV mortality during two years of follow-up.

A123: LA TROMBOSI DELLA BIOPROTESI MITRALICA IMPIANTATA CON TECNICA PERCUTANEA DI VALVE-IN-VALVE: PROSPETTIVE FUTURE PER PROFILASSI E TRATTAMENTO

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L'impianto percutaneo di una bioprotesi valvolare mediante la procedura valve-in-valve è considerato una valida opzione terapeutica per il trattamento della degenerazione di una valvola protesica biologica in pazienti ad alto rischio chirurgico. Nonostante esista una maggiore esperienza per l'impianto di bioprotesi valve-in-valve in posizione aortica, anche quello in posizione mitralica è ritenuto efficace e sicuro. Una possibile complicanza di queste procedure è la trombosi della valvola impiantata. Esistono attualmente poche evidenze sul tipo e sulla durata della profilassi e del trattamento della trombosi valvolare dopo una procedura percutanea di valve-in-valve. In questo case report verrà analizzato il caso di una paziente che ha sviluppato una trombosi su una bioprotesi mitralica impiantata con tecnica valve-in-valve mentre era in trattamento con warfarin e clopidogrel.



A124: TRANSCATHETER AORTIC VALVE REPLACEMENT AND COMPLEX CORONARY STENOSIS: A SINGLE CENTER EXPERIENCE OF PCI WITH INTRAVASCULAR LITHOTRIPSY

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Aims. Patients with severe aortic stenosis undergoing TAVI often present a significant coronary artery disease (CAD) with complex lesions and extensive calcification, requiring PCI. Recently intravascular lithotripsy has been introduced for PCI of calcified lesions through a balloon catheter using pulsatile mechanical energy. Limited data exist on the outcome of patients undergoing combined TAVI and complex PCI. We present a case series based on the experience of our center with the aim to provide support to the feasibility of combined procedure of TAVI and intravascular lithotripsy-assisted PCI.

Methods. We analyzed data from patients with complex coronary lesions undergoing PCI and TAVI between January 2019 to December 2019. When indicated PCI with intravascular lithotripsy (Shockwave, Medical Inc) was performed in the same procedure of TAVI. Procedural time, amount of contrast medium and length of intensive care unit and in-hospital stay were collected and compared with mean results of TAVI alone procedures in our center. In-hospital and 30-day major adverse cardiac events were also evaluated.

Results. A total of 34 consecutive patients (38% male; age 83 ± 7 years) underwent transfemoral TAVI procedure during the index timeframe. 3 patients (9%) received TAVI and intravascular lithotripsy-assisted PCI during the same procedure. Those patients presented at least one high-risk features, as reduced left ventricle ejection fraction (LVEF) (N=1), chronic kidney disease (N=1), multivessel coronary artery disease (N=1), left main lesion (N=1). Complete revascularization was achieved in all cases. No procedural complications were recorded. Procedural time was 83 ± 16 min, with no significant increase compared to mean of TAVI procedure in our center (62 ± 22 min; $P=0.11$). Use of contrast medium did not differ among the only TAVI group patients (169 ± 75.5) and those who received combined procedure (165 ± 100 ; $P=0.93$). Patients treated with combined procedure did not present a longer intensive care unit (1 vs 1.54 ± 1.47 ; $P=0.53$) or in-hospital length of stay (9.6 ± 3.6 vs 6.9 ± 3.2 ; $P=0.17$). No major adverse cardiac events were recorded during in-hospital stay and at 30-day follow-up.

Conclusions. Our early experience suggests that a strategy of combined treatment with TAVI and intravascular lithotripsy - assisted PCI is feasible for treatment of patients with both severe aortic stenosis and severe calcified coronary artery disease without increasing procedural time and complexity. Further studies are needed to validate this treatment strategy in larger population.

A125: A BOMB ON LEFT VENTRICULAR WALL: PERCUTANEOUS TREATMENT OF A LEFT VENTRICULAR PSEUDOANEURYSM

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Introduction. Left ventricular pseudoaneurysm (LVP) is a saccular structure communicating with ventricular cavity through neck entrance. LVP is generally related to contained cardiac rupture enclosed by adherent pericardium and scar tissue. Surgical repair is still considered the standard therapy such treatment is associated to high risk. In fact, repair of LVP is technically challenging due to tissue friability and the difficulty in the hemostasis achievement. In the recent years percutaneous closure for pseudoaneurysms with occluder devices emerged as an alternative strategy, however its systematic use is still controversial.

Case presentation. A 70-year-old male patient was referred to our institution for an abnormal cardiac mass detected as incidental finding at transthoracic echocardiography. Cardiac magnetic resonance revealed a large cavity (depth= 67 mm; max. longitudinal diameter= 88 mm), with characteristics for pseudoaneurysm, communicating with left ventricle through a neck (11 mm) in lateral wall. Coronary angiography showed diffuse coronary ectasia with chronic total occlusion of right coronary artery. Due to the high-risk profile of the patient, the Heart Team opted for percutaneous closure of the ventricular wall defect with an Amplatzer septal occluder (AGA Medical Corporation, 682 Mendelssohn Avenue, Golden Valley, MN 55427 USA). The closing procedure was performed under intraoperative transesophageal echocardiography (TEE) monitoring. TEE and subsequent left ventriculography confirmed the absence of communication between ventricular cavity and the pseudoaneurysm. After one-week, despite the normal post-procedure course, cardiac arrest due to ventricular tachycardia occurred. It was promptly treated with a single 250 DC shock. Subsequently internal cardioverter defibrillator was implanted. The patient is in good general conditions after six month follow-up.

Discussion. Left ventricular pseudoaneurysm is a saccular structure in communication with ventricular cavity generating after contained cardiac rupture which is enclosed by adherent pericardium and scar tissue commonly caused by myocardial infarction and cardiac surgery. The most important complication associated to LVP is rupture leading to a sudden fatal bleeding. Other possible complications are related to thrombus formation with risk of systemic embolization and compressive phenomenon due to the progressively increasing of the mass sizing. Due to the coexistence of several comorbidities' patient was considered at high-risk for surgery and a less invasive approach was preferred. In recent years small series of percutaneous closure of LVP with occluder devices have been described, but further data about middle-long term outcome are lacking. Intraoperative TEE, together with left ventriculography, is a useful tool to guide the procedure and monitor the adequate release of the device. The occurrence of ventricular arrhythmias after percutaneous closure of interventricular septal defect with the same device have been already reported, but further data to identify patients at higher risk for such complication are needed. For this reason, prolonged ECG monitoring and/or intracardiac electrophysiological study could be useful in this patient cohort to identify those requiring a cardiac defibrillator in primary prevention.

(OR: 1.7 per 1mm decrease; 95% CI: 1.3-2.3;p<0.01) were found independent predictors of unsuccessful coronary cannulation after TAVR. A model combining these factors demonstrated to predict with very high accuracy the risk of unsuccessful coronary cannulation after TAVR (area under the curve 0.94;p<0.01).

Conclusions. Unsuccessful coronary cannulation following TAVR was observed in 7.7% of patients, and occurred almost exclusively in patients receiving Evolut TAV. The combination of Evolut TAV, a higher TAV/SoV relation and implantation depth predicts with high accuracy the risk of unsuccessful coronary cannulation after TAVR. (ClinicalTrials.gov: NCT04026204)

A127: WHEN THE WIRE WITHIN THE YIN AND YANG MAKES A DIFFERENCE – COMPLEX CORONARY DISSECTION SEALING

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Left main (LM) dissection is a rare complication of cardiac surgery but it is associated to a high peri-procedural mortality. Hemodynamic instability with ST elevation after cardiac surgery requires urgent coronary angiography and revascularization by percutaneous coronary intervention (PCI) or redo coronary artery bypass surgery. PCI has a high complication rate in patients with LM coronary dissection, especially in difficult settings such as after aortic valve cardiac surgery. Coronary imaging has a critical role for guidance of PCI in these challenging scenarios.

We herein describe a case of a 78-year-old man suffering from severe symptomatic aortic valve stenosis and hypertension who underwent surgical aortic valve replacement through mid-sternotomy.

During the immediate post-operative course in Intensive Care Unit, reintervention was necessary due to sudden bleeding from chest drainages. Concomitantly, ST segment elevation developed in the anterolateral leads. Transesophageal echocardiography revealed severe left ventricular dysfunction (30% ejection fraction) with akinesia of the whole cardiac apex and hypokinesia of anterior and lateral walls. The patient was therefore immediately transferred to catheterization laboratory where coronary angiography revealed a long dissection with TIMI flow grade 1, extending from the origin of the LM towards the left anterior descending coronary artery up to the third segment and involving the first diagonal branch (Figure 1). We performed intravascular ultrasound (IVUS) that delineated the sharp contours of a "Yin and Yang" sign (Figure 2) confirming the longitudinal extent of the dissection and the presence of the wire in the true lumen. Thanks to IVUS we could confidently deploy two 3.5 x 23 mm and 3.0 x 18 mm everolimus eluting stents with a successful final result (Figure 3) and TIMI 3 flow. At the end of the procedure, intraaortic balloon pump was positioned in view of persistent hypotension.

This case confirms the pivotal role of intracoronary imaging in complex left main disease scenarios even in high-risk patient. PCI in left main coronary dissection is technically challenging, mainly for the uncertainties rising from wiring into the real true lumen and danger of extending the dissection by catheter tip deep intubation and contrast injection into the false lumen. Once IVUS imaging confirmed that the wire (we preferred the non polymer jacketed guidewire Asahi Sion) passed through the real true lumen of the left main we were able to safely complete stenting.

A126: CORONARY CANNULATION AFTER TAVR: THE REACCESS STUDY (REOBTAIN CORONARY OSTIA CANNULATION BEYOND TRANSCATHETER AORTIC VALVE STENT)

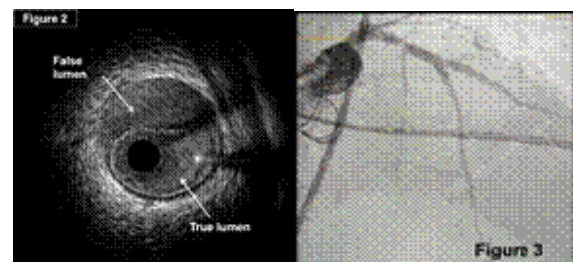
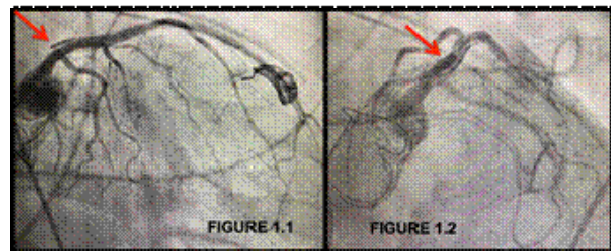
Giuliano Costa (a), Marco Barbanti (a), Andrea Picci (a), Enrico Criscione (a), Roberto Valvo (a), Claudia Reddavid (a), Carmelo Sgroi (a), Corrado Tamburino (a) (a) AOU POLICLINICO RODOLICO-SAN MARCO, CATANIA

Objectives. To investigate the feasibility of coronary ostia cannulation after transcatheter aortic valve replacement (TAVR), and to assess potential predictors of coronary access impairment.

Background. Certain data concerning the feasibility and reproducibility of coronary cannulation after TAVR are lacking.

Methods. This is an investigator-driven, single-center, prospective, registry-based study that enrolled consecutive patients undergoing TAVR using all commercially available devices. All patients performed coronary angiography before and after TAVR. The primary endpoint was the rate of unsuccessful coronary ostia cannulation after TAVR. Secondary endpoints were the identification of factors associated with the inability to selectively cannulate coronary ostia after TAVR.

Results. Among 300 patients enrolled in the RE-ACCESS study from December 2018 to January 2020, a total of 23(7.7%) cases of unsuccessful coronary cannulation after TAVR were documented. This issue occurred in 22 of 23 cases with the use of Evolut R/PRO transcatheter aortic valves (TAVs) (17.9% vs. 0.4%, p<0.01). At multivariate analysis, the use of Evolut R/PRO TAVs (OR: 29.6; 95% CI: 2.6-335.0;p<0.01), the TAV/sinus of Valsalva (SoV) relation (OR: 1.1 per 1mm increase; 95% CI: 1.0-1.2;p<0.01) and the mean TAV implant depth



A128: LONG-TERM OUTCOME OF PCI OF UNPROTECTED CORONARY ARTERY. PRELIMINARY DATA FROM GRAVITY

Edoardo Elia (a), Giorgio Marengo (a), Fabrizio D'Ascenzo (a), Gianni Casella (d), Daniela Trabattoni (b), Emad Abu-Assi (c), Giulio Stefanini (g), Fabrizio Ugo (e), Sebastiano Gili (b), Carla Giustetto (a), Roberto Manfredi (a), Gulgiemo Gallone (a), Francesco Bruno (a), Roberto Verardi (a, d), Imad Sheiban (f), Sergio Raposeiras-Roubin (c), Gaetano Maria De Ferrari (a) (a) DIPARTIMENTO DI CARDIOLOGIA, CITTÀ DELLA SALUTE E DELLA SCIENZA - UNIVERSITÀ DI TORINO; (b) DIPARTIMENTO DI CARDIOLOGIA CENTRO CARDIOLOGICO MONZINO; (c) DIPARTIMENTO DI CARDIOLOGIA, PRESIDIO ALVARO CONQUEIRO, VIGO; (d) DIPARTIMENTO DI CARDIOLOGIA, OSPEDALE MAGGIORE DI BOLOGNA; (e) DIPARTIMENTO DI CARDIOLOGIA OSPEDALE SANT'ANDREA, VERCELLI; (f) DIPARTIMENTO DI CARDIOLOGIA, CLINICA PEDERZOLI, PESCHIERA DEL GARDA; (g) DIPARTIMENTO DI CARDIOLOGIA, ISTITUTO HUMANITAS, MILANO

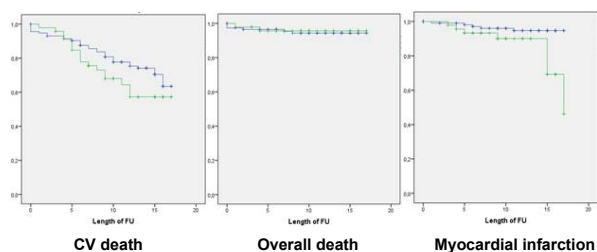
Introduction and aim. Long-term outcome after percutaneous treatment (PCI) of unprotected left main coronary artery (ULMCA) disease is still uncertain despite the widespread this therapeutic option. Indeed there is no data regarding survival after 15 years and how repeated revascularization on target lesion (TVR) or not-target lesion can influence patients' prognosis.

Consequently, we performed an European multicenter collection of PCI on ULMCAD to describe 15 years outcomes of patients and their potential clinical and procedural determinants.

Methods. GRAVITY is a multicenter retrospective registry including consecutive patients underwent PCI of ULMCAD between June 2002 and 2005 at nine European centers. At this moment, data from only seven centers were received and consequently included in this preliminary analysis. The chosen primary end-point is cardiovascular (CV) mortality, the secondary end-point are overall mortality, freedom from myocardial infarction and stent thrombosis.

Results. 200 patients were included with a mean age of 67 years (± 12), of which 98% hypertensive, 22% diabetics, 72% dyslipidemic and 39% smokers. The mean SYNTAX score was 24 (± 10), mean percentage of stenosis 73% (± 17), lesion length 13.2 mm (± 6.4 mm), Medina class 1,1,1 and 0,1,1 occurred in 33% and 4% respectively. Regarding procedural characteristics provisional strategy was more common than two-stents strategy (74% vs 26%) and were more used DES compared to BMS (91% vs 9%). The mean LVEF at discharge was 42% (± 12). After 15 (13-17) years, 23.5% of patients underwent rePCI of ULMCA, the majority during the first year (58%). rePCI on ULMCA did not modify the CV mortality (6% vs 12%; $p=0.372$), overall mortality (36% vs 27%; $p=0.156$) and stent thrombosis (4% vs 5%; $p=0.817$) but myocardial infarction was more common in who underwent rePCI on ULMCA (17% vs 4%; $p=0.006$). At multivariate analysis only diabetes mellitus was found to predict CV death (HR 1.56, 95% CI 1.15-2.11, $p=0.004$)

Conclusion. Percutaneous treatment of atherosclerotic disease of left main coronary artery is a safe therapeutic option and repeat revascularization on TVR does not influence cardiovascular and overall mortality.



A129: EMERGENT AORTIC VALVULOPLASTY IN A PATIENT WITH TAKO-TSUBO CARDIOMIOPATHY AND AORTIC STENOSIS PRESENTING WITH CARDIOGENIC SHOCK

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A 84-year-old woman contacts EMR for chest pain and dyspnoea whose onset followed an anxious nightmare that had awakened her from sleeping. In her clinical history arterial hypertension in therapy with ACE inhibitors and a known aortic valve stenosis in echocardiographic follow-up (last Eco-doppler of 4 months earlier with evidence of normal left ventricular function and a moderate aortic valve stenosis). At the arrival of emergency team the patient was in shock (TA 75/50 mmHg) and in respiratory failure. A prompt intubation was performed and an EKG was obtained with evidence of diffuse alteration of the repolarization and a slight elevation of ST segment in the anterior leads. The patient was transferred directly to the cath-lab and a coronary angiography was performed. No significant coronary obstructions were found and the patient was transferred to the Coronary Care. Despite inotropic support with Dobutamine 8mcg/kg/min and norepinephrine 0,08 mcg/kg/min no hemodynamic improvement was observed. At the echocardiography a

severe left ventricle dysfunction with an apical balloon shape consistent with a Takotsubo syndrome (TTS) was observed. The aortic valve appeared heavily calcified and the movement of the cusps was severely reduced. The aortic doppler confirmed a severe low-flow low-gradient aortic stenosis with an aortic valve area (AVA) less than 1 cm². However, given the low stroke volume a pseudo-severe aortic stenosis caused by the abrupt decrease in left ventricle systolic function couldn't be excluded. Moreover, a dynamic left ventricular outflow tract obstruction (LVOTO) has been reported in 20% of TTS (typically in patients with pre-existing septal bulge) and could precipitate the scenario. Inotropic support response was poor and given the echocardiographic presentation Dobutamine was suspended. The choice of inotropes was limited since increasing exogenous catecholaminergic inotropes in a highly suspected Takotsubo cardiomyopathy was useless and even dangerous and levosimendan or milrinone use was precluded because of their important vasodilators effects. So we thought a mechanical support, but in the context of LVOTO also intra-aortic balloon pump should be avoided.

For the persistency of severe cardiogenic shock and the worsening of the clinical scenario, we decided to perform an urgent valvuloplasty. After the procedure arterial pressure progressively improved and norepinephrine support was progressively suspended in the same day. In the following days a complete recovery of left ventricle function was observed, with a complete recovery of systolic function (LVEF 55%), an improvement of the aortic valve area at the control echocardiography (mean gradient 22 mmHg, AVA 1.1 cm²). Aortic valvuloplasty in patients affected by severe aortic stenosis is a known therapeutic weapon in patients in critical situations. However the most important limit of the procedure is connected to the low persistency of the result obtained. In the context of temporary decrease of the left systolic function and an hemodynamically relevant aortic stenosis, valvuloplasty could be an useful therapeutic tool to overcome critical situation. In this case was particularly useful because of the abrupt decrease and the fast recovery of the left ventricle function. However after 6 months, for the progression of the aortic valve disease, the patient successfully underwent transcatheter aortic valve implantation (TAVI) with an Edwards Sapien 3 26 mm valve. The following 12-months ambulatory follow-up was uneventful.

A130: THERMODILUTION-DERIVED RESTING CORONARY FLOW MEASUREMENT: A REVERSE DOSE FINDING STUDY

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Background. Hyperemic absolute coronary blood flow (in mL/min) can be safely and reproducibly measured with intracoronary continuous thermodilution of saline at room temperature at an infusion rate of 20 mL/min. This study aims at assessing the best infusion rate to measure resting flow by thermodilution, i.e. low enough to avoid microvascular dilation but high enough to allow reliable thermodilution tracings

Methods and Results. In 26 coronary arteries (24 patients) with angiographic non-significant stenoses, absolute flow was assessed by continuous saline thermodilution at infusion rates of 10 mL/min and 20 mL/min using a pressure/temperature sensed guide wire, a dedicated infusion catheter (RayFlow™, Hexacath, Paris, France) and a dedicated software (CoroFlow™ System, Uppsala, Sweden). Average peak velocity (APV) was measured simultaneously using an intracoronary Doppler-wire (FloWire, Volcano/Philips). In addition, in a subgroup of 10 arteries, absolute flow and APV were also measured during saline infusion at 6 ml/min and 8 ml/min. In 26 coronary arteries there was no significance difference in the Pd/Pa and in the APV at baseline and during the infusion of saline at 10 ml/min (Pd/Pa: 0.94±0.057 vs 0.94±0.059, $p=0.82$; APV: 22.2±8.40 vs 23.2±8.39 cm/s, $p=0.63$). In contrast, at an infusion rate of 20 mL/min, we observed a significant decrease in Pd/Pa compared to baseline (0.85±0.089 vs 0.95±0.053 vs, respectively, $p<0.001$) and a significant increase in APV (22.2±8.4 cm/s to 57.8±25.5 cm/s, respectively, $p<0.001$). The coronary flow reserve (CFR) evaluated by Doppler and intracoronary continuous thermodilution correlated well ($r=0.87$, 95% CI = 0.72-0.94, $p<0.001$) and Bland-Altman analysis documented a mean bias of -0.003 (limit of agreement -1.05 to 1.04) thus indicating the presence of resting coronary blood flow during the infusion of 10 mL/min of saline. In 10 coronary arteries saline infusions at 6 and 8 ml/min did not produce any significant changes in Pd/Pa and in the APV compared to baseline and both Doppler and Thermodilution derived CFR correlated well at each infusion rate (6 ml/min: $r=0.71$, 95% CI 0.14-0.92, $p=0.02$; 8ml/min: $r=0.78$, 95% CI=0.31-0.95, $p=0.007$). However, with an infusion rate of 6 mL/min, an unstable thermodilution tracing was observed. Accordingly, Bland Altman analysis showed a significantly larger dispersion of the CFR values when 6 ml/min was used to measure resting coronary flow (as compared with 8 ml/min): mean bias at 6 ml/min:

-0.53, limits of agreement: -2.25 to 1.20: mean bias at 8 ml/min: 0.004, limits of agreement: -0.72 to 0.73.

Conclusion. Absolute resting coronary flow can be measured by intracoronary continuous thermodilution of saline at infusion rate of 8-10 ml/min.

A131: HYPEREMIC HEMODYNAMIC CHARACTERISTICS OF SERIAL CORONARY LESIONS ASSESSED BY PULLBACK PRESSURE GRADIENT (PPG) INDEX

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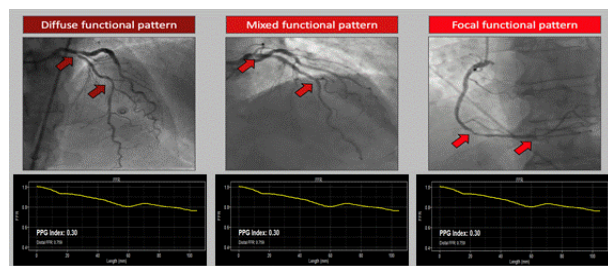
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Introduction. To describe the functional characteristics of angiography-defined serial coronary lesions using fractional flow reserve (FFR)-derived motorized pullback tracings, and to describe the Pullback Pressure Gradients (PPG) index - in these lesions.

Methods. Prospective, multicenter study with independent core laboratory analysis. Patients undergoing coronary angiography due to stable angina were enrolled. Serial lesions were defined angiographically as the presence of 2 or more narrowings with visual diameter stenosis >50% separated at least by 3 times the reference vessel diameter in the same coronary vessel. Continuous IV adenosine-FFR measurements were obtained using a motorized-pullback device at a speed of 1 mm/s. Pullback curves were assessed to determine the presence of focal step-ups (FFR >0.05 units over 20 mm). In addition, the PPG index was computed for all vessels. PPG index values close to 0 define functional diffuse disease whereas values close to 1 define focal disease.

Results. From a total of 159 vessels (117 patients), 25 vessels were adjudicated as presenting serial lesions (mean PPG index 0.48 ± 0.17 , range 0.26-0.87). Two focal pressure step-ups were observed in 40% of the cases (n = 10; mean PPG index 0.59 ± 0.17), whereas 8% of the vessels presented a progressive pressure losses (n = 2; mean PPG index 0.27 ± 0.01). In the remaining 52% of the cases, a single pressure step-up was recorded (n = 13; mean PPG index 0.44 ± 0.12 ; ANOVA p-value = 0.01). The PPG index independently predicted the presence of two focal pressure step ups.

Conclusion. Hyperemic FFR curves in tandem stenoses revealed high prevalence of functional diffuse CAD. Two pressure step-ups occurred in less than half of the vessels. High PPG index identified vessels with two focal pressure drops. FFR tracings and the PPG index provide a more objective CAD evaluation, which can lead to changes in the therapeutic approach.



A132: VESSEL FRACTIONAL FLOW RESERVE AND GRAFT VASCULOPATHY IN HEART TRANSPLANT RECIPIENTS

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Background. Cardiac allograft vasculopathy (CAV) remains the Achilles' heel of long-term survival after heart transplantation (HTx). The severity and extent of CAV is graded with conventional coronary angiography (COR) which has several limitations. Recently, vessel fractional flow reserve (vFFR) derived from COR has emerged as a diagnostic computational tool to quantify the functional severity of coronary artery disease.

Purpose. The present study assessed the usefulness of vFFR to detect CAV in HTx recipients.

Methods. In HTx patients referred for annual check-up, undergoing surveillance COR, the extent of CAV was graded according to the criteria proposed by the international society of heart and lung transplantation (ISHLT). In addition, three-dimensional coronary geometries were constructed from COR to calculate pressure losses using vFFR.

Results. In 65 HTx patients with a mean age of 53.7 ± 10.1 years, 8.5 years (IQR 1.90, 15.2) years after HTx, a total number of 173 vessels (59 LAD, 61 LCX, and 53 RCA) were analyzed. The mean vFFR was 0.84 ± 0.15 and median was 0.88 (IQR 0.79, 0.94). A vFFR ≤ 0.80 was present in 24 patients (48 vessels). HTx patients with a history of ischemic cardiomyopathy (ICMP) had numerically lower vFFR as compared to those with non-ICMP (0.70 ± 0.22 vs. 0.79 ± 0.13 , $p=0.06$). The use of vFFR reclassified 31.9% of patients compared to the anatomical ISHLT criteria. Despite a CAV score of 0, a pathological vFFR ≤ 0.80 was detected in 8 patients (34.8%).

Conclusion. The impairment in epicardial conductance assessed by vFFR in a subgroup of patients without CAV according to standard ISHLT criteria suggests the presence of a diffuse vasculopathy undetectable by conventional angiography. Therefore, we speculate that vFFR may be useful in risk stratification after HTx.

A133: ISCHEMIA O NON ISCHEMIA? VALORE AGGIUNTO DELLO STUDIO MULTIPARAMETRICO DI UNA FISTOLA CORONARICA COMPLESSA

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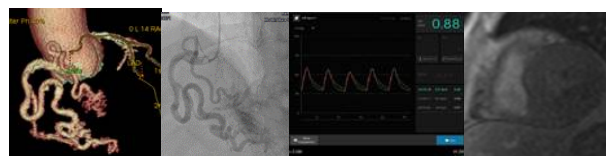
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Presentiamo il caso di un paziente di 68 anni- con plurimi fattori di rischio cardiovascolare- giunto alla nostra attenzione per un quadro di dolore toracico tipico con dimostrazione alla angio-TC coronarografia di aterosclerosi coronarica ostruttiva severa e diffusa, associata ad una fistola tra coronaria destra e ventricolo destro.

Per recidiva di angina associata ad alterazioni ECG, il paziente è stato sottoposto a studio coronarografico ed angioplastica con impianto di stent medicato su coronaria destra sub-occlusa (vaso culprit). L'esame ha mostrato inoltre stenosi 70% del tronco comune, stenosi 60% di arteria interventricolare anteriore al I tratto, occlusione cronica di arteria circonflessa ed ha confermato la presenza di fistola (principalmente rappresentata dal primo ramo marginale acuto, tortuoso e di grosso calibro) tra il sistema coronarico destro ed il ventricolo destro.

Nel medesimo ricovero è stata completata la rivascularizzazione mediante angioplastica ed impianto di stent su tronco comune ed arteria interventricolare anteriore. A completamento, è stata eseguita valutazione funzionale della coronaria destra mediante instant-wave free ratio (iFR) ottenendo valori patologici di 0.88. Dopo occlusione con pallone del ramo marginale, responsabile della fistola, abbiamo ottenuto la normalizzazione dell'iFR, confermando la completa ed efficace ricanalizzazione della coronaria destra ed il furto attivo da parte della fistola coronarica. Una successiva valutazione ecografica ha dimostrato $Qp/Qs=1$. Per escludere che il furto potesse determinare ischemia miocardica, il paziente è stato sottoposto a RMN stress con dipiridamolo. L'esame non ha mostrato alterazioni né della perfusione né della cinetica del ventricolo destro, confermando l'assenza di effetto ischemizzante del furto. Ha altresì dimostrato la presenza di delayed enhancement della parete laterale del ventricolo sinistro, senza segni di ipoperfusione del territorio rifornito dall'interventricolare anteriore. L'attività del tramite fistoloso è stata confermata dall'aumento dell'enhancement contrastografico del ventricolo destro mentre il ventricolo sinistro non era contrastato (RMN perfusion). Prima della dimissione, il paziente è stato valutato mediante test ergometrico che non ha mostrato segni di ischemia miocardica.

Sulla base della valutazione multiparametrica della fistola, abbiamo ritenuto non indicata l'esclusione della fistola ed iniziato un programma di follow-up. L'integrazione di metodiche invasive Hi-Tech (iFR) e metodiche più tradizionali (CT, RMN, ecocardiografia e test ergometrico) possono avere un valore aggiunto nella difficile interpretazione delle fistole coronariche complesse e nella scelta del trattamento più appropriato.



A134: PREDICTORS OF OUTCOMES IN PATIENTS WITH MITRAL REGURGITATION UNDERGOING PERCUTANEOUS VALVE REPAIR

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Objectives. We sought to investigate predictors of clinical outcomes in patients with mitral regurgitation undergoing percutaneous valve repair.

Background. Percutaneous mitral valve repair has been increasingly performed worldwide after approval.

Methods. The MITRA-UMG registry retrospectively collected data from consecutive patients with symptomatic moderate-to-severe or severe mitral regurgitation who underwent MitraClip implantation. The primary endpoint of interest was the composite of cardiovascular death or rehospitalization for heart failure. Between March 2012 and July 2018, a total of 150 consecutive patients admitted to our institution were included.

Results. Acute procedural success was obtained in 95.4% of patients, with no intraprocedural death. The composite primary endpoint of cardiovascular death or rehospitalization for heart failure was met in 50 patients (38%) with cumulative incidences of 7%, 25%, at 30 days and 1 year, respectively (Table I). In the Cox multivariate model, NYHA functional class IV, left ventricular end-diastolic volume index (LVEDVi), EuroSCORE II, independently increased the risk of the primary endpoint at long-term follow-up (Table II). At Kaplan-Meier analysis, a LVEDVi >92 ml/m² was associated with an increased incidence of the primary endpoint (Figure).

Conclusions. In this study, patients presenting with dilated ventricles (LVEDVi >92 ml/m²), high operative risk (EuroSCORE II >7%) or advanced heart failure symptoms (NYHA IV) at baseline carried the worst prognosis after percutaneous mitral valve repair.

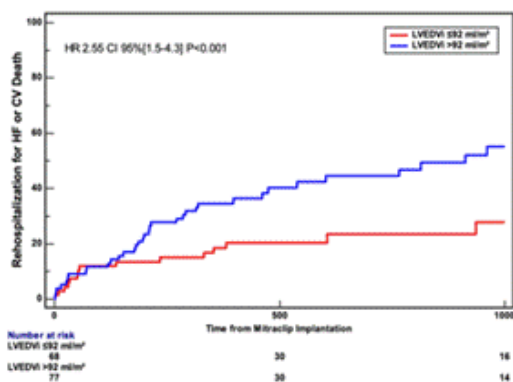


Table I – 1-year Clinical Outcomes

Primary Endpoint	1-year rate, n(%)
Rehospitalization for HF or CV death	33(25)
Secondary Endpoints	
All-cause mortality	17(13)
- cardiac	13(10)
- non-cardiac	4(3)
All-cause rehospitalization	42(32)
- heart failure	27(21)
- other	15(12)
New-onset AF	2(2)
Severe bleeding	4(3)

HF= Heart Failure; CV= Cardiovascular; AF= Atrial Fibrillation

Table II – Predictors of CV Death or Rehospitalization for HF

Variable	Univariate		Multivariate	
	Hazard Ratio [95% Confidence Interval]	P-value	Hazard Ratio [95% Confidence Interval]	P-value
NYHA IV	1.72 [1.71, 8.74]	0.0012	18.53 [5.78, 59.36]	<0.0001
LVEDVi >92ml/m ²	3.56 [1.83, 6.94]	0.0002	4.59 [2.07, 10.18]	0.0002
LVEF <42%	2.39 [1.29, 4.42]	0.0058		
DAP >303 G ₂ * cm ²	2.29 [1.16, 4.51]	0.0173		
Euroscore II >7%	2.26 [1.27, 4.03]	0.0060	2.01 [1.01, 4.02]	0.049

NYHA= New York Heart Association; LVEDVi= Left Ventricular End-Diastolic Volume index; LVEF= Left Ventricular Ejection Fraction; DAP= Dose Area Product.

A135: ANGIOPLASTICA CORONARICA MEDIANTE ATERECTOMIA ROTAZIONALE COME STRATEGIA INIZIALE O DI SALVATAGGIO: DIFFERENZA NELL'OUTCOME DA UN REGISTRO MONOCENTRICO

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Introduzione. Le lesioni coronariche calcifiche sono tecnicamente difficili da affrontare durante angioplastica coronarica. L'adeguata preparazione della placca mediante dispositivi che fratturano e riducono la componente calcifica è fondamentale per il successo procedurale. Tra questi l'aterectomia rotazionale (AR) è una delle tecniche attualmente più utilizzate e può essere scelta come approccio di prima intenzione o come approccio di salvataggio conseguente a tentativo inefficace di angioplastica semplice.

Obiettivi. a) studiare le differenze di outcome procedurale e peri-procedurale tra i pazienti sottoposti ad AR come approccio in prima intenzione (Gruppo 1) e quelli sottoposti ad AR mediante strategia di salvataggio (Gruppo 2); b) effettuare una valutazione globale delle complicanze che derivano dall'utilizzo dell'AR; c) ricercare singoli fattori associati alla comparsa di complicanze dell'angioplastica con AR.

Materiali e metodi. Il presente è uno studio retrospettivo osservazionale. Sono stati reclutati un totale di 240 pazienti sottoposti a coronarografia ed angioplastica con AR in prima intenzione o come strategia di salvataggio tra il 2011 e il 2019. I dati sono stati ottenuti attraverso il sistema di archiviazione elettronico dei referti procedurali e dalle cartelle cliniche digitalizzate. È stato infine costruito un database elettronico anonimizzato in formato Excel, successivamente analizzato mediante software statistico SPSS 23.

Risultati. L'analisi comparativa tra i due gruppi ha mostrato una sostanziale omogeneità dei campioni per caratteristiche cliniche e laboratoristiche di base. Alcune differenze sono emerse dai dati angiografici e procedurali: a) pazienti ai quali è stato somministrata dose da carico di Clopidogrel durante angioplastica (Gruppo 1: 69,2% contro 55,7%, p=0,033); b) pazienti con malattia trivasale, (Gruppo 1: 13,3%, Gruppo 2: 5,15%; p=0,039); c) pazienti che hanno trattato il tronco comune, (Gruppo 2: 9,3% contro 2,1%; p=0,012); d) pazienti per i quali è stata utilizzata esclusivamente una fresa di diametro 1,25 mm, (Gruppo 2: 57, 73%, Gruppo 1: 39, 16%; p=0,004). L'incidenza di complicanze procedurali e/o peri-procedurali è stata sovrapponibile nei due gruppi (Gruppo 1: 8%, gruppo 2: 8,8%; p=ns). All'analisi di regressione univariata la strategia con AR in prima intenzione o di salvataggio non ha mostrato associazione con le complicanze; il diabete è risultato associato ad una maggiore incidenza di eventi avversi procedurali e post-procedurali (OR 2.632, 95.0% CI 1.024-6.762, p=0.044), mentre la dislipidemia (OR 0.288, 95.0% CI 0.096-0.866; p=0.027) ha mostrato associazione inversa con gli stessi.

Conclusioni. Nei pazienti con malattia coronarica calcifica, la strategia con AR in prima intenzione piuttosto che come strategia di salvataggio non ha mostrato un vantaggio in termini di outcome procedurale e peri-procedurale. La tecnica è risultata sicura se in mani esperte e nel nostro campione è stata associata ad una percentuale di complicanze compatibili con la letteratura.

A136: "PRIMARY" TAVI IN A PATIENT WITH CARDIOGENIC SHOCK: THE FUTURE IS NOW

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Background. The introduction of TAVI (transcatheter aortic valve implantation) has revolutioned the way to treat patients with severe aortic stenosis (AS) and high-intermediate surgical risk. TAVI is often performed in the elective setting. We describe the case of a 85 years old woman with severe AS developing cardiogenic shock and treated with "primary" TAVI. During the procedure the patient has been assisted with non-invasive ventilation (NIV) and analgo-sedation. We want to highlight the mini-invasiveness and the feasibility of a procedure like TAVI, which is already spreading its indication to low and intermediate risk population, and it could be even performed as a life-saving intervention in the emergency setting of severe AS with cardiogenic shock.

Case report. A 85-year-old woman with diabetes mellitus type II and hypertension was admitted to our CICU for the occurrence of hypertensive pulmonary oedema. On her arrival the patient was sent to the cathlab where coronary artery disease was ruled out. The echocardiography revealed severe AS. Because of the high surgical risk (Logistic EuroSCORE 37.77; STS mortality and morbidity 20.5) the Heart Team contraindicated surgical aortic valve replacement (SAVR) and addressed the patient to TAVI. While the patient was in the Radiology Department to take an angio-CT for the evaluation of the vascular access and the assessment of valvular planimetry, she developed pulmonary

oedema and cardiogenic shock. Skin rash and other allergic manifestations were ruled out. The anesthesiologist promptly started NIV with an inotropic support provided by the administration of i.v. Norepinephrine. The patient's unstable condition led us to send her straight to the cathlab: every minute could be important to save her life. Percutaneous balloon aortic valvuloplasty (PBAV) was performed with a Nucleus 22 mm balloon. Subsequently, a CoreValve R23 mm (Medtronic) was implanted. The positioning of the valve (Device Time) took 20 minutes and the residual gradient was not significant without periprosthetic leaks. During the whole procedure the patient, after the induction of analgo-sedation, has been assisted by NIV using a facial mask (FlexiFit 431). The weaning from NIV occurred after few hours the patient came back to the CICU because of the evidence of a net improvement of the respiratory parameters. Before discharging, we optimized the diuretic therapy and set a dual antiplatelet therapy with cardioaspirin and clopidogrel (one-month duration). At 30 days' follow-up the patient was well and in good general condition.

Discussion. Several case series suggest PBAV in patients with heart failure due to severe AS as a bridge therapy to SAVR or TAVI. As reported from Masha et al. in patients presenting with severe AS and acute cardiogenic shock, TAVI appears to be a viable treatment option although such patients population remains at elevated risk of death. TAVI might be the best strategy in selected patients with cardiogenic shock and aortic stenosis while PBAV should be performed as a bridge to a definitive therapy in the sickest patients yet to avoid futility. Whether primary PCI is the milestone for the treatment of the acute coronary syndrome, "primary" TAVI could become a procedure to be performed in patients with severe AS developing cardiogenic shock, thus becoming a life-saving procedure.

Conclusion. We present a case where a successful emergency TAVI was performed in a patient with cardiogenic shock. This is the first reported case in which an emergency TAVI has been performed using NIV and analgo-sedation further reducing the invasiveness of such procedure into an emergency setting.

A137: PREDICTORS AND CLINICAL IMPACT OF PROSTHESIS-PATIENT MISMATCH AFTER SELF-EXPANDABLE TAVI IN SMALL ANNULI – FROM TAVI SMALL REGISTRY

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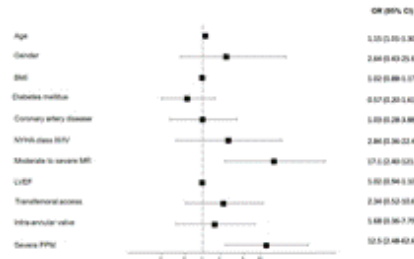
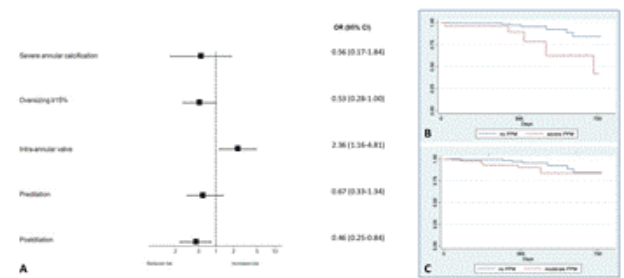
(a) HUMANITAS RESEARCH HOSPITAL; (b) SAN RAFFAELE SCIENTIFIC INSTITUTE; (c) MONTEFIORE MEDICAL CENTER; (d) ZURICH UNIVERSITY HOSPITAL; (e) ERASMUS MEDICAL CENTER; (f) POLICLINICO VITTORIO EMANUELE; (g) KERCKOFF HEART AND LUNG CENTER; (h) POLICLINICO SAN DONATO; (i) CIVIL HOSPITAL OF BRESCIA; (j) CENTRO HOSPITALAR DE LISBOA OCCIDENTAL; (k) MARIA CECILIA HOSPITAL

Objectives. Define predictors of prosthesis-patient mismatch (PPM) after transcatheter aortic valve implantation (TAVI) with self-expandable valve (SEV) in patients with small annuli, and compare outcomes in patients with and without PPM.

Background. TAVI seemed to reduce the risk of PPM incidence as compared with surgical aortic valve replacement, especially in patients with small aortic annuli. Nevertheless, predictors and outcomes of PPM in this population have not been clarified yet.

Methods. A total of four-hundred forty-five patients with (n = 129) and without PPM (n = 316) were included from TAVI-SMALL study, a retrospective registry of patients with severe aortic stenosis and small annuli treated with transcatheter SEV. Predictors of PPM and all-cause death were investigated.

Results. Intra-annular valves were found to confer an augmented risk of PPM (odds ratio [OR] 2.36, 95% confidence interval (CI) 1.16-4.81), while postdilatation (OR 0.46, 95% CI 0.25-0.84), and valve oversizing (OR 0.53, 95% CI 0.28-1.00), seemed to protect against PPM occurrence. Patients with severe PPM suffered a higher all-cause mortality when compared to those without PPM (14.6% vs 6.6%, p=0.069), and severe PPM resulted to be independent predictor of all-cause death (OR 12.5, 95% CI 2.48-62.6).



Conclusions. Patients with small aortic annuli undergoing TAVI are at higher risk of PPM, especially if implanted with intra-annular valves; conversely, postdilatation and valve oversizing are protective factor against PPM occurrence. Severe PPM is an independent predictor of all-cause death.

A138: A CASE REPORT OF CORONARY ARTERY SPASM AND TAKO-TSUBO SYNDROME: EXPLORING THE HIDDEN SIDE OF THE MOON

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Background. Tako-Tsubo syndrome (TTS) is a disease characterized by an acute and reversible myocardial injury typically precipitated by stressful and/or emotional triggers. Despite extensive research, its pathogenesis remains incompletely understood. Spasm of epicardial coronary arteries has been proposed as a potential pathogenic factor in TTS.

Case summary. Herein we report the case of a 68-year-old female admitted to the emergency department after developing chest pain in concomitance with an intense emotional stress. A diagnosis of non-ST-segment elevation myocardial infarction (NSTEMI) was made. Coronary angiography disclosed normal coronary arteries, and left ventriculography showed an inferior focal akinesia with basal and apical hyperkinesis, so that a diagnosis of focal TTS was made. Two months later, the patient was re-admitted with NSTEMI, and repeat coronary angiography showed an irregular subocclusive stenosis of a well-developed first obtuse marginal branch. After intracoronary nitroglycerine infusion, a complete recover of the vessel patency was noted, and a diagnosis of epicardial spasm was made. Intracoronary optical coherence tomography was performed to assess a residual "hazy" region, which confirmed a normal vessel morphology and a residual focal area of spasm without signs of instability.

Discussion. Whether TTS and coronary artery spasm are two expressions of the same disease, or rather two separate entities with overlapping mechanisms remains unknown, and further research is warranted to solve this issue. Meanwhile, the opportunity of performing provocative tests for coronary spasm in patients with suspected TTS might be considered to gain more insights into this hypothesis.

A139: THROMBOTIC VOLUME ASSESSED BY DUAL QUANTITATIVE CORONARY ANGIOGRAPHY PREDICTS MICROVASCULAR OBSTRUCTION AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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(a) UNIVERSITÀ CATTOLICA DEL SACRO CUORE; (b) IRCCS OSPEDALE SAN MARTINO, GENOVA

Background. To investigate the relation between the thrombotic volume detected by dual quantitative coronary angiography (QCA) and the occurrence of microvascular obstruction (MVO) assessed by cardiac magnetic resonance (CMR) in patients with ST-segment elevation myocardial infarction (STEMI).

Methods and Results. Forty-eight patients with STEMI undergoing primary percutaneous coronary intervention and receiving CMR within 7 days from admission were included. Pre-stenting thrombus volume at the site of the culprit lesion was measured by applying automated edge detection and video-assisted densitometry techniques (i.e., dual-QCA), and patients were categorized into tertiles of thrombus volume. The presence of delayed-enhancement MVO, as well as its extent (MVO mass), were assessed by CMR. Pre-stenting dual-QCA thrombus volume was significantly greater in patients with MVO than in those without (5.85 mm³ [2.05–16.71] vs. 1.88 mm³ [1.03–6.92], p=0.009). Patients in the highest tertile showed greater MVO mass compared to those in the mid and lowest tertiles (113.3 gr [0.0–203.8] vs. 58.5 gr [0.0–144.4] vs. 0.0 gr [0.0–60.225], respectively; p=0.031). The best cut-off value of dual-QCA thrombus volume for predicting the presence of MVO was 2.07 mm³ (AUC: 0.720). The addition of dual-QCA thrombus volume to the traditional angiographic indices of no-reflow enhanced the prediction of MVO by CMR (R=0.752).

Conclusions. Pre-stenting dual-QCA thrombus volume predicts the presence of MVO assessed by CMR in patients with STEMI. This methodology may aid the identification of patients at higher risk of MVO and guide adoption of preventive strategies.

A140: ACUTE HEART FAILURE EVENTS INCREASE THE LEVEL OF FRAILITY IN ELDERLY PATIENTS AFFECTED BY SEVERE AORTIC STENOSIS AND CHFpEF. A PRE TAVR EVALUATION BY MULTIDISCIPLINARY HEART TEAM

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Background. Frailty is prevalent in elderly patients (pts) with severe symptomatic aortic valve stenosis (AS) and heart failure; it associates with poor outcomes and mortality after trans-catheter aortic valve replacement (TAVR).

Purpose: To measure, by a comprehensive pre-TAVR assessment of elderly high risk pts with AS, the frailty level and its relation with chronic heart failure (CHF) and acute heart failure (AHF) to identify in advance a tailored treatment with TAVR, balloon aortic dilation (AVD), or medical therapy (MT).

Methods. In a pre-TAVR assessment of 53 pts (70% F; mean age 82.7±5.7) affected by severe AS and CHFpEF (EF=57%), we considered two groups for occurrence of AHF (average time 55 days). We evaluated Frailty (Fried score), Comorbidity (Charlson Index), disability (ADL, IADL), depression (GDS), nutritional status (MNA), cognitive impairment (MMSE) in addition to clinical features, STS score, imaging and laboratory data.

Results. AHF pts (n=20) were mainly females (85%), with higher STS score (P=0.013), NYHA III-IV (P<0.0002), EF=50% (P<0.0001), higher PAFs (P=0.008) and tricuspid valve regurgitation >2 (P=0.008). They were at risk of malnutrition (P=0.006), depression (P=0.03), with higher comorbidity (P=0.02) and disability (P=0.04). 75% of AHF pts had sarcopenia by handgrip test (P=0.004) and CPK value (P=0.002), higher N/L ratio (P=0.01), higher creatinine (P=0.02) and BNP (P=0.02). 10% of AHF pts were pre-frail, 30% frail, 90% severely frail. After Heart Team evaluation, the 75% of pre-frail and 47% of early-frail pts have been referred to TAVR (P<0.0001); they are mainly affected by CHF (75%). Instead, the 53% and 37% of late-frail pts were referred to medical therapy and AVD, respectively (P<0.0001); they were mainly affected by AHF (60%).

Conclusions. Patients with AS and CHF+AHF become late frail so losing indication for TAVR. Our data suggest the need of a precocious evaluation of elderly pts with severe AS for elective TAVR treatment before the occurrence of AHF, since this event associates with a worsening degree of individual frailty.

A141: INTRACORONARY BOLUS OF GLYCOPROTEIN IIB/IIIA INHIBITOR AS BRIDGING OR ADJUNCTIVE STRATEGY TO ORAL P2Y12 INHIBITOR LOAD IN THE MODERN SETTING OF STEMI

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Aims. In the acute management of ST-elevation myocardial infarction (STEMI), glycoprotein IIb/IIIa inhibitors (GPIs) bolus not followed by intravenous infusion as adjunctive or bridging therapy to oral P2Y₁₂ inhibitors is potentially advantageous given their fast onset and offset of action, but clinical evidence in their support is limited.

Methods and Results. Out of 423 consecutive STEMI patients, 297 met the inclusion and exclusion criteria and were enrolled. Of them, 107/297 (36%) received an intracoronary GPI bolus-only during primary percutaneous coronary intervention (PPCI) not followed by intravenous infusion and 190/297 (64%) received standard antithrombotic therapy. Of the 107 GPI-treated, 22/107 (21%) had P2Y₁₂ inhibitor pre-treatment (adjunctive strategy) and 85/107 (79%) did not (bridging strategy). During hospital staying, there was no difference in the primary safety endpoint of TIMI major-minor bleeding (p=0.283), TIMI major (p=0.267) or TIMI minor (p=0.685) bleeding between groups. No stroke event occurred in the GPI group. Despite patients receiving GPI having a significantly higher intraprocedural ischemic burden, no significant differences were found in the efficacy outcomes between groups. Consistent findings were observed for patients receiving GPIs bolus before (bridging strategy) or after (adjunctive strategy) P2Y₁₂ inhibitors, compared to those receiving standard therapy. Multivariate logistic regression analyses did not find any independent predictors significantly associated to the primary and secondary composite endpoints.

Conclusion. In a contemporary real world population of STEMI patients undergoing PPCI, the use of intracoronary GPIs bolus-only in selected patients at high ischemic risk is safe and could represent a useful

antithrombotic strategy both in those pre-treated and in those naïve to P2Y₁₂ inhibitors. Larger trials are warranted to test its efficacy.

A142: MACROPHAGE INFILTRATES IN CORONARY PLAQUE EROSION IN PATIENTS WITH ACUTE CORONARY SYNDROMES

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Introduction. Plaque erosion (PE) is responsible for at least one-third of acute coronary syndrome (ACS), and inflammation plays a key role in plaque instability. We assessed the presence of optical coherence tomography (OCT)-defined macrophage infiltrates (MØI) at the culprit site in ACS patients with PE, evaluating their clinical and OCT correlates, along with their prognostic value.

Methods. ACS patients undergoing OCT imaging and presenting PE as culprit lesion were retrospectively selected. Presence of MØI at culprit site was assessed. The incidence of major adverse cardiac events (MACEs), defined as the composite of cardiac death, recurrent myocardial infarction and target-vessel revascularization (TVR), was assessed [follow-up median (interquartile range, IQR) time 2.5 (2.03–2.58) years].

Results. We included 153 patients [median age (IQR) 64 (53–75) years, 99 (64.7%) males]. Fifty-one (33.3%) patients presented PE with MØI and 102 (66.7%) PE without MØI. Patients having PE with MØI compared with PE patients without MØI had more vulnerable plaque features both at culprit site and at non-culprit segments. MACEs were significantly more frequent in PE with MØI patients compared with PE without MØI [11 (21.6%) vs. 6 (5.9%), p=0.008], mainly driven by a higher risk of cardiac death and TVR. At multivariable Cox regression, PE with MØI was an independent predictor of MACEs [HR 2.95, 95% CI (1.09–8.02), p=0.034].

Conclusions. Our study demonstrates that among ACS patients with PE the presence of MØI at culprit lesion is associated with more vulnerable plaque features, along with a worse prognosis at a long-term follow-up.

A143: USO DI ADENOSINA INTRACORONARICA E DI INIBITORI GP IIB/IIIA IN CORSO DI ANGIOPLASTICA PRIMARIA IN PAZIENTI STEMI: ESPERIENZA DI UN SINGOLO CENTRO

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Background. In corso di STEMI l'impiego di inibitori Gp IIb/IIIa (GPI) è attualmente raccomandato solo in condizioni di bailout. Le evidenze concernenti la somministrazione intracoronarica di adenosina sono contrastanti. Il nostro studio si propone di valutare l'impatto prognostico a breve e a lungo termine della somministrazione di adenosina intracoronarica in associazione ad inibitori Gp IIb/IIIa in pazienti ad elevato rischio trombotico in corso di angioplastica primaria in pazienti STEMI.

Metodi. È stato condotto uno studio caso-controllo su una coorte di 178 pazienti sottoposti ad angioplastica coronarica primaria (pPCI) in corso di STEMI presso il reparto di Cardiologia dell'Azienda Ospedaliera Universitaria Paolo Giaccone di Palermo. I pazienti sono stati suddivisi in tre bracci di trattamento: somministrazione intracoronarica di GPI + adenosina (gruppo 1, n = 56); somministrazione intracoronarica di GPI (gruppo 2, n = 63); gruppo controllo (gruppo 3, n = 59). Gli endpoint primari erano: risoluzione completa del sopraslivellamento ST (STR) a 60 minuti dal termine della procedura, TIMI di grado 3 nel vaso culprit a fine procedura. Gli endpoint secondari erano: Myocardial blush grade (MBG) di grado 3 nel territorio dell'infarto a fine procedura; recupero della cinesi segmentaria nella zona interessata dall'infarto e della frazione d'ieiezione (FE), minor numero di eventi avversi cardiaci maggiori (MACE) al follow-up; minor numero di eventi emorragici maggiori o minori.

Risultati. L'STR nel gruppo 1 è stata di 1,96 mm vs 1,87 mm nel gruppo 2 vs 1,25 mm nel gruppo 3 (p<0,001); la percentuale di riduzione è stata dell'80,16% vs 81,8% vs 58,71% (p<0,001). Il recupero percentuale della frazione d'ieiezione (FE%), valutata al follow-up, è stata nettamente maggiore nel gruppo 1 rispetto al gruppo 3 (15,50% nel gruppo 1, 10,10% nel gruppo 2 e 2,35% nel gruppo 3, p<0,001). Analoghi risultati per il Wall Motion Score Index (18,14% gruppo 1 vs 10,73% gruppo 2 vs 6,82% gruppo 3, con p=0,004). I MACE nel gruppo 1 erano 10,71% vs 17,46% nel gruppo 2 vs 32,2% nel gruppo 3 (p=0,013); analogamente è stata evidenziata una percentuale minore di decessi nel gruppo 1 (3,57%) e nel gruppo 2 (4,76%) rispetto al gruppo 3 (18,64%), con p=0,006. Gli eventi emorragici maggiori e minori, non hanno mostrato una differenza statisticamente significativa tra i vari gruppi (1,79% nel gruppo 1, 7,93% nel gruppo 2 e 6,78% nel gruppo 3, con p=0,310). In merito ai parametri angiografici sono stati evidenziati dei risultati migliori nel gruppo 1 rispetto agli altri gruppi, in particolare la percentuale maggiore di pazienti con MBG 3 post-pPCI è stata rilevata nel gruppo 1 con una differenza statistica estremamente significativa (rispettivamente 60,71% nel gruppo

1, 38,1% nel gruppo 2 e 23,73% nel gruppo 3, con $p < 0,001$). Riguardo il TIMI post-pPCI invece non sono state riscontrate differenze statisticamente significative tra i gruppi.

Conclusioni. Sulla base dei risultati ottenuti nel presente studio è possibile affermare che i pazienti a cui, in corso di pPCI, sono stati somministrati congiuntamente, l'inibitore della GP IIb/IIIa e l'adenosina intracoronarica, hanno dimostrato di raggiungere migliori risultati rispetto al gruppo trattato con solo inibitore in quasi tutti gli end point primari e secondari.

A144: INTRAVASCULAR ULTRASOUND AND ITS APPLICATIONS IN THE CATH LAB: A CASE REPORT

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Background. Use of Intravascular Ultrasound (IVUS) can be very helpful in the catheterization laboratory, especially when coronary angiography alone leaves unresolved doubts. Among its possible applications, it can be fundamental to assist in three specific contexts: i) precise assessment of angiographical borderline or intermediate stenoses; ii) assessment of previously treated lesions; iii) PCI guidance and optimization. The present report exemplifies these three case-scenarios, underlying the synergic interaction between angiography and IVUS in case of synchronization and overlay of these two imaging modalities.

Case description. A 56-year-old male with hypertension and history of coronary artery disease (CAD) and previous PCI for NSTEMI one year back. At the 1-year follow-up, the patient reported progressively worsening effort angina over the previous weeks. A treadmill stress test revealed ischemic EKG-modifications at peak exercise. The patient was thus referred to our hospital for coronary angiography which showed disease progression with an intermediate stenosis of the left anterior descending artery (LAD) and an irregular intimal profile of the intra-stent segment. The patient had normal left ventricular function without regional wall motion abnormalities. The lesion was then assessed by means of IVUS with the SyncVision modality (Philips Volcano, Ca, USA), that synchronizes IVUS frames with the coronary angiogram, revealing moderate neointimal proliferation with underexpansion of the previously implanted stent and a severe stenosis close to the proximal edge of the stent with slight calcification. Thus, optimization of the previously implanted stent was obtained through high-pressure non-compliant balloon dilation (3,5 x 14 mm, expanded at 8 ATM for 120"), while an additional stent (3,5 x 15 mm, expanded at 16 ATM for 20") was implanted proximally to cover the severe stenosis close to the proximal edge of the stent. Thus we performed PCI of restenosis and stenting of proximal LAD, with a good angiographic result. Final assessment by means of IVUS showed an improved result within the previously implanted stent with an increase in lumen area and a good expansion of the newly implanted stent with proper apposition of stent struts. The patients was discharged asymptomatic the next day with dual antiplatelet treatment (ASA 100 mg o.d. and ticagrelor 90 mg b.i.d.).

Conclusions. IVUS is a useful tool in evaluating in-stent restenosis and understanding the underlying mechanisms. In particular, the use of IVUS and its synchronization with the angiography was very useful to: i) assess in-stenosis neointimal proliferation and the under-expansion of the previously implanted stent; ii) characterize the intermediate stenosis and evaluate the distal landing zone in relation to the proximal edge of the previously implanted stent; iii) guide PCI, thus helping to select stent size and assess and to optimize PCI result. The usefulness of IVUS in guiding PCI is supported by a growing wealth of data. In fact, recent meta-analyses including about 30.000 patients showed that IVUS guidance is able to prevent major adverse cardiovascular events (MACE) including early and late ST and myocardial infarction and mortality at 1 year.

A145: MINOCA: ERGONOVINE TEST FOR THE DIAGNOSIS

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Introduction. Myocardial infarction with non-obstructive coronary arteries (MINOCA) is diagnosed when a patient meets the three MINOCA criteria: AMI criteria according to the Fourth Universal definition; obstructive coronary arteries as per angiographic guidelines, with no lesions >50% in a major epicardial vessels; no other clinically overt specific cause that can serve an alternative cause. The diagnostic algorithm for MINOCA is based on several exams that need to be performed in order to detect the real cause of MINOCA, that could be detected in more than 75% of patients with chest pain, high-sensitive troponin I (hs-TnI) above 99% percentile and no obstructive lesions >50% of coronary vessels. Coronary artery vasospasm is a common and underestimated cause of MINOCA that required an intracoronary functional test for a correct diagnosis and proper management.

Case report. A 64-year-old man with a medical history of arterial hypertension presented to the emergency room because of a severe chest pain episode, radiating to the back and left arm, started 30 minutes previously. An electrocardiogram was performed and ST-segment elevation was recorded in I, aVL, V2-V6 leads and ST-segment depression was recorded in II, III, aVF leads. The time-0 hs-TnI was elevated at 941.840 pg/mL (normal value <34.2). Because of the suspect of a ST-segment elevation myocardial infarction (STEMI), the patient was immediately transferred to the cardiac catheterization laboratory: coronary angiography (CAG) showed a mild atherosclerosis plaque of the left coronary artery (LCA). In consideration of the clinical and laboratory presentation, an ergonovine test was performed, resulting positive for diffuse epicardial coronary spasm with a completely spasm of first and second diagonal arteries and distal portion of circumflex artery. The patient was subsequently transferred to the Intensive Care Unit (ICU) and an echocardiogram was performed showing an ejection fraction of 60% with a mild hypokinesis of the apical region. MINOCA on coronary arteries spasm was the final diagnosis and the patient was discharged home on a daily aspirin, statin, angiotensin-converting enzyme inhibitor (ACE-i), nitrates and calcium channel blocker (CCB).

Discussion. With this case report, we described a possible diagnostic and therapeutic management of a patient with AMI criteria and no relevant coronary arteries obstruction. In evaluating MINOCA patient, the first step is to find the cause of myocardial injury during the coronary angiography: coronary artery thrombosis or spasm or plaque rupture should be considered at this level and intracoronary functional test with ergonovine or intravascular imaging (IVUS or OCT) should be performed. Once these conditions have been excluded, cardiac magnetic resonance (CRM) could help detecting ischemic or non-ischemic patterns related to myocarditis or Takotsubo. In the presented case, provocative test with ergonovine was fundamental for the diagnosis and the correct therapeutic management. When coronary artery spasms are diagnosed, CCB and nitrates are the first therapeutic choice, also reducing the risk of vasospastic angina episodes.

In conclusion, coronary artery spasm is a condition that can be underestimated and for this reason provocative test is crucial when a patient with suspect of STEMI has no lesions during CAG.

A146: DOUBLE ANTEROGRADE AND RETROGRADE APPROACH FOR LARGE PULMONARY ARTERIOVENOUS MALFORMATION EMBOLIZATION

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Pulmonary arteriovenous malformations (PAVMs) are an underappreciated cause of respiratory failure and life-threatening neurological events. Recanalization represents a possible long-term complication of percutaneous treatment, associated with recurrence of embolic events. We present a clinical case of a successfully treated PAVM using a double access technique, transfemoral transeptal (retrograde) and transfemoral transpulmonary artery (anterograde) for contemporary percutaneous embolization of both arterial and venous branches to minimize subsequent recanalization, in a patient with systemic desaturation and thrombophilia, thus at high risk for paradoxical ischemic stroke.

A147: NUOVE PROSPETTIVE PER TAVI CON APPROCCIO TRANS-FEMORALE IN PAZIENTI CON ESTESA MALATTIA CALCIFICA ED ESTREMA TORTUOSITÀ DELL'ASSE ILIACO-FEMORALE

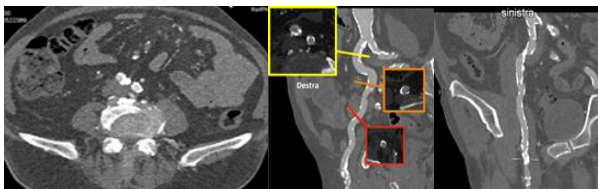
Marco Russo (c), Marco Gambardella (c), Guido Grossi (c), Pierluigi Demola (a, c), Alessio Mattesini (a), Francesco Meucci (a), Carlo Pratesi (b, d), Carlo Di Mario (a, d)

(a) INTERVENTISTICA CARDIOLOGICA STRUTTURALE, AZIENDA OSPEDALIERA UNIVERSITARIA CAREGGI; (b) CHIRURGIA VASCOLARE, AZIENDA OSPEDALIERA UNIVERSITARIA CAREGGI; (c) UNIVERSITÀ DEGLI STUDI DI FIRENZE, SCUOLA DI SPECIALIZZAZIONE IN MALATTIE DELL'APPARATO CARDIOVASCOLARE; (d) UNIVERSITÀ DEGLI STUDI DI FIRENZE

Presentiamo il caso del paziente S.G. di 82 anni, affetto da stenosi aortica severa (G max 80/med 48 mmHg) sintomatica per dispnea da sforzo (NYHA III) con indicazione alla correzione della valvulopatia mediante TAVI. Il paziente presenta plurime comorbidity tra cui coronaropatia critica trattata mediante bypass in mammaria ad Y su discendente anteriore e ramo marginale, impianto di stent su tronco comune verso l'arteria circonflessa (2011) e su coronaria destra ed arteria interventricolare anteriore prossimale (2017). Alla valutazione mediante Angio TC toraco-addominale vi erano grossolane calcificazioni parietali a carico dell'aorta toraco-addominale con quadro di aorta a porcellana sull'aorta ascendente, aneurisma fusiforme (31 mm) dell'aorta addominale sottorenale con severe diffuse placche calcifiche a carico della iliaca esterna e comune destra (calcio circonferenziale, diametro minimo 3,5x5,5 mm) e della femorale comune di destra ed occlusione della femorale comune sinistra. All'ecodoppler dei tronchi sovraortici, ateromasia carotidea bilaterale calcifica non critica (50%). Dato il rischio di compromissione dei grafts con approccio succlavio, la cattiva qualità

delle carotidi e la severità dell'aterosclerosi polidistrettuale associate all'importante tortuosità dell'asse iliaco femorale, si è deciso di procedere all'esecuzione di TAVI mediante esposizione chirurgica dell'accesso arterioso femorale destro in collaborazione con i colleghi della chirurgia vascolare. Dopo aver punto al di sopra delle calcificazioni subocclusive dell'arteria femorale comune destra, per estrema calcificazione dell'arteria iliaca esterna e comune destra, è stata eseguita litotripsia intravascolare con pallone Shockwave 7.0 x 60 mm (300 emissioni) e successiva dilatazione mediante pallone periferico 9.0 x 40 (sino a 12 atm) e 8.0 x 40 mm (sino a 14 atm). Si è quindi proceduto con valvuloplastica aortica mediante pallone VACS II 18 x 40 mm con successivo impianto di protesi CoreValve Evolut R 26 mm. Al controllo angiografico finale, insufficienza residua di grado lieve. All'ecocardiografia post procedura, dimostrazione di normoposizionamento della protesi aortica con leak laterale di grado lieve. Il decorso post operatorio è stato complicato da iniziale anemia; alla TC addome completo dimostrazione radiologica di limitato ematoma a livello della radice femorale destra, non rifornito. In terza giornata il paziente è stato mobilizzato.

La collaborazione multidisciplinare tra emodinamisti e chirurghi vascolari e l'utilizzo di tecniche di litotripsia intravascolare mediante Shockwave permette di completare con successo la TAVI mantenendo l'approccio transfemorale che si è dimostrato il più sicuro nei trial controllati anche nei casi più estremi di polivasculopatia.



A148: A CHALLENGING ANOMALOUS ORIGIN OF THE LEFT CORONARY ARTERY

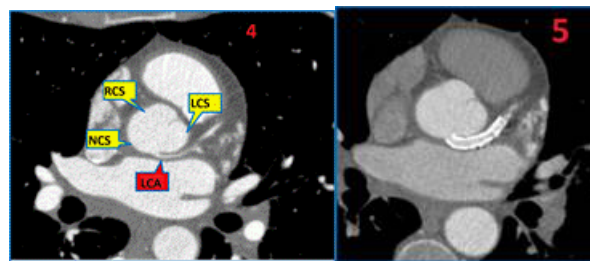
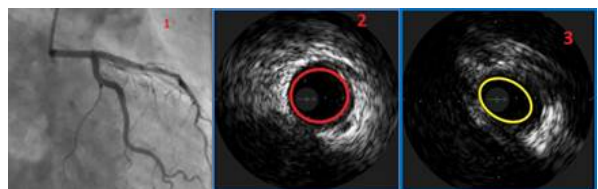
Maria Sabatini (a), Gino Duronio (b), Stefania Uguccioni (b), Giuseppe Ciliberti (a), Giulia Stronati (a), Alessandro Rosario Parisi (b), Francesca Mirabella (b), Alessia Urbinati (a), Lucia Uguccioni (b), Michela Casella (a), Lucia Marinucci (b), Federico Guerra (a), Antonio Dello Russo (a)

(a) CARDIOLOGY AND ARRHYTHMOLOGY CLINIC, UNIVERSITY HOSPITAL MARCHE POLYTECHNIC UNIVERSITY, ANCONA; (b) HEMODYNAMICS AND INTERVENTIONAL CARDIOLOGY, NORTH MARCHE UNITED HOSPITALS, PESARO

Background. Anomalous aortic origin of a coronary artery (AAOCA) is a congenital condition in which a major coronary artery arises from the wrong sinus of Valsalva. It has an estimated incidence of 0,1-0,3% in the general population. Although the first-choice approach to AAOCA is currently surgery, some successful cases of stenting the right coronary artery (RCA) with an anomalous origin have been described in literature.

Case report. A 42-year-old female presented to the emergency department complaining of exertional chest pain as well as some episodes of thoracic discomfort at rest. She underwent an exercise stress test which was positive for symptoms and ECG modifications. She then underwent a coronary angiography that showed an anomalous origin of the left coronary artery (LCA) from the non-coronary sinus (NCS) (Figure 1). IVUS showed a dynamic compression of the proximal part of the LCA during heart systole (Figures 2; 3). Such a finding suggested an intramural course. The LCA was studied with a CT coronary angiography (CTCA) (Figure 4) and surgical management was established. After a few days, she had a sudden cardiac arrest for a ventricular fibrillation treated with DC shock and ventilation management. The coronary angiography was repeated, and the patient was treated with a new generation DES placed from the origin of the LCA along the axis of left descending artery. The circumflex artery was treated with POBA. A new CTCA confirmed the success of the percutaneous intervention (Figure 5). Six days after, the patient underwent a second exercise test. She reached the maximum loading phase and the test was negative both for symptoms and ECG modifications.

Conclusions. The adverse event rate linked to the surgical correction of an AAOCA is reported to be 15%. Moreover, in the postoperative period, some patients continue to have evidence of ischemia. This case shows an effective and safe PCI of an extremely rare anomalous origin of the LCA in an acute setting.



A149: ACS IN THE YOUTH: COULD THE VARICELLA ZOSTER VIRUS BE ONE OF THE MAIN PLAYERS?

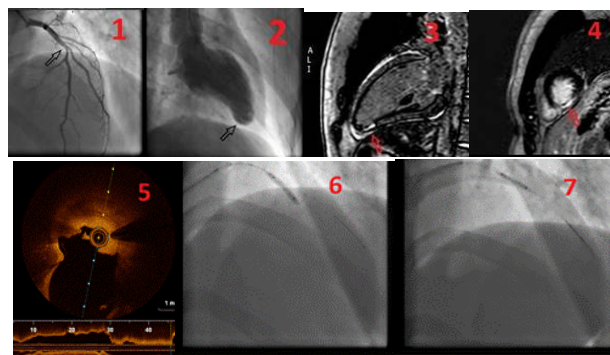
Maria Sabatini (a), Gino Duronio (b), Giuseppe Ciliberti (a), Alessandro Rosario Parisi (b), Stefania Uguccioni (b), Giulia Stronati (a), Francesca Mirabella (b), Alessia Urbinati (a), Lucia Uguccioni (b), Michela Casella (b), Lucia Marinucci (b), Federico Guerra (a), Antonio Dello Russo (a)

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Background. An association between the Varicella Zoster virus (VZV) and an increased risk of cardiovascular events can be found described in current literature. A possible mechanism seems to be related to the inflammatory response to the infection, based on pro thrombotic antibodies and cytokines. The virus itself can therefore lead to a vasculopathy.

Case report. A 22-year-old male with occasional smoking habit and without other cardiovascular risk factors presented to the emergency department complaining of acute chest pain while resting. The electrocardiogram showed an ST elevation in the inferior leads and in the precordial leads (V3-V4). He was brought in the emergency department and then into the Cath Lab. When he arrived, he presented a skin rash compatible with chickenpox. The patient underwent a coronary angiography which detected an eccentric plaque with borderline significance in the middle tract of the left anterior descending artery (LAD) with a TIMI 3 flow (Figure 1). The ventriculography showed a pronounced apical hypokinesia (Figure 2). The suspicion of a myopericarditis came out and needed to be urgently confirmed through a cardiac magnetic resonance (CMR). The CMR showed an apical transmural damage in line with an acute myocardial infarction (Figures 3; 4). A PCI was performed with the support of the intravascular optical coherence tomography (OCT) which confirmed a thrombotic formation (Figure 5). The LAD was treated with a bioabsorbable stent and the first diagonal with POBA for a shift of the thrombotic material in that branch (Figures 6; 7).

Conclusion. In current literature, risk of experiencing cardiovascular events in the first year after the reactivation of VZV is 10 to 30% higher to those with no reactivation. Our case shows how the primary infection as well could be linked with the development of an acute coronary syndrome, even in patients with low cardiovascular risk.



A150: A SINGULAR PRESENTATION OF CORONARY FISTULA

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(a) DIPARTIMENTO DI MEDICINA, STRUTTURA COMPLESSA DI MEDICINA INTERNA, AZIENDA OSPEDALIERA SANTA MARIA DI TERNI; (b) UNIVERSITÀ DEGLI STUDI DI PERUGIA; (c) CENTRO SERVIZI GROCCO, RIABILITAZIONE CARDIOLOGICA, PERUGIA

Case report. A 39-year-old runner was evaluated at the "Grocco Cardiac Rehabilitation Center" for the occurrence of dyspnea and mild precordial discomfort during intense efforts. Such symptoms were attenuated with reducing the effort. Apart for being a former smoker, his previous disease

history was unremarkable. At the physical examination of the heart, the cardiac impulse was palpable at the left fifth intercostal space; cardiac activity was rhythmic and normofrequent; a continuous systo-diastolic murmur with a trill was appreciated at the left sternal border in the third intercostal space, suggesting intra-cardiac shunt. There were no signs related to heart failure. Blood pressure and electrocardiography trace were within the normal limits.

A trans-thoracic echocardiography revealed enlarged right cardiac chambers: right superior-inferior x latero-lateral atrial diameters, evaluated at the four chambers view, were 52 x 47 mm, with a corresponding right atrial area of 21 cm². The right ventricle was dilated (basal diameter 49 mm); the diameter of inferior vena cava (IVC) was enlarged (25 mm); the inferior cava index was reduced by 30%, suggesting elevated systolic pulmonary arterial pressure (47 mmHg). Based on the absence of clear signs revealing the source of the appreciated heart murmur, the diagnostic work-up was implemented with trans-esophageal echocardiography, which revealed a continuum solution at the level of interatrial septum, of about 1 cm length. At the color-Doppler examination, a left-to-right interatrial shunt was demonstrated, suggesting inter-atrial defect. An indication to cardiac surgery consult was made, and a coronary angiography with right cardiac catheterization was planned in order to complete the diagnostic work-up. This exam revealed an ectasic right coronary artery with a fistula, and a significant interatrial shunt with elevated QP/QS ratio. The interventricular posterior artery originating from the fistula was vascularized by heterocoronary collateral circulation. To better define the anatomical boundaries of the right coronary artery and the fistula, a coronary CT scan was performed, that showed ectasic right coronary artery and the presence of distal fistula connecting the aforementioned artery with the right atrium and vena cordis magna, inducing significant shunt.

Discussion and Conclusions. Coronary fistulas are rare abnormalities found in about 0,1% of patients undergoing cardiac catheterization. Fistulas may originate from any tract of the coronary arteries; in half of cases, the fistula originates from the right coronary artery, and often involves the right atrium, the right ventricle and the pulmonary arteries. Fistulas can be asymptomatic or not, being the symptoms related to the extent of the shunt. Asymptomatic forms are occasionally found, and generally occur in adult patients. Conversely, symptomatic forms can be detected due to the presence of angina, "coronary theft", heart failure or ventricular overload, and are associated with higher morbidity and mortality. In the American College of Cardiology guidelines, percutaneous or surgical closure represents a Class I recommendation for large fistulae regardless of symptoms and for small- to moderate-size fistulae with evidence of myocardial ischemia, arrhythmia, ventricular dysfunction, ventricular enlargement, or endarteritis. The conservative treatment is reserved for small fistulas accidentally discovered in asymptomatic patients, provided that a periodic echocardiographic evaluation is performed to quantify the possible growth and/or hemodynamic changes that may occur.

A151: COMBINED TWO-STEP PROCEDURE OF MITRACLIP AND LEFT ATRIAL APPENDAGE OCCLUSION IN THE SAME PATIENT: A CASE REPORT

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(a) UNIVERSITÀ DI ROMA TOR VERGATA

Background. Percutaneous transcatheter mitral valve repair (MVR) using the MitraClip system is a consolidated procedure to treat selected patients with degenerative or functional mitral regurgitation (MR). Its safety and efficacy in high surgical risk-patients has been consistently demonstrated, both in clinical trials and in real-world settings. Atrial fibrillation is frequently observed in this setting, and the presence of contraindication to oral anticoagulant therapy is also common in these patients. In this context, percutaneous left atrial appendage occlusion (LAO) may be a valid alternative.

Purpose. This clinical case shows the efficacy of a combined two steps procedure of percutaneous transcatheter MVR using the MitraClip system and LAO in patients with contraindications to anticoagulant therapy.

Methods. We report the case of a patient with severe primary MR, symptomatic for heart failure despite optimal medical therapy and cardiac resynchronization, with atrial fibrillation and contraindication for anticoagulant therapy due to high bleeding risk. Therefore, it was decided to perform a combined two-steps transcatheter procedure of MVR and LAO.

Results. A 78-year-old patient, previous smoking, affected by hypertension and permanent atrial fibrillation in treatment with oral anticoagulant therapy was hospitalized for progressive and severe dyspnea. His comorbidities included chronic Kidney disease, chronic anemia and previous kidney cancer. Trans-thoracic (TTE) and trans-esophageal echocardiogram (ETE) showed normal left ventricular ejection fraction (LVEF 55%) and severe primary MR with eccentric jet due to P2 prolapse. The patient, deemed inoperable due to prohibitive surgical risk,

symptomatic despite optimal medical therapy, underwent a percutaneous edge-to-edge procedure. A single XTR clip was implanted in A2-P2 position with residual mild moderate MR and mean transvalvular gradient of 3 mmHg without peri and post procedural complications. Six months after the procedure, the patient reported a functional improvement; TTE showed the persistence of a mild moderate MR but he referred several hospitalizations for melena anemia. Considered long-term oral anticoagulant therapy indication, concomitant high bleeding risk (HAS-BLED score 5) and clinical frailty, the patient underwent to percutaneous LAO with Amplatzer device. During follow-up, the patient reported an improvement of quality of life with lower rates of hospitalizations.

Conclusions. In selected patients with high surgical risk, atrial fibrillation and increased bleeding risk, a combined two-steps procedure with MitraClip and LAO is feasible, safe and effective.

A152: NEUTROPHIL TO LYMPHOCYTE RATIO PREDICTS HEART FAILURE ADMISSIONS AFTER TRANCATHETER AORTIC VALVE REPLACEMENT

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(a) DEPARTMENT OF CARDIOVASCULAR DISEASE, GEMELLI MOLISE SPA, CAMPOBASSO; (b) DEPARTMENT OF RADIOLOGY, GEMELLI MOLISE SPA, CAMPOBASSO; (c) DEPARTMENT OF MEDICINE AND HEALTH SCIENCES "V. TIBERIO", UNIVERSITY OF MOLISE, CAMPOBASSO

Background. Neutrophil-to-lymphocyte ratio (NLR) has prognostic value in cardiovascular disease. The role of NLR in predicting HF admissions in TAVR patients is not fully clarified. It is theorized to be two pronged: firstly, inflammatory reactions are known to contribute to the development of HF; and secondly, inflammatory stimuli lead to the release of cytokines and proteolytic enzymes causing destruction of the myocardium and decreased left ventricular function. In HF, the hypothalamic pituitary axis is activated leading to increased cortisol production resulting in decrease in the relative concentration of lymphocytes. Lymphopenia has also been associated with a poor prognosis in HF. In this study we have evaluated NLR as a predictor of HF admission in patients undergoing transcatheter aortic valve replacement (TAVR).

Methods. A total of 115 consecutive TAVR candidates, hospitalized at Gemelli Molise in Campobasso, were enrolled in this study. Baseline characteristics and laboratory tests were collected and analyzed. NLR was evaluated at admission, implantation day and discharge. Patients with HF hospitalization in 2 year follow-up (n=9) were compared to those without (n=106).

Results. There were no differences between the two groups in patient baseline characteristics. Higher NLR at admission (4,62±4,27 vs 3,13±1,59, p=0.003), was significantly associated with HF hospitalization during follow-up in patients undergoing TAVR. Multivariate analysis, adjusted for EF, age, CRP, sex, CKD, moderate to severe paravalvular leak (PVL), revealed that NLR calculated at admission was an independent predictor of AHF (OR 1,435; 95% IC 1,038-1,894; p=0,029).

Conclusion. In our patients, higher NLR at admission was significantly associated with HF hospitalization during follow-up in patients undergoing TAVI. These preliminary results need to be elucidated with larger and more specifically designed studies.

Multivariate analysis – predicting factors for AHF

Factor	P value	OR	95% CI for OR
NLR admission	0,029	1,435	1,038-1,984
EF	0,931		
Age	0,805		
Sex	0,828		
CRP	0,863		
CKD	0,960		
PVL (mod to sev)	0,126		

A153: CONTRAST-INDUCED ACUTE KIDNEY INJURY IN PATIENTS UNDERGOING TAVI COMPARED TO CORONARY INTERVENTIONS

Gabriele Venturi (a), Michele Pighi (a), Flavio Ribichini (a)
(a) AZIENDA OSPEDALIERA UNIVERSITARIA INTEGRATA - VERONA

Background. Differences in the impact of contrast medium on the development of contrast-induced acute kidney injury (CI-AKI) in patients undergoing transcatheter aortic valve implantation (TAVI) or coronary angiography/percutaneous coronary interventions (CA/PCI) have not been previously investigated.

Methods and Results. Patients treated with TAVI or elective CA/PCI were retrospectively analysed in terms of baseline and procedural characteristics including pre/post-procedural kidney function. CI-AKI was defined as a relative increase in SCr (serum creatinine) concentration of at least 0.3mg/dL within 72 hours of contrast-medium administration compared with baseline. The incidence of CI-AKI in the TAVI vs CA/PCI group was compared. After the exclusion of patients in dialysis and emergency procedures, 977 patients were analysed: 489 TAVI (50.1%), 488 CA/PCI (49.9%). TAVI patients were older, presenting a higher rate of anemia and chronic kidney disease (p<0.001 for all comparisons). Consistently, they also had a significantly lower glomerular filtration rate and higher SCr (p<0.001 for all). However, the occurrence of CI-AKI was

significantly lower in these patients compared to CA/PCI (6.7% versus 14.5%, $p<0.001$). At multivariate analysis, TAVI procedure had an independent protective effect on CI-AKI incidence among total population (OR 0.334; 95% CI 0.193-0.579; $p<0.001$). This observation was confirmed after propensity score matching among 360 patients (180 TAVI and 180 CA/PCI; $p=0.002$).

Conclusions. CI-AKI occurred less frequently in patients undergoing TAVI than in CA/PCI subjects, despite a worse risk profile. The impact of contrast administration on kidney function in TAVI patients may be better tolerated because of the hemodynamic changes following aortic valve replacement.

A154: CONTRAST-INDUCED NEPHROPATHY IN PATIENTS WITH AORTIC STENOSIS UNDERGOING CONCOMITANT OR STAGED CORONARY AND VALVULAR PROCEDURES

Gabriele Venturi (a), Michele Pighi (a), Flavio Ribichini (a)
(a) AZIENDA OSPEDALIERA UNIVERSITARIA INTEGRATA - VERONA

Background. The impact of staged versus concomitant coronary procedures on renal function in patients with severe aortic stenosis (AS) undergoing transcatheter aortic valve implantation (TAVI) remains unclear.

Methods. Patients undergoing CA/PCI one week up to 4 months before TAVI (staged strategy), or during the same TAVI procedure (concomitant strategy), were retrospectively analyzed in terms of baseline, procedural characteristics and kidney function, both pre-and post-procedure. Contrast-induced acute kidney injury (CI-AKI) was defined as a relative increase in serum creatinine (Scr) concentration of at least 0.3 mg/dL, compared to baseline, within 72 hours after the index procedure (CA/PCI pre-TAVI for the staged group, TAVI, and CA/PCI for the concomitant group). Thirty-day follow-up data after TAVI were collected to assess the early safety outcomes of TAVI procedures.

Results. After the application of exclusion criteria, 334 patients were considered for this analysis: 151 (45.2%) underwent staged pre-TAVI coronary procedures, and 183 (54.8%) followed a concomitant strategy. CI-AKI occurred in 33 patients following pre-TAVI coronary procedures vs. 8 patients in the concomitant strategy group (21.9% vs. 4.4%, $p<0.001$). Staged pre-TAVI coronary procedures caused a higher incidence of CI-AKI than concomitant TAVI and coronary procedures at univariate and multivariate analyses ($p<0.001$). Furthermore, performing CA/PCI during the same TAVI procedure did not impact the overall early safety TAVI outcomes compared to the staged strategy ($p=0.609$).

Conclusions. Performing staged pre TAVI coronary procedures yields a significantly higher risk of CI-AKI compared with concomitant strategy. Moreover, the concomitant strategy did not increase the risk of procedure-related complications.

CARDIONCOLOGIA E CARDIOTOSSICITÀ

A155: PRE-TREATMENT HIGH-SENSITIVITY TROPONIN T FOR THE SHORT-TERM PREDICTION OF CARDIAC OUTCOMES IN PATIENTS ON IMMUNE CHECKPOINT INHIBITORS

Serena Petricciuolo (a), Maria Grazia Delle Donne (b), Alberto Aimo (a), Antonio Chella (b), Giacinta Guarini (b), Raffaele De Caterina (a, b)
(a) UNIVERSITÀ DI PISA; (b) AOU P

Background. Immune checkpoint inhibitors (ICIs) are an emerging option for several advanced metastatic cancers, but have been associated with cardiotoxicity. The prognostic value of high-sensitivity troponin T (hs-TnT) measured before treatment start has never been investigated.

Materials and Methods. Thirty consecutive patients underwent measurement of hs-TnT before starting ICI therapy (pembrolizumab, 23%; nivolumab, 12%; atezolizumab, 6%; durvalumab, 5%). The primary endpoint was a composite of cardiovascular death, stroke or transient ischemic attack, pulmonary embolism and new-onset heart failure. The secondary endpoint was progression of cardiac involvement according to the CARDIOTOX staging system.

Results. Patients (median age 68 years, 77% men, 13% with coronary artery disease, 90% current or former smokers, 67% overweight or obese, and 43% hypertensive) had a median hs-TnT of 12 ng/L (interquartile interval 8-23). At the 3-month timepoint, 7 patients (23%) had experienced the primary endpoint, and 13 (43%) the secondary endpoint. Area under the curve values were 0.909 for the primary, and 0.757 for the secondary endpoint. The best troponin-T cut-off was 14 ng/L for both the primary (100% sensitivity, 73% specificity) and secondary endpoint (sensitivity 75%, specificity 77%). Over a median follow-up duration of 2.6 months (2.0-3.6), survival free from the primary endpoint was shorter in patients with hs-TnT ≥ 14 ng/L (Log-rank: 10.3, $p=0.001$), and all patients developing the primary endpoint had hs-TnT ≥ 14 ng/L at baseline.

Conclusions. In patients on ICIs, baseline hs-TnT predicts a composite cardiovascular endpoint and the progression of cardiac involvement at 3 months, with 14 ng/L as the best cut-off.

A156: COMPARISON OF CLINICAL AND ECHOCARDIOGRAPHIC CHARACTERISTICS OF ATRIAL FIBRILLATION IN PATIENTS WITH OR WITHOUT ACTIVE CANCER

Valentina Capone (a), Federica Luciano (a), Ofelia Casciano (a), Mario Enrico Canonico (a), Silvia Orefice (b), Ludovica Fiorillo (b), Teresa Fedele (b), Vittoria Cuomo (b), Ciro Santoro (a), Roberta Esposito (b)

(a) DIPARTIMENTO DI SCIENZE BIOMEDICHE AVANZATE AOU FEDERICO II NAPOLI; (b) DIPARTIMENTO DI CLINICA MEDICA E CHIRURGIA AOU FEDERICO II NAPOLI

Background. It is known that active cancer patients show an increased risk of atrial fibrillation (AF) due to several proposed hemodynamical, biochemical and iatrogenic mechanisms. Moreover, AF may present an additional factor affecting the prognosis of malignant diseases and a challenge for the therapeutic management of active cancer patients. Little is known about eventual peculiar characteristics of active cancer patients AF.

Purpose. The aim of study was to compare clinical and echocardiographic phenotype of patients with non-valvular AF with or without active cancer.

Methods. In the NeAfib-Echo registry, we enrolled 211 consecutive adult patients with non-valvular AF (F/M: 43/57%; mean age 69.5 \pm 11.6 years), 89 (42.2%) patients with permanent/persistent AF (prAF) and 122 (57.8%) with paroxysmal AF (pxAF). Of these, 75 patients had active cancer (F/M: 52/48%; mean age 67.9 \pm 11.5 years) with 45 patients under chemotherapy treatment (56%). Anthropometric parameters and blood pressure (BP) were recorded and CHA₂DS₂-VASc score and HAS-BLED score was calculated. Patients underwent a complete echo-Doppler exam, including determination of peak atrial longitudinal strain (PALS) and left ventricular (LV) global longitudinal strain (GLS).

Results. No significant differences in sex prevalence, age, systolic and diastolic BP, heart rate and AF type was found between AF patients with or without active cancer. CHA₂DS₂-VASc and HAS-BLED score did not significantly differ between two groups. Also echocardiographic parameters (E/e' ratio, ejection fraction(EF), left atrial volume index (LAVi), left ventricular mass (LVM), relative wall thickness (RWT), pulmonary arterial pressure systolic (PAPs), PALS and GLS) were not significantly different between two groups. By multivariate regression analysis, with all echocardiographic parameters as covariates, in AF patients with active cancer group, best echocardiographic predictors of CHA₂DS₂-VASc were PALS ($\beta = -0.511$, $p<0.0001$) and EF ($\beta = -0.347$, $p<0.004$) (cumulative R² =0.45, SEE= 1.0%, $p<0.0001$). In addition, the presence of current chemotherapy treatment did not lead to significant differences in clinical and echocardiographic parameters.

Conclusions. Clinical and echocardiographic phenotype of AF did not significantly differ between patients with or without active cancer. In active cancer patients, PALS and EF were the best echocardiographic predictors of CHA₂DS₂-VASc. Current chemotherapy treatment did not impact on clinical and echocardiographic AF features.

A157: RIGHT VENTRICULAR DYSFUNCTION PARALLELS LEFT VENTRICULAR FUNCTIONAL INVOLVEMENT IN WOMEN WITH BREAST CANCER EXPERIENCING SUBCLINICAL CARDIOTOXICITY

Ofelia Casciano (a), Ciro Santoro (a), Rossana Soloperto (a), Federica Luciano (a), Mario Canonico (a), Mario Giuliano (b), Grazia Arpino (b), Sabino De Placido (b), Roberta Esposito (b), Giovanni Esposito (a)

(a) DIPARTIMENTO DI SCIENZE BIOMEDICHE AVANZATE AOU FEDERICO II; (b) DIPARTIMENTO DI MEDICINA CLINICA E CHIRURGIA

Background. Cancer therapy related cardiac toxicity disease (CRCTD) of the left ventricle (LV) can influence the outcome of oncologic patients. Little is known on CRCTD related right ventricular (RV) dysfunction even though RV involvement has been proven to be a remarkable prognosticator in heart failure.

Purpose. To analyse parallel changes in LV and RV function occurring during the course of cancer therapy in women affected by breast cancer by using both standard and speckle tracking echocardiography.

Methods. Fifty Her-2 positive breast cancer women (age = 53.6 \pm 11.7 years) underwent sequential cancer therapy protocol including anthracycline (ANT) epirubicine + cyclophosphamide (4 cycles) followed by a total amount of 18 cycles with trastuzumab (TRZ) + paclitaxel. A complete echo-Doppler exam, including LV and RV global longitudinal strain (GLS) as well as RV septal and free wall longitudinal strain (SLS and FWLS respectively) assessment, was performed at baseline, after ANT end and after TRZ completion. Patients with overt heart failure and LV ejection fraction <50%, coronary artery disease, atrial fibrillation, hemodynamically significant valve disease and inadequate echo were excluded. Overt CRCTD was defined according guidelines and both subclinical LV and RV CRCTD as a LV and RV GLS drop from baseline >15%.

Results. None of the patients experienced overt CRCTD but 6 patients (14%) showed subclinical LV dysfunction and 33 (66%) had a significant drop of RV longitudinal function. The comparison of standard echo-Doppler exam at baseline and after ANT and TRZ completion did not show significant changes of LV and RV systolic and diastolic parameters.

Conversely, a progressive significant reduction of RV GLS ($p < 0.002$ after TRZ), SLS and FWLS and, with a lower extent, of LV GLS ($p < 0.02$ after TRZ) was observed after ANT and TRZ completion. Percentage reduction in RV GLS (DRV GLS) from baseline to ANT end correlated with LV GLS both at EC end ($r = -0.40$, $p = 0.006$) and after TRZ completion ($r = -0.62$, $p < 0.0001$).

Conclusions. Detrimental cardiac effects of cancer therapy involve both LV and RV systolic longitudinal function. Progressive RV dysfunction is evident through ANT and TRZ treatment. Early RV dysfunction parallels LV involvement and predicts subsequent LV subclinical dysfunction. A comprehensive LV and RV longitudinal function assessment might better predict the onset of CRCTD in breast cancer patients.

A158: ROLE OF METABOLOMICS IN THE IDENTIFICATION OF EARLY PATTERNS OF CARDIOTOXICITY IN PATIENTS WITH BREAST CANCER TREATED WITH ANTHRACYCLINES

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Background. Anthracycline (ANT) therapy has been associated to a significant dose-dependent cardiotoxicity (CTX). Cardiac biomarkers like troponin and brain natriuretic peptide together with 2D echocardiography proved limited use in detecting early CTX. Metabolomic analysis has been proposed as a powerful tool to detect early changes in metabolic profiles related to several pathological settings.

Purpose. To diagnose early CTX via speckle tracking echocardiography (STE) and characterize the metabolomic fingerprint of ANT-mediated CTX.

Methods. In 2019, patients with breast cancer and normal baseline ejection fraction (EF) were enrolled and longitudinally monitored through clinical assessment, blood sample collection and echocardiography before initiation of ANT therapy and at 180, 270 and 360 mg/m² of ANT. CTX – defined as >15% reduction in global longitudinal strain (GLS) – was monitored at each ANT dose increment. Unsupervised principal component analysis, supervised partial least square and partial least-square discriminant analyses were used to compare the metabolomic profiles of patients who did and did not develop CTX.

Results. Out of 33 enrolled patients 8 patients (25%) developed CTX by GLS criteria. Patients with CTX had a significant decrease in GLS compared to patients without CTX at 270 mg/m² (GLS 20.47% vs 17%, $p = 0.01$) and 360 mg/m² ANT (GLS 21.63% vs 17.7%, $p < 0.001$), but no significant differences in EF or other 2D echocardiographic parameters. The PLS-DA model at 360 mg/m² ANT ($R^2 = 0.92$, $Q^2 = 0.53$, $p = 0.03$) identified a significantly higher prevalence of Krebs cycle intermediates like fumarate and succinate, and fatty acids like linoleic acid in patients with CTX. On the contrary, patients without CTX had significantly higher level of the cardioprotective metabolite like tryptophan.

Conclusions. Our data show in a human population of breast cancer patients, that early ANT-induced CTX (diagnosed via asymptomatic GLS reduction) is associated with a unique metabolomic profile that affects molecular pathways of energy production. Notably, CTX damage upregulates similar metabolites to those previously identified in clinical heart failure and in mouse CTX models. Our results suggest that a metabolomic fingerprint can be used to create prediction models to identify patients at higher risk of developing cardiovascular complications from ANT therapy, in order to personalize chemotherapy and cardioprotective treatment.

A159: DEFINING THE METABOLOMIC PROFILE RELATED WITH CARDIOTOXICITY IN PATIENTS WITH BREAST CANCER TREATED WITH ANTHRACYCLINES

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Background. Anthracycline (ANT) cardiotoxicity is associated with progressive impairment of cardiac function, which proceeds slowly and continues irreversibly for years after treatment cessation therapy. Global longitudinal strain has been suggested as the more sensitive parameter to detect subclinical myocardial impairment, however, not all treated patients appear to suffer cardiotoxicity (CTX). Metabolomic analysis has been proposed as a powerful tool to detect metabolic profiles related to several pathological settings.

Purpose. To characterize the metabolic factors related to ANT-mediated CTX.

Methods. In 2019, patients with breast cancer and normal baseline ejection fraction (EF) were enrolled and longitudinally monitored through clinical assessment, blood sample collection and echocardiography before initiation of ANT therapy. CTX – defined as >15% reduction in global longitudinal strain (GLS) – was monitored at each ANT dose increment. Unsupervised Principal Component Analysis, supervised Partial Least Square and Partial Least-Square Discriminant Analyses were used to compare the metabolomic profiles of patients who did and did not develop CTX.

Results. Out of 33 enrolled patients 8 patients (25%) developed CTX by GLS criteria. Patients with CTX had a significant decrease in GLS compared to patients without CTX at 360 mg/m² ANT (GLS 21.63% vs 17.7%, $p < 0.001$), but no significant differences in EF or other 2D echocardiographic parameters. The PLS-DA model at T0 ($R^2 = 0.895$, $Q^2 = 0.502$, $p = 0.003$) identified a significantly metabolic difference between patients who did and did not develop CTX. Lower levels of the cardioprotective metabolite tryptophan and of other oxidative stress modulating factors like Hipoxantine and aminomalonic acid were found in patients who developed CTX. On the contrary, patients without CTX had significantly lower levels of miristic acid.

Conclusions. Our data show in a human population of breast cancer patients, that ANT-induced CTX (diagnosed via asymptomatic GLS reduction) is associated with a unique metabolomic profile that affects molecular pathways of energy production and oxidative stress modulating factors. Our results suggest that a metabolomic fingerprint can be leveraged to create prediction models to identify patients at higher risk of developing cardiovascular complications from ANT therapy, in order to personalize chemotherapy and cardioprotective treatment.

A160: IMPROVEMENT IN HEART RATE VARIABILITY, CARDIORESPIRATORY FITNESS AND QUALITY OF LIFE IN BREAST CANCER SURVIVORS ACROSS THE COVID-19 PANDEMIC: INSIGHT FROM THE "MOVEMENT AND HEALTH BEYOND CARE" (MOVIS) CLINICAL TRIAL

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Background. Breast cancer (BC) is the most common invasive cancer in women and evidence has shown that exercise can significantly improve the outcomes of BC survivors. Movis: 'Movement and health beyond care' is an ongoing randomized controlled trial comparing the benefits of exercise and proper nutritional plan versus usual care on quality of life (QoL) in BC survivors within the 12 month post-surgery period.

Methods. The study included the first group of the MOVIS trial with patients enrolled up to January the 30th 2020. Thirty women (17.4% of the total planned cohort of 172 women) with stage I-III non-metastatic BC recruited (age: 53.5 ± 7.6; BMI: 25.3 ± 4.9) were randomized in two groups: intervention arm (IA) underwent 3-month aerobic training (3-day/week) with increasing exercise intensity (40 to 70% heart rate reserve) and duration (20 to 60 min); control arm (CA) received usual care recommendations. As the planned protocol was changed due to the unexpected COVID-19 pandemic, both groups were recommended to train at home, with a more frequent and strict follow-up for the IA group. Cardiorespiratory fitness [by estimated maximal oxygen uptake (VO_{2max})], QoL (by EORTC QLQ-C30 questionnaire), fatigue, cardiac function indexes (by echocardiography with speckle tracking imaging), and heart rate variability (HRV; by 24-Holter monitoring) were evaluated at baseline and after 3 months.

Results. There were no adverse events during training. Baseline evaluation revealed no systolic dysfunction (mean LVEF 60.4 ± 4.5) and a mild reduction (values >-18% in global longitudinal strain (GLS) in 26% of patients. Statistical analysis revealed a significant improvement in cardiorespiratory fitness level (VO_{2max} from 30.7 ± 5.7 to 33.9 ± 6.6 mL/kg/min, coefficient of variation (CV) 10.3%; $p = 0.000$). HRV improved in both time and frequency domains: average SDNN/5min and VLF increased from 50.6 ± 14.4 to 55.2 ± 16.7 msec ($p = 0.033$) and from 1597 ± 967 to 1881 ± 963 msec ($p = 0.04$), respectively. Mean and resting heart rate decreased from 76.6 ± 7.8 to 73.7 ± 8.3 bpm ($p = 0.009$) and from 68 ± 7.5 to 63.2 ± 8 bpm ($p = 0.001$), respectively. QLQ scale score FOR QoL assessment increased even during the pandemic: in global health status (from 64.7 ± 17 to 15.9 ± 13 var 15.9; $p = 0.0015$); physical functioning (from 54.4 ± 12.3 to 62 ± 6.6 CV 13.9%; $p = 0.0005$); fatigue (from 26.3 ± 23.4 to 11.9 ± 14.3 CV -54.9%; $p = 0.0008$), and showed a general

improvement over time even on the social functioning (from 47.2 ± 22.8 to 66.7 ± 00 CV 41.2%; $p=0.0001$). There was no difference between the two groups probably due to small sample size (17.4% of the total planned cohort of 172 women).

Conclusion. In BC survivors, short-term remotely-supervised exercise training and recommendations of a healthy life-style lead to a significant improvement in HRV parameters, cardiorespiratory fitness, and QoL.

A161: CARDIOVASCULAR MONITORING IN METASTATIC MELANOMA PATIENTS UNDERGOING COMBINATION THERAPY WITH BRAF AND MEK INHIBITORS

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Introduction. Combination of BRAF and MEK inhibitors (BRAFi + MEKi), as compared to monotherapy, improves survival rate in BRAF-mutated metastatic melanoma. However, this treatment may be burdened by cardiovascular adverse events (CVAEs), such as reduction in left ventricular ejection fraction (LVEF), arterial hypertension (HT), and prolongation of corrected QT (QTc) interval. Consensus regarding the best strategy for CV monitoring during BRAFi + MEKi therapy is still lacking. Aim of this study was to describe occurrence of CVAEs in a real-world BRAFi +MEKi cohort, focusing on the role of Cardio-Oncology and of serial transthoracic echocardiograms (TTEs).

Materials and methods. Data of all metastatic melanoma patients treated with BRAFi + MEKi and evaluated at the Cardio-Oncology Outpatient Clinic of Ospedale Policlinico San Martino, in Genova, from April 2016 to December 2019, were reviewed. CV risk factors, medical history and treatments were recorded at baseline. Follow-up consisted of TTE every 3-4 months, whereas a complete cardiology evaluation was only performed when judged clinically necessary by the referring oncologist. CVAEs during anticancer treatment were defined as drop in LVEF >10 percentage points to a value below 55%, new-onset HT and QTc prolongation >500 ms.

Results. Study population consisted of 28 patients, with a slight predominance of males (15, 53.6%) and a median age of 60 years [52.5-68.5]. Three (10.7%) patients were current and 5 (17.9%) former smokers. Eight patients (28.6%) had HT, 6 (21.4%) dyslipidaemia, 4 (14.3%) type 2 diabetes mellitus, 5 (17.9%) obesity, 1 (3.6%) chronic kidney disease and 4 (14.3%) family history of coronary artery disease (CAD). Only 1 (3.6%) patient had CAD and none had known heart failure or atrial fibrillation. Three (10.7%) patients were on beta-blockers, 6 (21.4%) were treated with angiotensin-converting-enzyme inhibitors/angiotensin receptor blockers, 5 (17.9%) with diuretics, 1 (3.6%) with antiplatelet drugs, and 2 (7.1%) with statins. Twenty-three patients (82.1%) had at least 2 clinical evaluations; among the remaining, 3 were lost at follow-up and 2 died because of early cancer progression. Overall, 170 TTE were performed, with a mean of 6 per patient. CVAEs occurred in 5 (17.9%) patients: drop in LVEF >10 percentage points to a value below 55% (1), new-onset HT (3) and QTc interval prolongation >500 ms (1). Of note, serial TTE monitoring did not reveal asymptomatic LV dysfunction, and the only case of LVEF drop was in a symptomatic patient presenting with dyspnoea and peripheral oedema, who required anticipation of the scheduled TTE. The patient partially responded to diuretics and disease-modifying therapy, but a switch to another anticancer drug was eventually needed.

Conclusions. Most of metastatic melanoma patients have ≥ 1 CV risk factors. CVAEs rate in our population is in agreement with what previously reported. Our preliminary data do not support strict TTE monitoring in metastatic melanoma patients receiving BRAFi + MEKi. Nevertheless, careful clinical surveillance remains mandatory. Further studies with larger population and longer follow-up are needed to better define the best monitoring strategy for this anticancer treatment.

A162: PONATINIB INDUCES VASCULAR TOXICITY THROUGH THE NOTCH-1 SIGNALING PATHWAY

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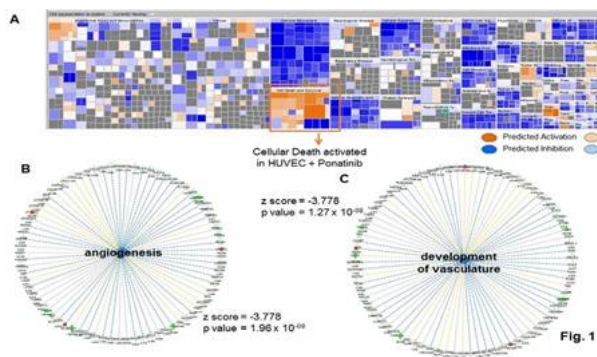
Background. Ponatinib, a third-generation tyrosine kinase inhibitor (TKI), is the only approved TKI that is effective against T315I mutations in

patients with chronic myeloid leukemia (CML). Specific activation of Notch signaling in CML cells by ponatinib can be considered as the "on-target effect" on the tumor and represents a therapeutic approach for CML. Nevertheless, ponatinib-induced vascular toxicity remains a serious concern, with underlying mechanisms poorly understood.

Aims. We aimed at determining mechanisms of ponatinib-induced vascular toxicity, defining associated signaling pathways and identifying potential rescue strategies.

Methods and Results. We exposed human umbilical endothelial cells (HUVECs) to ponatinib or vehicle in the presence or absence of the neutralizing factor anti-Notch-1 antibody for exposure times of 0-72 hours. Label-free proteomics and network analysis showed that protein cargo of HUVECs treated with ponatinib triggered apoptosis, and inhibited vasculature development (Fig. 1). We validated the proteomic data showing the inhibition of matrigel tube formation, an upregulation of cleaved caspase-3 and a downregulation of phosphorylated AKT and phosphorylated eNOS. We delineated the signaling of ponatinib-induced vascular toxicity demonstrating that ponatinib inhibits endothelial survival, reduces angiogenesis and induces endothelial senescence and apoptosis via Notch-1 pathway.

Conclusion. Ponatinib induced endothelial toxicity in vitro. Hyperactivation of Notch-1 in the vessels can lead to abnormal vascular development and vascular dysfunction. By hyperactivating Notch-1 in the vessels, ponatinib exerts an "on-target off tumor effect", which leads to deleterious effects and may explain the drug's vasculotoxicity. Selective blockade of Notch-1 prevented ponatinib-induced vascular toxicity.



A163: ATRIAL STRAIN EVALUATION FOR DETECTION OF SUBCLINICAL ANTHRACYCLINE CARDIOTOXICITY IN BREAST CANCER PATIENTS

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Background. The purpose of this study compared standard echo, 2D left ventricular (LV) speckle tracking echocardiography (STE) and 2D left atrial strain STE for detection of subclinical chemotherapy-related cardiotoxicity (CRT) in breast cancer (BC) patients undergoing anthracyclines (ANTs) therapy.

Methods. One hundred two consecutive breast cancer patients free of cardiac symptoms were treated by multiple chemotherapeutic protocols including ANT for 4 cycles. Before and after treatment, at a follow-up time of 3, 6 and 12 months, patients underwent general cardiological evaluation including physical examination, electrocardiogram (ECG), conventional transthoracic echocardiogram (TTE) with tissue Doppler imaging (TDI), 2D left ventricular global longitudinal strain (GLS) and 2D left atrial strain, measured as peak atrial longitudinal strain (PALS) and left atrial strain (LAS).

Results. All patients completed the chemotherapy cycles. No significant cardiovascular adverse events were observed during treatment. Neither 2D left ventricular ejection fraction (LVEF) nor E/e' ratio evaluation at TDI were significantly changed after treatment. Conversely, GLS was significantly reduced at T1, T2, and T3 compared to baseline (GLS -21, 1% IQR -21,9 -20,2 at T0 vs -18,8% IQR -19,5 -18,1% at T1, $p<0,01$; -18% IQR 19,8-17,8 at T2, $p<0,01$ and -18% IQR -20,1;-15,9% at T3, $p<0,01$). Consensually, a significant reduction of PALS has been measured (PALS 34,4% IQR 31,4-37,4% at T0 vs 28,5% IQR 26,2-30,8% at T1, $p<0,001$; 30,8% IQR 27,6-34% at T2, $p<0,001$ and 30,6% IQR 28,2-32,9% at T3, $p<0,001$). Finally, LAS was significantly increased at T1 and T2 (0,2057%⁻¹ IQR 0,1-0,2%⁻¹ at T0 vs 0,2853%⁻¹ IQR 0,2-0,3%⁻¹ at T1, $p<0,001$ and 0,351%⁻¹ IQR 0,2-0,4%⁻¹ at T2, $p<0,001$).

Conclusion. Our study demonstrates that CRT induced by ANTs treatment give a reduction of myocardial function as detected by GLS reduction and also an impairment of atrial function detected by 2D left

atrial strain. A multiparametric assessment of the myocardial and atrial function, including GLS and 2D atrial strain, could improve the accuracy of risk stratification of cardiotoxicity in patients undergoing ANTs treatment.

A164: USE OF MYOCARDIAL WORK FOR MULTIPARAMETRIC DETECTION OF OF SUBCLINICAL ANTHRACYCLINE CARDIOTOXICITY IN BREAST CANCER PATIENTS

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Background. The aim of our study was to assess subclinical cardiac effects of anthracyclines (ANTs) in women treated for breast cancer (BC).

Methods. We enrolled 46 female patients with BC undergoing adjuvant treatment with anthracycline-containing chemotherapy (CT) followed by taxane (paclitaxel/docetaxel). Patients underwent physical examination, electrocardiogram (ECG) and standard transthoracic echocardiography (TTE) including evaluation of diastolic and systolic function, measured as left ventricular ejection fraction (LVEF), left ventricular global longitudinal strain (GLS) and myocardial work (MW) expressed as global work index (GWI), global constructive work (GCW), global work waste (GWW), and global work efficiency (GWE). The parameters were measured at baseline (T0) and at 3 months (T1) and 6 months (T2) follow-up.

Results. All patients completed the chemotherapy cycles. No significant cardiovascular adverse events were observed during treatment. Neither 2D left ventricular ejection fraction (LVEF) nor E/e' ratio evaluation at T1 were significantly changed after treatment. Conversely, GLS was significantly reduced at T1 and T2 since baseline (GLS -19,99% IQR -20,6 -19,3% at T0 vs -17,88% IQR -18,8 -16,9% at T1, $p < 0,001$ and -16,71% IQR 17,6 -15,7% at T2, $p < 0,001$). Consensually, a significant reduction in myocardial work was also measured (GWI 2115 mmHg IQR 1888-2342 mmHg at T0 vs 1714 mmHg IQR 1557-1870 mmHg at T1, $p < 0,0001$ and 1694 mmHg IQR 1482-1907 mmHg at T2, $p < 0,0001$).

Conclusion. Our study demonstrates that evaluation of myocardial work allows very early detection of subclinical cardiac damage induced by chemotherapy, consensually to the reduction of the GLS. A multiparametric assessment of the myocardial function, including myocardial work and GLS, could improve the accuracy of risk stratification of cardiotoxicity in patients undergoing ANTs treatment.

A165: EVENTI AVVERSI CARDIOVASCOLARI NEI PAZIENTI CON LMC: L'IMPORTANZA DELLA PREVENZIONE CARDIOVASCOLARE

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Introduzione. Nilotinib e ponatinib utilizzati nel trattamento della leucemia mieloide cronica (LMC) possono provocare eventi avversi cardiovascolari (aterosclerosi accelerata, infarto miocardico, ictus, arteriopatia obliterante periferica - PAD). Il dasatinib può provocare ipertensione polmonare. Obiettivo dello studio è analizzare gli effetti tossici cardiovascolari dei farmaci inibitori di BCR-ABL nei pazienti con LMC e correlare tali eventi avversi con il profilo di rischio cardiovascolare dei pazienti e dose del farmaco utilizzata.

Metodi. È uno studio osservazionale, retrospettivo. Abbiamo arruolato 44 pazienti con LMC in trattamento inizialmente con imatinib e successivamente nilotinib e/o ponatinib o dasatinib. Il 58% dei pazienti era in trattamento con nilotinib (gruppo A); il 15% con ponatinib (gruppo B), il 27% con dasatinib (gruppo C). Tutti i pazienti hanno effettuato una valutazione cardiologica (valutazione del profilo di rischio cardiovascolare in accordo alle linee guida ESC, elettrocardiogramma ed ecocardiogramma) dopo una durata media di trattamento di circa 3 anni; solo il gruppo B ha effettuato una valutazione cardiologica basale prima di iniziare il trattamento con correzione dei fattori di rischio cardiovascolare modificabili. Sono stati valutati i seguenti eventi avversi in corso di terapia: ipertensione arteriosa di nuova insorgenza, sindrome coronarica acuta (SCA) e cronica (SCC), ipertensione polmonare, PAD.

Risultati. Prima di iniziare il trattamento antineoplastico nessun paziente aveva avuto un evento cardiovascolare; il 52% presentava un profilo di rischio cardiovascolare elevato, il 21% intermedio, il 27% basso. Nel gruppo A, il 12% ha avuto una SCA in corso di terapia, il 12% ha manifestato SCC ed è stato sottoposto a rivascolarizzazione coronarica. Il 50% dei pazienti con SCA e SCC presentava una patologia coronarica trivasale alla CVG. Tutti i pazienti che hanno presentato al follow-up una complicanza coronarica avevano un profilo di rischio cardiovascolare elevato prima di iniziare il trattamento ed erano trattati con elevate dosi giornaliere di nilotinib (800 mg/die). Nel gruppo B (ponatinib 15 mg/die) nessun paziente ha presentato SCA o SCC, il 14% ha sviluppato ipertensione arteriosa, il 14% PAD. Il 100% dei pazienti del gruppo B presentava un profilo di rischio cardiovascolare elevato vs il 56% del gruppo A e il 16% del gruppo C. L'8% dei pazienti del gruppo C ha sviluppato ipertensione polmonare regredita dopo sospensione del dasatinib. Nessun paziente presentava scompenso cardiaco.

Conclusioni. Nilotinib e ponatinib possono causare eventi avversi cardiovascolari seri. Il rischio di sviluppare cardiotoxicità sembra dipendere dal profilo di rischio cardiovascolare del paziente e in parte anche dal dosaggio del farmaco utilizzato. Infatti la minore incidenza di eventi avversi nel gruppo B potrebbe essere dovuta al dosaggio ridotto di ponatinib assunto nonché alla correzione dei fattori di rischio cardiovascolare effettuata prima di iniziare il trattamento antineoplastico. Quindi nei pazienti con LMC è importante procedere alla correzione dei fattori di rischio cardiovascolare prima di iniziare il trattamento con anti BCR-ABL, nonché effettuare un regolare follow-up cardiologico in corso di terapia, soprattutto nei pazienti a maggiore rischio cardiovascolare.

A166: ANTI-VEGF AND CARDIOTOXICITY: BEWARE OF THE WOLF

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S. R. è un paziente di anni 61, ex fumatore (40 sigarette/die per 30 anni), non altri fattori di rischio cardiovascolare. Gentilizio riferito negativo. Nel 2014 riscontro occasionale di adenocarcinoma colo-rettale con metastasi epatiche; sottoposto a resezione anteriore del retto e confezionamento di ileostomia. Nel 2017 intervento di termoablazione RFTA delle lesioni metastatica epatica a livello del segmento S7 con scarso beneficio. In considerazione della stabilità della malattia, seppur in stadio metastatico, si optava per chemioterapia di mantenimento con bevacizumab e capecitabina, in seguito interrotta in previsione di intervento di ernioplastica inguinale (ultima seduta di chemioterapia il 6/12/2019). In corso di valutazione cardiologica preoperatoria (ernioplastica) veniva eseguito ECG che mostrava: bradicardia sinusale a FC di 47 bpm, T negative da V4 a V6, difasiche in sede /inferiore. Veniva posta indicazione ad ecocardiogramma e test ergometrico. Il primo mostrava cardiopatia ipertensiva con frazione di eiezione conservata e assenza di difetti di cinesi segmentaria. Il test ergometrico risultava positivo per segni ECGrafici di ischemia inducibile (comparsa al picco dell'esercizio di sottoslivellamento orizzontale ST in V4-V6) e negativo per sintomi. Si procedeva dunque l'iter diagnostico con esame coronarografico che mostrava un albero coronarico esente da stenosi emodinamicamente significative. In data 07/03/2020 si sottoponeva al consueto follow-up oncologico e a TC total body veniva evidenziata progressione di malattia con comparsa di multiple linfoadenomegalie in sede sovraclaveare e laterocervicale sinistra, ilare polmonare, celiaca, ilare epatica, paracavale e paraaortica; si riscontravano, inoltre, multiple formazioni nodulari polmonari bilaterali e aumento delle dimensioni delle lesioni secondarie a livello surrenalico ed epatico, pertanto si poneva indicazione a ripresa di terapia con bevacizumab nello schema terapeutico. Durante la visita accusava improvvisa insorgenza di dolore retrosternale; all'ECG: bradicardia sinusale (50 bpm), ritardo di conduzione intraventricolare destro, segmento ST sottoslivellato e T negative in V4-V6, T isodifasiche in V3. Sulla scorta di tale quadro clinico strumentale il paziente veniva ricoverato in cardiologia e sottoposto a esame coronarografico che documentava un albero coronarico angiograficamente indenne. Si dava quindi indicazione ad ottimizzazione della terapia medica con nitrati TD e ranolazina (paziente bradicardico).

Il bevacizumab è un anticorpo monoclonale umanizzato che agisce bloccando il legame del VEGF al suo recettore, che può causare ischemia miocardica, silente e non. Il suo meccanismo lesivo è legato ad una tossicità diretta o mediata sul microcircolo coronarico con riduzione della sintesi di NO, aumento dello stress ossidativo, sovraccarico funzionale dei miocardiociti e disfunzione endoteliale, come quello plausibile nel nostro paziente. Inoltre può favorire uno stato procoagulante e trombotico arteriosa. Per questa classe di farmaci il rischio di IMA è tutt'altro che trascurabile, specie se utilizzati in associazione a fluoropirimidine, ed è perciò necessario che i pazienti prima e durante il trattamento siano sottoposti a valutazione cardiologica ed eventuali test diagnostici d'ischemia inducibile poiché un'eventuale coronaropatia non nota aumenta il rischio di sviluppare cardiotoxicità. In caso di tossicità vascolare da bevacizumab è necessaria la sospensione del trattamento, eventuale rechallenge solo dopo ottimizzazione della terapia antischemica ed sotto attento follow-up cardiologico.

A167: DIFFUSE CARDIAC METASTASES IN A PATIENT WITH MELANOMA, ACUTE HEART FAILURE AND PULMONARY EMBOLISM: A CASE REPORT

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Cardiac tumors are rare, affecting 0.002-0.3% of the population. Metastatic cardiac tumors are more common (95% of cases) than primary heart tumors (<5%). Lung cancer (especially adenocarcinoma), breast cancer, lymphoma and melanoma are the most frequent causes of cardiac metastases. Cardiac involvement is generally identified postmortem, since >90% of patients with cardiac metastases are

asymptomatic. The most common symptoms are dyspnea and peripheral edema due to blood inflow obstruction, arrhythmia, chest pain and pericardial effusion due to tumor infiltration, and thromboembolic events. Melanoma represents 4.4% of all cardiac metastases. The prognosis of stage IV melanoma is poor, with a 5 year relative survival rate of 25%.

Case description. A 66-year-old male with metastatic melanoma was referred to our ER for severe ascites, peripheral edema, asthenia and lower limbs hyposthenia. He was diagnosed 3 years ago with melanoma of the right upper limb, for which he underwent excision with ipsilateral axillary node dissection, followed by chemotherapy and hyperthermia therapy. He subsequently had a progression of disease with bone, adrenal glands and liver metastases with inferior vena cava thrombosis. Cardiac examination was unremarkable, except for paraphonic tones, lower extremities edema and jugular vein distention. Pulmonary examination showed decreased chest expansion, bibasilar lung hypophonesis with diffuse crackles, no wheezes. Blood pressure was 100/60 mmHg and heart rate was 100 bpm. He presented multiple painless subcutaneous nodules (0.5 cm diameter). Blood tests showed anemia (Hb 9.4 g/dl), hypoalbuminemia (albumin 2.3 g/dl) and acute renal failure (creatinine 2.9 mg/dl) with severe hyperkalemia (K^+ 8.3 mEq/L), so he underwent urgent hemodialysis. The ECG documented sinus tachycardia with 1st degree AV block, right bundle branch block, low voltages, inverted T waves in V1 – V4 and DIII. Chest x-ray documented multiple diffuse bilateral radiopacities and pleural effusion. TTE showed preserved EF, multiple hyperechogenic masses in the right atrium and RV epicardium, bulging of RV free wall, infiltrative hypertrophy in the LV with granular sparkling pattern, large circumferential pericardial effusion without hemodynamic compromise. The abdominal echography showed severe ascites, hepatomegaly with coin lesions in the V segment and in the IVC lumen and bilateral adrenal gland masses. We started iv administration of furosemide, albumin, ceftriaxone and saline. The patient was also given prednisone, enoxaparin sodium, O₂ therapy. During the following 24 h the patient developed acute kidney failure, acute heart failure, acute respiratory failure and metabolic acidosis, that resulted in death. The post-mortem examination revealed acute pulmonary edema, hydropericardium, pulmonary arteries thromboembolism, IVC thrombosis, bilateral pleuric effusion, and large cell undifferentiated metastatic carcinoma in the myocardium, valvular apparatus, coronary tree, adrenal glands, kidneys, liver and spleen.

Discussion. An accurate study of the heart should be undertaken during initial staging and follow-up of melanoma patients. A multimodality approach with echocardiography, cardiac magnetic resonance and computed tomography will provide better anatomic definition and tissue characterization that may allow early detection of cardiac masses. A quick and accurate diagnosis can in some cases allow for a surgical resection to reduce a mass before chemotherapy and prevent cardiac failure.

A168: HYPERGLYCEMIA INCREASED NIVOLUMAB-INDUCED CARDIOTOXICITY, ENHANCED IMMUNORESISTANCE IN ER+ BREAST CANCER CELLS MODULATING GROWTH FACTORS AND NLRP3 EXPRESSION

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Introduction. Type 2 diabetes, obesity and metabolic syndrome are negative prognostic factors in breast cancer patients. Immune checkpoint inhibitors (ICIs) that target cytotoxic T lymphocyte antigen 4, programmed cell death-1, and PD-ligand 1 have revolutionized cancer treatment, achieving unprecedented efficacy in multiple malignancies. However ICIs are characterized by a broad spectrum of toxicity reactions, termed immune-related adverse events (irAEs) like cardiotoxicity and induction of diabetes.

Purpose. We aimed to study if hyperglycemia could enhance ICI-induced cardiotoxicity in cardiomyocytes and immunoresistance in human breast cancer cells. Finally, we evaluated if the treatment with an SGLT-2 inhibitor (empagliflozin) could revert these effects during hyperglycemic condition.

Methods. Human cardiomyocytes (HL-1 cells) and PD-1+ ER α +, PR+, HER2- breast cancer cells (MCF-7 cell line) were exposed to nivolumab (100 nM) at high glucose (25 mM) low glucose (5.5 and 2.5 mM) for 72 h. After the incubation period, we performed the following tests: determination of cell viability, through analysis of mitochondrial dehydrogenase activity; NLRP3, p65/NF- κ B and leukotrienes expression through ELISA method.

Results. Nivolumab-induced cardiotoxicity was enhanced by 2,7-fold during exposure to 25 mM glucose (High Glucose; HG) compared to 5.5 mM glucose (Low Glucose; LG) in human adult cardiomyocytes. Moreover, IC50 value of nivolumab against MCF7-cells increased significantly under HG vs LG ($P < 0.01$). Moreover, during high glucose condition, cardiomyocytes and human breast cancer cells exposed to nivolumab, increases the expression of NLRP3, p65/NF- κ B, leukotrienes and cytokines. Notably, hyperglycemia increases significantly the

intracellular calcium (iCa²⁺) content in cardiomyocytes during incubation with nivolumab, probably increasing the metabolic susceptibility to damages induced by ICI. Shifting from HG to LG, as well as the administration of 50 nM empagliflozin (anti SGLT2 drug with hypoglycemic properties) reduced the magnitude of cardiotoxic effects, indicating cardioprotective and immuno-enhancing properties.

Conclusion. To our knowledge these results are the first evidence that hyperglycemia exacerbates ICI-induced cardiotoxicity and immunoresistance and set the stage to preclinical and clinical trials aimed to decrease glucose through dietary or lifestyle changes or through new hypoglycemic drugs (gliflozins).

A169: THE SGLT-2 INHIBITOR DAPAGLIFLOZIN ENHANCED ANTICANCER ACTIVITIES AND EXERTS CARDIOPROTECTIVE EFFECTS AGAINST IPILIMUMAB-INDUCED TOXICITY THROUGH MYD88 AND NLRP2-MEDIATED PATHWAYS

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Introduction. The clinical trial "DECLARE-TIMI 58" (Dapagliflozin Effect on Cardiovascular Events-Thrombolysis in Myocardial Infarction 58), demonstrated that dapagliflozin, a Sodium glucose cotransporter 2 inhibitor, reduces the composite end point of cardiovascular death/hospitalization for heart failure in a broad population of patients with type 2 diabetes mellitus.

Purpose. We aimed to study if dapagliflozin could exert cardioprotective effects in ipilimumab-induced cardiotoxicity through the analysis of multiple biochemical mechanisms.

Methods. HL-1 adult cardiomyocytes in co-culture with hPBMC cells, were exposed to subclinical concentration of ipilimumab (200 nM) alone or in combination with dapagliflozin at 50 nM. Determination of cell viability was performed through analysis of mitochondrial dehydrogenase activity and the study of lipid peroxidation (quantifying cellular Malondialdehyde and 4-hydroxynonenal), and of intracellular Ca²⁺ homeostasis by spectrophotometric methods. Moreover, anti-inflammatory studies were also performed (activation of NLRP3 inflammasome; expression of TLR4/MyD88; transcriptional activation of p65/NF- κ B and secretion of cytokines involved in cardiotoxicity (Interleukins 1 β , 8 and 6)).

Results. Dapagliflozin increases significantly the cardiomyocytes viability during exposure to ipilimumab. Its cardioprotective properties are explainable by the reduction of intracellular Ca²⁺ overload (-34,5% vs ipilimumab; $p < 0,001$), of the lipid peroxidation phenomena (mean reduction of 30,5% vs ipilimumab; $p < 0,001$). Moreover, cardiomyocytes exposed to dapagliflozin during ipilimumab reduced the expression of pro-inflammatory cytokines involved in cardiotoxicity (- 43,5% for Interleukin-1 β ; -32,8 for Interleukin 8; -53,3% for Interleukin 6; $p < 0,05$ for all). Notably, dapagliflozin reduces p65-NF- κ B activation (- 32,2% vs ipilimumab) and inhibits of 43,5% the expression of NLRP3 inflammasome.

Conclusion. Dapagliflozin demonstrated for the first time cardioprotective properties during ipilimumab exposure. The main biochemical effects of dapagliflozin are related to MYD88, NLRP3 complex and pro-inflammatory cytokines Interleukin 1 and 6. This study provides the proof of concept for translational studies designed to investigate the cardioprotective use of dapagliflozin in preclinical models of cardio-immuno-oncology.

A170: CARDIOTOXICITY OF IPILIMUMAB AND NIVOLUMAB INVOLVES NLRP3 INFLAMMASOME AND MYD88-RELATED PATHWAYS

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Introduction. Several strategies based on immune checkpoint inhibitors (ICIs) have been developed or are under investigation for cancer therapy, opening to advantages in cancer outcomes. However, several ICIs-induced side effects emerged in these patients, especially a rare but clinically significant cardiotoxicity with high rate of mortality.

Purpose. We studied cytotoxic and pro-inflammatory properties of ipilimumab and Nivolumab, underlying pathways and cytokine storm involved.

Methods. Co-cultures of human cardiomyocytes and lymphocytes were exposed to Ipilimumab or Nivolumab; cell viability and expression of

leukotrienes, NLRP3, MyD88 and p65/NF- κ B were performed. C57 mice were treated with Iplimumab (15 mg/kg); analysis of fractional shortening, ejection fraction, radial and longitudinal strain were made before and after treatments through 2D-echocardiography. Expression of NLRP3, MyD88, p65/NF- κ B and 12 cytokines have been analyzed in murine myocardium. **Results.** Nivolumab and Iplimumab exert effective anticancer but also significant cardiotoxic effects in co-cultures of lymphocytes and tumor or cardiac cells. Both ICIs increased NLRP3, MyD88 and p65/NF- κ B expression compared to untreated cells, however the most pro-inflammatory and cardiotoxic effects were seen after exposure to Iplimumab. Mice treated with Iplimumab showed a significant decrease of fractional shortening and radial strain with respect to untreated mice coupled to a significant increase of myocardial expression of NLRP3, MyD88 and several interleukins. **Conclusion.** Nivolumab and Iplimumab exert cytotoxic effects mediated by NLRP3/IL-1 β and MyD88 pathways leading to pro-inflammatory cytokine storm in heart tissue.

A171: CARDIOPROTECTIVE EFFECTS OF PCSK9 INHIBITOR EVOLUCUMAB AGAINST DOXORUBICIN-TRASTUZUMAB SEQUENTIAL TREATMENT: THE ROLE OF MYD88/NFKB/MTORC PATHWAYS

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Introduction. Inhibition of proprotein convertase subtilisin/kexin type 9 (PCSK9) has emerged as a novel therapy to treat hypercholesterolaemia and related cardiovascular diseases. Evolocumab, a PCSK9 inhibitor, reduced the risk of cardiovascular events in patients with atherosclerotic cardiovascular diseases when added to maximally tolerated statin therapy (\pm ezetimibe), and recent data from the ODYSSEY OUTCOMES trial indicate that alirocumab added to maximally tolerated statin therapy (\pm other lipid-lowering drugs) reduces the risk of cardiovascular events in patients with a recent acute coronary syndrome.

Purpose. Considering the expression of PCSK9 in heart tissue, we aimed to study for the first time the direct biochemical effects of evolocumab in cardiomyocytes during exposure to doxorubicin, trastuzumab, their sequential treatments

Methods. Human fetal cardiomyocytes (HFC cell line) were exposed to subclinical concentration of doxorubicin, trastuzumab, sequential treatment of both (all 100 nM), alone or in combination with evolocumab (50 nM) for 48h. After the incubation period, we performed the following tests: determination of cell viability, through analysis of mitochondrial dehydrogenase activity, study of lipid peroxidation (quantifying cellular Malondialdehyde and 4-hydroxynonenal), intracellular Ca²⁺ homeostasis. Moreover, pro-inflammatory studied were also performed (activation of NLRP3 inflammasome; expression of TLR4/MyD88; mTORC1 FoxO1/3a; transcriptional activation of p65/NF- κ B and secretion of cytokines involved in cardiotoxicity (Interleukins 1 β , 8, 6).

Results. Evolocumab co-incubated with doxorubicin alone or in sequence with trastuzumab exerts cardioprotective effects, enhancing cell viability of 35-43% compared to untreated cells ($p < 0,05$ for all); Evolocumab reduced significantly the cardiotoxicity through MyD88/NF- κ B/cytokines axis and mTORC1 FoxO1/3a mediated mechanisms.

Conclusion. We demonstrated, for the first time, that the PCSK9 inhibitor evolocumab exerts direct effects in cardiomyocytes during doxorubicin and trastuzumab exposure turning on a new light on its possible use in cancer patients.

A172: OXIDIZED LOW-DENSITY LIPOPROTEIN EXACERBATES APOPTOSIS IN CARDIOMYOCYTES EXPOSED TO NIVOLUMAB BY MODULATING TLR4/NFKB AND NLRP3 PATHWAYS

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Introduction. Atherosclerosis is now recognized as a chronic inflammatory disease, and the main character is a focal atheromatous plaque formation. Oxidized low-density lipoprotein (Ox-LDL) is oxidatively modified form of LDL and it contributes to the atherosclerotic plaque formation and progression. Ox-LDL is toxic to cells via trigger of oxidative mechanisms and it is quite clear that few cells are completely refractory to the toxicity of ox-LDL. Recent findings reported that cardiovascular events (myocarditis and atherosclerosis) were higher after initiation of immune check-point inhibitors (ICIs), potentially mediated by accelerated progression of atherosclerosis. Optimization of cardiovascular risk factors and increased awareness of cardiovascular risk, prior to, during and after treatment, should be considered among patients on an ICI.

Purpose. We evaluated whether ox-LDL-induced apoptosis depended in part on the activation of toll-like receptor-4 (TLR4)/Nuclear factor κ B (NF-

κ B) signaling pathway and NLRP3 during exposure of cardiomyocytes to Nivolumab turning the light on the role of OxLDL in ICI-s induced cardiotoxicity.

Methods. Human fetal cardiomyocytes (HFC cell line) in co-culture with hPBMC, were exposed to clinically relevant concentration of Nivolumab (100 nM) alone or combined to OxLDL at 1, 10 and 50 μ g/mL for 24h. After the incubation period, we performed the following tests: determination of cell viability, through analysis of mitochondrial dehydrogenase activity, study of lipid peroxidation (quantifying cellular Malondialdehyde and 4-hydroxynonenal), intracellular Ca²⁺ homeostasis and apoptosis. Moreover, pro-inflammatory studied were also performed (activation of NLRP3 inflammasome, expression of TLR4 and NF- κ B). In order to evaluate the pathways involved in OxLDL damages, TLR4 and NLRP3 inhibitor (TAK-242 and dapsanutrile, respectively) were added during cell viability and apoptosis studies.

Results. Nivolumab exerts cytotoxic and pro-apoptotic effects in co-culture of cardiomyocytes and hPBMC. OxLDL increases nivolumab-induced cardiotoxicity in a manner that is sensitive to TLR4 and NLRP3. Incubation of cardiomyocytes with ox-LDL (10 and 50 μ g/mL) for 24 hours increased TLR4 and NF- κ B expressions significantly. Ox-LDL had pro-apoptotic effects in a concentration-dependent manner with the involvement of lipid peroxidation but not of intracellular calcium.

Conclusion. We demonstrated, for the first time, that Ox-LDL exacerbates apoptosis and inflammation in cardiomyocytes during exposure to Nivolumab turning the light on their role in ICIs-induced cardiotoxicity. These results place the first step to preclinical studies aimed to reduce ox-LDL during treatment with ICIs.

CARDIOPATIA ISCHEMICA

A173: OVERLAPPING EFFECTS OF MI-R-21 INHIBITION AND ORAL ANTI-FIBROTIC AND ANTI-INFLAMMATORY DRUGS: RATIONALE FOR DRUG REPURPOSING TO RELIEVE ISCHEMIA/REPERFUSION INJURY

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Background. Reperfusion strategies have reduced the mortality of ST-segment elevation myocardial infarction (STEMI), but ischemia/reperfusion (I/R) injury still represents an important issue, and the prevalence of heart failure (HF) after STEMI is raising. Intracoronary infusion of miR-21 inhibitors after reperfusion has been reported to reduce cardiac fibrosis and hypertrophy and improve cardiac function in pigs. Possible drawbacks of miR-21 inhibitors are their high costs and the need for intracoronary administration. Oral drugs with anti-fibrotic or anti-inflammatory actions could have similar effects on protein expression than miR-21 inhibition. We examined the 2 drugs approved for idiopathic pulmonary fibrosis (nintedanib and pirfenidone) and colchicine, which is being evaluated for the prevention of adverse ventricular remodeling after STEMI (NCT03156816).

Methods. We identified the regulatory profile of miR-21 (588 target genes). Only 99 of these interactions were supported by robust experimental data (i.e., information from reporter gene assays), and were then considered for further examination. The biological significance of these 99 targets was evaluated through over-representation analysis, and 13 genes were identified as potentially related to cardiovascular diseases. We retrieved all known targets and main downstream interactions of nintedanib, pirfenidone and colchicine (source: www.drugbank.ca). We cross-validated these datasets by using neural network analyses to search for protein-protein interactions, focusing on those shared by miR-21 inhibition and each one of the 3 drugs.

Results. Nintedanib and miR-21 inhibition shared many targets, which could indicate overlapping mechanisms of action. The proto-oncogene SRC, which participates in gene transcription, immune response, apoptosis and migration, emerged as the leading signaling effector. By blocking SRC expression and many downstream effectors of SRC, as well as platelet derived growth factor, nintedanib could decreased miR-21 expression. The molecular effects of nintedanib include an inhibition of inflammation, fibrosis and angiogenesis, and then ultimately a relief from I/R injury, in a similar fashion than anti-miR-21. Contrary to nintedanib, no overlap between the effects of pirfenidone and miR-21 inhibition was found. Conversely, colchicine seems to determine an indirect blockade of the important pro-inflammatory signaling pathway AKT/NF κ B, similarly to miR-21 inhibition. Colchicine has also been proposed to inhibit SRC, but few published data are available.

Conclusion. miR-21 inhibition is emerging as a potential treatment for I/R cardiac injury, but its applicability in clinical practice is burdened by several limitations. Drug repurposing could aid this situation by mimicking the molecular activity of miR-21 inhibition. Through a bioinformatic approach, we found that nintedanib could exert beneficial effects similar to those reported for miR-21 inhibition, with a lower degree of overlap between the effects of colchicine and anti-miR-21. If confirmed by

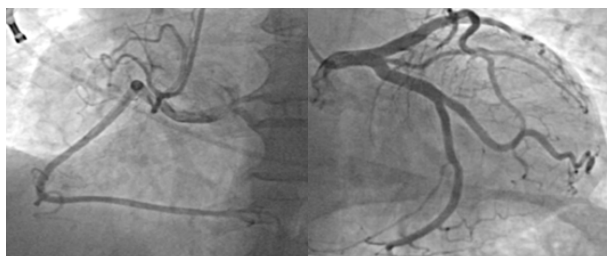
experimental evidence, nintedanib or colchicine could enter the stage of clinical trials to assess their efficacy as cardioprotective therapies in human patients with STEMI.

A174: A RARE CAUSE OF MINOCA

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A 63-year-old man was admitted to the cath-lab with posterior ST-segment elevation myocardial infarction and sudden onset of chest pain, swelling and headache. Pulmonary congestion was found at thoracic auscultation. Echocardiography revealed moderate ejection fraction reduction with posterolateral wall akinesia and basal segments hypokinesia. Elevated levels of troponin I, CK-MB, B-type natriuretic peptide and white blood cells were found. Angiographic evaluation of coronary arteries was unremarkable.

In the next days, patient experienced several episodes of hypertensive crisis treated with iv metoprolol. In one case, severe hypotension requiring fluids occurred after beta-blocker administration. A thoracic and abdomen CT revealed interstitial pneumonia and a giant mass of 15x12x11 cm occupying the right adrenal situs. After a proper wash out from potentially interfering antihypertensive agents, very high levels of urinary adrenaline of 33737 nmol/24h (url <77) confirmed the diagnosis of giant pheochromocytoma. Therapy with doxazosine first and metoprolol then was started achieving an adequate control of blood pressure. Discharge echocardiography revealed the complete recovery of the left ventricle systolic function, while signs of ischemia persisted at the EKG. After six days from the beginning of symptoms, the patient was transferred to the department of general surgery, where he underwent a MIBG-SPECT followed by laparotomic right adrenal gland asportation. Histological exam confirmed the presence of pheochromocytoma. This is a rare endocrine neoplasia, able to cause heterogeneous cardiovascular manifestations such as type-2 myocardial infarction and transient cardiomyopathy. The pathophysiological mechanism responsible for this manifestation of the tumor is not well known. High levels of circulating catecholamines could cause ischemia and consequent left ventricle dysfunction due to coronary vasospasm, increased oxygen demand or direct toxic effects. Although the ESC guidelines on STEMI do not report pheochromocytoma as a potential cause of MINOCA, our case underlies the importance of considering this diagnosis, especially in patient with concomitant transient cardiomyopathy and hypertensive crisis.



A175: MYOCARDIAL INFARCTION WITH NON-OBSTRUCTIVE CORONARY ARTERIES DEMANDS A BIOLOGICAL SIGNATURE

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Myocardial Infarction with non-obstructive coronary arteries (MINOCA) population are increasingly recognized. Up to 10% of patients presenting with myocardial infarction (MI) undergoing angiography are found with no obstructed coronary arteries. However, the biological pathways underlying these condition are still unknown. Therefore, focal point of the scientific community is to identify a biological signature for this clinical category, to provide easier and less expensive diagnostic tools.

The aim of the study is to explore the molecular peculiarities underlying the pathophysiologic mechanisms of myocardial infarction with non-obstructive artery disease, performing a biological profile of the MINOCA group compared to Non ST Segment Elevation Myocardial Infarction (NSTEMI) population.

We performed a gene expression array on two groups of pooled cDNA from peripheral blood mononuclear cells, from MINOCA (n = 22) and NSTEMI (n = 12) patients, followed by gene expression validation for each patient, by qRT-PCR.

Our preliminary data showed a significantly increased gene expression in NSTEMI as compared to MINOCA group for the following molecules: CD44 (p<0.05), hyaluronan receptor involved in inflammation and cell adhesion, and molecules acting as redox-balancers or involved in

extracellular matrix turnover and homeostasis such as glutathione peroxidase 1 (GPX1, p<0.001), Matrix metalloproteinase 1 (MMP1, p<0.0001), Tissue Inhibitor of Metalloproteinase (TIMP1, p<0.05), and Superoxide dismutase 1 (SOD1, p<0.05).

These results demonstrate the existence of different molecular signatures underlying two condition with a similar clinical manifestation and represent the clue of a different underlying pathophysiology. This study paves the way to novel diagnostic tools to improve the early stratification of this particular subgroup of acute patients and to tailor treatments.

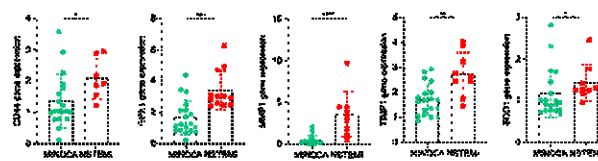


Figure 1. Biological profile showing gene expression of endothelial, tissue remodeling, and redox molecules in MINOCA and NSTEMI groups

A176: ISCHEMIA WITH NON-OBSTRUCTIVE CORONARY ARTERIES: NEED OF A BIOLOGICAL PROFILE

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Ischemia with non-obstructive coronary arteries (INOCA) population is far from an uncommon condition. According to the ACC-National Cardiovascular Data registry and National, Heart, Lung and Blood institute databases, up to 4 million patients with clinical signs of myocardial ischemia have no obstructive coronary artery disease (CAD). The absence of precise guidelines for diagnosis and treatment in non-obstructive CAD, lead the scientific community to fill the gap knowledge for this clinical category, in order to provide non-invasive and less expensive diagnostic tools.

The aim of the study is to explore the molecular peculiarities underlying the pathophysiologic mechanisms of non-obstructive artery with myocardial ischemia, performing a biological profile of the INOCA group compared to Stable angina (SA) population.

We performed a gene expression array on two groups of pooled cDNA from peripheral blood mononuclear cells, from INOCA (n = 7) and SA (n = 19) patients, with subsequent gene expression validation by qRT-PCR technique.

Our preliminary data showed a significantly increased gene expression in SA as compared to INOCA group of molecules involved in cell adhesion, signaling, vascular motion and inflammation. In details, we found increased expression of Endothelin-1 (EDN1, p<0.0001), Intercellular Adhesion molecule-1 (ICAM1, p<0.05), Galectin 8 (LGALS8, p<0.05), Tumor Necrosis Factor (TNF p<0.05), Tissue Inhibitor of Metalloproteinase (TIMP1, p<0.05), and Vascular Endothelial Growth Factor A (VEGFA<0.001).

The different expression of molecular biomarkers might allow the differentiation of SA and INOCA patients and improve diagnosis and treatment options, in the era of personalized medicine.

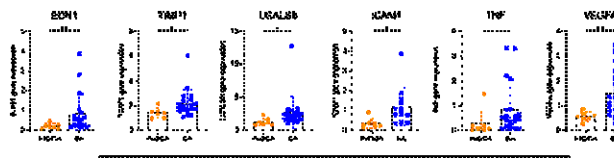


Figure 1. Molecular profile showing gene expression of endothelial, tissue remodeling, and redox molecules in INOCA and SA groups

A177: EPICARDIAL ADIPOSE TISSUE AND IL-13 RESPONSE TO MYOCARDIAL INJURY DRIVES LEFT VENTRICULAR REMODELLING AFTER ST-ELEVATION MYOCARDIAL INFARCTION

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Introduction. Left ventricular (LV) remodeling after ST-elevation myocardial infarction (STEMI) is explained only in part by the infarct size, and the inter-patient variability may be ascribed to different inflammatory response to myocardial injury. Epicardial adipose tissue (EAT) is a source of inflammatory mediators which directly modulates the myocardium. EAT increase is associated to several cardiovascular diseases, however its response to myocardial injury is currently unknown. Among inflammatory

mediators, IL-13 seems to play protective role in LV regeneration, but its variations after STEMI have not been described yet. In the present study we analysed the impact of infarct-related changes of EAT and IL-13 in post-STEMI LV remodelling.

Methods. We enrolled 100 patients with STEMI undergoing primary angioplasty. At the enrolment (T0) and after 3 months (T1), we measured EAT thickness by echocardiography and circulating levels of IL-13 by ELISA.

Results. At T1, the 60% of patients displayed increased EAT thickness (DEAT>0). DEAT was directly associated to LV end-diastolic volume ($r=0.42$; $p=0.014$), LV end-systolic volume ($r=0.42$; $p=0.013$) and worse LV ejection fraction (LVEF) at T1 ($r=-0.44$; $p=0.0094$), independently of the infarct size. In the overall population IL-13 levels significantly decreased at T1 ($p=0.0002$). The DIL13 was directly associated to DLVEF ($r=0.42$; $p=0.017$) and inversely related to DEAT ($r=-0.51$; $p=0.022$), thus confirming a protective role for IL-13.

Conclusions. The variability of STEMI-induced 'inflammatory response' may affect the post-infarct LV remodelling. DEAT thickness and DIL-13 levels could be novel prognostic markers in STEMI patients.

A178: PLIN2 IS AN AGE-RELATED BRIDGE BETWEEN OXIDATIVE STRESS AND INFLAMMATION-DEPENDENT METABOLISM IN CORONARY INSTABILITY

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Aims. Aging is the leading risk factor for atherosclerotic lesions formation and is related to plaque stability decreasing; however, age-related plaque instability pathways remain unclear. Lipid Droplet (LD) accumulation leads to the alteration of the macrophage in foam cell, a central key aspect in the pathogenesis of atherosclerosis. Upregulation of PLIN2 leads to cytoplasmic accumulation of LD. PLIN2 is a substrate for chaperone-mediated autophagy and ubiquitin-proteasomal degradation. In the present work, we sought to delineate the role of PLIN2 and its regulation mechanisms in human atherosclerosis and plaque instability in patients with a diagnosis of ST-elevation myocardial infarction (STEMI) and stable chronic angina (SA). In particular, we focused on the study of PLIN2 expression and oxidative stress mechanisms.

Methods and Results. We enrolled 136 symptomatic patients with STEMI and SA conditions. PBMCs, isolated from peripheral blood, were incubated with monoclonal antibodies (mAb) conjugated with anti-CD14, and anti-CD36 fluorochrome, for surface analysis. For intracellular analysis, PBMCs were fixed, permeabilized and then incubated with fluorochrome conjugated anti-PLIN2 mAb. PLIN2 protein expression was significantly increased in STEMI as compared to SA patients ($p<0.0001$), while LDL scavenger receptor CD36 did not show differences between the two groups. At the flow cytometer, CD14⁺ monocytes showed a positive correlation of PLIN2 protein expression with age in STEMI ($p=0.003$) and in SA patients ($p=0.01$). Proteasome activity is negatively correlated with age in the STEMI population and in the SA population. PBMCs were seeded at a density of 1×10^6 cells/ml and cultured in RPMI containing fetal bovine serum, penicillin/streptomycin, and L-glutamine. After 24h, cells were treated with hydrogen peroxide for 4h, then washed and stained for cytometry analysis of PLIN2. We proposed that oxidative stress was a trigger of reduced proteasome activity and PLIN2 degradation.

Conclusions. In the present study, we established that age-related PLIN2 protein expression in STEMI patients was higher compared to SA patients, merging the underlying mechanisms of PLIN2 expression to oxidative stress and inflammation-dependent metabolism pathways in coronary instability. A weakening in the ability of proteostatic balance during aging leads the body susceptible to several chronic diseases. Studying the machinery that controls the pathophysiology of age-related disease is imperative for understanding whether treatments that modulate the pathways can be valuable in patients with age-related coronary instability.

A179: HIGH-RISK PERCUTANEOUS CORONARY INTERVENTION IN A THREE-VESSEL CORONARY ARTERY DISEASE PATIENT WITH MULTIPLE RECURRENT ACUTE CORONARY SYNDROMES

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A 74-year-old patient with family history of coronary artery disease, hypertension, type 2 diabetes mellitus, dyslipidemia, hyperuricemia, peripheral artery disease, chronic obstructive pulmonary disease and chronic kidney disease was admitted to our Cardiology Unit for a recurrent myocardial infarction without ST-segment elevation (NSTEMI). He had a diagnosis of severe two-vessel coronary artery disease (CAD), in stable

angina, treated with stenting on first tract of the left circumflex coronary artery (LCX) and proximal-mid tract of the left anterior descending coronary artery (LAD) in 1990. In the same year, for unstable angina, a coronary angiography showed a severe three-vessel CAD with LAD stenting restenosis. Therefore, a percutaneous coronary intervention (PCI) with multiple bare-metal stents implantation was performed on the right coronary artery (RCA), on the obtuse marginal branch (OM) and on LAD. In 2016, for the recurrence of exertional angina, a new coronary angiography revealed RCA stenting restenosis treated with multiple balloon angioplasty and overlapping drug-eluting stents implantation. In 2019 the patient was admitted to our department complaining of low threshold angina. An EKG documented sinus rhythm, first-degree atrio-ventricular block and non-specific repolarization disorders. Levels of high-sensitivity cardiac troponin I (hs-cTn I) rose rapidly. The transthoracic echocardiography showed normal size, function and kinesis of the left ventricle. Coronary angiography revealed a severe and calcific three-vessel disease with restenosis intrastent of LAD (99%) and OM (80%) with ostia involvement. The Heart Team excluded the surgical treatment option because of patient comorbidities and percutaneous myocardial revascularization was planned. Consequently, T and protrusion double stenting technique on left main (LM) bifurcation was performed and two overlapping stents on the first tract of LCx-OM and on the first tract of LAD were implanted. The procedure was complicated by LCx no-reflow phenomenon with progressive hypotension poorly responsive to inotropic support. For progressive hemodynamic instability, right femoro-femoral venous-arterial extracorporeal membrane oxygenation (V-A ECMO) was placed. Intra-coronary adenosine infusion and balloon angioplasty partially restored coronary flow on distal LCx. At the end of the procedure, hemodynamic stability was supported by adrenaline infusion (0.05 mcg/kg/min) and V-A ECMO flow rate set on 2.5 L/min. Bedside cardiac ultrasound evidenced severe reduction of left ventricular ejection fraction (LVEF) without pericardial effusion and severe valvulopathy. Anterior leads repolarization abnormalities on the EKG were found. Post procedural hs-cTn I peak was 114000 ug/L. Afterwards, adrenaline infusion was stopped and V-A ECMO was removed on day three with progressive recovery of left ventricular ejection fraction.

The patient was discharged on dual antiplatelet therapy (DAPT) with ticagrelor 90 mg twice daily and Cardioaspirin 100 mg. After one year from the discharge there was no evidence of anemia, bleeding events or increased bleeding risk. DAPT score was ≥ 3 (74 years-old -1; diabetes mellitus +1; MI at presentation +1; prior PCI or prior MI +1; stent diameter <3mm +1) and taking into account the diffuse three vessel coronary artery disease, long term DAPT with ticagrelor 60 mg twice daily was started. Long-term use of DAPT is helpful for the prevention of late ST and ischemic events in selected patient with right DAPT score.

A180: THE ROLE OF OBESITY AND ADIPOKINES IN CORONARY MICROVASCULAR DYSFUNCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background. Patients with obesity present structural and functional changes in the heart and in the coronary circulation, which ultimately leads to an increased risk of cardiovascular disease. Obesity is associated with a low chronic state of inflammation which seems to be linked to a compromised coronary vasoreactivity, which is shown to be a forerunner and a long-term predictor of clinically relevant cardiovascular events.

Methods. A systematic review was performed by searching PubMed, Embase and Cochrane Library database. Selection criteria were applied leading to the inclusion of studies of any level of evidence published in peer-reviewed journals reporting clinical or preclinical results. Relative data were extracted and critically analysed. PRISMA guidelines were applied and risk of bias was assessed, as well as the methodological quality of the included studies. After this assessment, we excluded all the articles with serious risk of bias and/or low quality. Meta-analysis was conducted on the data collected regarding coronary blood flow (CFR) and hyperemic myocardial blood flow (MBF), while for the other parameters a descriptive analysis was performed.

Results. After applying the described criteria, we included 15 articles on human and animal literature assessed as medium or high quality. The data of 1399 patients were examined, 456 of which with obesity (BMI ≥ 30). A pooled effect size analysis shows that coronary flow reserve (CFR) is significantly reduced in patients with obesity [Random Effect (RE): -47.7%, 95% confidence interval (CI) -80.2% - -15.2%; $n=422$]. Increased BMI is associated with reduced CFR. The same trend is found evaluating pharmacological induced stress MBF, which was reduced in patients with obesity [RE: -47.8%, 95% CI -73.7% - -21.8%; $n=409$]. Nevertheless, MBF at rest did not show a significant difference in patients with obesity from our analysis [RE: 15%, 95% CI -24%-53%; $n=409$]. Pro-inflammatory adipokines secretion, as leptin and CRP, seems to correlate with a significant decrease of stress-induced MBF and reduced CFR.

Conclusions. Obesity is associated with a significant higher risk of coronary microvascular dysfunction, which is reflected by diminished CFR and stress MBF. Systemic inflammation and the imbalance of adipokines related to obesity has been closely linked to a blunt coronary flow. CMD is a pre-clinical heart conditions that often remains undiagnosed. Further evidence is required to clear out the role of Obesity from a molecular point of view on the coronary endothelium.

A181: COMPARISON BETWEEN EXERCISE ELECTROCARDIOGRAPHY AND STRESS ECHOCARDIOGRAPHY AS FIRST DIAGNOSTIC APPROACH IN PATIENTS WITH SUSPECTED CHRONIC CORONARY SYNDROME

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Background and purpose. Non-invasive imaging tests, including exercise stress echocardiography (ESE) or radionuclides studies and coronary computed tomography angiography (CCTA), are recommended in recent guidelines as the first-line approach for the diagnosis of obstructive coronary artery disease (CAD), whereas exercise electrocardiography (Ex-ECG) is recommended only when imaging tests are not available. However, there are scarce data directly comparing the diagnostic accuracy of ESE and Ex-ECG in patients with suspected CAD. Our study aimed to compare the accuracy of ESE and Ex-ECG in identifying the presence of obstructive CAD in patients undergoing for the first time a diagnostic stress test.

Methods. We studied consecutive patients referred to our department to perform Ex-ECG because of a clinical suspect of CAD. Patients with a previous history of heart disease or significant comorbidity were excluded. Each patient underwent a symptom-limited Ex-ECG according to a standard Bruce protocol. Echocardiographic images were acquired at baseline and at peak exercise and analyzed by two expert cardiologists. A clinical follow-up was undertaken to ascertain the clinical outcome of patients.

Results. Overall, 97 consecutive patients (55 male, mean age 57.4±15 years) were enrolled in the study. Twenty-six patients (27%) had a positive ex-ECG, whereas 11 (11%) had a positive ESE. In particular, 66 patients (68%) had both negative Ex-ECG and ESE, 20 (21%) had a positive ex-ECG but negative ESE, 5 (5%) had a negative Ex-ECG but positive ESE, and 6 (6%) had both positive ex-ECG and ESE.

After 4.4±2.8 months, 7 patients (7.2%) underwent invasive coronary angiography (ICA), showing obstructive CAD in 6; 9 (9.3%) patients underwent CCTA, which was negative in all. All 6 patients with obstructive CAD at ICA had positive ex-ECG, whereas 2 of these patients had negative ESE. Among the 10 patients with no obstructive CAD at ICA/CCTA, 5 had positive Ex-ECG, whereas 3 had positive ESE.

Conclusions. Our data show that in patients without previous history of CAD, ESE does not seem to present a significantly higher diagnostic accuracy compared to Ex-ECG for the identification of patients with or without obstructive CAD. Our data suggest that large controlled studies are warranted to true pros and cons of ESE as the first test for the diagnosis of obstructive CAD compared to Ex-ECG.

A182: MYOCARDIAL INFARCTION WITH NON-OBSTRUCTIVE CORONARY ARTERY DISEASE: THE PROGNOSTIC ROLE OF INFARCT SIZE PREDICTORS

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Background. In patients with Acute Myocardial Infarction (AMI), the levels of cardiac troponin T and absolute neutrophil count have been shown to correlate with infarct scar size and left ventricular ejection fraction (LVEF) as well as conferring a risk for major cardiovascular adverse events (MACE). In the context of myocardial infarction with non-obstructive coronary arteries (MINOCA) the prognostic role of such indicators has never been explored.

Purpose. To evaluate the prognostic role of known myocardial infarct size indicators in a MINOCA population compared to patients with obstructive AMI (Ob-AMI).

Methods. Among 1990 patients admitted to our coronary care unit from 2016 to 2019 with AMI, we enrolled 186 consecutive MINOCA patients according to the current ESC diagnostic criteria. We compared troponin peak levels, absolute neutrophil count at the time of hospital admission and LVEF in MINOCA patients versus Ob-AMI. Furthermore, we assessed the prognostic value of these indicators. All-cause mortality and a composite end - point of all-cause mortality and myocardial re-infarction were evaluated. The median follow-up time was 19.6 ± 12.9 months.

Results. MINOCA patients were more frequently females (64.9% vs 35.1%; $p < 0.001$), non-smokers (42.3% vs 61.8%; $p < 0.001$) with a lower prevalence of diabetes (9.9% vs 23.7%; $p < 0.001$) compared to the Ob-AMI population. Conversely, no differences were found in hypertension and dyslipidemia. As far as infarct size predictors are concerned, MINOCA patients showed lower levels of troponin value and absolute neutrophil count measured at the time of hospital admission (1838.27 ± 601.0 ng/L vs 13543 ± 3350.6 ng/L; $p < 0.001$, $6.7 \pm 1.36 \times 10^9/L$ vs $7.1 \pm 1.29 \times 10^9/L$; $p = 0.001$, respectively). Moreover, these patients exhibited a higher LVEF ($56.1 \pm 10\%$ vs $49.3 \pm 11\%$; $p < 0.001$) as compared to Ob-AMI. Among our MINOCA patients, 13 (10.6%) all-cause deaths and 3 (4.3%) myocardial re-infarction were observed during follow-up. Multivariable Cox-regression model demonstrated that mean troponin level, absolute neutrophil count and LVEF were not independent predictors of MACE (HR 1.0, 95% CI 0.9-1.1, $p=0.6$; HR 0.96, 95% CI 0.9-1.1, $p=0.187$; HR 0.9, 95% CI 0.79-1.02, $p=0.12$, respectively).

Conclusion. MINOCA patients show a similar prognosis compared to the worldwide AMI population. However, in this study the outcome in the MINOCA population was not influenced by commonly used infarct size predictors, in contrast to what is observed in Ob-AMI patients. These results once again emphasize both the complexity of MINOCA patients and the importance of a better understanding of the different underlying pathophysiological mechanisms.

A183: TYPE 2 MYOCARDIAL INFARCTION IN PATIENTS WITH COVID-19

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Background. In the setting of coronavirus disease 2019 (COVID-19) myocardial injury has been associated with an unfavourable outcome. Among different forms of myocardial injury, type 2 myocardial infarction (T2MI) is usually a poorly studied clinical entity, with no guidelines or consensus documents available to aid physicians in clinical management. As a matter of fact, there are no data regarding COVID-19 patients experiencing a T2MI during hospitalization.

Methods. We performed a retrospective, observational, single-centre cohort study of 60 consecutive patients with T2MI: 12 (admitted between 1 March and 15 April 2020) with and 48 (admitted in the same period in 2019) without COVID-19. T2MI diagnosis was performed in the presence of acute myocardial injury associated with clinical of myocardial ischemia in the context of imbalance between oxygen supply and demand. Other reasons of troponin elevation have been excluded.

Results. Patients with COVID-19-related T2MI had a significantly higher rate of hypoxemia as compared to control T2MI patients, as well as a trend toward a higher heart rate. Moreover, blood test showed significantly higher values of haemoglobin, ferritin, D-dimer and C-reactive protein in patients with COVID-19 as compared with those without. On the contrary, patients with COVID-19 had a significantly lower peak troponin I values than non-infected patients. Left ventricular systolic function by echocardiography was similar in the 2 study groups. Finally, patients with COVID-19-related T2MI showed a two-fold higher in-hospital mortality (50% vs 23%; $p=0.025$) as compared with the control T2MI patients.

Conclusions. Our data underline that T2MI may occur in the setting of COVID-19 syndrome secondary to hypoxemia, increased heart rate, inflammatory status and/or decompensated heart failure. While, in T2MI without COVID-19, anaemia seems to be a more prevalent mechanism of myocardial ischemia. Despite the lower degree of myocardial damage, revealed by troponin peak, and similar systolic left ventricular function, COVID-19-related T2MI patients showed a significantly higher in-hospital mortality than control patients. Thus, given the medical complexity due to the viral infection and the other associated comorbidities and the high expected rate of non-cardiovascular mortality, a multidisciplinary approach is mandatory in COVID-19 patients with T2MI. Finally, the optimal treatment of T2MI is still unknown, since therapeutic agents currently used for type 1 myocardial infarction (antiplatelets, statins, beta-blockers and ace-inhibitors) are not been tested in T2MI so far. Thus, every effort should be performed to prevent T2MI trying to control all the factors involved in the balance between myocardial oxygen supply and demand.

A184: IMPACT OF CORONARY STENTING ON TOP OF MEDICAL THERAPY ON HARD COMPOSITE ENDPOINTS IN PATIENTS WITH CHRONIC CORONARY SYNDROMES: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction. Whether percutaneous coronary intervention (PCI) with stent implantation on top of optimal medical therapy (OMT) modifies hard composite clinical outcomes in chronic coronary syndromes (CCS) patients remains controversial.

Methods. This study was registered in PROSPERO (CRD42020166754) and follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Cochrane Collaboration reporting. Randomized controlled trials (RCTs) that compared PCI with stent implantation on top of OMT versus OMT alone in CCS patients were included. Main exclusion criteria were left main disease, severe left ventricular dysfunction and severe kidney failure. To overcome the potential limitations deriving from different follow-up durations among studies or multiple events by the same person, Incidence Risk Ratio (IRR) with 95% confidence intervals (CIs) were calculated.

Results. Six RCTs enrolling a total of 10,751 patients were included. At an average follow-up of 3.6 years, PCI+OMT compared with OMT alone was associated with no difference in the two co-primary composite endpoints of all-cause death/myocardial infarction (MI)/stroke (IRR, 1.00; 95% CI, 0.91-1.10) and cardiovascular (CV) death/MI (IRR, 0.97; 95% CI, 0.86-1.11). There was no significant difference in the individual secondary endpoints constituting primary outcomes between groups. Consistent results were found when limiting analysis to RCTs enrolling patients with moderate-to-severe ischemia or using DES in the PCI arm or enrolling patients since the year 2000 or using a definite and more specific definition of periprocedural MI.

Conclusion. In CCS patients with inducible myocardial ischemia and without severely reduced ejection fraction or left main disease, adding PCI to OMT does not reduce the incidence of hard composite or individual outcomes.

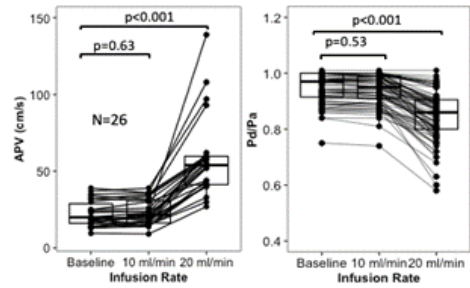
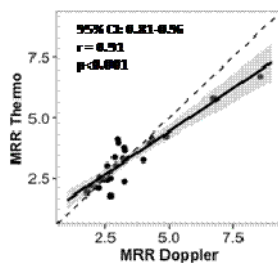
A185: QUANTIFYING CORONARY MICROVASCULAR DISEASE: ASSESSING ABSOLUTE MICROVASCULAR RESISTANCE RESERVE (MRR) BY CONTINUOUS CORONARY THERMODILUTION

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Background. Hyperemic absolute coronary blood flow (in mL/min) can be safely and reproducibly measured with intracoronary continuous thermodilution of saline at room temperature at an infusion rate of 20 mL/min. This study aims at assessing whether continuous thermodilution can also measure resting flow and microvascular resistance.

Methods and Results. In 87 coronary arteries (58 patients) with angiographic non-significant stenoses absolute flow was assessed by continuous thermodilution of saline at infusion rates of 10 mL/min and 20 mL/min using a pressure/temperature sensed guide wire, a dedicated infusion catheter (RayFlow™, Hexacath, Paris, France) and a dedicated software (CoroFlow™ System, Uppsala, Sweden). In addition, in 26 arteries, average peak velocity (APV, FloWire, Volcano/Philips) was measured simultaneously. There was no significant difference between P_d/P_a at baseline and during saline infusion at 10 mL/min, (0.95 ± 0.053 vs 0.94 ± 0.054 , respectively ($p=0.53$)) and there was no significant difference in APV at baseline and during the infusion of saline at 10 mL/min (22.2 ± 8.40 vs 23.2 ± 8.39 cm/s, respectively, $p=0.63$), thus indicating presence of resting coronary blood flow during the infusion of 10 mL/min of saline. In contrast, at an infusion rate of 20 mL/min, a significant decrease in P_d/P_a was observed compared to baseline: (0.85 ± 0.089 vs 0.95 ± 0.053 vs, respectively, $p<0.001$) and a significant increase in APV was observed (22.2 ± 8.4 cm/s to 57.8 ± 25.5 cm/s, respectively, $p<0.001$). The coronary flow reserve calculated by thermodilution and by Doppler flow velocity were similar (2.73 ± 0.85 vs 2.72 ± 1.07 , respectively and their individual values correlated closely ($r=0.87$, 95% CI 0.72 - 0.94, $p<0.001$). Microvascular resistance (R_{μ}), defined as the distal coronary pressure divided by the absolute flow was calculated both at rest ($R_{\mu-rest}$) and during hyperemia ($R_{\mu-hyper}$). Microvascular Resistance Reserve (MRR), is calculated as the ratio of $R_{\mu-rest}$ and $R_{\mu-hyper}$ and showed a good correlation with the analogous Doppler-derived parameter (using the APV instead of absolute flow). Mean doppler and thermodilution derived MRR were similar (3.32 ± 1.50 vs 3.23 ± 1.16) and values correlated closely ($r=0.91$, 95% CI 0.81 - 0.96, $p<0.001$); Bland-Altman analysis: mean bias= 0.071 , limit of agreement -1.195 to 1.338).



$$MRR = \frac{R_{\mu-rest}}{R_{\mu-hyper}}$$

Conclusion. Absolute coronary blood flow (in mL/min) can be measured by continuous thermodilution both at rest and during hyperemia. This allows accurate, reproducible, and operator-independent direct volumetric calculation of CFR and MRR. The latter is a quantitative metric which is specific for microvascular function and independent from myocardial mass.

A186: UTILITY OF CARDIAC TROPONIN T IN PATIENTS ADMITTED TO THE EMERGENCY DEPARTMENT

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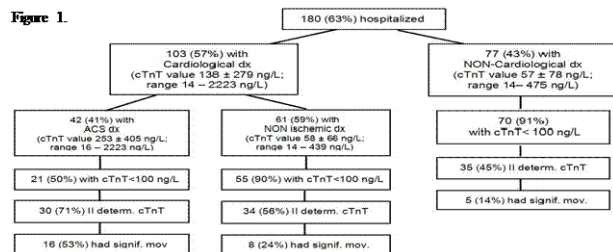
Background. Cardiac troponin (cTn) is the preferred biomarker to rule out or to confirm the diagnosis of acute coronary syndrome (ACS). New generation troponin assays have high analytical sensitivity but at the cost of a reduced diagnostic specificity.

Aim. The aim of this retrospective study was to evaluate the clinical utility of cTnT and its possible predictive value in consecutive patients admitted to the emergency department (ED).

Methods. We analyzed data of patients (pts) admitted to the ED during an enrolment period of 30 consecutive days; values of cTnT, discharge diagnosis (dx), and the clinical decision taken in each case were also recorded. cTnT values ≥ 14 ng/L were considered abnormal. Significant cTnT changes at serial samples was defined by a 50% increase from an initial normal value, or a 20% increase from an initial abnormal value.

Results. Overall, data from 711 pts were analyzed. Abnormal cTnT values were recorded in 288 pts (41%; 169 males, mean age: 77 years); 5 died during hospitalization, 103 were discharged and 180 were hospitalized. Diagnosis of acute cardiac diseases were present in 103 (57%) patients (Figure 1): 41 (40%) had a dx of ACS and showed higher cTnT values when compared to those without an ACS dx ($p<0.01$). Furthermore, among those with an ACS, serial changes in cTnT values were recorded as abnormal only in 53% of cases. Discharged pts had cTnT values of 31 ± 33 ng/L (range 14 - 322 ng/L). As a final analysis, cTnT values did not appear to be independent and absolute predictors for the type of dx made for each case ($p>0.05$).

Conclusions. Positive cTnT values were found in a considerable proportion (41%) of pts presenting to the ED in 30 consecutive days. Pts with an ACS dx had higher cTnT levels compared to the other pts while a significant cTnT increase at serial samples was limited to 50%. Abnormal cTnT values did not prevent the discharge based on clinical evaluation. As other biomarkers, cTnT measurement is not an independent predictor of the type of dx.



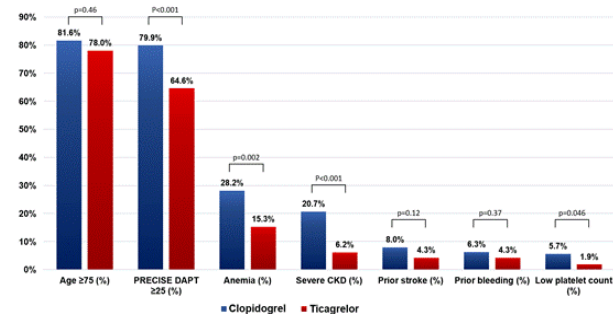
A187: TICAGRELOR VERSUS CLOPIDOGREL IN PATIENTS WITH ACUTE CORONARY SYNDROMES AND HIGH BLEEDING RISK: INSIGHTS FROM THE MULTICENTER START-ANTIPLATELET REGISTRY

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Optimal dual antiplatelet therapy (DAPT) strategy in high bleeding risk (HBR) patients presenting with acute coronary syndrome remains debated. We sought to investigate the use of clopidogrel versus ticagrelor in HBR patients with acute coronary syndrome and their impact on ischemic and bleeding events at 1 year.

In the START-ANTIPLATELET registry (NCT02219984), consecutive patients with ≥ 1 HBR criteria were stratified by DAPT type in clopidogrel versus ticagrelor groups. The primary endpoint was net adverse clinical endpoints (NACE), defined as a composite of all-cause death, myocardial infarction, stroke, and major bleeding. Of 1,209 patients with 1-year follow-up, 553 were defined as HBR, of whom 383 were considered eligible for the study as on DAPT with clopidogrel (174 or 45.4%) or ticagrelor (209 or 54.6%). Clopidogrel was more often administered in patients at increased ischemic and bleeding risk, while ticagrelor in those undergoing percutaneous coronary intervention. Mean DAPT duration was longer in the ticagrelor group. At 1 year, after multivariate adjustment, no difference in NACEs was observed between patients on clopidogrel versus ticagrelor (19% vs. 11%, adjusted hazard ratio 1.27 [95% CI 0.71-2.27], $p=0.429$). Age, number of HBR criteria, and mean DAPT duration were independent predictors of NACEs.

In a real-world registry of patients with acute coronary syndrome, 45% were at HBR and frequently treated with clopidogrel. After adjustment for potential confounders, the duration of DAPT, but not DAPT type (stratified by clopidogrel vs. ticagrelor), was associated with the risk of ischemic and bleeding events at 1 year.

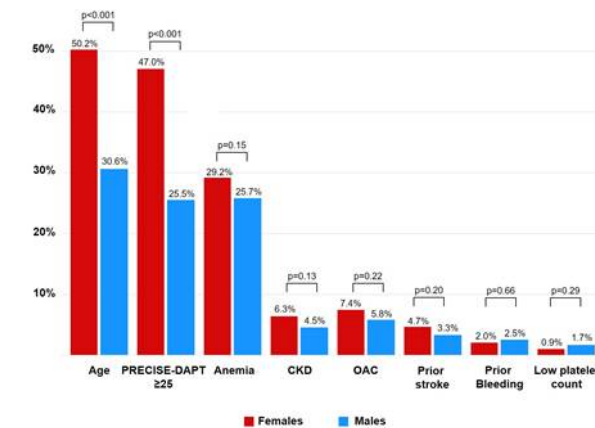


A188: CLINICAL IMPLICATIONS OF HIGH BLEEDING RISK FACTORS IN FEMALE VERSUS MALE PATIENTS WITH ACUTE CORONARY SYNDROMES: DATA FROM THE START-ANTIPLATELET REGISTRY

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Bleeding impairs outcomes and quality of life in patients with acute coronary syndrome (ACS), which supports routine assessment and management of established risk factors. Clinical factors predisposing to bleeding complications may differ in terms of prevalence and clinical implications in females and males. We sought to investigate the prevalence of high bleeding risk (HBR) factors in female and male patients with ACS from the START-ANTIPLATELET registry.

In the START-ANTIPLATELET registry (NCT02219984), consecutive patients were stratified by sex and HBR status – defined according to age ≥ 75 , PRECISE-DAPT ≥ 25 , anemia, chronic kidney disease (eGFR < 60 mL/min), long-term oral anticoagulant (OAC), prior stroke, prior bleeding requiring medical attention, or platelet count $< 100,000/\text{mm}^3$. The primary endpoint was net adverse clinical endpoints (NACE), defined as a composite of all-cause death, myocardial infarction, stroke, and major bleeding. Of 2,014 patients, 538 were females – of whom 352 (58.5%) were defined HBR – and 1,476 were males – of whom 697 (47.2%) were defined HBR. Among the HBR factors, advanced age (50.2% vs. 30.6%) and PRECISE-DAPT ≥ 25 (47.0% vs. 25.7%) were significantly more frequent in females compared with males (p -value < 0.001 for both), whereas the distribution of other HBR factors did not differ between sex. In a real-world ACS registry, 58% of females and 47% of males were at HBR. The distribution of HBR factors were similar between sexes, except for advanced age and PRECISE-DAPT ≥ 25 , which resulted more frequent among females. Our findings do support the adoption of similar strategies for the assessment of HBR factors in both sexes, while emphasizing the relevance of advanced age in characterizing of HBR status in females.

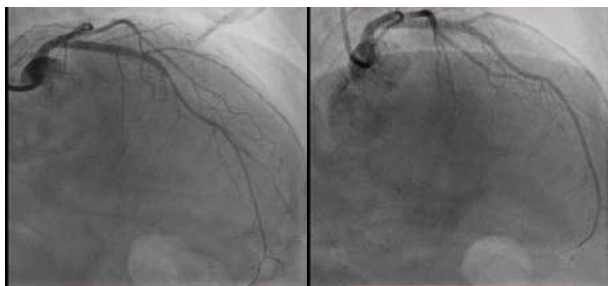


A189: MYOCARDIAL INFARCTION WITH NON OBSTRUCTIVE CORONARY ARTERIES IN PAZIENTE CON CARDIOPATIA ISCHEMICA CRONICA

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Il termine MINOCA (myocardial infarction with non obstructive coronary arteries) viene usato per descrivere una forma di infarto miocardico acuto (IMA) in assenza di stenosi coronariche angiograficamente significative. Il vasospasmo coronarico, una delle cause più frequenti di MINOCA, è l'espressione di una iper-reattività della muscolatura liscia vascolare a diversi stimoli vasoconstrictori tra cui l'iperventilazione. Spesso interessa soggetti giovani, di sesso femminile, con diversi fattori di rischio cardiovascolari come il tabagismo, l'alcolismo, il consumo di stupefacenti e condotte di vita stressanti. Si manifesta con dolore toracico a riposo associato a sopraslivellamento, o sottoslivellamento, del tratto ST all'ECG in diverse derivazioni, a seconda del vaso interessato. Riportiamo il caso di una donna di 65 anni giunta alla nostra osservazione per dolore toracico insorto improvvisamente prima di iniziare una procedura odontoiatrica, parzialmente regredito dopo l'assunzione di nitroderivati per via sublinguale. La paziente aveva una storia di cardiopatia ischemica (iniziata nel 2002 con un IMA antero-settale rivascolarizzato con PTCA ed impianto di stents); ipertensione arteriosa sistemica; intolleranza ai carboidrati; dislipidemia. All'ingresso al DEA si riscontrava un aumento dei markers di miocardionecrosi in assenza alterazioni specifiche all'ECG, per cui veniva fatta diagnosi di SCA-NSTEMI, impostata terapia antiaggregante con DAPT e indicazione ad eseguire coronarografia (CG) entro 24h. A 12 ore dall'accesso in UTIC ricompariva dolore toracico associato a sottoslivellamento del tratto ST ed inversione dell'onda T nelle derivazioni antero-laterali. La CG eseguita in urgenza evidenziava uno spasmo diffuso delle arterie circonflessa e discendente anteriore, risoltesi con somministrazione di nitrati intracoronarici. Veniva quindi impostata terapia medica con calcio antagonisti e nitrati, con completa risoluzione della sintomatologia. Questo è il caso di una presentazione non tipica di MINOCA che si è verificato in una paziente con storia di CAD. Non c'è stato un tipico sopraslivellamento dell'ST, verosimilmente per il carattere diffuso dello spasmo e la presenza di circoli collaterali favoriti dalla presenza della cardiopatia ischemica cronica. Lo sviluppo in una stessa paziente di IMA di tipo 1 e di tipo 2 suggerisce l'esistenza di meccanismi fisiopatologici comuni che, in presenza di fattori scatenanti, possano determinare in momenti diversi trombosi e vasospasmo dei vasi coronarici. Pertanto, in caso di MINOCA è importante caratterizzare bene

i triggers della malattia al fine di utilizzare terapie mediche più appropriate per questa condizione clinica che ancora presenta degli aspetti fisiopatologici non del tutto chiariti.



A190: STEMI CAUSED BY CATECHOLAMINERGIC CRISIS IN A PATIENT WITH PHEOCHROMOCYTOMA: A CASE REPORT

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(a) CARDIOLOGIA UNIVERSITARIA POLICLINICO DI BARI

Background. Tako-tsubo cardiomyopathy is a condition characterized by a transient left ventricular asynergy, induced by physical and emotional stress. A central role is supposed to be played by catecholamines, in fact in literature it is described the association between Takotsubo and pheochromocytoma. Pheochromocytoma is an adrenal tumor that produces catecholamines.

Case report. We describe the case of a 68-year-old, diabetic, hyperlipidemic and hypertensive man admitted for chest pain and high blood pressure: ECG showed ST elevation in leads V2-V3-V4. The echocardiogram showed global reduction in contractility (FE 38%) with apical akinesia and hyperkinesia of the base while coronarography was negative for atherosclerotic lesions and vasospastic features. Few months before, because of myeloproliferative syndrome abdomen MRI was made and it had revealed a 60 mm right adrenal gland mass diagnosed as pheochromocytoma, so we made the determination of urinary metanephrines and urinary vanilmandelic acid that were both high. The tumor was surgically removed and after 6 months an other echocardiogram was made: it showed a normal global contractility (FE 55%) and the patient had no longer experience episodes of chest pain.

Conclusions. This case confirmed that tako-tsubo cardiomyopathy without physical and emotional stress could alert clinicians of an underlying disorder such as pheochromocytoma and tumor detection is crucial to the prognosis.



A191: ACUTE CORONARY SYNDROME, PRESENTING WITH ISORHYTHMIC DISSOCIATION, IN ABSENCE OF ST SEGMENT DEVIATION OR CHEST PAIN

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A 60-year-old woman was admitted to our emergency department for dyspnoea. Past medical history: untreated essential hypertension; no other comorbidities.

Baseline electrocardiographic (ECG) evaluation showed junctional rhythm, isorhythmic dissociation, in absence of ST segment deviation. Laboratory tests: BNP and Troponin I levels were 2046 pg/mL (normal value 0-100) and 0,29 ng/mL (normal value 0,00-0,04), respectively. Chest x-ray documented bilateral pleural effusion. Bedside heart ultrasound (US) showed mildly dilated left ventricle, normal wall thickness, severe left ventricle dysfunction, akinesia of the mid-distal portion of posterior, inferior and lateral wall, and severe mitral regurgitation by posterior edge tethering. Intravenous diuretic therapy was started and patient was admitted to intensive coronary unit (ICU) with diagnosis of heart failure in silent previous myocardial infarction (MI).

After ICU admission, cardiac arrest with ECG evidence of ventricular fibrillation was documented; after successful advanced life support and cardiac defibrillation, ECG showed sinus rhythm and negative infero-lateral T waves. Coronary angiography (CA) (previous administration of dual antiplatelet therapy, anticoagulant, beta-blocker, statin and morphine) showed proximal sub-occlusion of left circumflex coronary artery (Cx). During angiography, a new episode of ventricular fibrillation was treated with cardiac defibrillation. Percutaneous transluminal coronary angioplasty (PTCA) was performed and a direct drug eluting stent (DES) was implanted. In the next few hours, two new episodes of ventricular fibrillation were treated with cardiac defibrillation, and amiodarone, potassium and magnesium sulphate infusions. Anti-remodeling therapy was also introduced. After the acute phase, the patient was transferred to a rehabilitation center. At the discharge, persistent left ventricular systolic dysfunction and negative infero-lateral T waves at ECG were documented.

In our report we discuss the case of a patient with acute sub-occlusion of left circumflex coronary artery not associated with ECG signs of acute ischemia (only rhythm disorders were documented) or with chest pain. In this context, Shen et al. (1991) described the relationships between ECG patterns and angiographic features of isolated and acute left circumflex coronary artery disease. The Authors highlighted that isolated left circumflex coronary artery disease is relatively uncommon, occurring in 2-3% of cases; more specifically, among 89 patients with isolated left circumflex coronary artery disease (46 with acute myocardial infarction), ECG abnormalities were documented in 75 patients, including Q waves, abnormal R wave in lead V1, and ST-T changes. No rhythm disorders (i.e. junctional rhythm) were documented at the baseline evaluation.

A192: MALATTIA CORONARICA CRONICA IN PAZIENTE AD ELEVATO RISCHIO CARDIOVASCOLARE: OTTIMIZZAZIONE DELLA TERAPIA A LUNGO TERMINE, DALLE ULTIME LINEE GUIDA ALLA PRATICA CLINICA

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(a) UNIVERSITÀ DEGLI STUDI DELL'AQUILA

Introduzione. Il progressivo incremento della vita media della popolazione ha determinato, nelle ultime decadi, l'esigenza di nuove strategie di gestione della patologia coronarica cronica. Le ultime linee guida sull'argomento, nel 2019, propongono l'associazione di un secondo farmaco antitrombotico all'aspirina in pazienti ad elevato rischio cardiovascolare. Tale raccomandazione è supportata dai dati dello studio COMPASS del 2017, studio a tre bracci in cui i pazienti vengono randomizzati 1:1:1 per ricevere in terapia rispettivamente: solo acido acetilsalicilico, acido acetilsalicilico associato a rivaroxaban 2,5/bid, solo rivaroxaban 5 mg/od.

Caso clinico. Paziente donna di 68 anni, fumatrice, affetta da ipertensione arteriosa, diabete, dislipidemia, cardiopatia ischemica cronica (NSTEMI) trattato con PTCA e impianto di DES su IVA nel 2015). Terapia medica ottimizzata con acido acetilsalicilico, statina, betabloccante, ace-inibitore, ranolazina, CCB diidropiridinico. Alla visita cardiologica di controllo, il cardiologo curante identifica la paziente come «paziente COMPASS» che si gioverebbe dell'aggiunta in terapia di rivaroxaban 2,5 mg/bid.

Discussione. Lo studio COMPASS 2017 è stato condotto su circa 27.000 pazienti in ritmo sinusale, con malattia coronarica stabile e/o arteriopatia periferica over 65 o più giovani di 65 anni con documentata patologia a carico di almeno due coronarie e/o almeno due fattori di rischio cardiovascolari. I risultati hanno evidenziato la superiorità di rivaroxaban 2,5 mg/bid insieme ad acido acetilsalicilico rispetto alla somministrazione di solo acido acetilsalicilico e rispetto al rivaroxaban 5 mg/od, per riduzione di morte cardiovascolare, stroke e infarto miocardico. Tra i

pazienti trattati con tale associazione è stata registrata una percentuale di emorragie maggiori non fatali superiore a quella osservata nel gruppo sottoposto alla sola somministrazione di aspirina, a fronte di un vantaggio significativo in termini di riduzione di mortalità dovuta alla combinazione degli eventi ischemici ed emorragici. Resta attualmente il limite della mancata rimborsabilità del farmaco a tale dosaggio, ancora in classe C e quindi totalmente a carico del paziente.

Conclusioni. L'utilizzo di rivaroxaban 2,5 mg/bid potrebbe costituire un'utile strategia terapeutica per pazienti con cardiopatia ischemica cronica che non abbiano indicazione ad assumere anticoagulanti a dosaggio pieno, in presenza di elevato rischio ischemico ed in assenza di elevato rischio emorragico.

A193: KEY ROLE OF IMPELLA FOR THE INTERVENTIONAL TREATMENT OF A YOUNG PATIENT WITH TWO CTOS AND DEPRESSED LV FUNCTION

Giovanni Monizzi (a), Luca Grancini (a), Paolo Olivares (a), Antonio Bartorelli (a)

(a) CENTRO CARDIOLOGICO MONZINO

During percutaneous coronary interventions (PCI) in patients with high-risk characteristics, use of advanced technologies is required. Novel percutaneous left ventricular assist device have been developed to provide hemodynamic support during complex high-risk indicated procedures (CHIP).

We present a case in which elective Impella hemodynamic support was essential to allow PCI in a patient with severely depressed LV function.

A 45-year-old male, smoker, with no previous history of cardiovascular disease presented to the emergency department for new onset of exertional dyspnoea. The echocardiography showed left ventricle (LV) dilatation with diffuse hypokinesia and an ejection fraction of 27%. The cardiac magnetic resonance (MRI) confirmed the echo findings. A coronary angiography was performed and two chronic total occlusions (CTOs) of the proximal right coronary artery (RCA) and left circumflex (LCx) were found. A PCI was planned using IMPELLA hemodynamic support. The right femoral access was used to introduce IMPELLA introducer (14 Fr) with preclosure by ProGlide. A double access, left femoral and right radial access (6 Fr) for CTO PCI were obtained. The CTO of the LCx was successfully crossed using a Fielder XT supported by Finecross microcatheter, and a predilatation of the obtuse marginal branch was performed. At this point ventricular fibrillation (VF) occurred. Surprisingly, the patient was still conscious because of IMPELLA support, and no DC shock was performed because, while the sedation was about to be prepared, we observed spontaneous termination of VF. In the end a bifurcation PCI was performed using a T stent technique with two sirolimus eluting stents. After that we attempted the RCA PCI. In this case a dual lumen catheter (Crusade) was used to perform a parallel-wire technique with a GaiaThird that successfully crossed the occlusion. As even in this case a bifurcation with a big acute marginal branch was involved, a supercross 120° microcatheter was used to wire the side branch (SB) and a PCI with a dedicated stent for bifurcation on the SB and a sirolimus eluting stent on the main branch were placed with a good final result. One day after the procedure, levosimendan was administered i.v. and well tolerated.

In-hospital stay was uneventful. The echo at 3 days post procedure showed LV volume reduction (TDV/TSV 130/53 mL), persistent inferior akinesia and normalization of global LV function (EF 59%)

In this case, elective Impella hemodynamic support was essential to allow PCI in a complex high-risk coronary anatomy in a patient with severely depressed LV function. It is remarkable that the patient remained conscious and hemodynamically stable during ventricular fibrillation that lasted about 1 minute and spontaneously terminated likely because of maintained coronary perfusion and LV unloading. This case confirms the Impella pivotal role in supporting complex high-risk PCI, particularly in patients with depressed LV function.

A194: PREDIRE I SANGUINAMENTI NEI SOGGETTI ANZIANI CON SINDROME CORONARICA ACUTA E SOTTOPOSTI AD ANGIOPLASTICA PRIMARIA. VALIDAZIONE ESTERNA DEGLI SCORE DI RISCHIO PRECISE-DAPT E PARIS

Claudio Montalto (a), Gabriele Crimi (b), Nuccia Morici (c), Luigi Piatti (d), Daniele Grosseto (e), Paolo Sganzerla (f), Giovanni Tortorella (g), Roberta De Rosa (h), Leonardo De Luca (i), Giuseppe De Luca (j), Tullio Palmerini (k), Marco Valgimigli (l), Stefano Savonitto (d), Stefano De Servi (m)

(a) FONDAZIONE IRCCS POLICLINICO SAN MATTEO, PAVIA, IT; (b) IRCCS POLICLINICO SAN MARTINO, GENOVA, IT; (c) ASST GREAT METROPOLITAN NIGUARDA, MILANO, IT; (d) ALESSANDRO MANZONI HOSPITAL, LECCO, IT; (e) INFERRI HOSPITAL OF RIMINI, RIMINI, IT; (f) OSPEDALE TREVIGLIO, TREVIGLIO, IT; (g) SANTA MARIA NUOVA HOSPITAL, REGGIO EMILIA, IT; (h) AOU S. GIOVANNI DI DIO E RUGGI DARAGONA, SALERNO, IT; (i) SAN GIOVANNI EVANGELISTA HOSPITAL, TIVOLI, IT; (j) HOSPITAL MAGGIORE DELLA CARITÀ, NOVARA, IT; (k) POLICLINICO SANT'ORSOLA MALPIGHI, BOLOGNA, IT; (l) BERN UNIVERSITY HOSPITAL, INSELSPIITAL, BERN, SWITZERLAND; (m) UNIVERSITY OF PAVIA, PAVIA, IT

Introduzione. La duplice terapia antiaggregante (DAPT) deve essere adattata al profilo di rischio ischemico e di sanguinamento di ciascun

paziente, e questo rappresenta una sfida nella pratica clinica quotidiana, in particolare per gli anziani che sono sottorappresentati nelle coorti di validazione dei punteggi di rischio disponibili. Pertanto, è poco chiaro se tali punteggi siano estendibili anche in questa popolazione di soggetti fragili.

Scopo. In questo studio abbiamo analizzato l'utilità clinica dei punteggi di sanguinamento PRECISE-DAPT E PARIS in coorti di pazienti anziani affetti da sindrome coronarica acuta (SCA) e trattate invasivamente.

Metodi. In questa iniziativa di validazione esterna sono stati inclusi 1,883 soggetti con >74 anni con SCA e trattati con angioplastica coronarica, a partire da 3 suti prospettici e multicentrici. Gli score di sanguinamento sono stati calcolati per ogni paziente e i soggetti sono stati stratificati in categorie di rischio sulla base della definizione offerta da ciascun punteggio analizzato.

Risultati. Dopo un tempo mediano di 365 giorni, i pazienti nella categoria di rischio elevata secondo il PRECISE-DAPT sono andati incontro ad un numero maggiore di sanguinamenti BARC 3-5 (log rank p=0.002) al contrario dei soggetti nella categoria di alto rischio per il punteggio PARIS (log rank p=0.3). Entrambi i punteggi di rischio hanno un potere discriminativo moderato (c-statistics 0.70 e 0.64) mentre la calibrazione è risultata accurata per entrambi i punteggi ($\chi^2 > 0.05$). Tuttavia, il PARIS è stato associato ad una sovra-stima maggiore degli eventi di sanguinamento (Delta medio tra probabilità degli eventi osservati e predetti: = -0.65 per il PRECISE DAPT e -4.62 per PARIS, p=0.02). L'analisi delle curve decisionali è risultata in favore del PRECISE-DAPT fino ad una soglia di rischio del 2%. In una analisi secondaria in cui abbiamo incluso anche gli eventi BARC 2, il potere di calibrazione e di discriminazione è risultato moderato per entrambi gli score di rischio.

Conclusioni. Per gli anziani trattati invasivamente per una SCA sia il punteggio PARIS che il PRECISE-DAPT sono risultati moderatamente accurati nel predire il rischio di sanguinamento. Ciononostante, l'uso del PRECISE-DAPT è associato ad una performance migliore e ad un vantaggio netto più elevato.

A195: OPTIMAL P2Y12 INHIBITION IN OLDER ADULTS WITH ACUTE CORONARY SYNDROMES: A NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Aims. Dual antiplatelet therapy (DAPT) with a P2Y₁₂ inhibitor on top of aspirin is the cornerstone of therapy after acute coronary syndromes (ACS). Nonetheless, the safest and most efficacious P2Y₁₂ for older patients who are both at high ischemic and bleeding risk remains uncertain. We aimed to examine the effect of available P2Y₁₂ inhibitors on ischemic and bleeding endpoints in older adults with ACS.

Methods. Randomized clinical trials that reported separately the results of adults older >70 years for at least the primary endpoint (composite of death, myocardial infarction [MI] and stroke). Seven studies (14,485 patients-years) were included.

Results. Network meta-analysis showed that prasugrel was associated with similar occurrence of the primary endpoint and of a secondary ischemic endpoint (composite of MI and stroke) and was most likely the best treatment (Surface Under the Cumulative Ranking curve Analysis [SUCRA] 54.5 and 59.8, respectively). With regards to major bleedings, clopidogrel showed the highest likelihood of event reduction (SUCRA 70.1%) while ticagrelor of stent thrombosis (SUCRA 55.6%). Our meta-regression with a fixed proportion of patients managed invasively of 100% confirmed these trends with increasing SUCRA.

Conclusion. Among older subjects with ACS, DAPT should be balanced upon ischemic and bleeding risks as prasugrel is associated with the highest probability of reduction of ischemic events and clopidogrel of bleedings. Ticagrelor had highest SUCRA for stent thrombosis reduction but seems suboptimal in older adults.

A196: INSTANTANEOUS WAVE-FREE RATIO AND NON INVASIVE CORONARY FLOW RESERVE IN THE EVALUATION OF INTERMEDIATE STENOSES ON THE LEFT ANTERIOR DESCENDING ARTERY

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Objectives. The severity of an intermediate left anterior descending artery (LAD) stenosis can be functionally assessed by non-invasive

coronary flow reserve (CFR) obtained by transthoracic echocardiography as well as, invasive methods such as the measurement of iFR in the cath lab. In this study we aimed to investigate the correlation between the two methods.

Methods. We enrolled 12 male patients with CAD, having no previous myocardial infarction in the LAD territory, who underwent coronarography studies for angina pectoris or NSTEMI or STEMI on territories other than that of the LAD. An intermediate LAD lesion (50-80%) was found at the quantitative evaluation by QCA. A functional assessment was carried out in all subjects using both an invasive iFR and a non-invasive method on evaluating the coronary flow reserve (CFR) using transthoracic echocardiography, and measuring the flow in the distal portion of the LAD in basal conditions and during coronary hyperemia induced by adenosine. In the event of significant stenosis with the presence of pathological iFR, elective angioplasty was performed on LAD.

Results. The CFR average values calculated with the peaks of diastolic velocities (mean \pm SD) were 2.13 ± 0.79 , range 1.21-3.7, and the iFR average values were 0.84 ± 0.09 , range 0.63-0.94. We found a correlation between the CFR values and the iFR values measured in the cathlab ($r = 0.67$, $p=0.02$). Based on pathological iFR values <0.89 , eight out of 12 patients (stenosis group A) underwent PCI and 4 patients with iFR normal value (group B) were referred for medical therapy. CFR was significantly reduced in group A compared to group B (1.7 ± 0.35 vs 2.98 ± 0.77 , $p < 0.03$). ROC analysis shows the best CFR cut-off in our population by distinguishing a pathological iFR was $CFR \leq 1.88$ (sensitivity 100%, specificity 80%, PPV 87.5%, NPV 100%, diagnostic accuracy 91.6%). Considering the standard CFR cut-off <2 , two patients (16%) presented a discrepancy between the CFR and iFR values. In fact, in one patient the CFR value was normal despite a critical stenosis of the LAD in its distal portion, while the second patient showed an altered CFR value (1.93) despite the absence of a hemodynamically significant coronary lesion. Considering the ROC curve derived cut-off, the discordance persists only for the patient with normal CFR and pathological iFR.

Conclusions. The non-invasive CFR measurement obtained by transthoracic echocardiography, in patients with LAD intermediate lesions, has a good correlation with the iFR measured in the cath-lab and is confirmed as a useful and accurate tool in detecting a functionally significant lesion and in the follow-up of patients with LAD intermediate stenosis. However, this method does not allow to assess particularly distal LAD stenosis and is affected by alterations of the microcirculation. For this reason, association of the dual imaging during stress echo with assessment of CFR and wall motion could further increase the accuracy of the method in the evaluation of functionally significant stenosis.

A197: GENDER DIFFERENCE IN REPERFUSION TIMES IN STEMI PATIENTS

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Background. Cardiovascular disease is the leading cause of mortality in women. There is a significant delay when treating Women with STEMI thus a higher mortality rate in females. Aim of the study: to assess the impact of gender on decision delay and system delay reperfusion therapy with primary angioplasty (PPCI) in patients with STEMI admitted to our Department.

Methods. Nine hundred forty-three consecutive patients with STEMI referred to our hospital for PPCI were studied. 223, 23.6% were female (FG) mean age 68.8 ± 13.7 and 720, 77.1% were men (MG), mean age 62.3 ± 11.8 , $p < 0.0001$. For each patient demographic data, clinical variables, examinations were collected and following intervals were calculated: 1) Pain to ECG, from the symptom onset to first diagnostic ECG (pain to ECG), 2) Door To Balloon (DTB) time, from hospital arrival to the first therapy 3) the first medical contact-to-balloon time (FMCTB time), from the first diagnostic ECG to the first therapeutic intervention; 4) Total Ischemic Time (TIT), from symptom onset to reperfusion.

Results. The pain to ECG was greater in FG (110 vs 91 min, $p=0.04$). Female patients more frequently had an interval Pain-to-ECG over 120 minutes (41.1%) than male patients (31.1%) ($p=0.02$). The DTB time, was comparable in both groups, (60 FG vs 61 min MG, $p=0.37$). But, the overall delay in the management of the patient presents statistically significant differences between groups (FMC in FG 100 vs 93 min of MG, $p=0.008$). In parallel, the proportion of patients with FMC time ≤ 90 min increased from 38.5% FG, to 47.7% MG, $p=0.02$. The TIT was higher in FG compared to MG (195 vs 150.5 min, $p=0.0047$), and the percentage of patients with a TIT ≤ 120 minutes was statistically different (FG 7.1% vs 13%, $p=0.017$).

Conclusion. Our study confirms a greater decisional delay in call for help in women and pre-hospital delay that leads to a longer Total Ischemic Time. Gender contributes to the pre-hospital delays to reperfusion but not to in-hospital delays. Thus highlights the need to increase campaigns aimed at informing the female population on how to recognize and not to underestimate myocardial infarct related symptoms, in order to provide an

effective reperfusion therapy. We also need a greater awareness of physicians in pre-hospital management of women with suspected myocardial infarction.

A198: SEX DIFFERENCES IN IN-HOSPITAL MANAGEMENT AND OUTCOMES OF PATIENTS WITH ACUTE ST-ELEVATION MYOCARDIAL INFARCTION

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The last decades have been characterized by a mortality rate decrease in patients with acute ST-elevation myocardial infarction (STEMI), due to a wide application of myocardial reperfusion therapy as recommended by STEMI ESC guidelines. However, several studies show worse outcomes in women, compared to men, among STEMI patients. The aim of our study is to evaluate if there exists a gender gap in cardiovascular risk factors, in-hospital management and outcomes of STEMI patients who underwent percutaneous coronary intervention (PCI) in our coronary care unit (CCU).

Methods. We evaluated 943 STEMI patients consecutively admitted to our CCU and underwent PCI within 12 hours after the onset of symptoms from 1st January 2008 to 29 September 2019. For each patient we collected demographic, clinical and angiographic characteristics and we calculated time from symptoms onset to reperfusion (identified as the moment of restoring flow in the culprit coronary).

Results. Among the 943 patients, 223 (23.62%) were women and 720 (77.1%) were men. Our study confirms differences in cardiovascular risk profile in female STEMI patients: women were older (68.8 ± 13.7 vs 62.3 ± 11.8 , $p < 0.0001$), with a higher prevalence of hypertension (64% vs 51.2%, $p=0.001$) and a worse glomerular filtration rate (63 ± 22.4 vs 73.9 ± 21.2 , $p < 0.0001$), while men had higher prevalence of smoking (51.2% vs 36.3%, $p < 0.0001$). In our case history, we experienced a good adherence to guidelines regarding pharmacological therapy both in acute and secondary prevention in both sexes and we found no differences between sexes in reperfusion therapy through PCI, that resulted equally effective in restoring flow in the culprit vessels (TIMI 3 flow post PCI 98.2% in women and 99% in men, $p=0.31$). But we found MINOCA in 1.34% of women, and no cases in men ($p=0.014$). Female patients had a significantly longer hospital stay than men (9.3 ± 4.8 vs 8.5 ± 4.6 , $p=0.031$). Women had a higher although not statistically significant tendency to cardiogenic shock (15 pts, 6.7%) compared to men (31 pts, 4.3%, $p=0.15$). In-hospital mortality rate in women resulted significantly higher than in men (6.7% vs 4.3%, $p=0.005$). Logistic regression analysis, correcting the mortality data for age and other clinical variables such as hypertension, smoking, diabetes, a Killip class >1 , pretreatment with DAPT, cardiogenic shock, glomerular filtrate, the FMC, an FE $<45\%$ and the use of the radial approach, the sex-related difference in in-hospital mortality, which was significant on univariate regression analysis, was no longer statistically significant (OR 2.37, 95% CI 1.17-6.58, $p=0.098$) and the independent factors of mortality in our population were age (OR 1.08, 95% CI 1.03-1.15, $p < 0.0001$), a fraction of ejection $<45\%$ (OR 4.95% CI 1.44-10.4, $p=0.007$) and the absence of pretreatment (OR 4.6, 95% CI 1.46-14.5, $p=0.009$).

Conclusions. Our study confirms a different risk profile between women and men with STEMI. In our population we found a good adherence to the guidelines for pharmacological treatment both in acute and in secondary prevention in both sexes. Our study confirms that, at least in the short term of hospitalization, women have a lower prognosis and expectation of surviving a heart attack than men. However, the increase in women mortality cannot be attributed, to a lower use in the acute phase of therapies such as DAPT or to the revascularization procedure. In fact, the procedural time of angioplasty and the effective result with TIMI 3 were similar in both sexes, rather, it appears to be due to a higher risk profile of women with STEMI.

A199: RUOLO DEI CANALI IONICI NELLA FISIOPATOLOGIA DELLA CARDIOPATIA ISCHEMICA: DALLA GENETICA, ALL'ESPRESSIONE MOLECOLARE, AL FENOTIPO CLINICO

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Introduzione. La patogenesi della cardiopatia ischemica viene usualmente correlata all'aterosclerosi dei vasi coronarici epicardici. Dati

angiografici, clinici e autoptici, tuttavia, evidenziano come la cardiopatia ischemica si manifesti anche in assenza di placche coronariche epicardiche, orientando verso un'attenzione sempre più ampia rivolta al microcircolo coronarico e, in particolare, ad alcuni polimorfismi di geni impiati nella sua regolazione, come fattori coinvolti nella patogenesi della cardiopatia ischemica, indipendentemente dai classici fattori di rischio cardiovascolari.

Obiettivo. L'obiettivo di questo studio è quello di riesaminare la letteratura in termini di associazione tra varianti geniche ed ischemia miocardica valutando, in particolare modo, il ruolo di alcuni SNPs del gene KCNJ11, codificante per la subunità Kir6.2 del canale del potassio ATP-dipendente (KATP). Inoltre, si vuole studiare l'eventuale associazione tra l'espressione dei geni KCNJ11 e SCN5A, quest'ultimo codificante per il canale per il sodio-voltaggio dipendente (Nav1.5), a livello del tessuto cardiaco e i livelli di RNA corrispondenti nel sangue periferico.

Materiali e metodi. In questo studio sperimentale, monocentrico, sono stati arruolati pazienti con indicazione ad essere sottoposti a coronarografia. I pazienti sono stati suddivisi in tre gruppi: G1 con placche coronariche; G2 con disfunzione del microcircolo ai test funzionali intracoronarici con acetilcolina e adenosina; G3 con coronarie anatomicamente e funzionalmente normali. Tutti i pazienti sono stati sottoposti ad analisi genetiche per il gene KCNJ11. In un sottogruppo di G1 costituito da pazienti sottoposti ad intervento cardiocirurgico di bypass aorto-coronarico (CABG) si è valutata l'espressione dell'RNA dei geni KCNJ11 e SCN5A su 3 campioni di biopsia cardiaca e 2 di sangue periferico; questo gruppo di pazienti è stato posto a confronto con un gruppo di pazienti di controllo sottoposti a intervento cardiocirurgico per cause non ischemiche.

Risultati. Sono stati arruolati 603 pazienti (G1: 409; G2: 76; G3: 118) su cui è stata eseguita l'analisi genetica per il gene KCNJ11, la quale ha evidenziato tra i tre gruppi una differenza significativa per i polimorfismi rs5215, rs5218 e rs5219 del gene KCNJ11 ($p < 0.0001$), così come confrontando G1-G3 (rs5215, rs5218 e rs5219 $p < 0.0001$); tra G1-G2 si confermano le differenze solo per rs5215 ($p < 0.0001$), rs5218 ($p = 0.005$) e rs5219 ($p = 0.024$); tra G2-G3 esistono differenze rs5215 e rs5219 ($p < 0.0001$). All'analisi multivariata, il polimorfismo rs5215_GG del gene KCNJ11 appare come fattore protettivo indipendente per cardiopatia ischemica ($p < 0.0001$; OR: 0.036; 95.0% CI: 0.018-0.069). Confrontando il sottogruppo di pazienti G1 sottoposti a CABG (20) con un gruppo di controllo (13) relativamente all'espressione dei geni KCNJ11 e SCN5A a livello cardiaco e del sangue periferico, questa è stata rilevata in tutti i campioni testati con una maggiore espressione di KCNJ11 e SCN5A nel tessuto cardiaco (con SCN5A più espresso di KCNJ11) e più bassi nel sangue (con valori simili per i due geni).

Discussione. Tali risultati confermano il ruolo di alcuni polimorfismi genetici codificanti, in particolare, per canali ionici coronarici, nel determinismo della cardiopatia ischemica, al di là dei fattori di rischio convenzionali, alimentando la prospettiva futura di una terapia per la cardiopatia ischemica a target genico. Inoltre, i dati preliminari relativi ai differenti livelli di espressione dei geni KCNJ11 e SCN5A nel cuore e nel sangue periferico, potrebbero, se approfonditi, stabilire un'eventuale correlazione tra i livelli di espressione di questi geni e il fenotipo clinico dei pazienti.

A200: ACUTE CORONARY SYNDROME: IS IT ALWAYS PLAQUE'S GUILTY?

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Introduction. Coronary embolism (CE) is an underdiagnosed cause of acute coronary syndrome (ACS). A coronary embolus may originate from an endocarditis of the aortic valve related to antiphospholipid syndrome. We show the decisive role of non-invasive and invasive diagnostic imaging techniques to define diagnosis and the proper treatment option in a such case.

Case presentation. A 29-year-old male was admitted to our hospital for anterior ST segment elevation myocardial infarction (STEMI). Echocardiography revealed a preserved left ventricular ejection fraction with an apical akinesis and aortic valve cusps thickening causing relevant aortic regurgitation. Coronary angiography revealed a distal left anterior descending artery (LAD) occlusion. No other significant coronary lesions were found. Primary PCI (PPCI) was performed through radial artery. After LAD artery recanalization with the guidewire, manual aspiration thrombectomy (MAT) was attempted several times using an aspiration catheter. No visible thrombus debris were aspirated. An intravenous bolus of glycoprotein (Gp) IIb/IIIa inhibitor was administered. Then, a 6-atm pre-dilatation with a semi-compliant balloon was performed with a modest endoluminal gain. Optical coherence tomography (OCT) was performed and it confirmed the presence of an endoluminal thrombus, white and red, without any finding suggesting underlying atherosclerosis or intimal tear. A more aggressive dilatation with a non-compliant balloon 12 atm was performed. The final angiogram showed a critical residual stenosis with a grade 3 TIMI flow without any distal embolization. According to the acceptable angiographic result, considering the

thrombus persistence at the final OCT evaluation, a deferred stenting strategy was adopted. Trans-oesophageal echocardiogram (TOE) showed isoechoic mobile formations in the ventricular side of cusps, causing severe aortic regurgitation. Serial blood cultures were negative. A total body computed tomography (CT) excluded other embolic systemic findings. A CT coronary angiography showed a complete thrombus resolution in LAD. Aortic valve replacement was performed with mechanical prosthesis in mini-thoracotomy. Macroscopic intraoperative examination of the aortic valve showed huge vegetations on the ventricular side of the cusps. Out of the autoimmunity markers dosed antiphospholipid antibodies titer (ACA-IgG; b2-GP1-IgG) was strongly positive. The discharge diagnosis was: non-bacterial thrombotic endocarditis (NBTE) related to APS.

Conclusions. Our case confirms that coronary embolism, probably underdiagnosed in clinical practice, must be suspected in young patients with ACS and no atherosclerotic risk factors. In addition, it underlines the importance to have available different diagnostic tools in the setting of ACS. Indeed, urgent trans-thoracic echocardiography (TTE) allowed to consider embolic hypotheses, subsequently confirmed by OCT. The latter is helpful in determining if there is a coronary atherosclerosis and if a percutaneous coronary intervention with stenting should be considered at the time of index procedure or deferred.

A201: REDUCTION OF TAKOTSUBO SYNDROME HOSPITALIZATION DURING THE COVID-19 PANDEMIC. RESULTS FROM THE GEIST (GERMAN AND ITALIAN STRESS CARDIOMYOPATHY) REGISTRY

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Background. Takotsubo syndrome (TTS) is an acute heart failure syndrome associated mainly to acute stress conditions.

Aim. To evaluate the impact of the COVID-19 pandemic on patient admissions to German and Italian cardiac care units (CCUs).

Methods. We enrolled consecutive TTS patients in the international multicenter GEIST (German and Italian stress cardiomyopathy) registry to collect data on admissions throughout six months period (January 1st to 30th June 2020) during the COVID-19 outbreak, compared with the equivalent months in 2019.

Results. During the first 6 month of 2020 there was a 9.5% reduction of TTS admissions (95% CI = 1.92 - 17.08, $p = 0.01$) when compared to 2019.

This trend was even more evident during the complete lockdown in Italy, that occurred between march 9th and may 4th, in which there was a 30.7% reduction of TTS admissions (95% CI = 1.65 - 59.75, $p = 0.03$).

There were no differences in term of clinical features and in-hospital complications among patients admitted in 2019 and 2020. However, during the Italian complete lockdown we observed a significantly longer hospitalization duration compared to 2019 (9 ± 3 days in 2020 vs 6 ± 2 days in 2019 $p = 0.03$).

Emotional trigger showed a tendency to decrease in the same period (33% in 2020 vs 46% in 2019, $p = 0.44$).

Conclusions. Admissions for TTS were significantly reduced during the COVID-19 pandemic mainly during the complete lockdown without a parallel increase in complication rates.

A202: DOLORE TORACICO IN ETÀ PEDIATRICA: UN CASO PIÙ UNICO CHE RARO

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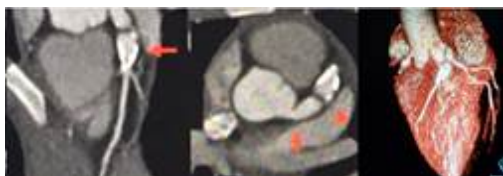
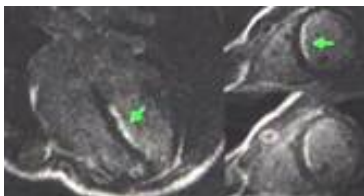
Donatella Manca (a), Sabrina Montis (a), Gildo Matta (b), Stefano Cossa (b), Paolo Siotto (b), Maurizio Porcu (c), Carlo Ballo (d),

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Anamnesi: non familiarità per cardiopatie. Nato a termine da parto spontaneo. All'età di 3 anni episodio febbrile in corso di faringite, otite e

linfadenopatie cervicali. Pratica calcio a livello agonistico in assenza di sintomatologia. Test da sforzo seriati per idoneità agonistica nella norma. 14 anni: durante una partita comparsa di dolore toracico, esacerbato dagli atti del respiro, durato circa 48 ore. Recatosi in PS di un centro Spoke riscontro all'ECG ST sopraslivellato V4-V6 con troponina positiva; immediato trasferimento presso centro Hub. All'ecocardiogramma evidenza di ipocinesia marcata apicale e settale con lieve riduzione della funzione sistolica globale FE 50%. Agli esami ematochimici conferma di positività della troponina e PCR lievemente aumentata. Iniziale inquadramento diagnostico di miocardite, trattato conservativamente; osservazione clinica, durante la degenza non recidive di dolore toracico. All'ecocardiogramma predimensione miglioramento della cinetica distrettuale con FE 50%. RMN cardiaca: delayed enhancement non compatibile con miocardite, ma bensì con necrosi ischemica su territorio di IVA. Non più alterazioni della cinetica distrettuale e recupero FE 60%. TC coronarie: Cdx e IVA occluse nel tratto prossimale, vasi aneurismatici con grossolane formazioni trombotiche calcificazioni parietali. Terapia: cardioaspirina, B-bloccanti e ACE-inibitore. 1 mese dopo l'evento acuto è stato ricoverato presso centro cardiocirurgico per le cardiopatie congenite di III livello e sottoposto a intervento di bypass con doppia arteria mammaria interna, mammaria dx su Cdx e mammaria sn su IVA. Iniziata terapia anticoagulante in aggiunta alla terapia di base. Al controllo 2 mesi dopo la dimissione non evidenti alterazioni della cinetica e FE conservata 60%, lieve discinesia del SIV. Evidenza di aneurismi coronarici Csx: TC e IVA 6 mm z score rispettivamente di +4.4 e 6.6, Cdx 10 mm z score + 14. Iniziata terapia con statina. Un anno dopo episodio di dolore toracico con sopraslivellamento concavo ST in sede precordiale; accesso in PS, troponina negativa, PCR positiva, ecocardiogramma normale, non versamento pericardico. Ricoverato per pericardite per una settimana, terapia con colchicina e ibuprofene. Questo caso clinico è peculiare perché molto spesso, si è portati in un giovane con dolore toracico a pensare a una miocardite, statisticamente molto più frequente di un problema ischemico durante l'adolescenza. Ma le coronarie giocano purtroppo brutti scherzi, dalle anomalie di sede, alle anomalie di calibro, come in questo caso, dove l'anomalia caratteristica con dilatazioni e restringimenti a "corona di rosario" ci porta a pensare ad una eziologia secondaria legata a una probabile pregressa malattia di Kawasaki.



A203: PROGNOSTIC IMPACT OF HYPERGLYCEMIA AND DIABETES IN PATIENTS WITH MYOCARDIAL INFARCTION WITH NON-OBSTRUCTIVE CORONARY ARTERY DISEASE (MINOCA)

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Background. Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a heterogeneous clinically entity and represents 5% to 10% of all patients with myocardial infarction (MI). Besides type 2 diabetes mellitus (DM), which is a common comorbidity in patients hospitalized for an acute coronary syndrome, high glucose levels (HGL) at admission are frequently observed in this context. The risk of major adverse cardiovascular events following acute coronary syndrome is increased in

people with DM and HGL. However, evidence regarding diabetes and high glucose level among MINOCA patients is lacking.

Purpose. To examine the incidence of major adverse cardiovascular events (MACEs) in diabetic and non-diabetic MINOCA patients as well as according to HGL at presentation.

Methods. Among 2644 patients with acute MI admitted to our coronary care unit from 2016 to 2020, we enrolled 291 consecutive MINOCA patients according to the current ESC diagnostic criteria. HGL at admission was defined as serum glucose level above 150 mg/dl. All-cause mortality and a composite end-point of all-cause mortality and myocardial re-infarction were compared. The median follow-up time was 19.6 ± 12.9 months.

Results. Diabetic MINOCA patients were older (mean age 75.5 ± 9.6 vs 66.5 ± 14.7; p=0.002) and with higher prevalence of hypertension (p=0.016). Conversely, there were no significant differences in gender, BMI, dyslipidemia and atrial fibrillation. Similarly, no significant differences were observed regarding clinical and ECG presentation, echocardiographic features and laboratory tests. The rates of death (30.8% vs 8.3%; p=0.013) and MACEs (22.2% vs 6.8%; p=0.025) were significantly higher in MINOCA-DM patients; conversely, no significant differences were observed for re-MI (p=0.58). At multivariate regression model adjusted for age and sex, type 2 DM was not an independent predictor of all cause deaths (p=0.36) and MACE (p=0.24).

Patients with admission HGL had similar baseline characteristics, cardiovascular risk factors, clinical presentations, echocardiographic features and troponin values as compared to patients with no-HGL. HGL at admission was associated with higher incidence of all-cause-death (p < 0.001) and MACE (p=0.003) during follow-up compared to patients with no HGL; conversely, no significant differences were observed in the incidence of re-MI (p=0.7). Multivariate analysis adjusted for age and sex demonstrated that HGL was an independent predictor of death (HR 6.25; CI 1.64-23.85; p=0.007) and MACEs (HR 6.17; CI 1.79-21.23, p=0.004).

Conclusion. In MINOCA patients, HGL was an independent risk factor for both MACEs and death while type 2 DM was not correlated with these hard endpoints. As a consequence, HGL could have a still unexplored pathophysiological role in MINOCA. Properly powered randomized trials are warranted.

A204: WHEN THE MICROCHANNEL IS HIDING AND THE TIP-IN TECHNIQUE FAILS: THE FACILITATED ANTEGRADE WIRING TECHNIQUE

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The success rate of percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) has increased over time, thanks to the more frequent utilization of the retrograde approach. Externalization is a crucial step of retrograde CTO-PCI, allowing to complete the revascularization through an antegrade system for balloons and stents delivery. In case of hampered crossing of the collateral vessel or CTO segment by the retrograde microcatheter (MC), the tip-in technique can be helpful. We present a clinical case through which we explain a novel technique that could be useful when antegrade MC does not cross the CTO segment after effective tip-in and when the antegrade approach is challenging. In the retrograde approach for percutaneous revascularization of chronic total occlusion (CTO), externalization represents a key-step consisting in creating an antegrade route for delivery of balloons and stents. The Tip-In technique represents an alternative to traditional externalization when retrograde microcatheter (MC) is not able to advance beyond the CTO segment or when it is not able to cross the collateral channel. An improvement of this technique ("The Facilitated Tip-In Technique") has been described that could be effective in case of failure to advance an antegrade MC beyond the CTO segment after effective Tip-in. In this manuscript, we present a novel technique ("The Facilitated Antegrade Wiring Technique") that could be useful when antegrade MC does not cross the CTO segment despite increased antegrade MC support and when the antegrade puncture of the proximal cap is challenging due to ambiguous cap and angulation of the occluded vessel, not allowing IVUS guidance.

A205: THE PRESENCE OF ARRHYTHMIAS IN ACUTE MYOCARDIAL INFARCTION PATIENTS AND HYPERGLYCEMIA

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Background. In patients with acute myocardial infarction (AMI), hyperglycemia is a common feature determining a worse prognosis.

During AMI, sympathetic stimulation and release of catecholamine cause an increase of serum glucose levels. Few studies have examined the relationship between hyperglycemic status and the occurrence of arrhythmias in-hospital stay in patients with AMI.

Purpose. To evaluate the relationship between elevated serum glucose levels and occurrence of arrhythmias in-hospital stay in patients with AMI.

Methods. We enrolled 2758 consecutive patients with AMI undergoing coronary angiogram between 2016 and 2019. Hyperglycemia was defined as a serum glucose level ≥ 150 mg/dl at the time of hospital admission. EKGs of each patient were assessed by expert cardiologists. Arrhythmias was defined by the presence of one of the following: atrial fibrillation, non-sustained and sustained ventricular tachycardia, ventricular fibrillation and sinus node or atrioventricular blocks.

Results. Among 2758 patients (32% were female, mean age was 68.5 ± 13 years) 22.5% were diabetic. At admission, the mean value of serum glucose levels was 146 ± 66 mg/dl. At hospital admission, hyperglycemic status was present in 32% of patients and 8.2% presented atrial fibrillation. Atrial fibrillation was significantly more frequent in hyperglycemic as compared to normoglycemic patients (6.7% vs 11.3% respectively; $p < 0.001$). During hospital stay, the onset of new arrhythmias was higher in hyperglycemic status than normoglycemic status (9.8% vs 4.4% respectively, $p < 0.001$). Multivariate analysis adjusted for age, sex and diabetes revealed that the presence of hyperglycemia was an independent predictor for the onset of new arrhythmias (OR 2.28; 95% CI 1.60-3.27; $p < 0.001$).

Conclusions. Hyperglycemia was an independent predictor of new arrhythmias during hospitalization in patients with AMI. Moreover, at hospital admission, patients with hyperglycemic status presented high incidence of atrial fibrillation. Further studies are needed to more fully understand the biologic mechanisms involved in the associations observed.

A206: HYPERGLYCEMIA, INFLAMMATORY RESPONSE AND INFARCT SIZE IN ACUTE MYOCARDIAL INFARCTION: OBSTRUCTIVE VERSUS MINOCA PATIENTS

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Background. Hyperglycemia has been associated with increased inflammatory indexes and larger infarct sizes in patients with obstructive acute myocardial infarction (AMI) while no studies have explored these correlations in non-obstructive acute myocardial infarction (MINOCA).

Purpose. We investigated the relationship between hyperglycemia, inflammation and infarct size in a cohort of AMI patients that included MINOCA.

Methods. Patients with AMI undergoing coronary angiography between 2016 and 2020 were enrolled in AMIPE Registry. The following inflammatory markers were evaluated at baseline: C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and neutrophil-to-platelet ratio (NPR). Myocardial infarct size was measured by peak high sensitivity troponin I (Hs-TnI) levels, left-ventricular-end-diastolic-volume (LVEDV) and left ventricular ejection fraction (LVEF). Hyperglycemia was defined as admission glucose level ≥ 140 mg/dL according to the American Heart Association and the Endocrine Society Clinical Guidelines.

Results. The final study population consisted of 2450 patients with obstructive-AMI and 239 with MINOCA. Hyperglycemia was more prevalent among obstructive-AMI than MINOCA cases (33.8% vs 12.9%, p -value < 0.001). In all hyperglycemic patients - obstructive-AMI and MINOCA - NLR, NPR, LPR and CRP were significantly markedly altered. Hyperglycemic obstructive-AMI subjects exhibited a higher Hs-TnI, a larger LVEDV and a lower LVEF compared to normoglycemic ones. Conversely, MINOCA patients showed similar myocardial damage, irrespective of glycemia.

Conclusions. Our data confirm the association of admission hyperglycemia with elevated inflammatory markers in obstructive AMI but also in MINOCA. Hyperglycemic obstructive-AMI had a larger infarct size, whereas MINOCA patients exhibited modest myocardial damage, regardless of admission glucose levels. Further prospective studies are needed to assess the role of hyperglycemia in the heterogenous MINOCA entity.

A207: COLCHICINE SIGNIFICANTLY INCREASES THE RISK OF NON-CARDIOVASCULAR DEATH IN PATIENTS WITH CORONARY ARTERY DISEASE

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Aims. Colchicine has recently emerged as a promising therapeutic option for patients with coronary artery disease (CAD). Indeed, several

randomized controlled trials (RCTs) have shown a remarkable effect of colchicine, as compared to placebo, in reducing hard ischemic events including cardiovascular (CV) death, resuscitated cardiac arrest, myocardial infarction (MI), stroke and ischemia driven coronary revascularization. This beneficial has been proposed to be attributable to the potent anti-inflammatory activity exerted by colchicine and was consistent among RCTs including patients with acute (ACS) or chronic coronary syndromes (CCS). Nevertheless, a trend towards increased incidence of death from non-cardiovascular causes was present in the colchicine group, as compared to the control group, in all the major trials on the topic. Since none of the published RCTs was powered to address the outcome of non-cardiovascular death, pooled analyses are particularly useful to address this relevant outcome and dispel any possible safety concerns on the broad use of colchicine among CAD patients.

Methods and Results. We included RCTs comparing low dose of colchicine versus placebo in patients with CAD. Trials in which the outcome of non-cardiovascular death was not reported or those randomizing less than 100 patients were excluded. A total of 11,555 patients from four RCTs were included. The Q Cochran test and Higgins I² statistics were calculated to estimate heterogeneity among the included studies. Odds Ratio (ORs) with 95% confidence intervals (CIs) by using Mantel-Haenszel fixed-effect models were calculated using RevMan software version 5.3 (Cochrane Collaboration). P-values < 0.05 were considered significant. A pre-specified subgroup analysis was performed according to the inclusion of acute (ACS) or chronic (CCS) coronary syndromes patients. Publication bias and meta-regressions were not performed given to the small number of studies included (< 10). At an average follow-up of 25.1 months, colchicine is associated with a significantly higher risk of non-cardiovascular death (OR 1.55; 95% CI 1.10 to 2.17; $P = 0.01$) as compared to the control group. The result is consistent at subgroup analysis including RCTs enrolling CCS patients (OR 1.63; 95% CI 1.07 to 2.49; $P = 0.02$) while a non significant increase of non-cardiovascular death is found at subgroup analysis including RCTs enrolling ACS patients (OR 1.40; 95% CI 0.78 to 2.48; $P = 0.25$).

Conclusion. The use of colchicine in patients with CAD is associated with a significant increase in non-cardiovascular death at a follow-up of 25 months. In the lack of pharmacological and clinical data reassuring from an excess of non-cardiovascular death, further investigations are warranted to determine whether colchicine could become a safe and widespread panacea for the treatment of CAD.

A208: RUOLO DELLA TERAPIA IN ACUTO CON STATINE NELLA DISFUNZIONE ENDOTELIALE NEL PAZIENTE STEMI: ROSUVASTATINA VS ATORVASTATINA

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Introduzione. Il trattamento con statine è parte integrante dell'approccio terapeutico nei pazienti con sindromi coronariche acute (SCA); il razionale risiede nel fatto che l'8-10% dei pazienti con recente STEMI va incontro a recidiva infartuale entro un anno dall'evento, e che circa il 44% della riduzione dei decessi è ascrivibile al controllo dei fattori di rischio coronarico. Il beneficio derivante dall'impiego di statine è da ricondurre alla riduzione del colesterolo LDL, il cui controllo garantisce circa il 24% di riduzione delle morti totali; esiste infatti un rapporto direttamente proporzionale tra la riduzione dei livelli di colesterolo LDL e la riduzione degli eventi cardiovascolari. Le linee guida ESC 2019 hanno identificato i nuovi target sulla base delle classi di rischio, ovvero very high risk (LDL-C < 55 mg/ml), high risk (LDL-C < 70 mg/dl), moderate risk (LDL-C < 100 mg/dl), low risk (LDL-C < 116 mg/dl). Al fine di raggiungere i target sopra indicati, in tutti i pazienti è raccomandata la terapia con statine ad alte dosi, iniziata il più precocemente possibile. In associazione alla statina è raccomandato l'utilizzo di ezetimibe in caso di mancato raggiungimento del target LDL-C dopo 4-6 settimane di terapia con la massima dose tollerata di statina. Qualora dopo ulteriori 4-6 settimane non sia ancora stato raggiunto il target di LDL-C, è raccomandata l'aggiunta degli inibitori di PCSK9.

Obiettivi. L'obiettivo di questo studio è la valutazione dell'equivalenza di efficacia di atorvastatina rispetto a rosuvastatina, somministrate immediatamente dopo intervento di PTCA in pazienti STEMI, nel normalizzare la funzione endoteliale (misurata strumentalmente a livello periferico) e i marker sierologici di infiammazione vascolare e di instabilità di placca.

Materiali e metodi. I pazienti sono stati reclutati entro 48 ore dalla diagnosi di STEMI e sono stati randomizzati ad atorvastatina 80 mg vs rosuvastatina 40 mg. La valutazione è stata svolta in quattro tempi: al momento dell'evento acuto (entro 48 ore dalla diagnosi), dopo 1 mese, dopo 4 mesi e dopo 4 anni. I parametri valutati sono stati principalmente hs-PCR e RHI (mediante EndoPAT), in particolare al momento dell'evento acuto e a distanza di 4 anni. Altri parametri analizzati sono stati la Pulse Wave Velocity e l'Augmentation Index, mediante EndoPAT e SphygmoCor.

Risultati e Conclusioni. Lo studio ha evidenziato come la riduzione di

colesterolo LDL risulti progressiva con l'utilizzo di rosuvastatina, ma non con quello di atorvastatina, che manifesta un effetto più rapido ma di minore entità a lungo termine; inoltre la riduzione della hs-PCR risulta molto più accentuata con l'utilizzo di rosuvastatina, se si considera un intervallo di tempo più lungo (anni). Tale concetto viene confermato anche dal miglioramento della funzionalità endoteliale (valutata misurando l'RHl tramite EndoPAT) che si è verificato nei pazienti in trattamento con rosuvastatina, ma non in quelli in trattamento con atorvastatina. Questo dato risulta evidente nella rivalutazione dei pazienti nel follow-up effettuato a 4 anni di distanza dall'evento acuto. Si può quindi ipotizzare che a lungo termine l'"effetto pleiotropico" della rosuvastatina sia maggiore di quello dell'atorvastatina. Infine, data la non significatività riscontrata nello studio in diverse variabili, è necessario confermare e ampliare questi risultati in un campione di pazienti più numeroso.

A209: CONTROVERSIAL INTERPRETATION OF VEGF-A IN THE PATHOGENESIS AND PROGNOSIS OF CARDIOVASCULAR DISEASE

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Vascular endothelial growth factor (VEGF) is a family of signaling proteins contributing to the growth of blood vessels. Angiogenesis plays a critical role in myocardial repair after AMI, and impaired neovascularization in the infarct area may contribute to the transition to heart failure. The isoform A of VEGF is a key mediator of angiogenesis and its correlation with coronary artery disease (CAD), in particular with STEMI, has been evaluated in many studies. In most studies, in STEMI patients high levels of VEGF-A were detected and were related with the extension of infarcted area and with a favorable clinical outcome. In recent works, adverse cardiac remodeling turned out to be associated with altered ratio between pro-angiogenic and anti-angiogenic isoforms of VEGF-A. As a matter of fact, the isoform VEGF-A165B is considered an anti-angiogenic factor able to influence adverse cardiac remodeling and plaque rupture. Overall, the interpretation of VEGF-A in pathogenesis and prognosis of cardiovascular disease is controversial and needs further investigation. VEGF-A is responsible for angiogenesis, neovascularization and tissue repair and the main trigger for its production is hypoxia. VEG-A stimulates vasodilation, capillary permeability, blood cells chemotaxis, mitosis and migration of endothelial progenitors that are necessary for blood vessel formation. In CAD VEGF-A promotes the development of collateral circulation, led by hypoxia. Also, in myocardial infarction, it is implicated in myocardial repair. In recent studies, it turned out that alternate splicing of exon 8 of VEGF-A mRNA generates the isoform VEGF-A165B that binds the same receptor as VEGF-A but fails to activate receptor fosforilation, impairing angiogenesis. Many studies investigated the correlation of the level of VEGF-A in serum and the presence of coronary lesions. Kucukardali *et al.* asserted that VEGF-A level was significantly higher in patients with critical coronary stenosis that in those with non-significant lesions. Lin *et al.* found that VEGF-A level was higher in total coronary occlusions than in partial stenotic injuries, indicating the role of VEGF-A in angiogenesis. In AMI most clinical studies determined an increase in the VEGF-A level compared to healthy subjects, patients with stable or unstable CAD. Also, Wojakowski *et al.* described higher values of VEGF-A in the blood serum in patients with AMI with multi-vessel injuries compared to those with single-vessel ones. No relation was found between the stenosis localization and VEGF-A level. Several studies were dedicated to measure the dynamics of VEGF-A in the acute phase of myocardial infarction. The VEGF-A level in AMI reached its peak on the 7th-14th day after PCI and returns to the norm after 6 months Hueso *et al.* affirmed that even before reperfusion VEGF-A was significantly increased in STEMI patients than in controls. As for isoform VEGF-A165B, it reached its peak 24h after reperfusion and remained elevated in the first days. Blood serum levels of aVEGF-A165b are altered after AMI and might reflect the extent of cardiac damage. According to Berezin *et al.* lowered levels of VEGF-A after AMI are related to impaired angiogenesis around the necrotic zone, that may expand due to the lack of adequate blood flow. Additionally, deficit of VEGF-A plays a central role in worsening cardiac repair and scar tissue formation, as a consequence of exaggerated inflammatory and fibrotic response. The pro-angiogenic role of VEGF-A is not the only effect of the molecule: indeed, it also has pro-inflammatory and vasodilatory properties that according to some studies may cause vascular leakage and myocardial edema contributing to vessel collapse, reperfusion arrhythmias, stunning, extended tissue lesions and increased infarct size. In conclusion, there are several controversial in interpretation of changes in VEGF-A levels after STEMI and the predictive value of VEGF-A needs to be further investigated in future.

A210: LA SINGOLARE PRESENTAZIONE DI ISCHEMIA MIOCARDICA "A CORRENTE ALTERNATA"

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Introduzione. La diagnosi di blocco di branca alternata si basa su due diverse condizioni: 1- che i pattern blocco di branca destro e sinistro siano presenti sulla stessa registrazione elettrocardiografica, 2- che i due pattern possano verificarsi con alcuni gradi di separazione temporale (cioè a distanza di ore o giorni). Prima dell'era della ri-perfusione il fenomeno dell'alternanza si verificava fino al 6% a seguito di infarto miocardico acuto, con una percentuale di progressione del 44% a blocco AV di alto grado. Con l'avvento della moderna terapia di ripercussione vengono riscontrati meno frequentemente nella pratica clinica.

Caso clinico. Giunge presso il nostro servizio di Cardiologia Riabilitativa soggetto di sesso maschile di anni 71 per effettuare ECG-Holter 24h di controllo. Il paziente era già a noi noto, in quanto aveva eseguito presso il nostro centro programmi di riabilitazione intensiva, il più recente dei quali effettuato dopo l'ultima rivascolarizzazione percutanea. In anamnesi presentava cardiopatia dilatativa post-ischemica in fase ipocinetica (pregressa rivascolarizzazione chirurgica- Graft venoso su IVA e D1; sostituzione valvolare aortica con protesi meccanica; PTCA su graft venoso e IVA prossimale; impianto di ICD in prevenzione secondaria per episodi di tachicardia ventricolare sostenuta). Dal diario ECG-Holter 24h si evinceva marcata astenia durante la giornata, per sforzi fisici anche minimi. Il tracciato evidenziava la presenza, per periodi piuttosto lunghi, di alternanza di blocchi di conduzione destra e sinistra, mai evidenziati in passato. Nel sospetto che tali blocchi avessero una genesi ischemica, il paziente veniva pertanto inviato presso la medicina nucleare per eseguire miocardiografia da sforzo e a riposo. La GATED-SPECT evidenziava diffusa riduzione dell'ispessimento e movimento in tutti i segmenti del ventricolo sinistro, frazione di eiezione ridotta (30%), reperti indicativi di ischemia inducibile nelle sedi sovradescritte. In considerazione di tale referto, il paziente veniva sottoposto ad esame coronarografico con evidenza di occlusione del bypass venoso singolo su IVA ed indicazione a terapia medica.

Discussione. I blocchi di branca possono verificarsi come parte di una malattia del sistema di conduzione diffusa, malattia del miocardio o rottura focale dovuta ad ischemia. A causa dell'estensione della ramificazione del fascio sinistro, il blocco di branca sinistro è più spesso associato al modello di malattia diffusa o all'ischemia prossimale nel territorio della discendente anteriore. Il verificarsi di un ritmo di fuga con morfologia a blocco di branca destro, in presenza di un blocco di branca sinistro, suggerisce che il focus dell'origine di quest'ultimo sia nel fascio sinistro, distale rispetto al blocco di conduzione.

Conclusioni. I blocchi di branca alternati rappresentano un campanello di allarme e pertanto devono essere valutati con attenzione. L'evidenza all'ECG-Holter 24h di tale aritmia ha permesso, nel caso in esame, di diagnosticare un'ischemia miocardica latente. Lo studio elettrofisiologico è indicato per valutare origine e meccanismo degli stessi. Data la storia clinica pregressa ed il forte sospetto per un'eziologia ischemica, nel caso in questione si è soprasseduto all'esecuzione di tale esame.

A211: IP3 RECEPTORS SELECTIVELY REGULATE DETRIMENTAL POST-INFARCTION CARDIAC FIBROSIS

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Background. Therapeutic strategies that specifically target excessive post-ischemic cardiac fibrosis are lacking but desperately needed; thus, it is critical to understand the molecular mechanisms underlying these processes. Genome-wide association studies have revealed an association between inositol 1,4,5-trisphosphate receptors (IP3Rs) and ischemic heart disease. However, experimental studies examining the exact role of IP3Rs in post-ischemic cardiac fibrosis are missing.

Aim. We hypothesize that IP3Rs play a key role in the regulation of cardiac myofibroblasts (myoFBs) in healing the infarcted heart after myocardial infarction (MI).

Methods. We performed an integrated set of *in vivo*, *ex vivo*, and *in vitro* experiments aiming at identifying the functional role of cardiac myoFB IP3Rs in post-ischemic cardiac remodeling. We generated cardiac myoFB-specific IP3R knock-out (IP3R^{KO}) mice (*Cre/lox* recombination technique; Promoter: *Periostin*), allowing us to overcome the difficulties encountered following the KO or KD of a single (of the three existent) IP3Rs, a strategy that has been shown to induce compensatory upregulation of the other isoforms.

Results. After MI, IP3Rs are significantly upregulated in myoFBs of the remote regions but not in the scar area. IP3RKO mice display a significantly reduced interstitial cardiac fibrosis and a markedly attenuated myocardial dysfunction following MI compared with control IP3R^{lox} or *Periostin*^{Cre} littermates. Moreover, FBs lacking IP3Rs exhibit significantly

reduced migratory and secretory capacities, a finding confirmed both in murine and human FBs. Mechanistically, we show that IP3Rs modulate apoptosis of myoFBs following ischemic injury.

Conclusions. Taken together, our findings indicate for the first time that IP3Rs are essential for the regulation of post-ischemic cardiac fibrosis.

A212: EXOSOMAL MICRORNAS REGULATE MYOFIBROBLAST ACTIVATION IN MYOCARDIAL INFARCTION

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Introduction. Recent evidence has shown that exosomal non-coding-RNAs play a pivotal role in cell-cell communication.

Hypothesis. We hypothesize that exosomal microRNAs (miRNAs, miRs) are involved in the activation of myofibroblasts following ischemic injury.

Methods. We tested our hypothesis through means of bioinformatic approaches and a murine model of myocardial infarction (MI), obtained via permanent ligation of the left anterior descending coronary artery; we measured the expression levels of a set of miRs in fibroblasts and cardiomyocyte-derived exosomes; we used miR inhibitors and mimics to evaluate post-MI myofibroblast phenocconversion.

Results. We found that, compared with SHAM conditions, miR-92a was significantly upregulated (absolute values) in cardiomyocyte-derived exosomes as well as in fibroblasts isolated at different time points after MI. This miR was shown to specifically target SMAD7, an established inhibitor of α SMA expression (a fundamental player in myofibroblast activation), such interaction was predicted using bioinformatic tools and biologically validated via luciferase assays. Furthermore, primary isolated cardiac fibroblasts were activated both when incubated with exosomes derived from ischemic cardiomyocytes and when cultured in conditioned medium of post-MI cardiomyocytes, whereas no significant effects were observed following incubation with exosomes or medium from sham cardiomyocytes. Myofibroblast activation was evaluated measuring the expression of α SMA, periostin, collagen I/III, fibroblast activation protein (FAP), fibronectin ED-A. Interestingly, miR-92a also regulated the post-MI inflammatory response (evaluated in terms of IL-6 and CXCL1). Inhibiting exosome release (GW4869 10 μ M for 12 h) significantly attenuated all these responses. The mechanistic contribution of miR-92a to fibroblast phenocconversion was further confirmed using miR-92a mimics and inhibitors.

Conclusions. Taken together, our findings indicate that miR-92a is transferred to fibroblasts in form of exosomal cargo, and is crucial for post-MI activation of myofibroblasts.

A213: DUAL MICRORNA-TARGETING RESCUES THE IMPAIRED MITOCHONDRIAL UNFOLDED PROTEIN RESPONSE IN HEART FAILURE

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Introduction. The mitochondrial unfolded protein response (UPR^{mt}) is an evolutionary conserved process evoked when the mitochondrial protein folding environment is compromised. The major regulators of the UPR^{mt} include *Activating Transcription Factor 5* (ATF5) and *Lon Peptidase 1* (LONP1). UPR^{mt} has been recently shown to be involved in cardiac pressure overload; however, its functional role in post-ischemic heart failure (HF) and its regulation by non-coding RNAs have never been investigated hitherto.

Hypothesis. We hypothesize that UPR^{mt} is a key process in the pathophysiology of post-ischemic HF and is regulated by specific microRNAs (miRNAs, miRs).

Methods. To test the mechanistic role of miRs in the modulation of UPR^{mt} in HF we combined bioinformatic approaches (to identify miRs targeting the crucial players of UPR^{mt}) with an *in vivo* murine model of ischemic HF (coronary ligation).

Results. We identified and biologically validated *in vitro* via luciferase assay two miRs, namely miR-129-5p and miR-489, as specific modulators of the expression of ATF5 and LONP1, respectively. Four weeks after LAD ligation both miRs were significantly ($p < 0.01$) upregulated in the left ventricle compared to sham conditions, whereas their respective targets, ATF5 and LONP1, were markedly downregulated, both at the mRNA and protein level. These alterations were accompanied by perturbations in UPR^{mt} and also in endoplasmic reticulum UPR (UPR^{ER}), including upregulation of HSP60, HSP10, and mtDNA, as well as the three main arms of ER stress. A dual miR *in vivo* targeting, using miR-129-5p and miR-489 antagonists, significantly improved the UPR^{mt} response and overall cardiac function, whereas single approaches yielded minimal results. Intriguingly, despite having as a main target a mitochondrial protease (LONP1), antagonist miR-489 alone had significant effects on the modulation of UPR^{ER}. These results were further supported by *ex vivo* experiments in primary isolated cardiomyocytes, in terms of contractility and mitochondrial dynamics and function (including fission/fusion and Seahorse assays).

Conclusions. Taken together our results indicate that miR-129-5p and miR489 regulate UPR^{mt} in cardiomyocytes in post-ischemic HF via specific targeting of ATF5 and LONP1.

A214: SECURE - SICUREZZA ED EFFICACIA DELLE PROCEDURE ESEGUITE IN SERVICE

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(a) ASP 5 MESSINA - UO EMODINAMICA PATTI; (b) POLICLINICO VITTORIO EMANUELE - CATANIA; (c) ASP 5 MESSINA - UOC CARDIOLOGIA CON UTIC MILAZZO; (d) ASP 5 MESSINA - UOC CARDIOLOGIA S. AGATA DI MILITELLO; (e) AO PAPPARDO MESSINA - UOC CARDIOCHIRURGIA; (f) ASP 5 MESSINA - RISK MANAGER AZIENDALE; (g) ASP 5 MESSINA - EX DIRETTORE SANITARIO AZIENDALE; (h) ASP 5 MESSINA - DIRETTORE GENERALE

Background. La coronaropatia rappresenta una delle cause di morte e morbilità più elevate sul territorio e tra le più frequenti cause di ricovero in UTIC. Lo studio coronarografico costituisce l'esame più importante nei pazienti che mostrano segni clinico-strumentali di coronaropatia acuta o cronica. Tuttavia non tutte le UTIC del territorio sono provviste di Emodinamica (centri spoke). Grazie al recente utilizzo dell'accesso arterioso radiale, al miglioramento delle performance dei devices coronarici e alla crescente esperienza dei centri, la coronarografia con eventuale angioplastica oggi rappresenta una procedura relativamente sicura.

Obiettivi. Dimostrare la fattibilità, la sicurezza e l'efficacia di specifici percorsi diagnostico/terapeutici (Service), autorizzati dalla Direzione Strategica dell'ASP Messina previa valutazione del rischio, per i pazienti affetti da sindrome coronarica acuta non STE (N-STEMI, angina instabile). Tali percorsi prevedono che il paziente venga trasferito presso il centro Hub con Emodinamica di Patti per essere sottoposto a coronarografia + eventuale angioplastica ed al termine della procedura ritorni all'Ospedale spoke di provenienza (transfer back). Unica controindicazione all'espletamento del Service è rappresentata dall'instabilità emodinamica in corso.

Razionale. Evitare la saturazione dei posti letto dei Centri Hub; ridurre i tempi di degenza; ridurre i rischi annessi ad un ritardo della rivascularizzazione miocardica; ridurre eventuali secondi ricoveri o trasferimenti presso altre Aziende Sanitarie, con risparmio di risorse economiche.

Metodi. Abbiamo analizzato 144 pazienti consecutivi trattati in "Service" da Agosto 2019 ad Agosto 2020 presso il nostro centro. Sono state valutate le principali complicanze intra-procedurali e peri-procedurali intraospedaliere: morte, trombosi acuta intrastent, insufficienza renale acuta, sanguinamento maggiore, complicanze vascolari, stroke, infarto miocardico.

Risultati. Di 144 pazienti trattati, il 72% erano uomini con età media di 69 \pm 5,2; nel 95% è stato usato l'accesso radiale; nel 78% era presente una malattia coronarica epicardica critica; nel 49,3% dei casi è stata effettuata l'angioplastica coronarica e nel 9,7% è stata posta indicazione a rivascularizzazione chirurgica. Abbiamo registrato una sola complicanza: insufficienza renale acuta post-procedurale in paziente affetto da IRC terminale (V stadio), con necessità di seduta emodialitica ospedaliera e successiva ripresa della diuresi spontanea.

Conclusioni. La coronarografia con eventuale angioplastica coronarica eseguita in service, dai dati emersi in questo studio, risulta essere fattibile, sicura, efficace ed economicamente vantaggiosa.

A215: INSTANTANEOUS WAVE-FREE RATIO IN ATRIAL FIBRILLATION: A SINGLE CASE-CONTROL PATIENT

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Background. The instantaneous wave-free ratio (iFR, Volcano Corporation) is a non-hyperemic pressure-derived ratio introduced as a diastolic resting measure for functional assessment of stenosis severity. iFR evaluation might be influenced by clinical and hemodynamic factors, such as age, heart rate and the presence of arrhythmias like atrial fibrillation (AF). Evidence found that coronary perfusion pressure during AF exponentially increases with higher heart rate (HR), but decreases over a cut-off of 90 bpm, leading to inaccurate iFR values. Moreover, the presence of highly irregular R-R intervals in AF might influence the iFR evaluation, leading to imprecise values. We present a unique "single case-control study" in a patient in AF evaluated by iFR before and after the restoration of sinus rhythm.

Case description. A 64-year-old man with a coronary computed tomography showing suspicious lesions underwent coronary angiography, which showed moderate stenosis of the mid-left anterior descending artery (LAD). Ventricular fibrillation was accidentally induced during the injection of the right coronary artery. Prompt return of spontaneous circulation was obtained after DC shock. After VF interruption, heart rhythm resulted in a high rate (170 bpm) atrial fibrillation. Intravenous amiodarone (300 mg) and metoprolol (5 mg) were given. After 20 minutes,

AF was persistent, but with proper heart rate control. Thus, an iFR assessment was performed to assess the severity of the LAD lesion. The lowest of four measures was a negative value (0.92, cut-off value <0.90). Due to the persistence of AF, the patient was electrically cardioverted with successful restoring of sinus rhythm. Therefore, iFR was reassessed resulting in a positive value (0.88). Successful percutaneous coronary angioplasty and drug-eluting stent implantation was then performed. **Conclusions.** The presence of AF, especially with high HR, might alter iFR values assessment in intermediate-grade coronary stenosis. In such a scenario, a careful interpretation of iFR results is required, and decision-making might need to integrate different diagnostic techniques.

A216: RUOLO PREDITTIVO DEL GLOBAL LONGITUDINAL STRAIN NELLA DIAGNOSTICA DI PRIMO LIVELLO IN PAZIENTI AFFETTI DA CARDIOPATIA ISCHEMICA

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Background. Il numero di decessi per malattie cardiovascolari a livello globale è aumentato nell'ultimo decennio e la maggior parte è attribuibile alla cardiopatia ischemica. La diagnosi precoce in questi pazienti rappresenta ancora oggi una delle sfide principali. L'analisi ecocardiografica della deformazione miocardica tramite il Global Longitudinal Strain (GLS) riesce ad evidenziare precocemente la disfunzione miocardica; tuttavia, il suo potere predittivo ed il suo ruolo nella diagnostica di primo livello in pazienti affetti da cardiopatia ischemica non sono ancora definiti.
Materiali e metodi. Sono stati arruolati 127 pazienti consecutivi con indicazione ad esecuzione di studio coronarografico per la presenza di una sintomatologia suggestiva e/o per evidenza strumentale di ischemia miocardica (scintigrafia miocardica, test da sforzo, coronaro-TC). Prima della coronarografia i pazienti sono stati sottoposti ad ecocardiogramma transtoracico con analisi dello strain miocardico tramite metodica speckle tracking. I risultati dello studio coronarografico sono stati analizzati al fine di registrare l'estensione e la localizzazione della malattia coronarica.
Risultati. 47 pazienti non hanno mostrato stenosi significative mentre 80 pazienti sono risultati affetti da cardiopatia ischemica. Sono stati esclusi dall'analisi i pazienti giunti a coronarografia per evidenza tomografica di malattia (14,2%) al fine di confrontare un parametro dinamico quale lo strain miocardico con test dinamici quali il test al treadmill e la scintigrafia da sforzo. Dall'analisi è risultata un'associazione tra positività del test funzionale di primo livello (test da sforzo al treadmill o scintigrafia miocardica) e presenza di malattia coronarica, per quanto statisticamente non significativa ($\chi^2(1, N=109) = 1,79, p=0,181$). L'analisi univariata ha mostrato un incremento dell'entità della stenosi coronarica dell'arteria discendente anteriore al crescere del valore di GLS-4ch ($\beta = 0,390, p<0,001$); dall'analisi multivariata gerarchica è emerso, inoltre, come quest'ultimo influisca sulla capacità del test ergometrico di associarsi alla malattia coronarica migliorando la predizione di stenosi significativa se aggiunto ad altri parametri ($F = 5,359, p = 0,002$). Il confronto di due curve ROC per la predizione di malattia dell'arteria discendente anteriore ha mostrato che entrambi i parametri GLS AVG e GLS 4ch stratificano in modo adeguato (AUC.605 e 0.649 rispettivamente).
Conclusioni. L'angiografia coronarica resta il gold standard nella determinazione di malattia coronarica. È tuttavia da tener presente la natura invasiva della stessa con le relative complicanze che possono derivarne. I risultati del nostro studio suggeriscono che l'aggiunta del GLS alla diagnostica di primo livello nella cardiopatia ischemica può risultare utile nel fornire informazioni circa l'entità della stenosi coronarica, specie nel caso di vasi principali, e di conseguenza migliorare la capacità predittiva di malattia coronarica aumentando l'appropriatezza dello studio angiografico invasivo.

A217: PLATELET REACTIVITY AND LONG-TERM CLINICAL OUTCOME FOLLOWING ELECTIVE PERCUTANEOUS CORONARY INTERVENTION IN COMPLEX HIGHER-RISK AND INDICATED PATIENTS

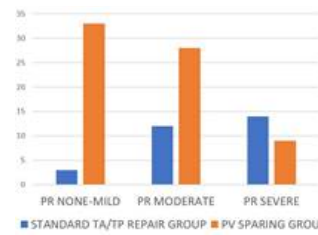
Michele Mattia Viscusi (a), Fabio Mangiacapra (a), Edoardo Bressi (a), Alessandro Sticchi (a), Iginio Colaiori (a), Marialessia Capuano (a), Elisabetta Ricottini (a), Ilaria Cavallari (a), Silvia Spota (b), Germano Di Sciascio (a), Gian Paolo Ussia (a), Francesco Grigioni (a) (a) UNIT OF CARDIOVASCULAR SCIENCES, DEPARTMENT OF MEDICINE, CAMPUS BIO-MEDICO UNIVERSITY, ROME, ITALY; (b) UNIT OF INTERNAL MEDICINE, DEPARTEMENT OF MEDICINE, CAMPUS BIO-MEDICO UNIVERSITY, ROME, ITALY
Background. Evidence regarding platelet reactivity and the prevalence of HPR in CHIP patients are lacking. Moreover, the impact of HPR on clinical outcomes of CHIP patients treated with PCI is unknown.
Methods. We enrolled 500 patients undergoing elective PCI for stable coronary artery disease (CAD) and treated with aspirin and clopidogrel. Patients were divided in four groups based on the presence of CHIP features and HPR. Primary endpoint was the occurrence of major adverse clinical events (MACE) at 5 years.
Results. The prevalence of HPR was significantly greater in CHIP population rather than non-CHIP patients (40.8% vs 30.5%, $p=0,014$). Patients with both CHIP features and HPR showed the highest estimates

of MACE (20.6%, log-rank $p=0,059$) and definite stent thrombosis (4.8%, log-rank $p=0,02$). At Cox proportional hazard analysis, the combination of CHIP features and HPR was an independent predictor of MACE (HR 2.61, 95% CI 1.25-5.44, $p=0,010$).
Conclusion. Among patients with stable CAD undergoing elective PCI and treated with aspirin and clopidogrel, the combination of CHIP features and HPR identifies a cohort of patients with the highest risk of MACE at 5 years, who might benefit of more potent antiplatelet strategies.

CARDIOPATIE CONGENITE E MALATTIE DEL CIRCOLO POLMONARE

A218: PULMONARY VALVE PRESERVATION AND TRANSANNULAR PATCH TECHNIQUES IN CHILDREN WITH REPAIRED TETRALOGY OF FALLOT; ECHOCARDIOGRAPHIC COMPARISON

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Introduction. To investigate pulmonary valve (PV) and right ventricular function by echocardiography in paediatric patients with repaired Tetralogy of Fallot (ToF), comparing PV preservation surgical strategies to standard transannular patch (TAP) repair.
Methods. All patients undergoing transatrial-transpulmonary repair for ToF at our institution between January 2007 and May 2020 were reviewed retrospectively. Patients were divided into 2 groups, according to the different techniques used (PV preservation strategy vs TAP repair). All patients underwent standard echo-Doppler study including RV areas, fractional area change (FAC) and tricuspid annular plane systolic excursion (TAPSE); Pulmonary regurgitation (PR) was assessed by color Doppler, continuous-wave (CW) Doppler, pressure half time (PHT) and PR index. By speckle tracking we measured also, in a subgroup of patients, right atrial strain (RAS), RV and left ventricle (LV) global longitudinal strain (RVGLS, LVGLS) and their time to peak (TTP) values.
Results. Eighty-two patients underwent a PV preservation strategy while 34 underwent a standard TAP repair. Five-year actuarial freedom from moderate/severe PV regurgitation was significantly higher in the PV preservation group compared to the TAP (61.3% [95% CI: 48-73%] vs 25.9% [95% CI: 12-43%], respectively; $p=0,02$). After adjusting for age, gender, BSA, and type of PV, the use of a TAP was still significantly associated with an increased risk for PV regurgitation at follow-up (HR: 1.85, 95% CI: 1.09, 3.15; $p=0,02$). At a mean follow-up of 6.9 ± 0.3 years, patients undergoing PV preservation showed an increased right ventricular fractional area change ($46.9\pm 0.8\%$ vs $42.5\pm 1.7\%$, $P<0,001$) and (TAPSE) z-score ($-3.36\pm 0.3\%$ vs $-4.7\pm 0.4\%$, $P=0,005$), while maintaining better PV competence in terms of pulmonary regurgitation index ($87.9\pm 1.2\%$ vs $82.7\pm 2.4\%$, $P=0,02$). At speckle tracking subanalysis, patients undergoing PV preservation ($n=23$), compared to the TAP group ($n=13$) showed also higher values of RAS ($37.5\pm 6.0\%$ vs $29.3\pm 8.2\%$, $P<0,006$), shorter right TTP ($319\pm 39\text{ms}$ vs $357.5\pm 45.2\text{ms}$, $P<0,01$) and higher values of LVGLS ($-20,6\pm 4,2\%$ vs $-17,5\pm 3,0$, $P<0,03$).
Conclusions. Surgical repair of ToF with PV preservation provides excellent outcomes in terms of PV competence and right ventricular function and should be advocated whenever possible.



	Surgical groups		P-value
	TA/TP repair group (n=29)	PV sparing group (n=70)	
Age at FU, years (range)	9,88 (7,95-11,1)	5,4 (2,4-7,2)	0,0001
RVFAC % (range)	42,3 (40-47)	47 (43-51)	0,01
Z-score TAPSE	-4,8 (-5,8;-3,3)	-3,2 (-4,9;-1,6)	0,0064
Degree of PV regurgitation, n (%)			
Grade 1 (none-mild)	3 (8, 33%)	33 (47%)	
Grade 2 (moderate)	12 (41%)	28 (40%)	
Grade 3 (severe)	14 (48, 28%)	9 (13%)	0,0003
PR index (range)	0,83 (0,75-0,93)	0,90 (0,85-0,94)	0,07

A219: LONG-TERM ECHOCARDIOGRAPHIC OUTCOMES, QUALITY OF LIFE AND PHYSICAL ACTIVITY OF DIFFERENT AORTIC VALVE SURGERY PROCEDURES: ROSS VS. AORTIC VALVE REPAIR

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Background. To compare long-term outcomes of aortic valve repair (AVr) and pulmonary autograft replacement (Ross procedure) in terms of echocardiographic parameters, quality of life (QoL), physical activity (PA).
Methods. In 2005-19, 129 patients (median age 22 [13, 33 IQR], 75% males) underwent aortic surgery in our Department: 40 were Ross (22 years [19, 51 IQR]), 67 AVr (17 years [1, 50 IQR]) and 22 aortic valve replacements (52 years [30, 80 IQR]). We focused on Ross and AVr. Retrospectively, relevant data were collected from medical records and phone re-calls. Physical activity (spontaneous and active) and QoL were assessed utilizing the IPAQ and SF-36 questionnaires. All patients underwent echocardiography pre/post-surgery and the follow-up lasted 12±4 years.

Results. At the baseline, Ross patients had more aortic stenosis than insufficiency (P = 0.045). At the follow-up, Ross procedures presented more right-ventricle and aortic annulus dilatation (P=0.002 and P=0.030, respectively), but higher left-ventricular global longitudinal strain (LV GLS: 18±3.2% vs. 16±3.3, P=0.0027). Conversely, AVr experienced more re-do operations (Log-rank P=0.005). Ross reported better QoL (SF-36: 0.8±0.07 vs. 19±0.4, P=0.045) and were also more active in daily PA (IPAQ ≥ 2500 Mets: 63.8% vs. 6%; P=0.006). Ross patients practiced more sports activities than AVr (P=0.011).

Conclusions. In a relatively small cohort of young and adults post aortic surgery patients, Ross procedures had better prognosis in terms of re-do operations; presented better ventricular function, as assessed by LV GLS. Ross patients had better long-term QoL and showed more spontaneous PA and involvement in sports activity.

A220: A VERY RARE LIKELY PATHOGENIC VARIANT IN ACVRL1 GENE IDENTIFIED IN A PATIENT WITH ATYPICAL HEREDITARY HEMORRHAGIC TELANGIECTASIA

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Hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant vascular dysplasia caused by heterozygous pathogenic variants in the *ACVRL1*, *ENG*, *GDF2*, *RASA1* or *SMAD4* genes. Peculiar clinical features are visceral arteriovenous malformations (AVMs) and mucocutaneous telangiectasias, leading to bleeding and anemia. Pulmonary arterial hypertension (PAH) is a rarer vascular manifestation of HHT. It can be a consequence of systemic arteriovenous shunting in the liver or be indistinguishable from idiopathic PAH. A 55-year old patient with dilated cardiomyopathy (DCM) was admitted to our hospital to investigate the idiopathic or acquired nature of the disease. No relevant clues emerged and no pathogenic variants in 12 DCM-related genes were identified by next generation sequencing. Due to unexplained persistent hypoxemia, after a transesophageal echocardiogram that ruled out the presence of a patent foramen ovale, the patient underwent a full body computed tomography with contrast agent that revealed seven bilateral pulmonary AVMs. A suspicion of HHT was proposed, despite the absence of other visceral AVM, telangiectasias and family history. Molecular analysis of *ACVRL1*, *ENG*, *GDF2* and *RASA1* identified the likely pathogenic variant c.914C>A (p.Ser305Tyr) in *ACVRL1*. This variant, involving a strongly conserved aminoacidic residue, was never described in HHT patients. It is reported in a single isolated PAH case as variant of uncertain significance. The substitutions of Ser305 with other aminoacids are instead known to be HHT causing mutations. Despite the patient being paucisymptomatic, the molecular diagnosis of HHT confirmed the clinical suspicion. After the diagnosis, the patient underwent transcatheter embolization of pulmonary AVMs. Familiar genetic tests are ongoing to better define the origin of mutation (inherited or de novo).

A221: DIAGNOSIS AND MANAGEMENT OF ANOMALOUS AORTIC ORIGIN OF CORONARY ARTERIES: A MULTICENTER STUDY

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Background. Diagnosis and management of the anomalous aortic origin of coronary arteries (AAOCA) remain a challenge because of the rare occurrence of these cardiac malformations and the absence of large multicentric study.

Aim. To assess the most common AAOCA clinical presentation and determine the most accurate diagnostic procedures.

Methods. Preliminary data from young patients referred for AAOCA to 17 European pediatric cardiac surgery centers were retrospectively collected. Demographics, clinical presentation and diagnostic pathway were investigated.

Results. Overall, 239 patients (138 females [58%], mean age 15 years) were included in the study. 154 patients presented a right coronary artery (RCA) anomalous origin, 62 presented an anomalous origin of the left main/circumflex/left anterior descending (LCA) coronary artery, 23 other malformations. The most common clinical presentations were exertional chest pain (73/239; 30%) and other non-specific symptoms (59/239; 25%). Symptoms appeared more frequently in patients suffering from RCA anomalous origin than LCA (123/154 [80%] vs 42/62 [67%], p=0.05). LCA anomalous origin was more frequently associated with exertional syncope comparing with RCA (11/62 [18%] vs 7/154 [5%], p=0.002), especially when characterized by an interarterial course (11/50 [22%] vs 7/147 [4.8%], p<0.001). Electrocardiographic and echocardiographic changes were traced in 37/228 (16%) and 123/232 (53%) patients respectively. Cardiac computed tomography angiography (CCTA) presented the highest diagnostic accuracy (162/177; 91%).

Conclusion. AAOCA represents a diagnostic challenge. The diagnostic algorithm, driven by the occurrence of exertion-induced chest pain or syncope, should be based on a second level radiological examination like CCTA.

A222: SHORT-TERM EFFECT OF SELEXIPAG IN COMPARISON TO PROSTACYCLIN ANALOGUES IN PULMONARY ARTERIAL HYPERTENSION PATIENTS STARTED ON DOUBLE-COMBINATION THERAPY WITH ERA AND PDE5 INHIBITORS

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Background. GRIPHON trial demonstrated that selexipag reduces the risk of death or morbidity events in patients with pulmonary arterial hypertension (PAH). Anyway its efficacy in comparison to prostacyclin analogues in patients already on oral double-combination therapy with endothelin receptor antagonist (ERA) and phosphodiesterase-5 inhibitor (PDE5-I) is unknown. Purpose: to compare the effects of selexipag (S) vs subcutaneous treprostinil (T) vs intravenous epoprostenol (E) in PAH patients initially started with double-combination therapy with ERA and PDE5-I.

Methods. We enrolled patients on double combination therapy with ERA + PDE5-I starting S, T or E. All patients were systematically assessed with WHO-functional class (FC), six minute walk test (6MWT) and right heart catheterization before treatment and 3 months after reaching a stable dose of the drug. Baseline characteristics and changes in 6MWT and hemodynamic parameters were analyzed using Wilcoxon signed-rank test and compared between the 3 drugs with Kruskal-Wallis test.

Results. 171 patients with PAH were enrolled. Results are shown in the Table. Patients with a complete reevaluation were 61% of S, 85% of T, 79% with E.

	Selexipag	Treprostinil s.c.	Epoprostenol e.v.	p-value
n	31	78	62	
Age (y)	61 (45 + 70) *	43 (37 + 52)	45 (31 + 60) *	0.002
WHO-FC III/IV, n (%)	19 (61)	56 (72)	50 (81)	0.131
6MWT (m)	456 (340 + 550) *	415 (325 + 510) *	372 (245 + 417) *	0.004
RAP (mmHg)	8 (5 + 10) *	9 (7 + 12)	12 (8 + 15) **	< 0.001
mPAP (mmHg)	53 (42 + 65)	64 (53 + 72)	60 (52 + 72) *	0.004
CI (l/min/m ²)	2.4 (2.3 + 2.8)	2.4 (2 + 2.6)	2.1 (1.8 + 2.7)	0.088
PVR (W.U.)	10 (8 + 12.8)	13 (10.6 + 16.3)	15.2 (12.1 + 22) **	< 0.001
SvO ₂ (%)	66 (60 + 70) *	65 (59 + 69) *	58 (50 + 63) **	< 0.001
Delta 6MWT (m)	7 (-10 + 24) *	35 (6 + 75)	66 (11 + 137) *	0.006
Delta RAP (mmHg)	-1 (-5 + 1)	-1 (-3 + 1)	-1 (-4 + 4)	0.526
Delta mPAP (mmHg)	-3 (-15 + 0)	-6 (-11 + 2)	-4 (-10 + 2)	0.260
Delta CI (l/min/m ²)	0.3 (0.1 + 0.4) *	0.5 (0.3 + 0.9)	0.7 (0.3 + 1.1) *	0.009
Delta PVR (WU)	-3.1 (-4.3 + -0.2)	-3.6 (-5.4 + -2.1)	-4.1 (-6.9 + -1.4)	0.142
Delta SvO ₂ (%)	3 (-4 + 6)	3 (0 + 6)	5 (-0.4 + 12)	0.075

*|| = p<0.05 between respective pair

CI, cardiac index; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; SvO₂, mixed venous oxygen saturation.

Conclusions. S was prescribed to the oldest and least severe PAH patients. E was prescribed to the youngest and most severe PAH patients

and led to the strongest improvement of exercise capacity and hemodynamic profile. T has intermediate characteristics.

A223: SURVIVAL OF PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION AND CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION LISTED FOR LUNG TRANSPLANTATION

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Background. Lung transplantation (LT) still remains a treatment option for patients with pulmonary arterial hypertension (PAH) and not operable chronic thromboembolic pulmonary hypertension patients (CTEPH).

Purpose. To compare the survival of transplant recipients (TR) and not-transplanted (NT) patients since listing.

Methods. We included all patients with PAH and not-operable CTEPH listed for LT. The survival of NT, TR and of all listed patients was evaluated starting from the date of listing (patients were censored as alive at the time of LT). The survival of TR was also evaluated starting from the date of the LT.

Results. 125 patients were included (90% had PAH). Fifty-eight (46%) patients were transplanted, after a mean time of 1.5 ± 1.3 years. Forty-one patients (33%) died while on the list and 25 (20%) patients were alive on the list on December 2019. The survival of NT patients at 1, 3 and 5 years after listing was 74%, 42%, 33%, respectively. The survival of TR patients at 1, 3 and 5 years after listing was 90%, 70%, 63%, respectively. The survival of all patients since listing (intention to treat analysis) at 1, 3 and 5 years was 85%, 59%, 48% respectively. The survival of TR at 1, 3 and 5 years since transplantation was 63%, 61%, 59%, respectively.

Conclusions. despite a non-randomized comparison, the data confirm a better long-term survival since listing of TR as compared with NT PAH or not-operable CTEPH patients.

A224: ROLE OF CARDIAC MAGNETIC RESONANCE IN STRATIFYING THE PROGNOSIS OF PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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Background. Pulmonary arterial hypertension (PAH) is a rare disease characterized by a complex remodeling of heart structures. Cardiac magnetic resonance (CMR) is the gold standard for a non-invasive evaluation of right ventricle (RV) volumes and mass.

Purpose. To define the relationship between clinical, functional, biochemical, haemodynamic and CMR parameters and survival in patients with PAH.

Methods. Consecutive patients with PAH referred to our centre underwent clinical, functional, brain natriuretic peptide (BNP) plasma levels, haemodynamic and CMR evaluation. All patients were treated according to current guidelines. Univariate Cox analysis for survival was performed. Parameters with a p-value < 0.1 at the univariate analysis were included in the multivariate analysis.

Results. One hundred forty-seven patients with PAH (mean age 49 ± 17 years, 69% female) were included in the study. Etiology of PAH was: idiopathic/heritable (49%), associated with connective tissue disease (19%), congenital heart disease (12%), portal hypertension/HIV infection (12%) and pulmonary veno-occlusive disease (8%). Thirty-six patients died during follow-up. Parameters significantly associated with mortality at the univariate analysis were age [Hazard Ratio (95% Confidence Interval): 1.043 (1.020-1.067); $p < 0.001$], six-minute walk test (6MWT) [HR: 0.995 (0.993-0.998); $p < 0.001$], WHO-functional class [HR: 2.489 (1.025-6.041); $p = 0.044$], idiopathic/heritable-congenital heart disease aetiology [HR: 0.182 (0.085-0.389); $p < 0.001$], connective tissue disease aetiology [HR: 2.274 (1.099-4.704); $p = 0.027$], pulmonary veno-occlusive disease aetiology [HR: 5.864 (2.328-14.773); $p < 0.001$], right atrial pressure [HR: 1.098 (1.032-1.169); $p = 0.003$], pulmonary artery oxygen saturation [HR: 0.947 (0.921-0.975); $p < 0.001$], BNP levels [HR: 2.214 (1.213-4.039); $p = 0.010$], RV wall thickness [HR: 0.633 (0.399-1.006); $p = 0.053$], RV end diastolic volume [HR: 1.012 (1.003-1.021); $p = 0.007$], RV end systolic volume [HR: 1.014 (1.003-1.024); $p = 0.011$]. Parameters independently associated with mortality at the multivariate analysis were age [HR: 1.035 (1.006-1.064); $p = 0.018$], idiopathic/heritable-congenital heart disease aetiology [HR: 0.355 (0.146-0.860); $p = 0.022$], pulmonary veno-occlusive disease aetiology [HR: 3.129 (1.071-9.143); $p = 0.037$], pulmonary artery oxygen saturation [HR: 0.953 (0.919-0.989); $p = 0.011$], RV wall thickness [HR: 0.527 (0.300-0.927); $p = 0.026$], RV end systolic volume [HR: 1.016 (1.003-1.029); $p = 0.014$].

Conclusions. RV wall thickness and RV end-systolic volume are associated with prognosis in patients with PAH independently from clinical and haemodynamic characteristics. These parameters may be used in the overall risk stratification of PAH patients.

A225: ECHOCARDIOGRAPHIC PREDICTORS OF LOW RISK HAEMODYNAMIC PARAMETERS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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Background. A periodic and multiparametric assessment of the risk profile of patients with pulmonary arterial hypertension (PAH) is essential for a low-risk oriented treatment strategy. Haemodynamic parameters anyway cannot be collected at each scheduled outpatients clinic follow-up visit. Purpose: to evaluate echocardiographic predictors of haemodynamic low-risk parameters in patients with PAH.

Methods. patients with PAH referred to our centre were included up to 31 December 2019. All patients underwent baseline demographic, clinical, WHO functional class, 6-minute walk test, brain natriuretic peptide (BNP), right cardiac catheterization and echocardiographic evaluation. Through a multivariate logistic regression analysis we evaluate the echocardiographic predictors of low risk for: 1) BNP/right atrial pressure (RAP): NT-proBNP < 300 ng/l/BNP < 50 ng/l AND RAP < 8 mmHg; 2) cardiac index (CI)/mixed venous oxygen saturation (SvO₂): CI ≥ 2.5 l/min/m² and SvO₂ $> 65\%$. Echocardiographic parameters cut-offs were chosen on the basis of the ROC curves or Literature data.

Results. 1020 patients were included. The two analysis were performed independently. (1) Independent echocardiographic predictors of low-risk BNP/RAP were: indexed right atrial area, mitral E/A ratio, dimension and inspiratory collapse of inferior vena cava and indexed left ventricular diastolic volume. We elaborated a score utilizing these parameter cut-offs: an indexed right atrial area of 10.4-15 cm²/m², a mitral E/A ratio of 0.8, dimension and inspiratory collapse of inferior vena cava indicative of 0-5 vs 5-10 vs 10-20 mmHg and an indexed left ventricular diastolic volume of 32 ml/m². The score has AUC: 0.62, specificity: 92%, sensitivity: 33%, negative predictive value: 70%, positive predictive value: 69%. (2)

Independent echocardiographic predictors of low-risk CI/SvO₂ were: S wave at TDI, Tei index, tricuspid annular plane systolic excursion (TAPSE), indexed left ventricular diastolic volume and the severity of the tricuspid regurgitation. We elaborated a score utilizing these parameter cut-offs: an S wave at TDI of 9.5 cm/s, a Tei index of 0.4, a TAPSE of 1.7 cm, an indexed left ventricular diastolic volume of 32 ml/m² and a mild vs more than mild tricuspid regurgitation. The score has AUC: 0.70, specificity: 89%, sensitivity: 50%, negative predictive value: 71%, positive predictive value: 77%.

Conclusions. Echocardiographic parameters can be used to rule out the presence of low-risk BNP/RAP values (indexed right atrial area, mitral E/A ratio, dimension and inspiratory collapse of inferior vena cava and indexed left ventricular diastolic volume) and low-risk CI/SvO₂ (S wave at TDI, Tei index, TAPSE, indexed left ventricular diastolic volume and severity of tricuspid regurgitation).

A226: CARDIAC MECHANICAL REMODELING AFTER ASD CLOSURE WITH GORE CARDIOFORM ASD OCCLUDER IN CHILDREN

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Background. Nowadays, trans-catheter closure of ostium secundum atrial septal defect (ASD) is considered as the first-line treatment. Previous studies demonstrated that ASD devices may impact on cardiac mechanics. The GORE® CARDIOFORM ASD Occluder (GCA, WL Gore & Associates, Flagstaff, AZ) is a recently approved double-disc, soft, conformable device, potentially innovative compared to other self-centering devices. It combines high softness and anatomic compliance with the potential to close defects as large as 35 mm.

Purpose. To study the mechanical changes in atrial and ventricular properties resulting from ASD closure using the GSO-ASD device.

Methods. Between January and June 2020, 16 consecutive pediatric patients with hemodynamically-significant ASD were enrolled to undergo transcatheter closure with the GCA device. Standard transthoracic echocardiography (TTE) with a GE Vivid E9 machine was performed the day before the procedure, 24 hours and 6 months after ASD percutaneous closure. Atrial and ventricular 2D speckle tracking analysis was performed offline by the use of Echopac v12 software (GE, Echopac, Horten, Norway). Left ventricle (LV) longitudinal, radial and circumferential strain (S) and strain rate (SR), right ventricle (RV), right and left atria (RA, LA) longitudinal S and SR were assessed from apical and short axis

views. Primary endpoint was to evaluate the impairment of the cardiac chambers mechanical properties after implantation of GCA.

Results. Population mean age was 8.7±2.6 years, and mean defect diameter was 14.9±4.6 mm. The rate of successful closure was 87.5% (14/16) at 24 hours and 100% at 6 months (0/14). One patient experienced transient supraventricular tachycardia. Longitudinal, circumferential and radial S and SR analysis of the LV, and longitudinal S and SR analysis of the RV and RA didn't show any global statistically significant difference between time 0 and 6 months after ASD closure (Table 1), although transient modifications were found at 24 hours. A reduction of LA septal segmental function was found after procedure, with a gradual LA global function recovery at 6 months.

Conclusion. This study shows that myocardial deformation remains unaltered 6 months after GCA implantation, differently from previously reported studies after surgical ASD closure and after Amplatzer ASD device implantation. These data highlight the softness and compliance of this new device towards the myocardial walls.

	T0	24 h FU	6 months FU	p (T0 vs 24 h FU)	p (T0 vs 6 months FU)
LV strain					
Longitudinal	-22.1 ± 1.8	-21.5 ± 1.7	-21.5 ± 1.1	0.32	0.15
Circumferential	-24.8 ± 5.0	-26.7 ± 4.1	-23.8 ± 2.7	0.19	0.73
Radial					
LA strain	40.7 ± 13.5	33.7 ± 11.0	37.7 ± 11.7	0.18	0.66
RA strain	53.3 ± 14.7	36.3 ± 9.2	43.5 ± 10.1	0.00	0.05
Long. RV strain	84.0 ± 24.0	74.1 ± 23.9	84.8 ± 42.1	0.25	0.90
Long. RV strain	-32.5 ± 4.1	-27.5 ± 4.8	-31.6 ± 2.2	0.01	0.44

A227: RIMODELLAMENTO ELETTRICO DOPO CHIUSURA DI DIFETTI INTERATRIALI TIPO OSTIUM SECUNDUM CON PROTESI GORE CARDIOFORM ASD OCCLUDER

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Introduzione. Al giorno d'oggi l'approccio percutaneo è il trattamento di prima scelta per la chiusura di difetti interatriali tipo ostium secundum. Gli studi di Letteratura si sono spesso focalizzati sul rimodellamento meccanico cardiaco, senza approfondire le consensuali modificazioni delle proprietà elettriche di conduzione atrio-ventricolare associabili al rimodellamento cardiaco.

Scopo. Lo scopo primario dello studio è la valutazione delle modificazioni elettrocardiografiche nel breve e medio termine dalla procedura emodinamica. Nello specifico si vuole andare ad analizzare l'eventuale variabilità di velocità di conduzione intra-atriale, atrioventricolare e di dispersione dell'onda P e dell'intervallo QTc, nonché l'eventuale presenza di aritmie iper-ipocinetiche, in tutti i pazienti sottoposti a chiusura di DIA II mediante Gore Cardioform ASD Occluder (GCA).

Metodi. Sono stati arruolati 15 pazienti pediatrici (età media 8.7±2.6 anni) affetti da DIA ostium secundum emodinamicamente significativi passibili di chiusura elettiva per via percutanea con GCA device. Per ogni paziente è stato registrato ECG di superficie il giorno prima della procedura, dopo 24 ore dalla stessa e a distanza di 6 mesi. Consensualmente è stata data indicazione ad esecuzione di ECG-Holter 24 ore ad 1 mese e 6 mesi dall'intervento.

L'analisi manuale dei tracciati elettrocardiografici è mirata alla valutazione di eventuali modifiche del ritmo cardiaco, della dispersione dell'onda P e dell'intervallo QTc, e della velocità di conduzione atrioventricolare nel breve e medio termine del follow-up. L'analisi dei referti ECG-Holter è inoltre dirimente per la valutazione nel breve e medio termine di eventuali tachiaritmie (TPSV) o bradiaritmie (tipo pause sinusali vs BAV di diverso grado), complicanze post-operatorie notoriamente attribuibili a tale intervento correttivo.

Risultati. L'analisi manuale di tutti i tracciati elettrocardiografici a 12 derivazioni ha evidenziato una riduzione della dispersione media dell'onda P già a distanza di 24h dalla procedura (P=0,003), poi confermato anche a distanza di 6 mesi (P=0,04)(pre-procedura: ΔP medio 0,028 s vs post-procedura ΔP medio 0,017 s, a 6 mesi ΔP medio 0,022 s). Tale andamento si registra anche a livello ventricolare, come confermato dalla riduzione della dispersione media dell'intervallo QTc (pre-procedura ΔQTc medio 39,8 s vs post-procedura ΔQTc medio 27,8 s) (P=0,002). La velocità di conduzione atrioventricolare ha presentato un transitorio, non significativo prolungamento a distanza di 24h con successiva normalizzazione a distanza di 6 mesi. In una paziente è stata rilevato un ritmo giunzionale, che ha poi presentato transitorio episodio di tachicardia sopraventricolare parossistica in settima giornata post-operatoria. Tale unica complicanza aritmica è stata efficacemente trattata farmacologicamente con flecainide, cui è seguita assenza di aritmie ipercinetiche come evidenziato all'ECG-Holter di 6 mesi.

Conclusioni. L'analisi elettrocardiografica nei pazienti sottoposti a

chiusura di difetto interatriale con GCA device mostra una omogeneizzazione della attivazione atriale già 24 ore dopo la chiusura del difetto, benefico confermato e stabilizzato al controllo a 6 mesi. L'omogeneizzazione di conduzione intracardiaca è associabile al consensuale rimodellamento meccanico cardiaco, avvalorando infine l'ipotesi che le modificazioni elettrocardiografiche sono talora anticipatorie e talora consensuali al miglioramento emodinamico post-procedurale.

A228: RUOLO PROGNOSTICO DELLA VALUTAZIONE ECOCARDIOGRAFICA NEI PAZIENTI CON FIBROSI POLMONARI

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Introduzione. La fibrosi polmonare è universalmente riconosciuta come una malattia interstiziale polmonare con prognosi sfavorevole. Sebbene la sua progressione sia variabile e dipenda dalla gravità del coinvolgimento polmonare, l'impatto del rimodellamento vascolare sulla pressione polmonare misurata in modo non invasivo e sul ventricolo destro (RV) è scarsamente segnalata. Pertanto, potrebbe essere utile un'analisi ecocardiografica specifica della funzione e delle dimensioni del ventricolo dx.

Obiettivi. In questo studio abbiamo valutato il diametro del ventricolo dx, la pressione polmonare sistolica e media e la funzione longitudinale del RV in pazienti con fibrosi polmonare; abbiamo inoltre valutato l'impatto prognostico di ciascuna misurazione durante un periodo di follow-up medio di 3 anni.

Metodi. I pazienti con diagnosi laboratoristica e radiologica di fibrosi polmonare sono stati inclusi in questo studio. In ogni paziente, l'ecocardiogramma è stato eseguito come screening durante una valutazione clinica completa, secondo le istruzioni fornite dalla American Society of Echocardiography. Abbiamo stimato la PAP sistolica a livello della valvola tricuspide e la pressione polmonare media tramite rigurgito protodiastolico della valvola polmonare mediante analisi Doppler continua. La TAPSE è stata ottenuta posizionando il cursore sul anulus laterale della tricuspide mediante tecnica M-mode; l'onda S è stata misurata mediante analisi Doppler tissutale sempre a livello dell'anulus laterale della valvola tricuspide. Il diametro telediastolico del RV è stato misurato a livello basale da una proiezione apicale 4 camere.

Risultati. Abbiamo arruolato 187 pazienti con fibrosi polmonare come diagnosi principale: 134 avevano un disturbo interstiziale primitivo, 27 istiocitosi, 15 sarcoidosi e 11 sclerodermia. L'aumento della pressione sistolica dell'arteria polmonare è stato riscontrato in 121 pazienti e l'elevazione di mPAP in 84; 78 soggetti avevano un diametro RV ingrandito a livello basale. Una funzione longitudinale ridotta in termini di TAPSE e onda S è stata rivelata in 83 e 90 pazienti, rispettivamente. È stata trovata una correlazione inversa tra PAP aumentata e ridotta funzione longitudinale (r = 0,67 p <0,001). Un cut-off di sPAP >40, mPAP >28 mmHg e diametro RV>44 mm è stato correlato ad una prognosi peggiore. Tuttavia, i fattori più importanti correlati ad un aumentato rischio di eventi avversi sono stati la riduzione delle TAPS <13 mm e la riduzione dell'S <9 (HR 2,09 e 2,3 rispettivamente).

Conclusioni. Si raccomanda quindi la valutazione ecocardiografica del RV in pazienti con malattie polmonari interstiziali. Un aumento del valore di sPAP è correlato ad un incremento del rischio, ma la compromissione della funzionalità longitudinale del RV costituisce il fattore prognostico più significativo.

A229: RELEVANCE OF TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSION/PULMONARY ARTERY SYSTOLIC PRESSURE RATIO FOR RISK ASSESSMENT IN PULMONARY ARTERIAL HYPERTENSION

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Background. The ratio of tricuspid annular plane excursion (TAPSE) to systolic pulmonary artery pressure (PASP) to assess right ventricular (RV) function adaptation to afterload has been shown to be of prognostic relevance in pulmonary arterial hypertension (PAH).

Objective. To test the hypothesis that improvement in TAPSE/PASP under targeted therapies is associated with the likelihood to achieve a low-risk status in PAH.

Methods. The study retrospectively enrolled 677 PAH patients (55% idiopathic) with follow-up clinical, right heart catheterization and echocardiographic evaluations within 12 months (IQR 180-344 days) after initiation of targeted therapies from 2005 to 2017 in 11 Italian centers. European guidelines-derived and United States Registry to Evaluate Early and Long-Term PAH Disease Management registry REVEAL 2.0 risk scores were assessed at baseline and follow-up.

Results. The patients improved their functional class and 6-min walk distance, but a minority of them achieved or maintained the low risk status as assessed either with the European or the REVAL score (30% and 27%, respectively). The TAPSE/PASP ratio increased curvilinearly in proportion to decreased pulmonary vascular resistance (PVR) more than 50%. Patients at low risk were respectively, 6.98 and 3.53 times more likely to have TAPSE/PASP ≥ 0.40 mm/mmHg than those at intermediate or high risk, according to the European (OR 6.98, CI 4.72-10.3; $p = 0.0001$) and the REVEAL score (OR 3.53, CI 2.43-5.11; $p = 0.0001$).

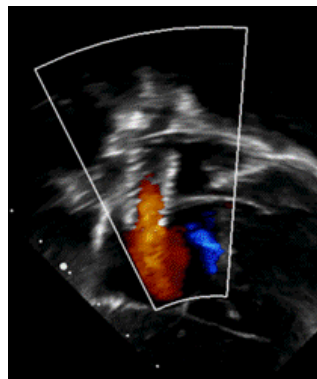
Conclusion. Improvement of TAPSE/PASP under targeted therapies in PAH is associated with a low risk status and more than 50% reduction in PVR.

A230: HYPOPLASTIC LEFT HEART SYNDROME: NORWOOD OR HYBRID PROCEDURE?

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Baby born at 38 weeks of gestation: Fetal echocardiography had revealed a severe Hypoplastic left heart syndrome (HLHS). The baby was intubated immediately after birth as a result of faint cry, severe cyanosis and a SpO₂ of 35%. Usually a patent oval foramen allows patients to have a better blood oxygen saturation at birth, but in our case the oval foramen was demonstrated severely restrictive at fetal echocardiography therefore an interventional catheterization was planned immediately after birth to perform left atrial decompression. Echocardiography and CT performed after the procedure showed correct positioning of the inter-atrial stent with a left to right shunt, mitral and aortic atresia associated with an atretic left ventricle and a very hypoplastic ascending aorta; coronary arteries, ascending aorta and aortic arch were perfused by retrograde flow through a large patent ductus arteriosus; right ventricle was moderately enlarged with good contractility. Transfontanellar and abdominal ultrasound findings were normal, as his newborn screen results and chromosomal analysis. On the 5th day of life the baby underwent a hybrid stage 1 palliation, so called "hybrid procedure", consisting of a palliative surgical procedure of bilateral pulmonary artery banding and ductal stenting through interventional catheterization. After surgery, switching from parenteral nutrition to oral feeding, he presented repetitive vomiting and gastroesophageal reflux, solved by using a nasojunal tube feeding. EKG showed no signs of possible ischemia. A balloon dilation of the interatrial stent was necessary to achieve an adequate atrial level communication as meanwhile the gradient between the atria was increasing over 10 mmHg. The baby was discharged on his 87th day of life in good clinical conditions weighing 4000 g, SpO₂ 90% in room-air, good cardiac activity with a systolic murmur 3/6, upper limbs pulses slightly weaker than inferior limbs pulses. He is slowly gaining weight to undergo the Glenn procedure at 6 months of age. HLHS is an uncommon congenital heart disease and a uniformly fatal lesion if untreated surgically. HLHS is in the spectrum of single ventricle defects that has a sequence of staged repairs. Initially the Norwood and its variations as a neonatal repair, with a bidirectional Glenn repair at 6 months of age and finally the bicaval pulmonary anastomosis (Fontan) after 4 years of age. Until recently, the Norwood procedure was the only treatment option. The more recent hybrid strategy is a less invasive procedure and is an alternative treatment for HLHS reserved for the most fragile patients (low birth weight

and/or restrictive atrial septum and/or those presenting in shock). The major advantage of the hybrid approach is the avoidance of early major heart surgery and extracorporeal circulation in high-risk patients. The goal is to create a stable and balanced circulation in the neonate, allowing the option to proceed to univentricular or biventricular repair in an older patient. Prenatal diagnosis is acquiring more and more importance in this field showing the potential of a targeted prenatal treatment planning that could be used to optimize postnatal management and even the potential of prenatal management of affected children.



A231: SUDDEN CARDIAC ARREST AND ITS WARNING SIGNS AND SYMPTOMS IN A PEDIATRIC POPULATION

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The first clinical manifestation of sudden cardiac arrest (SCA) is often lethal, therefore there is an active interest about identification of patients at risk for SCA. SCA in children and adolescents is rare compared with adult cases of cardiac arrest. The aim of the present study was to investigate the rate of and the features of (in-)patients admitted to the pediatric cardiology ward for sudden cardiac arrest (SCA) or for warning signs or symptoms of SCA defined as ventricular tachycardia or syncope.

We retrospectively reviewed the charts of patients admitted since January 2006 to July 2020. No sudden cardiac death was included. Syncope discharged from the emergency room or admitted to the neurology ward were excluded. For all patients we evaluated pre work-up history and risk factors, diagnostic work up, pharmacological and non-pharmacological interventions, discharge diagnosis and the latest follow-up. A negative outcome was defined as death or relapse of the admission signs and symptoms (SCA, syncope or ventricular tachycardia).

We selected 78 patients, 45 males and 33 females, aged between 1 month and 27 years (median 11,75 years) admitted for sudden cardiac arrest (21;27%), syncope (27; 34,5%) and for ventricular tachycardia (30; 38,5%). We defined pre work-up risk assessment with 5 criteria: positive family history for sudden cardiac death or channelopathies (12 patients;15%), known underlying cardiac disease as one between: congenital heart defects, cardiomyopathies or electrical disorders (31 pts; 40%), experience of previous cardiac symptoms (25, 32%) such as syncope or pre-syncope (16, recurrent in 10 patients), chest pain (4), dyspnea upon exertion or fatigue (4), ongoing antiarrhythmic treatment at the time of the event (16, 21%), exercise-related event (24, 31%).

Most patients (66%) had 0 or 1 known risk factor at the time of the event. Discharge diagnosis were heterogeneous: ventricular tachycardia in otherwise healthy heart 16, failing congenital heart disease 16, reflex neurocardiogenic syncope 15, channelopathies 11, cardiomyopathies 7, non-cardiogenic event 5, acute myocarditis 4, bradyarrhythmia 3, rhabdomyoma 1.

Comparing the risk assessment before work up with the discharge diagnosis there was some degree of mismatch: in 9 patients (11,5%) the discharge diagnosis was less serious than the risk criteria would have suggested and in 9 patients (11,5%), despite a low pre work up risk, a serious condition potentially lethal was diagnosed. In 60 patients (77%) the risk assessment matched the post-test risk. Notably only 5 out of 21 sudden cardiac arrest presented 2 or more risks criteria.

At follow-up there were 20 negative outcomes (2 deaths and 18 relapses), 4 patients were dismissed from regular follow-up, 53 patients are still on follow-up and did not presented any relapse. Patients sex or age did not impact on outcome at follow-up. There was no significant association between a negative outcome and higher pre work up risk (2 or more risk factors) nor the presence of an underlying cardiac disease or the event occurring during sport activity. A history of antiarrhythmic drug use was a predictor for a negative outcome ($p=0,0005$). Patients with a negative outcome (death or relapse) were more often admitted with a diagnosis of SCA or ventricular tachycardia than syncope ($p<0,001$) and required more often some non-pharmacological intervention (ECV, RFA, ICD or PM implantation) ($p=0,0002$).

A232: RISK REDUCTION AND HEMODYNAMICS WITH INITIAL COMBINATION THERAPY IN PULMONARY ARTERIAL HYPERTENSION

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Background. An initial oral combination of drugs is being recommended in pulmonary arterial hypertension (PAH), but the effects of this approach on risk reduction and pulmonary vascular resistance (PVR) are not known.

Objectives. To test the hypothesis that a low-risk status would be determined by the reversibility of PVR in PAH patients treated upfront with a combination of oral drugs.

Methods. The study enrolled 181 treatment-naïve PAH patients (81% idiopathic) with a follow-up right heart catheterization at 6 months after initial combination of endothelin receptor antagonist + phosphodiesterase-5 inhibitor drugs and clinical evaluation and risk assessments by European guidelines and REVEAL scores.

Results. Initial combination therapy improved functional class and 6-min walk distance, and decreased PVR by an average of 35% (median - 40%). A third of the patients had a decrease in PVR <25%. This poor hemodynamic response was independently predicted by age, male sex, pulmonary artery pressure and cardiac index, and at echocardiography a right/left ventricular surface area ratio >1 associated with low tricuspid annular plane systolic excursion (TAPSE) <18 mm. A low risk status at 6 months was achieved or maintained in only 34.8% (REVEAL score) to 43.1% (European score) of the patients. Adding criteria of poor hemodynamic response improved prediction of a low risk status.

Conclusion. A majority of PAH patients still insufficiently improved after 6 months of initial combinations of oral drugs is identifiable at initial evaluation by hemodynamic response criteria added to risk scores.

A233: THE EFFECTS OF PHYSICAL ACTIVITY ON NATRIURETIC PEPTIDES IN CHILDREN WITH HYPOPLASTIC LEFT HEART SYNDROME AFTER COMPLETE PALLIATION WITH FONTAN PROCEDURE

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Background. Hypoplastic left heart syndrome (HLHS) describes a heterogeneous group of pathologies characterized by underdevelopment of the structures of the left side of the heart. HLHS occurs in 0.16 - 0.36 per 1000 live births and represents 1.4 - 3.8% of congenital heart diseases. In the past, the syndrome was fatal within the first few weeks of life. Today, following the surgical and medical advances of the past four decades, many of these children undergo three surgical steps (the Norwood, Glenn and Fontan procedures) that enable them to survive childhood and reach adulthood with a univentricular heart. Recent studies have investigated the possible beneficial effects of physical activity in these patients with such a peculiar circulation, however this topic is not yet fully clarified. The aim of this study was to evaluate the effects of physical activity on NT-proBNP in patients with HLHS after complete palliation with Fontan procedure.

Methods. We enrolled 14 (9 male) patients with HLHS and univentricular heart. Each patient underwent a cardiologic examination, echocardiogram and blood tests. Physical activity was assessed by submitting the International Physical Activity Questionnaire (IPAQ) to the children together with their parents. Based on the score obtained, the patients were divided into two groups. In group I, children who carried out regular daily physical activity. In group II, on the other hand, the children who, according to the questionnaire scores, led a sedentary life were considered. NT-proBNP (pg/L) was measured for each patient.

Results. Among the echocardiographic parameters in the study, fractional area change (RVFAC) was considered to evaluate the function of the systemic right ventricle. Statistical analysis did not show a significant

difference in right ventricle function between the two groups: RVFAC $36.29 \pm 4.8\%$ vs $35.14 \pm 5.3\%$ ($p > 0.05$) in group I and group II respectively. We then assessed whether there was a difference between the NT-proBNP levels between the two groups and the data analysis showed a significant difference between group I and group II, 65.98 ± 20.03 ng/L vs 102.95 ± 23.65 ng/L ($p < 0.01$), respectively.

Conclusions. Our data showed a reduction of NT-proBNP levels in the group of children who perform physical activity compared to the group of sedentary children. To the best of our knowledge this is the first study that correlated NT-proBNP with physical activity in patients with HLHS and right univentricular heart.

A234: LONG-TERM PROGNOSTIC VALUE OF HIGH SYSTOLIC PULMONARY ARTERIAL PRESSURE AFTER ACUTE PULMONARY EMBOLISM: A RETROSPECTIVE STUDY

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The most important long-term complication of acute pulmonary embolism (APE) is chronic thromboembolic pulmonary hypertension (CTEPH). However long-term outcomes of APE and incidence of CTEPH are not well documented. We aimed to determine the incidence of pulmonary hypertension after APE and its prognostic value. Two-hundred eighty-four consecutive patients diagnosed with APE were monitored for a median period of 434 days (107-895) and data concerning PE recurrence, mortality and systolic pulmonary arterial pressure (PAPs) were collected. Population median age was 78 (67-84) and 52% were female. 57% of patients had a deep venous thrombosis at compressive ultrasonography and median PAPs at echocardiography at admission was 40 mmHg (22-50). In hospital death rate was 11%: at multivariable logistic regression cardiogenic shock and PAPs (per mmHg) were independent predictors of in hospital death (OR 7.2 (2.45-21.7), $p < 0.001$ and 1.06 (1.02-1.11), $p = 0.003$, respectively). Among survivors, at one month, 63 patients (22%) had PAPs >35 mmHg. Mortality rate at follow-up was as high as 24%, while PE recurrence rate was 0.4%. At multivariate Cox analysis including age, PAPs >35 mmHg, clinical relevant bleedings, PE recurrence and cancer, only age (per year) and PAPs >35 mmHg were predictors of all cause death (OR 1.08 (1.05-1.12), $p < 0.001$, and 3.60 (1.12-11.62), $p = 0.032$, respectively). Kaplan-Meier survival analysis stratified for pulmonary hypertension showed a clear negative trend of the latter factor, without reaching the statistic significance (Fig. 1). Our data show that pulmonary hypertension lasting after the acute phase is a negative prognostic factor in patients diagnosed with APE. Closer monitoring of patients with PAPs >35 mmHg at follow-up is recommended due to the high mortality rate in this subset of patients.

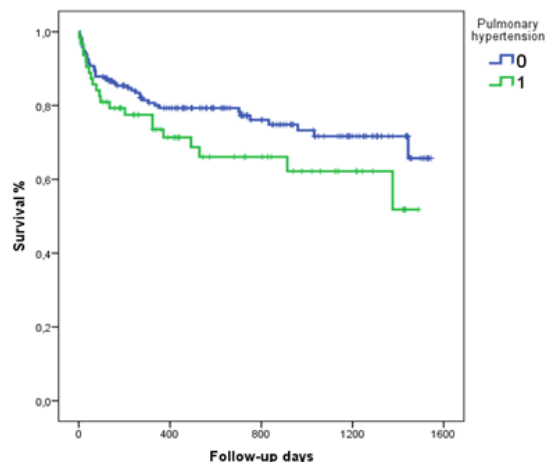


Figure 1. Kaplan-Meier survival analysis stratified for pulmonary hypertension.

A235: VENTRICULAR ARRHYTHMIAS IN A REPAIRED TETRALOGY OF FALLOT PATIENT

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Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart defect, representing 7% to 10% of congenital heart diseases (CHD). TOF is characterized by four defects: ventricular septal defect (VSD), pulmonary stenosis, overriding aorta and right ventricular hypertrophy; other associated cardiac abnormalities are aortic valve regurgitation, right aortic arch, abnormal coronary arteries, aorticopulmonary collaterals, patent ductus arteriosus and multiple septal defects. TOF presents a wide clinical spectrum, largely determined by RVOT obstruction (RVOTO)

degree. The standard treatment is surgical correction during the first year of life, that involves VSD closure and RVOTO relief. Common long-term complications in adults who underwent TOF surgery are pulmonary regurgitation, residual RVOTO, residual VSD, aortic complications, RV and LV dysfunction, supraventricular and ventricular arrhythmias, sudden cardiac death (SCD) and endocarditis.

Case presentation. A 23-year-old male with repaired TOF (rTOF), referred to our ER for syncope with buccal trauma and partial dental avulsion. The ECG showed sinus rhythm, normal AV and IV conduction and frequent monomorphic premature ventricular contractions (PVCs). Physical examination, routine blood tests and head and neck CT scan did not reveal any abnormalities. The patient's medications included ace-inhibitor, beta-blocker and spironolactone. The transthoracic echocardiogram showed IVS dysplasia, EF 50% and no significant valvulopathies. During the hospitalization, the patient underwent a 24 hours Holter ECG, which confirmed frequent monomorphic PVCs, rare isolated premature atrial contractions and also showed a single episode of unsustained monomorphic ventricular tachycardia. We excluded any other possible reversible cause of arrhythmias, such as hyperthyroidism and inflammatory processes. It was not possible to perform a Cardiac MRI due to patient's claustrophobia. In absence of any other evidence, we decided to provide a strict monitoring strategy based on remote control of the cardiac rhythm through an Implantable Loop Recorder. We also up-titrated beta-blocker therapy to maximum tolerated dose. We did not detect any other arrhythmic episode and the patient was discharged into good and stable clinical conditions. At three month follow-up, remote monitoring did not document any significant atrial or ventricular arrhythmias.

Discussion. rTOF patients should be monitored with a strict cardiologic follow-up in order to look for possible late complications such as arrhythmias. Ventricular arrhythmias include polymorphic VT/VF and monomorphic sustained VT; both are related to SCD, which has a reported frequency of 1-3.5%. Possible risk factors associated with any ventricular arrhythmias and SCD are QRS duration >180ms and LV dysfunction. According to ESC 2020 Adult CHD Guidelines, Holter monitoring, event recorder, and electrophysiology evaluation are required for high risk patients with suspected or clinical arrhythmias, and ICD implantation is recommended (class IC) only in patients with previous cardiac arrest or sustained VT. Therefore, the absence of any other arrhythmic clinical manifestation in our patient, led us to decide for a less invasive monitoring strategy.

A236: PULMONARY ARTERIAL HYPERTENSION IN A PATIENT WITH LONG-LASTING TREATMENT WITH INTRAVITREAL RANIBIZUMAB

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Introduction. Although vascular endothelial growth factor (VEGF) and its receptor are a known pathophysiological pathway in pulmonary arterial hypertension (PAH), their therapeutic role has not been thoroughly understood yet. The VEGF signalling inhibitor ranibizumab has been approved for the intravitreal treatment of neovascular age-related macular degeneration (nAMD). However, its potential link with PAH has not yet been described.

Case report. A 76-year-old Caucasian woman with progressive dyspnoea underwent cardiologic work-up. Background medical history included nAMD of the right eye, which was being currently under long-term therapy with intravitreal ranibizumab. At physical examination, cardiorespiratory findings were normal. Transthoracic echocardiography showed normal left ventricular systolic function and diastolic filling pressures, while the right ventricle was markedly dilated, with left ventricular D-shape and increased peak tricuspid regurgitation velocity. Full biochemical tests, including autoimmunity, hepatic and serologic panels were negative, as well as pulmonary function tests and chest CT scan. Then, right heart catheterization confirmed the diagnosis of severe pre-capillary pulmonary hypertension. Suspecting iatrogenic PAH, ranibizumab was discontinued and the patient was begun on macitentan 10 mg qd and sildenafil 20 mg tid. After a 6-month follow-up, she reported a greater exercise tolerance, with an increased 6-minute walking distance to 570 m from a baseline value of 510 m. A repeated cardiac catheterization showed a mild decrease in pulmonary artery pressures, with an improved cardiac output and reduced pulmonary vascular resistance.

Discussion. Ranibizumab is a fragment of the humanized monoclonal anti-VEGF antibody, which has been licensed for the treatment of nAMD. To the best of our knowledge, this is the first reported case of PAH in which a potential relation with long-lasting intravitreal ranibizumab for nAMD has been speculated. Further investigations are required to better discriminate the role of intravitreal antiangiogenic treatment in the pathogenesis of PAH.

A237: È POSSIBILE PREDIRE L'EVOLUZIONE CLINICA DI UN PAZIENTE CON EMBOLIA POLMONARE? UNA VALUTAZIONE RETROSPETTIVA DI 69 PAZIENTI OSPEDALIZZATI

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Introduzione. La stratificazione prognostica di pazienti con nuova diagnosi di Embolia Polmonare (EP) è il primo passaggio per l'adozione di un'ideale strategia di trattamento. In accordo con quanto suggeriscono le linee guida, i pazienti con EP senza shock o ipotensione dovrebbero essere considerati "non ad alto rischio". Questi pazienti andrebbero ulteriormente stratificati adottando uno score clinico-prognostico validato, PESI score o sua versione semplificata sPESI, per distinguere pazienti a rischio intermedio e basso. Tuttavia l'andamento clinico dei pazienti ricoverati per EP non sempre appare facilmente prevedibile.

Metodi. Abbiamo eseguito una valutazione retrospettiva di 69 pazienti consecutivi ricoverati presso la nostra U.O. di Cardiologia-Utic con diagnosi di EP tra l'Aprile 2016 ed il marzo 2020. Sono state raccolte per ogni paziente le caratteristiche demografiche e cliniche, i fattori predisponenti, le comorbidità, gli scores predittivi diagnostici (score di Wells e Ginevra score), i valori del D-Dimero, i risultati degli esami strumentali (ECG, ecocardiogramma, compressione ultra-sonografica: CUS, TC-angio del torace), e i punteggi PESI-sPESI score. Sono stati considerati outcomes clinici un combinato delle complicanze (infarto polmonare, emorragie, ictus, instabilità emodinamica, necessità di ventilazione), la morte, la durata del ricovero. Per calcolare la relazione tra caratteristiche dei pazienti e i relativi outcomes clinici sono stati calcolati i coefficienti di correlazione di Pearson-Spearman.

Risultati. Sono stati studiati 69 pazienti consecutivi (29 M, 40 F), con età media 72 anni (min. 27, max 94). Al momento della diagnosi, solo un terzo circa (32%) di essi presentava fattori di rischio temporaneo (setting-relati) per EP, tra i quali i più frequenti sono stati l'immobilizzazione per qualunque causa (15%), la chirurgia (10%), le fratture d'arto inferiore (7%). Per quanto riguarda i fattori di rischio permanenti (paziente-relati) o le morbidità associate, le più frequenti sono state l'ipertensione arteriosa (48%), la malattia respiratoria cronica (37%), la dislipidemia (25%), le patologie autoimmuni (23%), la fibrillazione atriale (22%) e il cancro attivo (19%). La proporzione di pazienti che ha presentato una CUS positiva per TVP è stata di 30/69 (43%). La percentuale di pazienti che presentava un D-Dimero significativamente elevato per età è stata di 64/69 (93%). Lo score di probabilità pre-test (Wells o Ginevra score) è stato predittivo per EP in circa 2/3 dei casi (67%). Nei casi rimanenti (34% Wells, 30% Ginevra) risultava un PE improbabile. I segni e sintomi clinici più frequenti sono stati la dispnea (75%), i segni di TVP (23%), la sincope (16%) e il dolore toracico (15%). I segni ECG più comuni sono stati la tachicardia sinusale (38%), inversione della T in V1-V4 (13%), BBdx (10%), S1Q3T3 (4%). Segni ecocardiografici più comuni sono stati l'ipertensione polmonare (65%), la dilatazione del VD (37%), la motilità ridotta del VD (28%), segno di McConnell (6%), segno 60-60 (4%). Gli outcomes clinici combinati (durata del ricovero - complicanze - morte) non hanno mostrato una correlazione statisticamente significativa con l'età dei pazienti, il sesso, la presenza di patologie associate, e nemmeno con gli scores di severità clinica (PESI score).

Conclusioni. Nei pazienti con EP che abbiamo avuto ricoverati tra aprile 2016 e marzo 2020, avere uno score di severità clinica validato (PESI score) più elevato, non ci ha permesso di individuare i pazienti con decorso clinico più sfavorevole. Forse è necessaria l'adozione di più complessi sistemi di inquadramento per migliorare la stratificazione prognostica di questi pazienti.

A238: UNA INCOMPLETA CORREZIONE DI RITORNO VENOSO POLMONARE ANOMALO TOTALE

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Il ritorno venoso polmonare anomalo totale (RVPAT) è una malformazione cardiaca rara caratterizzata da molteplici varianti anatomiche che ne condizionano presentazione clinica ed outcome. Un paziente di 30 anni giungeva alla nostra osservazione con diagnosi perinatale di RVPAT sopracardiacco con sbocco delle vene polmonari (vpvp) in vena verticale senza segni di ostruzione. A 26 giorni di età era stato sottoposto a correzione radicale mediante anastomosi del collettore comune all'atrio sinistro mentre non si eseguiva legatura della vena verticale per comparsa di edema polmonare. A 30 anni il paziente, asintomatico, eseguiva ecocardiogramma che evidenziava moderata dilatazione delle sezioni destre. Una risonanza magnetica cardiaca mostrava confluenza delle vpvp di destra in un unico condotto a regolare sbocco in atrio sinistro, mentre a sinistra vi erano due vpvp provenienti dal lobo inferiore con sbocco separato in atrio sinistro, la più piccola delle quali confluiva a monte con la vena verticale che riceveva le vpvp del lobo superiore sinistro e che drenava in vena anonima sinistra. Il cateterismo cardiaco riscontrava Qp/Qs 3.33, normali pressioni in arteria polmonare e

a catetere occludente. Si eseguiva quindi tentativo di chiusura della vena verticale con Vascular Plug, fallito per la repentina comparsa di dispnea e congestione polmonare. L'angiografia di controllo della vena verticale evidenziava stenosi dello sbocco venoso in atrio sinistro, confermata ad un'angio-TC del torace. Veniva successivamente eseguito test di occlusione in vena verticale che evidenziava aumento consensuale delle pressioni telediastoliche ventricolari sinistre e in arteria polmonare. Questo reperto poteva essere spiegato dalla presenza di una sottostante disfunzione diastolica ventricolare sinistra, non evidente in condizioni basali, e dalla presenza di ostruzione del ritorno venoso polmonare di sinistra. Quest'ultima inoltre ha favorito un aumento del flusso in vena verticale con persistenza di tale collettore venoso come via di scarico in atrio destro e conseguente dilatazione delle sezioni destre. Si poneva pertanto indicazione a correzione chirurgica rifiutata dal paziente.

La conoscenza delle varianti anatomiche di RVPAT e lo studio degli esiti di correzione chirurgica mediante metodiche di imaging di secondo livello, assieme ad una accurata valutazione fisiopatologica, sono fondamentali per un adeguato management medico e chirurgico.

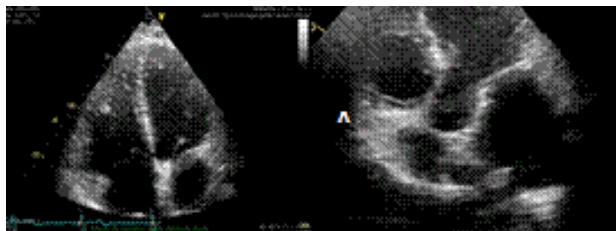


Figura 1. (A sinistra) Proiezione apicale 4 camere con evidenza di dilatazione del ventricolo destro. (A destra) Sbocco del collettore comune in atrio sinistro (freccia).

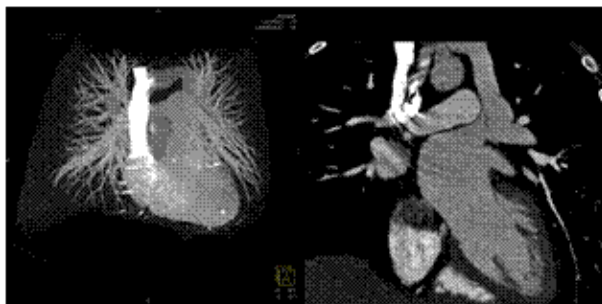


Figura 2. Angio-TC cardiaca. Ricostruzione maximum intensity projection e ricostruzione multiplanare con evidenza delle dimensioni e del decorso della vena verticale.

A239: AUTOIMMUNE-MEDIATED CONGENITAL HEART BLOCK: LONG-TERM CARDIOVASCULAR OUTCOME IN A TERTIARY CENTER EXPERIENCE

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Introduction. CHB is a rare disease due to the immune-mediated injury of the conduction system, as result of the transplacental passage of maternal anti-SSA/Ro and anti-SSB/La autoantibodies to the fetus. High rates of mortality and pacemaker (PM) implantation have been observed. Specific long-term management recommendations are not yet available.

Methods. Consecutive patients with autoimmune-mediated CHB referred to our Center from 2008 to 2019 were prospectively enrolled. *In utero* diagnosis was assessed by fetal echocardiography and confirmed at birth by electrocardiography (ECG). Serial clinical evaluation, ECG-monitoring and echocardiography were performed during follow-up. In patients with PM, a periodical device-monitoring was obtained. The aim of the study was to evaluate the long-term cardiovascular outcome and the clinical management of CHB. Data on self-perception of exercise tolerance were considered. CHB degree and mean ventricular heart rate (HR) *in utero*, at birth and during the latest follow-up were assessed. Pacing characteristics and device-related adverse events were also evaluated, involving LV dyssynchrony obtained by echocardiography.

Results. 22 cases of CHB from 21 anti-SSA/Ro antibody-positive mothers were enrolled (67% III-degree CHB at fetal diagnosis; 33% II-degree CHB). One intra-uterine death occurred. 16 cases were treated with a combination therapy protocol of steroids, plasmapheresis and intravenous immunoglobulin infusion. Among the 20 live births, 5 cases of incomplete

CHB were observed (3 cases of I-degree and 2 cases of II-degree CHB). Patients with III-degree CHB at birth most often presented LV dilation ($p=0,03$; incomplete CHB 1 vs III-degree CHB 15 patients). HR at birth was for I-degree 135 bpm [127,5-147,5], for II-degree 75 bpm [72,5-77,5] and for III-degree CHB 58 bpm [50-65]. Long-term follow-up was obtained in 21 patients (one late-diagnosis presented to our Institution at the age of 8 years) at 6,9 years [4,3-8,5]. HR remained stable over time (I-degree $p=0,1$; II-degree $p=0,18$; III-degree CHB $p=0,14$). No cases of impaired exercise tolerance were observed. LV dilation was detected in 4 patients. 1 patient with severe LV dilation and preserved ejection fraction presented non-sustained ventricular tachycardia. A borderline QT interval was observed in a child with LV dilation. No cases of R-R interval >3 sec were revealed. QRS interval was normal in all patients with spontaneous rhythm. 6 patients underwent PM implantation (5 within the first year and 1 within the fifth year): 2 epicardial dual chamber DDD, 1 endocardial dual chamber DDD, 1 epicardial biventricular CRT-P PM and 2 epicardial single-chamber VVI-R PM were implanted. Last device follow-up showed a range of ventricular pacing of 98-100%. PM dependency was confirmed in all cases. An early abdominal PM pocket infection was successfully treated with antibiotics. Endocarditis, pneumothorax and macroscopic lead fracture or dislodgment have all been excluded. All patients presented a recovery of LV dilation and no cases of LV dyssynchrony were observed.

Conclusions. In our experience, autoimmune-mediated CHB presented with a favorable long-term cardiovascular outcome. An adequate exercise tolerance was observed also in patients with spontaneous rhythm. Considering the stability of HR over time, an accurate selection of patients that need for PM should be performed. Long-term management of CHB should evaluate LV dyssynchrony in patients with PM and the presence of ventricular arrhythmias and LV dilation/dysfunction in patients with spontaneous rhythm.

COVID-19

A240: INCIDENCE, DETERMINANTS AND PROGNOSTIC RELEVANCE OF HS-TROPONIN AND NATRIURETIC PEPTIDES ELEVATION AT ADMISSION IN HOSPITALIZED COVID-19 PNEUMONIA PATIENTS

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Background. Myocardial involvement in the course of Coronavirus disease 2019 (COVID-19) pneumonia has been reported, though not fully characterized yet. Aim of the present study is to undertake a joint evaluation of hs-Troponin and natriuretic peptides (NP) in patients hospitalized for COVID-19 pneumonia.

Methods. In this multicenter observational study, we analyzed data from $n=111$ COVID-19 patients admitted to dedicated "COVID-19" medical units. Hs-Troponin was assessed in $n=103$ patients and NP in $n=82$ patients on admission; subgroups were identified according to values beyond reference range.

Results. Increased hs-Troponin and NP were found in 38% and 56% of the cases respectively. As compared to those with normal cardiac biomarkers, these patients were older, had higher prevalence of cardiovascular diseases (CVD) and more severe COVID-19 pneumonia by higher CRP and D-dimer and lower $\text{PaO}_2/\text{FIO}_2$. Two-dimensional echocardiography performed in a subset of patients ($n=24$) showed significantly reduced left ventricular ejection fraction in patients with elevated NP only ($p=0,02$), whereas right ventricular systolic function (tricuspid annular plane systolic excursion) was significantly reduced both in patients with high hs-Troponin and NP ($p=0,022$ and $p=0,03$ respectively). On multivariable analysis, independent associations were found of hs-Troponin with age, $\text{PaO}_2/\text{FIO}_2$ and D-dimer ($B=0,419$, $p=0,001$; $B=-0,212$, $p=0,013$ and $B=0,179$, $p=0,037$ respectively), and of NP with age and previous CVD ($B=0,480$, $p<0,001$ and $B=0,253$, $p=0,001$ respectively). In patients with in-hospital mortality ($n=23$, 21%) hs-Troponin and NP were both higher ($p=0,001$ and $p=0,002$ respectively), while increasing hs-troponin and NP were associated with worse in-hospital prognosis [OR 4.88 (95% CI 1.9-12.2), $p=0,001$ (adjusted OR 3.1 (95% CI 1.2-8.5), $p=0,025$) and OR 4.67 (95% CI 2-10.8), $p<0,001$ (adjusted OR 2.89 (95% CI 1.1-7.9), $p=0,04$) respectively]. Receiver operator characteristic curves showed good ability of hs-Troponin and NP in predicting in-hospital mortality (AUC 0.869, $p<0,001$ and AUC 0.810, $p<0,001$ respectively).

Conclusions. Myocardial involvement at admission is common in COVID-19 pneumonia and associated to worse prognosis, suggesting a role for cardiac biomarkers assessment in COVID-19 risk stratification. Independent associations of hs-Troponin with markers of disease severity and of NP with underlying CVD might point towards existing different mechanisms leading to their elevation in this setting.

A241: PERCUTANEOUS URGENT TREATMENT OF SEVERE AORTIC STENOSIS IN A PATIENT DURING SARS-CoV-2 PANDEMIC: ROLE OF BALLOON AORTIC VALVULOPLASTY

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Background. The majority of transcatheter aortic valve implantation (TAVI) procedures are performed on an elective basis and, therefore, have been postponed during Coronavirus disease 2019 (COVID-19) outbreak. However, delay in the treatment of severe aortic stenosis (AS) may increase the risk of adverse events, particularly in elderly patients with multiple comorbidities.

Case summary. An 86-year-old man, affected by severe AS was referred to our Institution from a spoke center due to decompensated heart failure refractory to optimal medical therapy. Three months before, the patient was evaluated by our Heart Team and was scheduled for TAVI. Since that time, he had been waiting for elective TAVI procedure, which was postponed due to the COVID-19 outbreak spark. Due to the clinical and computed tomography suspicion of SARS-CoV-2 infection he underwent nasopharyngeal swab and was temporarily isolated. However, the rapid deterioration of clinical and hemodynamic conditions required emergency treatment. We performed a balloon aortic valvuloplasty (BAV) as a bridge for TAVI, and achieved a reduction of the invasive transaortic gradient from 43 to 10 mmHg after one inflation. The patient's clinical and hemodynamic conditions markedly improved within a few hours; the next day, the result of the reverse-transcriptase polymer chain reaction for COVID-19 was negative. At day five, he underwent TAVI procedure with implantation of a CoreValve Evolut™ Pro 29. Subsequent clinical course was uneventful.

Discussion. In the context of COVID-19 pandemic, the deferral of TAVI procedure should be assessed on a case-by-case basis in order to avoid delay in patients at high risk for adverse events. BAV may be an option in heart failure patients with severe AS when TAVI is temporarily contraindicated such as in patients suspected for COVID-19.

A242: IMPACT OF RAAS INHIBITORS ON CLINICAL OUTCOME AND MORTALITY IN STEMI PATIENTS DURING THE COVID-19 ERA: A MULTICENTRE OBSERVATIONAL STUDY

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Background. Conflicting results are available regarding the influence of ACEi/ARBs on the risk of COVID-19 infection, while less is known about their impact on clinical outcome of STEMI patients with confirmed diagnosis of COVID-19. Our aim was to evaluate the impact of ACEi/ARBs therapy on in-hospital mortality and clinical outcomes of STEMI patients during COVID-19 pandemic.

Methods. We retrospectively analysed consecutive STEMI patients hospitalised from February 20, to May 10, 2020 at four Hospitals in Lombardy. SARS-COV-2 diagnosis was performed by nasopharyngeal swab test. Procedural outcome, respiratory complications and in-hospital mortality were reported. Univariate and multivariate analysis were performed by logistic regressions.

Results. Our population was represented by 182 STEMI patients, 76.9% male, mean age 67±12.5. Hypertension was reported in 53.3%, treated with ACEi/ARBs in 29.1%. COVID-19 diagnosis was confirmed in 17.1%. In-hospital mortality (13.2%) was significantly higher in COVID-19 patients (31% vs 10%, p=0.003), even if ejection fraction (OR 0.93 [95% CI] 0.87–0.99; p=0.03) and respiratory complications (OR 9.39 [95% CI] 1.91–45.9; p=0.006) result the only two independent predictors. The incidence of COVID-19 infection was not influenced by ACEi/ARBs (16.5% in naïve vs 18.8%) whose presence at admission did not correlate with respiratory complications or mortality both in case of discontinuation or maintenance.

Conclusion. In a high-risk population, such as that of STEMIs, the potential benefit of ACEi/ARBs discontinuation in COVID-19 patients is overcome by its detrimental effect. Intensive care, additional preventive respiratory investigations, regardless from swab test result, should be suggested among all patients admitted for STEMI during pandemic.

A243: HUMAN MESENCHYMAL STROMAL CELLS DO NOT EXPRESS ACE2 AND TMPRSS2 AND ARE NOT PERMISSIVE TO SARS-CoV-2 INFECTION

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Background. Cell-based therapy has been proposed for the treatment of both pulmonary and cardiac damage derived from SARS-CoV-2 infection. Mesenchymal stromal cells (MSCs) have acquired particular interest for the well documented immunomodulatory functions. However, some critical issues regarding the possibility that MSCs could be infected by the virus have been raised. Angiotensin-converting enzyme 2 (ACE2) and TMPRSS2 are the main host cell factors for the Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2) entry. To this purpose, we evaluated if human MSCs from both fetal and adult tissues constitutively express ACE2 and TMPRSS2, and if they can be infected by SARS-CoV-2.

Methods. We studied 8 hMSC lines: 4 of fetal origin isolated from human placentas (hA-MSC) and 4 of adult origin isolated from bone marrow aspirates (hBM-MSCs). The lung epithelial cancer cell line Calu-3, which expresses high levels of ACE2 and TMPRSS2, and is permissive to SARS-CoV-2, was used as positive control. We quantified ACE2 and TMPRSS2 mRNA levels by RT-qPCR and verified protein content by western blot on both cell lysates and serum-free 48 hrs-conditioned media (MSC-CM). ACE2 levels in MSC-CM were also quantified by ELISA assay. Finally, to test MSC viral susceptibility, we produced replication-defective, GFP-tagged retroviral particles bearing the SARS-CoV-2 Spike envelope protein; the pantropic VSV glycoprotein (VSV-G) was used as positive control.

Results. ACE2 and TMPRSS2 mRNA levels in both amniotic and bone marrow MSC were about 400-fold and 250-fold lower respectively compared with Calu-3. ACE2 and TMPRSS2 protein expression were undetectable by western blot in MSC lysates. Moreover, we were not able to detect any soluble ACE2 in MSC conditioned media both by western blot and ELISA. Finally, Calu-3 but not MSC were infected by SARS-CoV-2 Spike pseudovirus, whereas both cell types were susceptible to VSV-G pseudovirus infection.

Conclusions. Both fetal and adult MSC do not express biologically significant levels of ACE2 and TMPRSS2 and are refractory to SARS-CoV-2 infection. These data support MSC-based approaches in COVID-19 patients, even in the acute phase of disease, as a possible useful approach to mitigate the cytokine storm complicating the most severe cases of the disease.

A244: IMPACT OF THE COVID-19 PANDEMIC ON CLINICAL OUTCOMES OF ACS: RETROSPECTIVE ANALYSIS FROM A CARDIOLOGY NETWORK IN ABRUZZO, CENTRAL ITALY

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Background. The reorganization of healthcare services due to the COVID-19 pandemic has radically changed the management of inpatients and outpatients affected by cardiovascular disorders. Moreover, several authors worldwide have reported a significant decrease in hospital admissions for acute coronary syndromes (ACS) during the most recent months of the COVID-19 outbreak. To prepare for a second wave of the pandemic, the causes of this pattern and its impact on patients and hospital management have been studied.

Methods. We conducted a monocentric, observational, retrospective study aimed at evaluating consecutive patients discharged from our local network with a diagnosis of ACS from the 20th of February 2020 to the 30th of April 2020.

Results. A total of 201 patients with ACS were included in the analysis. All patients with ACS in 2020 were free of Sars-nCoV2 infection. Seventy-two ACS cases occurred during the February 20-April 30, 2020 period, while 129 were recorded in the same period of 2019 (44.4% reduction). In particular, the number of patients with NSTE (Non-STelevation)-ACS dropped from 84 (65%) in 2019 to 21 (44.4%) in 2020 (62% reduction, p=0,01), while more patients with a diagnosis of STEMI (ST elevation myocardial infarction) were admitted in 2020. Thirty-eight composite events (mortality, life-threatening arrhythmias, mechanical complications and acute heart failure) were observed in 2020, while only 34 patients were free from events. Conversely, in the 2019 ACS group, 37 events were recorded, while 92 patients did not develop any events (RR 1,82; 1,29- 2,6 95% CI; p= 0,01).

Conclusions. It is still matter of debate why the incidence of ACS has decreased during the COVID-19 pandemic, and the fear of seeking medical aid in high-risk environments such as hospitals has been proposed as a possible explanation. However, the delay in diagnosis and

treatment of these patients has a significant impact on public health costs and sustainability of care, since delayed diagnosis has been shown to be associated with a significant increase in short-term complications and deaths. Public health messaging and proper healthcare services organization should play a crucial role in adjusting the system to the new needs of public health.

A245: STEMI AND PRIMARY PCI DURING COVID-19 PANDEMIC PEAK PHASE IN ITALY: PATIENT AND SYSTEM DELAYS TO REPERFUSION

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 Timely reperfusion with primary percutaneous coronary intervention (pPCI) improves outcomes in patients with ST-segment elevation myocardial infarction (STEMI). The efficiency of the primary percutaneous coronary intervention (pPCI) system during the COVID-19 pandemic in terms of reperfusion delay and clinical results has been slightly evaluated. The implementation of dedicated measures to minimize the risk of nosocomial transmission and the patient's perception of an increased risk of in-hospital infection have to be taken into account.

In an Italian institution an internal protocol to minimize the risk of COVID-19 nosocomial transmission was implemented since the beginning of the outbreak. Therefore, we assess and characterize ischemic time and outcome of ST-elevation myocardial infarction (STEMI) patients treated with pPCI at an Italian hub center during the peak phase of the outbreak (n=85) compared to those treated during the same three months period in 2019 (n=67), with a 21% drop of STEMI cases rate. Patients with cardiogenic shock and out-of-hospital cardiac arrest were excluded. Baseline characteristics and comorbidities were similar in both groups, except for a higher rate of male in 2019. Compared to previous year, we highlighted a significantly longer total reperfusion delay in 2020 STEMI patients mainly due to pre-hospital delay, and a trend with higher in-hospital mortality rate with an increased rate of acute myocardial infarction (AMI) related complications. Since no hospital system reperfusion delay was found in STEMI patients admitted during the peak phase of the pandemic, we suggested that a dedicated COVID-19 protocol did not affect quality of in-hospital life-saving procedures.

A246: IN-HOSPITAL CARDIOVASCULAR EVALUATION OF COVID-19 PATIENTS DURING SARS-CoV-2 PANDEMIC: RESULTS FROM A SYSTEMATIC APPROACH

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Background. An increasing number of evidences, limited to sporadic cases or to echocardiography evaluation, reported that cardiovascular involvement is common in COVID-19 patients. Aim of this study was to assess the occurrence of cardiovascular diseases (CD) in confirmed COVID-19 patients admitted to hospital by clinical evaluation including Focus Cardiac UltraSound (FoCUS), integrated by further examinations when indicated.

Methods. During an interval time of 30 days, n=76 consecutive confirmed COVID-19 patients were undergone to cardiovascular evaluation within 48 hours from admission to our hospital. Twelve-standard electrocardiogram (ECG), high-sensitive Troponin and FoCUS evaluation by portable ultrasound were performed integrated by further test if clinically indicated. Baseline characteristic, arterial-blood gas, blood test, chest computed tomography and treatment were recorded. CD was defined as the occurrence of a new cardiovascular disease during the hospitalization for COVID-19.

Results. On the overall cohort 28% had CD. A final diagnosis was reached in 13 patients: acute myocarditis (n=7) and pericarditis (n=2), acute pulmonary embolism (n=2), Takotsubo syndrome (n=1), myocardial infarction (n=1). Ventricular dysfunction was identified in other 8 patients but further test could not be performed due to instable condition/death, acute renal failure, patients refusal. Death occurred more often in patients

presenting with CD compared to patients without CD (29% versus 5%, p=0.011).

Conclusions. Systematic cardiac evaluation during hospitalization for COVID-19 revealed the occurrence of a wide spectrum of cardiac conditions. Death occurred more often in patients with cardiovascular condition. FoCUS scan was easy and quick to perform and useful to screen patients requiring further test.

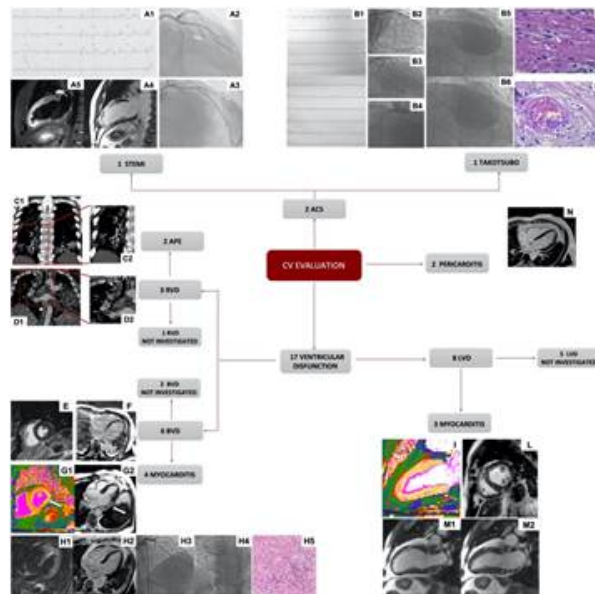


Figure 1. Summary of cardiovascular events occurred during COVID-19 hospital admission.

A247: AGGRESSIVE, MULTISITE VASCULAR COMPLICATIONS IN COVID-19 INFECTION: A CASE REPORT

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Background. COVID-19 has relevant cardiovascular implications, and patients with previous cardiovascular disease display an higher risk for detrimental outcomes.

Case presentation. A 68-year-old female patient was admitted to the emergency department complaining fever (38°C) for seven days, dyspnea and neurological deficit (aphasia and hemiplegia). Her past medical history was characterized by hypertension, bilateral carotid and mild peripheral artery disease (PAD). Home drug therapy was: aspirin and beta-blocker. Chest X-ray showed an infiltrative opacity and interstitial thickening prevalent on the inferior left lung. A nasopharyngeal swab was obtained resulting positive for SARS-CoV-2. Head CT showed acute lacunar infarction in the temporal right region. The day after, an electrocardiogram showed a postero-lateral myocardial infarction (MI) with ST elevation (STEMI for single-vessel arterial occlusion) which required urgent intervention (percutaneous coronary intervention (PCI) using drug-eluting stents (DES) on circumflex coronary artery). Blood tests showed: myoglobin 449.0 ng/mL; Hs-troponin I 2406.0 pg/mL; aPTT 37 SEC; PT/INR 1.22, CK MB 23.50 ng/dL; BNP 1292.0 pg/dL. After few days, lower limb PAD showed a very critical progression to necrosis of the feet (more relevant on the right foot) who required a partial amputation of the right foot. After 1 month, the patient experienced a moderate recovery with a substantial resolution of pneumonia.

Conclusion. SARS-CoV-2 induces blood hypercoagulability and severe inflammation, thus leading to an increased risk of vascular injury and thrombosis.

A248: STEMI IN THE LOCKDOWN PERIOD: FIRST OUTCOMES FROM ITALIAN REAL-WORLD COVID-19

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Background. The aim of our study is to evaluate the impact on ST-segment elevation myocardial infarction (STEMI) care during coronavirus disease 2019 (COVID-19) pandemic, through the analysis of cases of patients with STEMI who underwent percutaneous coronary intervention (PCI) at our department.

Methods. We performed an observational study on early data collected during social restrictions of Italian Government in our PCI center with 24/7 on-site interventional cardiologist availability. All consecutive patients affected by STEMI, from March, 9 to May, 4 2020, were collected and compared with STEMI treated during the same period of 2019.

Results. During the lockdown, we observed a 55% reduction of STEMI patients admitted to our catheterization laboratory, when compared to the same period of 2019 (26 vs 47 patients). Changes in all time components of STEMI care were notably observed, particularly for longer median times of symptom-to-first medical contact [382 minutes (IQR 63.2–1440) vs 96.5 minutes (IQR 62.2–212), $p=0,019$]. Procedural data and in-hospital outcomes were similar between the two groups, while the length of hospitalization was longer in patients of 2020 [6 days (IQR 5–8) vs 5 days (IQR 4–6), $p=0,003$]. In this group was also observed a worse left ventricular ejection fraction at baseline and discharge ($43\% \pm 9,5\%$ vs $47,4\% \pm 9,7\%$, $p=0,011$) ($45,1\% \pm 9,2\%$ vs $49,2\% \pm 9,6\%$, $p=0,013$).

Conclusions. COVID-19 outbreak induced a reduction of hospital access for STEMI with an increase in treatment delay, longer hospitalization and worse left ventricular function both at baseline and discharge.

A249: ACUTE COR PULMONALE IN A COHORT OF PATIENTS WITH COVID-19 RELATED ACUTE RESPIRATORY DISTRESS SYNDROME

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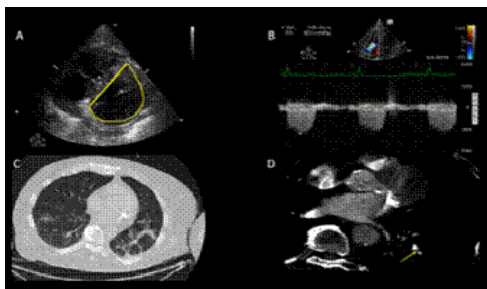
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Background. COVID-19 is often characterized by severe hypoxemia, regardless of respiratory system compliance, high rate of pulmonary thromboembolism and diffuse thrombosis of pulmonary microcirculation at necropsy. Although these mechanisms can conspire to determine rapid onset of right ventricle (RV) overload and failure, the impact of acute cor pulmonale (ACP) in severe COVID-19 is still unclear.

Methods. Between March 27 and April 23, 2020 all patients hospitalized in our ICUs with COVID-19 related acute respiratory distress syndrome (ARDS) underwent systematic echocardiographic evaluations. The presence of RV overload and paradoxical movement of the interventricular septum defined ACP. At every time point of examination we collected all available clinical, laboratory and respiratory parameters and evaluated potential association with ACP.

Results. We enrolled 27 consecutive patients (59% males), mean age 69 ± 13 years. The first trans-thoracic echocardiogram was performed at a median time from ICU admission of 6 days. Mean ICU stay was 22 ± 16 days. Each patient underwent a mean of 2.4 ± 0.9 echocardiographic examinations. ACP was diagnosed in 7/27 (26%) at first echocardiographic evaluation. At univariate analysis, elevated plasma D-dimer (OR 1.41, 95% CI 1.02-1.94; $p=0.04$) and troponin (OR 1.21, 95% CI 1.04-1.40; $p=0.01$) on ICU admission presented significant association with ACP. During the 30 day follow-up, 7/27 (26%) patients died, 4/7 (57%) with ACP and 3/20 (15%) without ACP. Mortality was significantly higher in patients with ACP than in the other patients ($p=0.048$). During the follow-up, we did not observe any further ACP onset or worsening right ventricular function in non-ACP patients.

Conclusions. Transthoracic echocardiography may reveal ACP in a sizeable proportion of patients with COVID-19 related ARDS. In our cohort, ACP was associated with higher blood levels of D-dimer and troponin on ICU admission and with higher 30-days mortality as compared with ARDS patients without ACP.



A250: THE NEGATIVE IMPACT OF COVID-19 PANDEMIC FOR NON-COVID PATIENTS WITH ACUTE CORONARY SYNDROMES

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Background. Coronavirus disease-2019 (COVID-19) affects cardiovascular patients in various way, both directly, because patients with previous cardiovascular disease face excess risks of severe illness

and cardiovascular events, and indirectly, as demonstrated by the decline in the total number of hospitalizations, a decrease of primary percutaneous coronary intervention and a significantly longer median length of stay (LOS) in non-COVID patients admitted during the pandemic.

Objectives. The aim of this study is to assess the impact of COVID-19 pandemic on the management and outcomes of patients presenting with STEMI during the period of the Italian lockdown.

Methods. We conducted a retrospective analysis on non-COVID patients admitted in Policlinico A. Gemelli of Rome for STEMI during the Italian lock-down, from March 9th to May 3th 2020, making a comparison with the same period of 2019. We collected data about the delays between the onset of symptoms and the culprit lesion treatment (symptoms onset to first arrival to ED; ED arrival to first diagnosis by EKG; ED arrival to ED discharge; ED discharge to cath-lab arrival; cath-lab arrival to wire crossing; symptoms onset to wire crossing; arrival at PCI center to wire crossing) and about the in-hospital outcomes (MACEs).

Results. We reported a mild decrease in the number of hospitalization due to STE-ACS in 2020 (22) compared with 2019 (26) and a significant increase of in-hospital MACE in 2020 (27.3% vs 3.8%; $p=0.038$). No remarkable "patient delay" was observed in 2020 compared to 2019 (311 vs 216 minutes; $p=0.541$), but a significant prolongation of the time from patient arrival at PCI center to wire crossing (94 vs 196 minutes; $p=0.038$) was reported, due to the need to certainly assess the negativity to SARS-CoV-2. Interestingly, we did not report differences between 2020 and 2019 in LOS (7,5 vs 9,5 days; $p=0.395$).

Conclusions. Implementing STEMI chain of survival with adjunctive measures required by COVID-19 pandemic may negatively impact on the management of patients presenting with acute cardiovascular conditions. Prolongation of total ischemic time in non-covid patients is not justified and should be avoided, as it does not provide clinical advantage and, conversely, worsen clinical in-hospital (and probably out-hospital) outcomes.

A251: UNUSUAL STROKE DURING THE COVID-19 PANDEMIC

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During the coronavirus disease 2019 (COVID-19) pandemic there was a dramatic drop of admissions of patients with acute coronary syndrome. There are plenty of theories circulating as to what could possibly drove STEMI rates down during this pandemic: patient's reluctance to go to a hospital during COVID-19 outbreak, lack of availability of local doctors and overload of emergency systems. A 54 years old male man was admitted to emergency department because of brain stroke-related symptoms. The patient's sister called the emergency number reporting the brother didn't answer the phone and he was at least a week that was suffering of stomach-ache. She also reported that the patient refused to go to hospital because was afraid about COVID-19. At health staff arrival the patients showed global aphasia and right hemisindrome; head-neck CT scan revealed ischemic areas in right frontal lobe and left parietal lobe. The patient was negative at COVID-19 test. ECG revealed anterolateral ST elevation with associated diffuse Q-waves and extreme QRS axis deviation. Transthoracic echocardiography showed lateral and inferolateral akinesia, severely depress left ventricular function, hematic pericardial effusion and a laceration of medium segment of lateral wall of the left ventricle. Coronary angiography revealed 70% stenosis of proximal, 80% of medium tract of left descending anterior coronary, 80% of proximal circumflex coronary, occlusion of I° obtuse marginal artery (culprit lesion) and dominant right coronary artery with no-significative stenosis. The patient, after heart team's discussion, underwent to urgent heart surgery. During surgery hematic pericardial clot was removed and a blood clot with a small bleeding area was found on infero-lateral wall of left ventricle; was also performed a single coronary artery by-pass on left anterior descending coronary. This case shows an important and rare complication of STEMI. Although cases on myocardial wall rupture are widely reported in literature, must be considered that in this case the patient refused to went to hospital due to COVID-19 outbreak. This case may help to consider that during COVID-19 pandemic infection, some patients died because they refused to go to the hospital or seek for medical help. Also this case may highlight the importance of telemedicine: if there was a telemedicine service, this patients we consider that this patients could have contacted the doctor by phone and be encouraged to go to the hospital earlier.

A252: COVID-19 E TELEMEDICINA IN CARDIOLOGIA

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Introduzione. La telemedicina consiste nell'erogare servizi sanitari a distanza grazie all'utilizzo di strumenti informatici e di telecomunicazione. Essa trova impiego in diversi ambiti e, in modo significativo in cardiologia, dimostrando vantaggi in termini di anni di vita guadagnati, di qualità di vita del paziente e di cost-saving. Nel periodo attuale, la pandemia da SARS-

CoV-2 ha sollevato numerose problematiche nella gestione dei pazienti affetti da COVID-19, soprattutto in coloro che mostrano un rischio cardiovascolare elevato e che sono sottoposti alla terapia con farmaci antivirali, che si associa al rischio di complicanze aritmiche, indotte dall'allungamento dell'intervallo QT.

Obiettivo. L'obiettivo dello studio è quello di confrontare uno strumento di telemedicina per il monitoraggio dell'intervallo QT e di altri parametri, quali temperatura corporea, saturazione di ossigeno e pressione arteriosa, con i metodi di misurazione standard, che possa essere utilizzato per il monitoraggio domiciliare dei pazienti affetti da COVID-19.

Materiali e metodi. Il dispositivo utilizzato per lo studio è stato testato su 23 pazienti stabili, ricoverati presso il Dipartimento di Scienze Cliniche, Interne, Anestesiologiche e Cardiovascolari, del Policlinico Umberto I. Tramite il device è stato possibile ottenere un tracciato elettrocardiografico (ECG) in singola derivazione, da cui è stato misurato il QT e calcolato il QTc, la temperatura corporea, la saturazione di ossigeno (SpO₂) e la pressione arteriosa (PA) sistolica e diastolica. Gli stessi parametri sono stati misurati, sui medesimi pazienti, mediante le metodiche di misurazione standard e sono poi stati comparati.

Risultati. L'analisi statistica effettuata non ha mostrato una differenza significativa dei valori di intervallo RR, QT/QTc e di temperatura corporea, tra i due metodi di misurazione (QT: t=1,438, p=0,1646; QTc Bazett: t=1,438, p=0,1646; QTc Fridericia: t=1,398, p=0,1762; temperatura corporea: t=1,664, p=0,1103) mentre i valori di SpO₂ e di PA hanno mostrato una differenza significativa, tra i due metodi di misurazione (SpO₂: t=4,646, p=0,0001; PA sistolica: t=5,385, p<0,0001; PA diastolica: t=4,502, p=0,0002).

Conclusioni. I risultati ottenuti permettono di sostenere la correlazione tra i valori di intervallo QTc e temperatura corporea, rilevati dal nostro dispositivo, e quelli rilevati mediante le metodiche di misurazione standard. Inoltre, sebbene i valori di SpO₂ e di PA misurati con il dispositivo e, messi poi a confronto con i valori ottenuti tramite metodiche di misurazione standard, non siano statisticamente correlati, tendono a presentare un errore con un andamento noto e non casuale.

A253: ADMISSION QT INTERVAL AND HYDROXYCHLOROQUINE TREATMENT IN SARS-CoV-2 PATIENTS

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Objectives. During the SARS-CoV-2 outbreak, hydroxychloroquine (HCQ) has been suggested as an active antiviral agent, but iatrogenic effects were a warning for its large use in such patients. Early February, in the absence of international guidelines, we used HCQ for treating SARS-CoV-2 patients. The effects of this drug on QTc interval and incident arrhythmias were investigated between February and April 2020.

Methods. Among all patients admitted to hospital for confirmed SARS-CoV-2 disease HCQ treatment was established based on clinical needs and the absence of left bundle branch block, G6PD deficiency, congenital long QT, and basal QTc >550ms. HCQ was administered at a daily dose of 400-600 mg in selected patients, and ECG and clinical findings (heart rhythm, heart rate, QT and QT corrected, arrhythmic events) were measured on admission (T0), treatment course (T1) and at the end of drug administration (T2).

Results. A total of 76 patients, aged 69.3±15.4 years, were studied. Interstitial pneumonia was found in 84% of cases. On admission, prolonged QTc was detected in 30 frail patients (39%) at T0, who entered the control group together with another 16 patients unsuitable for HCQ. Overall, 30 patients were eligible to receive HCQ for a maximum of 10 days. In some case azithromycin was given in combination. QTc prolongation (>500ms in 4 cases) was seen in 50% of treated patients, but no serious arrhythmic events (except from premature ventricular beats) were encountered during and after the treatment.

Conclusions. In the present study population, the occurrence of QTc prolongation was observed in most frail patients admitted for SARS-CoV-2 infection before antiviral treatment. Fifty percent of HCQ recipients at a daily dose of 400-600 mg showed iatrogenic QTc prolongation, albeit no ventricular arrhythmias were observed. Though HCQ treatment has not been definitely demonstrated to be effective against SARS-CoV-2 infection, its use in our patient series was uneventful.

A254: CARDIAC POINT-OF-CARE ULTRASOUND IN HOSPITALIZED COVID-19 PATIENTS: FINDINGS AND ASSOCIATION WITH OUTCOME

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Aims. Cardiovascular involvement has been reported in hospitalized COVID-19 patients. Primary outcome was to describe cardiac point-of-care ultrasound (POCUS) findings in a COVID-19 cohort patients. Secondary outcomes were to assess the association between echocardiographic findings and intensity of care expressed by respiratory distress (RD) grade, as well as the length of hospital stay and all-cause in-hospital mortality.

Methods. We performed a retrospective, observational cohort study, including all COVID-19 patients admitted to a tertiary Italian university hospital undergoing cardiac POCUS, and stratified according to the degree of RD at examination.

Results. Of 138 patients included in our study, 38 (27.5%) had mild RD, 35 (25.4%) had moderate RD, and 65 (47.1%) had severe RD. Most common abnormalities were left ventricular (LV) hypertrophy (38.4%), mild pericardial effusion (35.6%) and right ventricular (RV) dilatation (26.8%) (Figure 1). LV and RV systolic dysfunction were rare (13.0% and 5.1%, respectively) (Figure 1). LV hypertrophy was more frequent in severe RD. No cardiac POCUS parameter was independently associated with in-hospital mortality, whereas RV dilatation was associated with longer hospital stay (Figure 2).

Conclusion. In COVID-19 patients, cardiac POCUS parameters independently associated with need for more intensive or longer care are LV hypertrophy and RV dilatation, respectively. LV and RV dysfunction are uncommon.

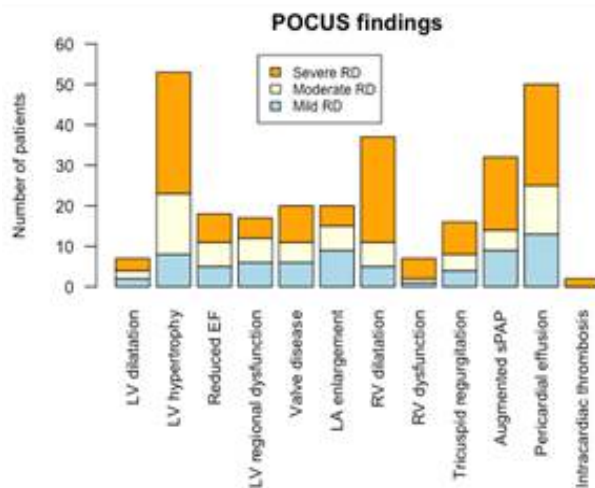


Figure 1

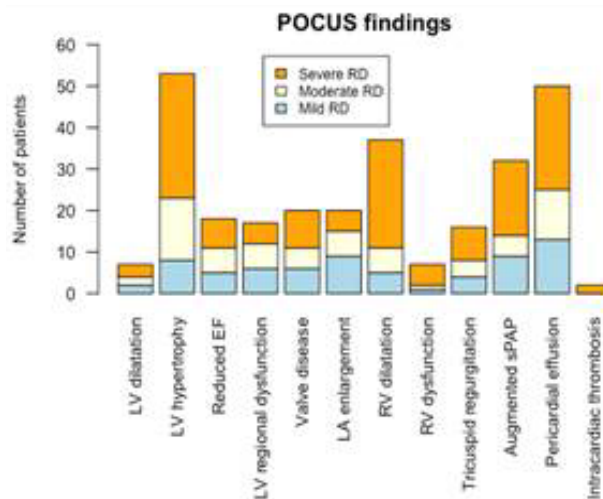


Figure 2

A255: PREVALENCE AND PROGNOSTIC VALUE OF AN INCREASE IN CARDIAC TROPONIN IN ELDERLY PATIENTS HOSPITALIZED FOR COVID-19

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Objective. An increase in cardiac troponin (cTn) in coronavirus disease 2019 has been associated with worse prognosis. Nonetheless, data about the significance of cTn in elderly subjects with COVID-19 are lacking.

Methods. From a registry of consecutive patients with laboratory-confirmed COVID-19 admitted to a hub hospital in Italy from 26/02 to 03/07/2020, we selected those ≥60 year-old and with cTn I (cTnI) measured within 3 days from the molecular diagnosis of COVID-19. When available, a second cTnI value within 48 hours was also extracted. The relationship between increased cTnI and all-cause in-hospital mortality was evaluated by a Cox regression model and restricted cubic spline functions with three knots.

Results. Of 343 included patients (median age 75.0 (68.0-83.0) years, 34.7% men), 88 (25.7%) had cTnI above the upper-reference limit (0.046 µg/L). Compared with subjects with normal cTnI, they had more comorbidities, more impaired respiratory exchanges and higher inflammatory markers on admission. Furthermore, they died more often (73.9% vs. 37.3%, p<0.001) over 15 (6-25) days of hospitalization (Figure 1). The association of elevated cTnI with mortality was confirmed by the adjusted Cox regression model (HR: 1.61, 95% CI: 1.06-2.52, p=0.039) and was linear until 0.3 µg/L, with a subsequent plateau (Figure 2). Of 191 (55.7%) patients with a second cTnI measurement, 49 (25.7%) had an increasing trend, which was not associated with mortality (univariate HR 1.39, 95% CI 0.87-2.22, p=0.265).

Conclusions. In elderly COVID-19 patients, an initial increase in cTn is common and predicts a higher risk of death. Serial cTn testing may not confer additional prognostic information.

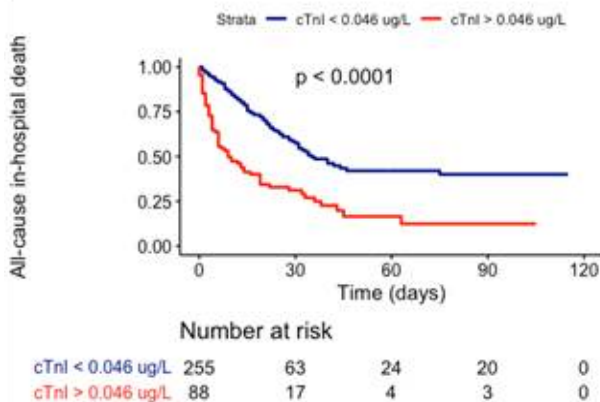


Figure 1

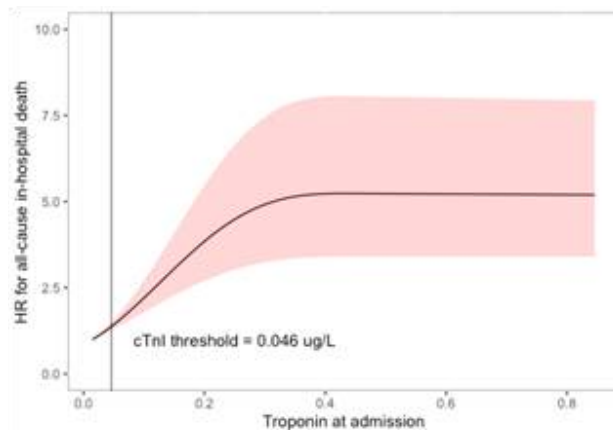


Figure 2

A256: PROSPECTIVE CARDIOPULMONARY STRESS TESTING EVALUATION OF NON-SEVERE COVID-19 PATIENTS AT THREE MONTHS AFTER HOSPITAL DISCHARGE

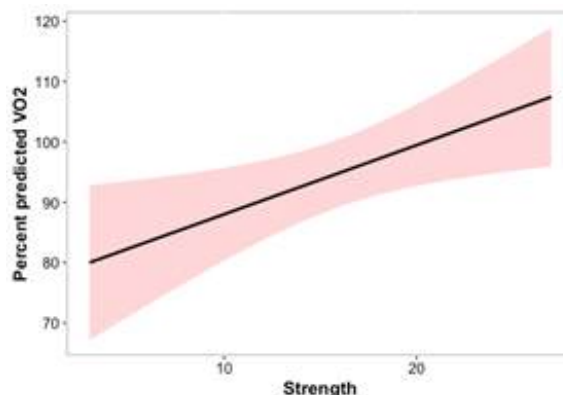
Vincenzo De Marzo (b, c), Piero Clavario (a), Roberta Lotti (b, c), Cristina Barbara (a), Annalisa Porcile (a), Carmelo Russo (a), Luigi Bottaro (a), Marta Caltabellotta (a), Arto Hautala (d), Roberta Della Bona (b, c), Marco Canepa (b, c), Pietro Ameri (b, c), Italo Porto (b, c)
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Background. Coronavirus disease 2019 (COVID-19) pandemic accounts for several millions confirmed cases. Long-term effects of this infection and their sustainability in a huge number of patients are of the utmost relevance. We sought to determine pulmonary, cardiac, and functional capacity of non-severe COVID-19 survivors by cardiopulmonary exercise testing (CPET), and also those characteristics associated to worse performance at CPET.

Methods. In a prospective study we included the first 100 consecutive subjects undergoing post-COVID-19 evaluation at the Outpatient Cardiac Rehabilitation center of Genoa, Italy. The local healthcare authority (Azienda Sanitaria Locale, ASL 3 Genovese) set up a structured follow-up program for all patients with a history of laboratory-confirmed COVID-19, admitted to ASL 3 COVID-19 wards from 1st of March 2020 to date (recruitment is still ongoing). As we focused on non-critical cases, we excluded those who needed invasive ventilation during hospital stay. We also excluded those patients with lack of data on hospital stay and those unable to perform CPET. At 3 months from COVID-19 diagnosis, all patients received complete clinical evaluation, trans-thoracic echocardiography, maximal CPET, pulmonary function test (PFT), and dominant leg extension (DLE) maximal strength evaluation.

Results. After exclusion of severe cases and incomplete/missing data, 75 patients were included in the final analysis. Median age was 58.8 (52.0-68.8) years, 28 (37.3%) were female. Median percent predicted oxygen uptake (%VO₂) was 90.7 (78.9-109.0)%. Twenty-seven (36.0%) patients had %VO₂ below, whereas 48 (64.0%) above the 85% predicted value (indicating normality). At PFT, median FEV₁, FVC, and DLCO were all within normal limits. Seven patients (25.9%) had a mainly respiratory, 3 (11.1%) a mainly cardiac, 1 (3.7%) a mixed cardiopulmonary, and 16 (59.3%) a non-cardiopulmonary limitation of exercise. At multivariate linear regression analysis, only DLE maximal strength (β=1.90, p=0.037) and active smoke (β=-7.02, p=0.041) were independently associated with %VO₂.

Conclusions. More than 1/3rd of non-severe COVID-19 survivors show exercise capacity limitation at CPET that could be mainly explained by muscular impairment, albeit cardiopulmonary causes are possible. These findings lay the foundation for future research to identify patients at higher risk of long-term effects which may benefit from careful surveillance and targeted rehabilitation programs.



A257: ELECTROCARDIOGRAPHIC FINDINGS AT PRESENTATION AND CLINICAL OUTCOME IN PATIENTS WITH SARS-CoV-2 INFECTION

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Background. The main severe complications of SARS-CoV-2 infection are pneumonia and distress respiratory syndrome. Recent studies, however, reported that cardiac injury, as assessed by troponin levels, is

associated with a worse outcome in these patients. No study hitherto assessed whether the simple standard electrocardiogram (ECG) may be helpful for risk stratification in these patients.

Methods. We studied 324 consecutive patients admitted to our Emergency Department with a confirmed diagnosis of SARS-CoV-2 infection. Standard 12-lead ECG recorded on admission was assessed for cardiac rhythm and rate, atrio-ventricular and intra-ventricular conduction, abnormal Q/QS wave, ST segment and T wave changes, corrected QT interval and tachyarrhythmias.

Results. At a mean follow-up of 31 ± 11 days, 44 deaths occurred (13.6%). Most ECG variables were significantly associated with mortality, including atrial fibrillation ($p=0.002$), increasing heart rate ($p=0.002$), presence of LBBB ($p<0.001$), QRS duration ($p<0.001$), a QRS duration ≥ 110 ms ($p<0.001$), ST segment depression ($p<0.001$), abnormal Q/QS wave ($p=0.034$), PVCs ($p=0.051$) and presence of any ECG abnormality (HR 4.58; 95% CI 2.40-8.76; $p<0.001$). At multivariable analysis, QRS duration ($p=0.002$), QRS duration ≥ 110 ms ($p=0.03$), LBBB ($p=0.014$) and presence of any ECG abnormality ($p=0.04$) maintained a significant independent association with mortality.

Conclusion. Our data show that standard ECG can be helpful for an initial risk stratification of patients admitted for SARS-CoV-2 infectious disease.

A258: COMPARISON OF ELECTROCARDIOGRAPHIC FINDINGS AND CLINICAL OUTCOME IN PATIENTS WITH COVID-19 OR OTHER RESPIRATORY INFECTIOUS DISEASE

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Background. The coronavirus SARS-CoV-2 is causing a pandemic outbreak of severe respiratory disease. Some studies showed that coronavirus disease (COVID-19) is associated with myocardial injury in 20-25% of hospitalized patients. However, whether the prevalence of cardiac involvement is increased in these patients compared to other infectious respiratory diseases is unknown.

Methods. We studied 556 consecutive patients admitted to our Emergency Department with an acute respiratory infectious disease. 324 of whom were diagnosed to have SARS-CoV-2 infection (COVID-19 group) and 232 other kinds of infectious respiratory disease (no-COVID-19 group). Standard 12-lead electrocardiogram (ECG) recorded on admission was assessed for cardiac rhythm, atrio-ventricular and intra-ventricular conduction, abnormal Q/QS wave, ST segment and T wave changes, corrected QT (cQT) interval and tachyarrhythmias.

Results. Overall, any ECG abnormality was found in 120 COVID-19 patients (37%) and 101 (43.5%) no-COVID-19 patients ($p=0.13$). Atrial fibrillation was present in 6.2% and 12.1% of patients in COVID-19 and no-COVID-19 group respectively ($p=0.021$). QRS duration was similar in the 2 groups ($p=0.62$), but there was a higher prevalence of left bundle branch blocks in no-COVID-19 group (1.9% vs. 6%, $p=0.011$). The prevalence of premature supraventricular complexes was lower among COVID-19 patients ($p=0.029$), whereas the prevalence of premature ventricular complexes ($p=0.42$), prolonged cQT interval ($p=0.43$), ST-segment depression ≥ 0.5 mm ($p=0.68$) or ≥ 1 mm ($p=0.13$) and T wave inversion ($p=1.00$) did not differ between the 2 groups. However, no differences in ECG variables were found between the 2 groups in a comparison of propensity score matched subgroups of 336 patients (168 in each group). During a follow-up of 45 ± 16 days, 51 deaths (15.7%) occurred in the COVID-19 group and 30 (12.9%) in the no-COVID-19 group. QRS duration ($p=0.016$), ST segment depression ≥ 0.5 mm ($p=0.016$) and the presence of any ECG abnormality ($p=0.027$) maintained a significant association with mortality at multivariable analysis. In the propensity score matched cohort, mortality was significantly higher in COVID-19 patients (23.2% versus 13.7%; HR 1.76; $p=0.032$).

Conclusions. Our data show that standard ECG does not show significant different rates of abnormal findings in patients with COVID-19 compared to those with other kinds of acute infectious respiratory disease. Among patients with an acute respiratory illness an abnormal ECG and, in particular, the presence of ST-segment depression on admission identify a population at increased risk of in-hospital death.

A259: PULMONARY EMBOLISM AS FIRST MANIFESTATION IN NON-SEVERE COVID-19

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Introduction. A typical clinical manifestation of COVID-19 is pneumonia. Fever is the most common presentation, followed by cough and dyspnoea. Patients could also present tachycardia, hemogasanalysis alterations and increased D-dimer levels. Recent studies have reported that COVID-19 is often accompanied by coagulopathy, and a significant number of patients with severe or critical COVID-19 develop concomitant

thrombosis, including pulmonary embolism (PE). Here, we report a case of pulmonary embolism as first clinical presentation of non-severe COVID-19 in a woman without any risk of thrombosis.

Case report. A 49-year-old female, in treatment with low dose beta-blockers for mild hypertension, was admitted to the Emergency Department for an atypical, dorsal, stinging chest pain, without fever neither cough nor dyspnoea. She had no risk factors for venous thromboembolism. An ECG showed sinus tachycardia with non-specific repolarization abnormalities. Laboratory data showed no lymphopenia, normal kidney and liver function, normal serum electrolytes, negative troponin, minimal elevation of CRP and a significant increase of D-dimer levels (3484 ng/ml FEU). A contrast chest computed tomography scan was performed and revealed endoluminal filling defects affecting the bilateral lower lobar branches of the pulmonary artery. Moreover, ground glass areas were described in the basal back of the lungs due to interstitial inflammation. Oropharyngeal swab was performed and tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Therapeutic dosage of low molecular weight heparin (LMWH) was administered and, at the same time, antiviral therapy with darunavir/cobicistat and hydroxychloroquine have been started. A Doppler examination of the lower limbs revealed no thrombi in the deep venous circle. Doppler echocardiography showed no signs of increased right ventricular pressure. Screening tests for autoimmune disease and congenital coagulation abnormalities, such as activated protein C, activated protein S, anti-double stranded DNA, antinuclear antibody, anti-cardiolipin- β 2-glycoprotein I complex antibody, and lupus anticoagulant were all negative. On day 7 post-admission, we replaced heparin with apixaban. D-dimer levels gradually decreased. During the hospitalization, the patient was treated with low flow oxygen, without need for non-invasive ventilation.

Conclusion. As demonstrated by this clinical case, pulmonary embolism can occur as first manifestation of SARS-CoV2 infection, also in patients with non-severe disease. For this reason, we believe that therapeutic doses of LMWH could be administered and possibly play a favorable role in preventing thrombotic complications. Hence, LMWH should be tested in randomized clinical trials in patients with COVID-19.

A260: OUT-OF-HOSPITAL CARDIAC ARREST IN THE COVID-19 ERA

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(a) U.O. CARDIOLOGIA OSPEDALE VALTIDONE AUSL PIACENZA; (b) OSPEDALE "G. DA SALICETO" PIACENZA

Introduction. The coronavirus disease 2019 (COVID-19) pandemic has affected health and economy worldwide. Adverse cardiovascular sequelae, such as myocarditis, acute myocardial infarction, heart failure and pulmonary embolism have been reported in patients with COVID-19, but it is unclear whether there is an association between Covid-19 and out-of-hospital cardiac arrest. Piacenza is a border town between Emilia Romagna and Lombardy, located near to the epicenter of the COVID-19 pandemic. Hence, it was the city most affected by COVID-19 in Emilia Romagna.

Aim. The aim of the study was to compare the occurrence of out-of-hospital-cardiac-arrest (OHCA) during COVID-19 pandemic with that of pre-COVID era.

Methods. Using the Progetto Vita Registry, we compared OHCA that occurred in Piacenza province during the first three months of COVID-19 outbreak (from February to April 2020) with those that occurred during the same period in 2019 (from February to April 2019). We collected data from the electronic database of the emergency medical system to identify patients affected by COVID-19, including both patients with symptoms suggestive of Sars-CoV-2 infection (history of fever before out-of-hospital cardiac arrest, with cough, dyspnea, or both) and patients with positive results of pharyngeal swabs test to detect SARS-CoV-2 obtained before the event or after death.

Results. From February to April 2020, 156 cases of OHCA were identified, as compared with 78 cases of the same period in 2019. Among patients with OHCA, we reported 68 cases of COVID-19. The 44.9% (n:70) of the population were women. Overall median age was 79.2 years (female: 83.5 years; male: 75.6 years). Demographic characteristics of patients were similar in 2020 and 2019. The median arrival time was 5.3 min longer in 2020 compared with 2019; the incidence of out-of-hospital death was 6.4% higher in 2020 than in 2019 and no one received cardiopulmonary resuscitation from bystanders in 2020. Initial cardiac rhythm was shockable in 6.4% (n:10) of patients in 2020 compared with 15.4% (n:12) in the same period of 2019.

Conclusion. During COVID-19 pandemic in Piacenza there was an increase in OHCA compared to the pre-COVID era. A total of 68 patients who experienced OHCA were suspected to have or had a diagnosis of COVID-19; these numbers account for 87.2% of the increase in cases of out-of-hospital cardiac arrest observed in Piacenza in 2020. This may be mainly due to an increased number of acute thromboembolic events occurred during COVID pandemic. Anticoagulant therapy should be considered in COVID-19 patients and the evaluation of D-Dimer could guide patient selection for this therapy.

A261: HOSPITAL MORTALITY AND SAFETY OF THERAPEUTIC VS. PROPHYLACTIC DOSES OF LOW MOLECULAR WEIGHT HEPARIN IN COVID-19 PATIENTS

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(a) CARDIOLOGY UNIT, EMERGENCY DEPARTMENT, CASTEL SAN GIOVANNI HOSPITAL, AUSL PIACENZA; (b) PLASTIC SURGERY UNIT, CASTEL SAN GIOVANNI HOSPITAL, AUSL PIACENZA; (c) EMERGENCY CARE UNIT, CASTEL SAN GIOVANNI HOSPITAL, AUSL PIACENZA; (d) RESPIRATORY INTENSIVE CARE UNIT, CASTEL SAN GIOVANNI HOSPITAL AUSL PIACENZA; (e) ORTHOPEDIC UNIT, CASTEL SAN GIOVANNI HOSPITAL, AUSL PIACENZA; (f) GENERAL MEDICINE UNIT, CASTEL SAN GIOVANNI HOSPITAL, AUSL PIACENZA; (g) DISES AND DSS, UNIVERSITÀ CATTOLICA DEL S.CUORE, PIACENZA; (h) DEPARTMENT OF TRANSLATIONAL AND PRECISION MEDICINE, SAPIENZA UNIVERSITY, ROME; (i) DEPARTMENT OF BIOMEDICAL AND NEUROMOTOR SCIENCE, ALMA MATER STUDIORUM UNIVERSITY, BOLOGNA

Objective. To compare the hospital mortality of COVID-19 patients treated with low molecular weight heparin, administered at prophylactic dose (P-LMWH) or at therapeutic dose (T-LMWH).

Design. Retrospective cohort study

Setting. Patients with COVID-19 pneumonia consecutively admitted to Castel San Giovanni COVID-Hospital from February 29, to April 7, 2020.

Main outcome measure. Hospital mortality.

Results. Of the 257 patients enrolled, 49 (19.1%) died during the hospitalization. Hospital mortality was significantly lower in patients treated with T-LMWH (17/126, 13.5%), compared with patients treated with P-LMWH (32/131, 24.4%; $\chi^2=4.98$, $p=0.02$). Crude and adjusted odds ratios of mortality for patients treated with T-LMWH were OR=0.483, 95% CI 0.252-0.923 and OR=0.374, 95% CI 0.177-0.792. In a stratified analysis by ventilation type, the only subgroup of patients who benefited from therapeutic doses of heparin were those receiving non-invasive mechanical ventilation (OR=0.099, 95% CI 0.028-0.354, $p<0.001$). No fatal bleedings were observed.

Conclusion. Treatment with therapeutic doses of LMWH is safe and reduces mortality in COVID-19 patients with severe pneumonia, especially among those who need non-invasive mechanical ventilation.

A262: EFFECTIVENESS OF HELMET CPAP TO REDUCE INTUBATION AND MORTALITY RATE IN PATIENTS WITH COVID-19

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Background. Effective respiratory support is crucial in the management of COVID-19. The objective of this study was to evaluate the effectiveness of helmet continuous positive airway pressure (CPAP) in reducing mortality and delaying mechanical ventilation.

Methods. Demographic and clinical records from patients admitted to Castel San Giovanni Hospital (Piacenza, Italy), with a confirmed COVID-19 diagnosis, between the 15th and 30th of March 2020, were analyzed.

Results. A total of 200 patients were included in the analysis, 78% were male, median age was 68.5 years, and 121 (69%) had at least 1 comorbidity. Of the 200 patients, 110 (55%) used only oxygen; 90 (45%) underwent CPAP treatment, 16 of whom (18.6%) were not compliant to CPAP (non-compliant group). In the subgroup compliant with CPAP, the need for intubation was slightly lower compared to the non-compliant group (33.3% vs 37.5%). A total of 32 (16.1%) patients died overall. The lowest mortality was in the CPAP-compliant group (8.3%) as compared to the non-compliant and no CPAP groups (68.8% and 13.4%, respectively). Mortality was higher in smokers (30%) and in obese patients (19.2%). The number of previous comorbidities had an impact on the mortality rate, especially for COPD, hypertension and malignancy.

Conclusion. This retrospective study indicated the effectiveness of helmet CPAP, in hospitalized patients with ARDS secondary to COVID-19, in reducing both mortality and the need for endotracheal intubation.

A263: L'EMERGENZA SANITARIA DA COVID-19 IN EMODINAMICA: ANALISI DEL CONTESTO, OSSERVAZIONI E SUGGERIMENTI PER IL TECNICO SANITARIO DI RADIOLOGIA MEDICA

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(a) ASL SALERNO - PO "SAN LUCA" VALLO DELLA LUCANIA; (b) SAINT CAMILLUS INTERNATIONAL UNIVERSITY OF HEALTH AND MEDICAL SCIENCES (UNICAMILLUS)

Obiettivi. Il lavoro presenta una raccolta sistemica delle indicazioni delle autorità al fine di fornire ulteriori chiarimenti e/o suggerimenti utili e chiari

al lavoro dei Tecnici sanitari di radiologia medica impegnati nei laboratori di emodinamica, al fine di migliorare, ottimizzare o razionalizzare, secondo la propria organizzazione (tecnologica, strutturale e di personale), le modalità operative, nel corso dell'emergenza sanitaria e comunque per garantire, in linea generale, un adeguato livello di sicurezza per i contagi in ambito nosocomiale.

Metodi. L'infarto è un evento altamente tempo-dipendente, in cui ogni minuto perso compromette il buon esito delle cure ed aumenta la mortalità. Nel periodo di emergenza si è registrato un ampio dimezzamento degli accessi nei Pronto soccorso (diretti o con chiamata al 118), per infarto del miocardio. È per questo indispensabile la definizione di appositi percorsi differenziati e protetti per i pazienti che, affetti da problemi cardiologici acuti, necessitano di assistenza in urgenza. Le differenti figure afferenti le sale di emodinamica, nella considerazione che un caso trattato in emodinamica, possa essere sospetto, probabile o confermato, è opportuno fornire indicazioni precise supportate da protocolli codificati, chi fa cosa e come, considerando anche il personale TSRM, afferente le sale di emodinamica, al fine di efficientare e sostenere la partecipazione alla prestazione con l'applicazione di tutte le misure di prevenzione e controllo delle infezioni del caso. Nel corso dei mesi di particolare emergenza il personale afferente è stato formato ed istruito, anche attraverso simulazioni, in maniera tale da garantire una migliore e perfetta performance dell'equipe nell'applicazione dei protocolli previsti

Risultati. Protocolli ben definiti e le simulazioni hanno garantito, nelle situazioni necessarie, una perfetta rispondenza del personale ad ogni aspetti di garanzia.

Conclusioni. L'ottimizzazione degli aspetti operativi, organizzativi e gestionali non possono essere esclusivamente diretti alle prestazioni di diagnosi e cura per i pazienti affetti da Covid-19, ma necessariamente, devono considerare anche il contenimento della trasmissione nosocomiale dell'infezione, preservando gli altri pazienti, l'ambiente e anche e soprattutto, gli operatori sanitari: uno dei principali valori su cui si fonda la strategia di risposta, per ridurre e combattere l'attuale pandemia. Una continua attenzione alla problematica, l'aggiornamento e la formazione sugli aspetti clinici, infettivologici e di igiene delle infezioni, l'istruzione e la formazione del personale sui comportamenti da utilizzare, le procedure da applicare e i dispositivi da utilizzare, nonché simulazioni e problem solving rappresentano elementi importanti per garantire sicurezza per gli operatori, l'ambiente ed i pazienti.

A264: IMPACT OF COVID-19 OUTBREAK ON WORKLOAD AND CASE-MIX IN A DEDICATED CMR LABORATORY

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Background. Cardiac magnetic resonance (CMR) is an extremely valuable imaging tool for diagnosis and monitoring of multiple cardiac conditions. During the spring of 2020, the rapid spreading of COVID-19 outbreak in Italy required political and societal responses that significantly affected social life, economy, and healthcare. During the worse phase of the outbreak, the entire national health service has been reshaped in order to manage the incident cases and be prepared to the new potential cases of COVID-19. CMR laboratories throughout the Country either completely stopped their clinical activity, with staff reassigned to other hospital activities, or performed only urgent scans, meaning those possibly impacting on the correct management of serious clinical entities. Aim of this study was to describe the characteristics of scanning activity performed during the period of national lockdown in a dedicated CMR laboratory.

Methods. From the general log-book of the CMR laboratory at Clinica Villa dei Fiori Acerra (Naples), operating in an Italian region only mildly involved by the outbreak, data about scanning activity as performed during the lockdown period (March-May 2020) were collected and compared with the level and type of activity in 2019 as a reference. We focused on the total number of exams performed, frequencies of clinical indications as well as modality of patient referral (inpatient vs outpatient).

Results. In 2019, the CMR laboratory performed a total of 889 exams, with the majority of them in an outpatient setting (75%) (Figure 1A). The most common clinical indications were cardiomyopathies (37%) and ischemic heart disease (27%, when including both acute and chronic presentation), followed by congenital heart diseases (13%) (Figure 1B). The relative prevalence of each clinical indication remains substantially unchanged when only the March-May 2019 period was considered. In the corresponding time period of 2019 (March-May), a significant reduction in the total number of performed scans was observed ($D=-47\%$). During the lockdown period in 2020, the inpatients accounted for 71% of all the CMR exams (Figure 2A), with the main clinical indications being acute cardiac conditions (44%, when including acute coronary syndrome, myocardial infarction with no coronary obstruction and myocarditis) and advanced heart failure from known or suspected cardiomyopathy (29%) (Figure 2B).

Conclusion. During the most acute phases of COVID-19 outbreak in Italy, CMR scanning activity was significantly impacted both in quantitative and qualitative terms. In agreement with specific SCMR scientific

recommendations, mostly urgent and acute clinical conditions led to the execution of a CMR exam during those months. More studies are needed to fully assess the short-term and long-term impact of this pandemic on the patterns of use of advanced cardiovascular imaging and consequences on clinical management of cardiac patients.

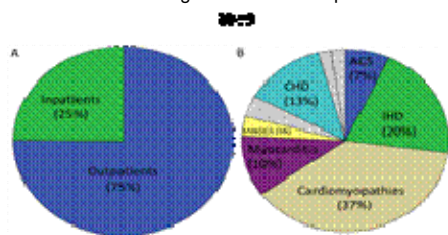


Figure 1

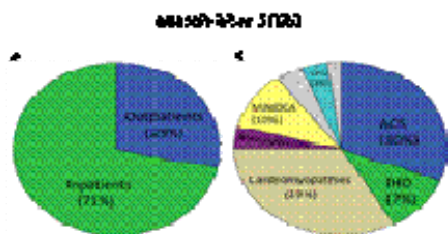


Figure 2

A265: COVID-19-RELATED ARRHYTHMIC STORM AS EARLY MANIFESTATION OF THE INFECTION: A CASE REPORT

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 (a) CARDIOLOGIA CLINICA ED INTERVENTISTICA - AZIENDA OSPEDALIERA UNIVERSITARIA DI SASSARI

Background. Cardiovascular manifestations of COVID-19 are mainly related to thrombotic complications induced by the viral infection. However, some epidemiological report suggests a role of COVID-19-related electrical instability as a contributor to the disease's mortality. This electrical vulnerability could be even more evident in patients with previous coronary artery disease, as occurred in the case here reported.

Case presentation. A 63-year-old man was admitted in March 2020 in our hospital for chest pain and ECG manifestation of extensive anterior STEMI and hemodynamic instability. His past medical history was remarkable for arterial hypertension, type-1 diabetes mellitus and dyslipidemia. Immediate coronary angiography was performed, that showed diffuse coronary artery disease of the right coronary artery (*chronic total occlusion*), the left main trunk, and the origin of anterior descending (LAD) and circumflex arteries. The proximal circumflex artery and obtuse marginal branch were also involved. An emergency percutaneous coronary intervention was performed. After staged PTCI and multiple implantations of drug-eluting stents complete coronary revascularization was achieved. Transthoracic echocardiography, that in the acute phase showed extensive wall motion abnormalities with severe left ventricular systolic dysfunction (EF= 30%), after revascularization gradually improved (EF= 40%). In the following days, the clinical conditions were stable. A routine chest X-ray indicated no pleural effusion or pulmonary congestion. Arterial Blood Gas (ABG), without oxygen support, showed no impairment in gas exchanges; blood tests were also normal apart for blood glucose levels which remained unstable and substantially elevated despite appropriate insulin therapy. During the night of the day 10th, after admission, the patient reported dry cough and fever (37.5° C). No remarkable symptoms were reported in the day after. However, in the morning of the 12th day, the patient suddenly presented with a witnessed cardiac arrest. Cardiopulmonary resuscitation was promptly initiated and ventricular fibrillation (VF) was rapidly identified and treated with 200 Joules DC shock. However, cardiac rhythm rapidly degenerated to new repeated episodes of VF despite appropriate Advanced Cardiovascular Life Support protocol was promptly initiated. ABG showed no electrolytes imbalance. To rule out potential acute-stent-thrombosis as a cause of recurrent VF, an emergency coronary angiography was performed showing the patency of the implanted stents and a TIMI flow grade 3 in all the main coronary branches. The patient was in the same day tested positive for Sars-CoV-2 infection. In the next day, interstitial pneumonia appeared at a chest high-resolution computed tomography. In the following days the patient developed multi-organ failure and after recurrent episodes of VF refractory to therapy eventually died 18 days after initial admission.

Conclusions. This case confirms that electrical instability might severely complicate COVID-19 in the very early phases of the disease. The concomitant presence of previous cardiovascular disease might act as a facilitator for the occurrence of an arrhythmic storm. In the context of COVID-19 pandemic, if the infection is suspected or proved, we suggest

that a 24h ECG monitoring should be considered in patients with established cardiovascular diseases.

A266: ACUTE MYOCARDIAL INFARCTION IN AN ASYMPTOMATIC PATIENT IN SUBACUTE PHASE OF SARS-CoV-2 DISEASE: A CASE REPORT

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Background. The clinical manifestations of SARS-CoV-2 infection are mostly dominated by respiratory tract symptoms, but the cardiovascular complications increase risk of morbidity and mortality in these patients. SARS-CoV-2-related cardiac involvement is mostly described in patients with cardiovascular risk factors and in the acute phase of viral disease.

Case report. A 43-year-old man, who had SARS-CoV-2 viral syndrome two months before, without cardiovascular risk factors, was admitted to our emergency department for acute chest pain and shortness of breath. At admission, he still tested positive for Covid-19, despite complete regression of typical SARS-CoV-2 viral syndrome 30 days before. His hemodynamic parameters showed a regular heart rate of 85 beats/minute and blood pressure of 110/80 mmHg. The electrocardiogram showed an anterior ST-elevation myocardial infarction (STEMI). The patient was immediately addressed to cathlab for primary percutaneous coronary intervention (pPCI). The invasive coronary angiogram revealed a proximal occlusion of left descending coronary artery, with other coronary vessels free of atherosclerotic disease. After recanalization of the culprit vessel, an elevated thrombotic burden was found requiring aspiration of the thrombus, successfully performed. Then, a biolimus eluting stenting (3.00x24mm) was implanted with a TIMI 2 flow recorded after the procedure. An echocardiogram revealed a mildly depressed left ventricular systolic function with an ejection fraction of 45% with hypokinesia of apex and mid-distal anterior wall. In-hospital permanence was free of any complication and the patient was eventually discharged after 7 days, with negative naso/oropharyngeal swab for SARS-CoV-2.

Conclusions. Acute coronary syndrome is a possible late complication of paucisymptomatic SARS-CoV-2 disease. Immediate diagnosis of myocardial infarction is crucial in suspected COVID-19 patients, even in patients without classic cardiovascular risk factors. Monitoring these patients in the late asymptomatic phase of the infection may be useful to detect early sign or symptoms of any cardiovascular complications. A longer-term antithrombotic treatment also in patient without critical symptoms of COVID-19 may be suggested to prevent thrombotic complications.

A267: ATRIAL FIBRILLATION IN COVID-19: AN ASSOCIATION WITH IN-HOSPITAL MORTALITY

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Background. Pneumonia caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection and its' related disease (COVID-19) emerged in Wuhan City, Hubei Province, China in December 2019. Among the most vulnerable and frail, those with a history of coronary artery disease (CAD), hypertension, heart failure, history of stroke/TIA. In this study we focused specifically on those presenting with atrial fibrillation (AF) as primary comorbidity, since AF and COVID-19 share some critical risk factors.

Methods. We prospectively collected data from patients admitted to Careggi University Hospital, Florence, from March 3rd to July 18th with COVID-19 diagnosis. Variables assessed on hospital admission included: demographics, number of drugs prescribed, cardiovascular (CV) risk factors. Arterial blood gases, laboratory findings and chest-x-ray were collected as well. AF was defined according to current guidelines. Aim of the study was to compare patients' characteristics by presence or absence of AF, to assess the association of AF with survival status (mortality vs. discharge from hospital) and determine its predictors.

Results. Of 318 enrolled patients, 62 (19.5%) had a history of AF both before and during hospital stay. We observed that patients in the AF group were older (78±11 vs. 65±15 years, p<0.001), were prescribed with more drugs (6.6±3.6 vs. 3.1±3.1, p<0.001), had more comorbidities (5.1±2 vs. 2.6±2.1, p<0.001). In addition, patients with an history of AF, shown higher CV-risk profile, with significant higher prevalence of hypertension (74.2% vs. 50.4%, p<0.001), CAD (45.2% vs. 17.4%, p<0.001), heart failure (46.8% vs. 16.4%, p<0.001) and history of stroke/TIA (22.6% vs. 8.2%, p<0.001). Patients with AF presented with a cancer history more frequently and had a higher prevalence of cognitive decline (36.1% vs. 15.7%, p<0.001). Among laboratory findings, patients with AF had lower levels of lymphocytes, higher creatinine levels (1.5 vs 1.1 mg/dL, p<0.001), LDH (430.3 vs. 325.8U/L, p<0.001), C-reactive protein (CRP,

113.4 vs 83mg/L) and aPTT. The most important differences between the two populations were reported in the destination at discharge and in-hospital mortality.

Mortality rate was higher in AF patients (36.1 vs 14.1%, p<0.001). AF patients were discharged towards a rehabilitation facility more frequently (16.4 vs 11.3%, p<0.05). Baseline independent predictors of AF were age (OR:1.04 95% CI 1.01-1.08, p=0.008), number of comorbidities (OR:1.41 95% CI 1.21-1.64, p=0.001), CRP (OR:1.01 95% CI 1.01-1.02, p=0.035) and aPTT (OR:1.11 95% CI 1.04-1.18, p=0.002)

Conclusion. AF is common in COVID-19 patients and is associated with worse outcome. Given the similar risk factors between AF and COVID-19, AF should be regarded as a synergistic and precipitating factor which should warrant prompt and specific care.

A268: GIANT RIGHT VENTRICULAR THROMBUS AND COVID-19: A BAD LUCK CASE?

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We describe the case of a 49-year-old woman hospitalized for COVID-19-related bilateral interstitial pneumonia with severe adult respiratory distress syndrome.

Chest CT scan performed in emergency department showed a large mass in the right ventricle, bilateral peripheral pulmonary embolism and extensive ground-glass opacifications involving both lungs (Fig. 1). The patient was admitted to our sub-intensive care unit and treatment with lopinavir/ritonavir, hydroxychloroquine and continuous positive airway pressure was immediately started. Trans-thoracic echocardiography confirmed a floating mass in the right ventricle, which diameters were about 27 x 12 mm (Fig. 2). RV size and function were normal and systolic pulmonary arterial pressure was 60 mmHg. Surgery was contraindicated because of pneumonia and unfractionated heparin infusion was started. The following day we performed a cardiac magnetic resonance that confirmed the presence of a mass consistent with thrombosis. Since the patient was hemodynamically stable but became intolerant to the continuous intravenous infusion, we switched UH to dabigatran 150 mg bid. Echocardiography performed at 15 days (4 days after starting dabigatran) showed complete thrombus resolution. *Ex adiuvantibus* diagnosis of RV thrombosis was performed after thrombus resolution.

In conclusion, although thrombotic complications have been reported in COVID-19 patients, this case represents the first report of intracardiac COVID-19-related thrombosis. After 4 weeks of hospitalization, the patient was discharged at home in good general condition; no oxygen supplementation was needed and a 6-month treatment with dabigatran was prescribed.

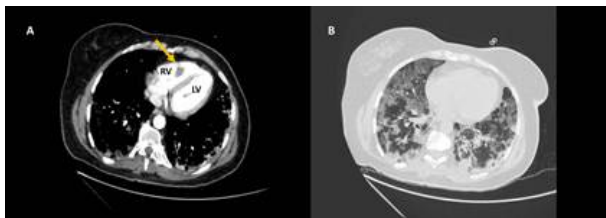


Figure 1

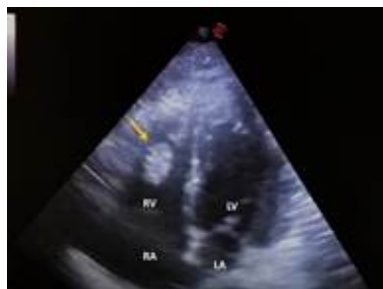


Figure 2

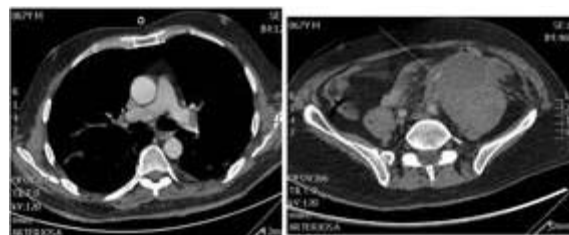
A269: A RARE AND SILENT CASE OF DISSEMINATED INTRAVASCULAR COAGULATION IN COVID-19 SEVERE PNEUMONIA

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A 67-year-old man admitted for COVID-19 bilateral pneumonia rapidly evolved in ARDS requiring CPAP support. He received antiretroviral therapy, hydroxychloroquine, dexamethasone, two tocilizumab doses in

addition to LMWH 75 IU/kg/die. On 10th day D-Dimer raised (105000 µg/l, ULN 500), right axillary venous thrombosis was detected, no right ventricle impairment was observed at echocardiography; dose of LMWH was doubled. Respiratory conditions were then getting better and CPAP support stopped. On 20th day of hospitalization patient presented acute lower abdominal pain with hypotension and sudden 3gr/dl hemoglobin loss. CT scan showed a voluminous psoas hematoma with active bleeding and bilateral pulmonary embolism (Figure). He underwent transcatheter embolization of three lumbar arteries with angiographic success, no further blood loss site identified. Few hours later he evolved into multi organ failure shock. Laboratory testing shown hemoglobin loss despite ongoing blood transfusion, normal platelet count, D-dimer 6500 µg/l with a trend toward reduction, mild fibrinogen reduction (115mg/dl), mild INR raise (1,9 from a range 1,2-1,7) and reduction in anti-thrombin (AT) III activity (45%), confirming disseminated intravascular coagulation diagnosis. Hemorrhagic shock support therapy was provided, including fresh frozen plasma and blood transfusions but patient died two days later.

In novel COVID-19 infection, coagulation disorder set off by inflammation are frequent and abnormal coagulation parameters are associated with poor prognosis. In these patients, DIC incidence seems to be 71,4% among deaths; haemorrhagic events are considered rare. To properly detect coagulopathy during sepsis the International Society of Thrombosis and Hemostasis (ISTH) guidelines recommends Sepsis-Induced-Coagulopathy (SIC) score considering: PT/INR, platelets count and presence of organ failure. In recent interim guidelines targeted to recognition and treatment of coagulopathy in COVID-19 patients, ISTH recommend to dose and monitoring: D-Dimer, PT, fibrinogen and platelet count, despite these last are often normal. SIC score performed during hospital stay for our patients was not significant (2 points: INR and respiratory impairment), daily measurements of platelets were not alarming, INR was slight constantly altered as often seen in COVID-19 severe infection and D-Dimer was in reduction after doubling LWWH dose for axillary thrombus. Despite these findings we observed a rare DIC with both thrombotic and hemorrhagic important manifestation, thus giving less diagnostic significance to proposed scores in COVID-19 patients. Major clinical manifestations then occurred, not responsive to conventional treatment.



CT scan images: (left) pulmonary bilateral embolism, (right) psoas hematoma.

A270: ACE-I AND ARBs DO NOT INFLUENCE THE CLINICAL AND CHEST CT PRESENTATION OF PATIENTS WITH COVID-19 AT THE ONSET OF DISEASE: AN ITALIAN MULTICENTER REGISTRY

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Background. In recent months every effort has been made to understand the possible interference of ACE-i or ARBs with ACE-2 receptor and SARS-CoV-2 pathway. Observational studies have shown no clinical impact of home therapy with ACE-i or ARBs on COVID-19, however these drugs are often discontinued upon hospitalization or diagnosis.

Objectives. To evaluate the influence of home therapy with RAAS inhibitors on the chest CT severity score and clinical presentation within 24 hours of diagnosis of SARS-CoV-2 infection, before stopping medications or starting specific therapy for COVID-19.

Methods. This is a multicenter, retrospective observational study. All admitted patients diagnosed with SARS-CoV-2 infection who performed chest CT within 24 hours of arrival were consecutively enrolled from March 1 to June 1, 2020. A severity score was attributed to Chest CT by two radiologists in blind to the patient's clinical information and, as validated by Ran Yang et al., a cut-off of 19.5 was considered to define severe radiological pneumonia.

Results. We included 593 patients and 156 were on home therapy with ACE-i/ARBs. In the ACE-i/ARBs group 95% of patients were hypertensive and there was a higher prevalence of diabetes mellitus (ACE-i/ARBs: 26.3% vs non-ACE-i/ARBs 11.3% p <0.01). Univariate and multivariate

analysis showed that home therapy with ACE-i, ARBs or ACE-i/ARBs were not associated with the risk of CT severity score ≥ 19.5 . Factors associated with CT score ≥ 19.5 were male sex (HR - 95% CI - p =), Diabetes mellitus (HR - 95% CI - p =), older age (HR - 95% CI - p =), the presence of dyspnoea and worse PF ratio on arrival were also associated with severe radiological pneumonia. Furthermore, therapy with ACE-i, ARBs, ACE-i / ARBs was not associated with the risk of a more severe clinical presentation on arrival in terms of fever, dyspnoea, P / F ratio or intestinal symptoms. Finally, the same was true for the outcome of COVID-19 in terms of death, intubation or non-invasive ventilation. The results were consistent in the subgroup with hypertension.

Conclusions. ACE-i and ARBs do not influence the clinical and chest CT presentation of patients with COVID-19 at the time of diagnosis, before discontinuation of therapy or hospitalization.

A271: RIGHT VENTRICULAR FUNCTION AND PULMONARY PRESSURES AS INDEPENDENT PREDICTORS OF SURVIVAL IN PATIENTS WITH COVID-19 PNEUMONIA

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Introduction. We sought to determine the possible association of right ventricular (RV) function and pulmonary pressures with mortality in patients with COVID-19 pneumonia.

Methods. We studied 115 consecutive patients (64.6 mean age, range 20-88 years; 40% female) with positive SARS-CoV-2 laboratory test results and TC-confirmed interstitial pneumonia. We defined cardiac injury as high sensitivity Troponin I (hs-TNI - ECLIA method) blood levels above the 99th-percentile upper reference limit. RV end-diastolic basal and mid tract diameters, tricuspid annular plane systolic excursion (TAPSE), pulmonary artery systolic pressure (PASP), mean pulmonary artery pressure (mPAP), tricuspid inflow E/A ratio and tricuspid regurgitation peak velocity (TRV) were assessed.

Results. A total of 26 out of 115 patients had cardiac injury (mean age 73.5), had more frequently systemic hypertension (61.5% vs 29.2%; $P < 0.001$), higher levels of C-reactive protein (mean 98.8 [45.8-130.4] vs 38.9 [22.2-96.3] mg·L⁻¹; $P < 0.001$) and of D-dimer (mean 4.8 [3.2-7.1] vs 2.1 [0.5-3.4] mg·L⁻¹; $P < 0.001$); multiple ground-glass opacities in CT-findings (69.2%/33.7%) and multiple consolidations by lung ultrasound (76.6%/38.2%) were found. LV-diameters and ejection fractions were comparable between the two groups. Conversely, RV end-diastolic basal tract (35.8±4.2 vs 31.2±2.6, $P < 0.01$) and mid tract (32.4±3.9 vs 28.6±3.7, $P < 0.01$), TRV (3.4±0.6 vs 2.9±0.5; $P < 0.001$) and mPAP (29.6±2.9 vs 23.6±2.7; $P < 0.001$) were significantly increased in patients with cardiac injury, while tricuspid inflow E/A ratio (0.77±0.5 vs 1.1±0.6; $P < 0.01$) and TAPSE (15.4±3.2 vs 20.3±4.7; $P < 0.001$) were reduced. Patients with cardiac injury had a higher mortality than those without cardiac injury (50%/7.8%; $P < 0.0001$).

Conclusions. Increase of mPAP and RV dysfunction are associated with higher risk of in-hospital mortality in patients with COVID-19 pneumonia and cardiac injury.

A272: ATRIAL FIBRILLATION IN A PATIENT PRESENTING WITH CORONAVIRUS DISEASE-2019 (COVID-19) INFECTION

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SARS-CoV-2 is a novel virus that has spread rapidly throughout the world causing a potentially life-threatening disease, COVID-19, causing disproportionately high mortality among elderly patients with concomitant pulmonary and cardiovascular diseases. The clinical cardiovascular manifestations of covid-19 include elevation of cardiac biomarkers (ischaemic or non-ischaemic aetiology), cardiac arrhythmia, arterial and venous thromboembolism (VTE), and cardiogenic shock and arrest. Multiple mechanisms have been proposed to explain influenza triggering arrhythmias, among them severe systemic, arterial, and myocardial inflammatory reaction seems to be one of the most plausible. In patients with underlying ischemic cardiomyopathy, the worsening of ischemia by increased oxygen demand and potential acute coronary syndromes led by influenza can also have a role in the increase of arrhythmic events. Furthermore, the systemic inflammatory response would make anticoagulation therapy for atrial fibrillation very complex. Arrhythmia could be the first presentation of covid-19, and new-onset and/or progressive arrhythmia could indicate cardiac involvement. We describe the case of a male presenting with COVI-19 infection who experienced atrial fibrillation (AF) which resolved with rate and rhythm control strategies, and supportive care.

Case report. A 80-year-old male presented to the emergency room with a

symptom of fever, shortness of breath and cough over the preceding 4 days. His Vital signs indicated heart rate of 160 beats/minute blood pressures of 160/90 mmHg, respiratory rate of 32 breaths per minute with an oxygen saturation of 86% on room air. A 12-lead electrocardiogram revealed atrial fibrillation and rate-related ST-T segment changes. A chest radiograph did not reveal any acute cardiopulmonary disease. Diagnostic laboratory investigations revealed a high D-dimer 500 ng/dl and pro-BNP : 600 pg/mL, while cardiac biomarkers were normal. In this room he was initiated on a amiodarone an 1 digoxin bolus. In the interim, the patient's COVID-19 test was positive. He reverted to normal sinus rhythm within 48 hours. This patient revealed several electrolyte abnormalities, including hypokalemia, hypomagnesemia, all of which were aggressively repleted. Further observational studies are required to characterize the nature and classification of arrhythmias in this COVID-19 pandemic.

A273: EFFECTS OF COVID-19 ON CARDIOVASCULAR FELLOWSHIP IN ITALY

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Background. Italy has been the first European Country to be hit hard by the COVID-19 pandemic. It is probable that, in the midst of the emergency, the impact that the pandemic could have had on the training of cardiovascular fellows in training (FITs) has been overlooked.

Aim. To investigate the perception of cardiovascular FITs about the effects of COVID-19 pandemic on cardiological education in Italy.

Methods. A 23-item survey has been created on Google form and subsequently sent to 1443 Italian cardiovascular Fellows in Training (FITs) registered on the database of the Italian Society of Cardiology (ISC). The participation was completely voluntary and the system has been set to avoid double entries.

Results. 633 FITs - 44% of the Italian FITs in cardiology- completed the survey. 24.5% of respondents have been employed in COVID-19 units and 95% affirmed that the cardiological training program (clinical activities, didactics or both) has been somewhat changed during the pandemic (Fig. 1A). For 61% of the FITs the COVID-19 had a negative effect on their education (Fig. 1B). Moreover, 59% of the respondents believe that they would not be able to completely fill the gap gained during that period over the rest of their training. The top five penalized aspects of cardiological education were frontal teaching, participation to scientific conferences, training in advanced echocardiography, circulation within the training network and the acquisition of skills on outpatient clinic care. Preferred activities during the lockdown were studying, working on research projects and learning about SARS-CoV-2 infection. Finally, a negative impact on psycho-physical well-being has been reported by 86% of the trainees.

Conclusion. This is the first European survey on the impact of Covid-19 on cardiological training. The results of our survey demonstrate that cardiological education has been severely compromised by the pandemic, pointing out the urge to adapt the current training programs to the new scenario, in order to guarantee safety but at the same time an adequate education of FITs during the COVID-19 era.

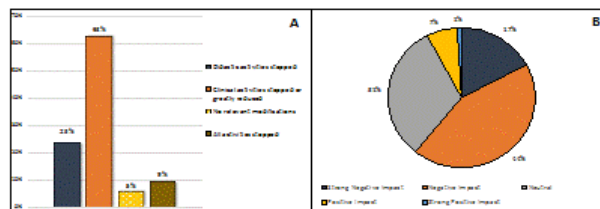


Figure 1. Impact of COVID-19 on cardiological education.

A274: IMPATTO DELLA SOMMINISTRAZIONE DEGLI INIBITORI DEL SISTEMA RENINA-ANGIOTENSINA SULLA SOPRAVVIVENZA IN PAZIENTI OSPEDALIZZATI PER INFEZIONE SARS COVID-19

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Introduzione. Il virus SARS-CoV-2 (COVID-19) utilizza il recettore dell'enzima di conversione dell'angiotensina-2 (ACE-2) per entrare nelle cellule umane. La ridotta espressione di ACE-2 nella polmonite indotta dal virus può svolgere un ruolo nella patogenesi di un'infezione fatale. Sia gli inibitori dell'enzima di conversione dell'angiotensina (ACEI) che gli antagonisti del recettore dell'angiotensina II (ARB) sono associati a una sovra-regolazione dell'enzima ACE-2. È stato ipotizzato che l'uso antecedente di ACEI/ARB possa essere associato a mortalità nel COVID-19.

Metodi. Abbiamo utilizzato il registro CORACLE, che contiene i dati dei pazienti COVID-19 ospedalizzati in 4 regioni d'Italia restringendo le analisi a quelli di età ≥ 50 anni. Il COVID-19 è stato confermato mediante test con tampone nasale o faringeo e reazione a catena della polimerasi di trascrizione inversa in tempo reale. L'outcome primario era la mortalità intraospedaliera.

Risultati. Su un totale di 781 pazienti acuti con COVID-19, 133 (17,0%) stavano usando un ARB e 171 (21,9%) stavano usando un ACEI. Sebbene né il sesso né il fumo di sigaretta differissero in modo significativo nei rispettivi gruppi, i pazienti trattati con ACEI/ARB tendevano ad essere più anziani e con maggiori probabilità di essere affetti da ipertensione, diabete mellito e insufficienza cardiaca congestizia. Il tasso di mortalità complessivo è stato del 15,1% (118/781) ed è stata rilevata una tendenza all'aumento con l'età (P Trend $<0,0001$). Nel complesso, gli odds ratio grezzi per la morte di coloro che hanno utilizzato ACEI e coloro che hanno utilizzato ARB erano rispettivamente 0,98, IC 95%: 0,60-1,60, $p=0,9333$ e 1,13, IC 95%: 0,67-1,91, $p=0,6385$. Dopo aggiustamento per età, storia di ipertensione, diabete mellito e insufficienza cardiaca congestizia, la somministrazione di ACEI antecedente è stata associata ad una mortalità ridotta OR = 0,553, IC 95%: 0,311-0,983, $p=0,0436$, mentre l'utilizzo di ARB non era associato in modo significativo ad un aumento del rischio (OR: 0,586, IC 95%: 0,322-1,065, $p=0,0796$).

Conclusioni. Nei pazienti di età superiore ai 50 anni ospedalizzati con COVID-19, l'uso antecedente di ACEI è stato indipendentemente associato a un ridotto rischio di morte. I nostri risultati confermano il ruolo protettivo dell'inibizione del sistema ACE nei pazienti con alto rischio cardiovascolare affetti da COVID.

A275: PREVALENCE AND CHARACTERISTICS OF MYOCARDIAL INJURY DURING THE COVID-19 PANDEMIC

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Background. Coronavirus disease 2019 (COVID-19) is a pandemic disease that is causing a public health emergency due to its high rapid spread, to the high mortality rate, and the high percentage of patients requiring hospitalization and intensive care. According to limited information on cardiac complication of COVID-19, characteristics and clinical significance of myocardial injury remain unclear.

Purpose. In this study, we determined the pattern of high sensitivity

troponin elevation in patients affected by SARS-CoV-2 and the prevalence of myocardial injury in this population; furthermore, we investigated the predictive value of Hs-Tn on disease severity and mortality.

Methods. This retrospective single-center study analyzed all 758 patients in whom hs-TnI was determined in our hospital from 20 February 2020 to 09 April 2020. One hundred-eighty nine of these patients received SARS-CoV-2 diagnosis. Demographic data, laboratory findings, comorbidities, and treatments were collected and analyzed in patients with COVID-19.

Results. A total of 189 hospitalized patients with COVID-19 were included in the final analysis. The median age was 66 years old (SD 12) and 61 (32.35) were female. During the stay, a total of 28 patients (14.8%) needed admission in Intensive Care Unit and 32 patients (13.7%) died. The prevalence of myocardial injury in our COVID-19 population is of 16% (31 subjects out of 189). The patients with cardiac injury were older, and had a greater number of cardiovascular comorbidities, in particular history of hypertension and ischemic heart disease; in addition, they had higher values of acute phase and inflammatory markers and leucocytes. The patients with hs-TnI above the 99th percentile cut-off required more frequently hospitalization in ICU (10 [32.3%] vs 8 [11.4%]; $P = .003$) and the mortality rate was significantly higher (17 [54.8%] vs. 15 [9.5%], $p < 0.001$). A multiple regression analysis was carried out to investigate whether hs-TnI could significantly predict the degree of COVID-19 disease: hs-TnI and CRP contributed significantly to the model ($B = 0.525$, $p < 0.001$; $B = 0.001$, $p = .020$, respectively). In addition, we included 189 patients with complete data for all variables (32 non-survivors and 151 survivors) in the multivariable logistic regression model. We found that hs-Tn at admission, older age and CRP levels were associated with increased odds of death.

Conclusions. Myocardial injury is prevalent in patients affected by SARS-CoV-2 and the patients with hs-Tn value above the upper reference limit are older and had a greater number of cardiovascular comorbidities. In this study we demonstrate a high positive predictive value of hs-Tn for disease severity and in-hospital death. Therefore, it may be reasonable to use high sensitivity troponin as a screening tool in COVID-19 population in order to triage them into high and low risk groups.

A276: FEASIBILITY OF REMOTE HOME MONITORING WITH A T-SHIRT WEARABLE DEVICE IN POST-RECOVERY COVID-19 PATIENTS

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Background and aim. During the last months, a pandemic by a novel coronavirus (Sars-Cov-2) has spread worldwide, putting hospitals under enormous pressure. Although follow-up data in this setting are scarce, early reports suggested that more than 80% of patients who had recovered from CoronaVirus Disease 19 (COVID-19) reported persistence of at least one symptom during follow-up, particularly fatigue and dyspnea. Therefore, a prolonged post-discharge monitoring for long-lasting effects is advisable. We assessed the feasibility of cardiorespiratory home monitoring through a wearable device in post-COVID-19 patients.

Methods. In this pilot study, we enrolled subjects with a confirmed diagnosis of COVID-19 after hospital discharge at home. A wearable device used (L.I.F.E.) (a technologically advanced T-Shirt device composed of ink-based dry electrodes linked to standard 12-lead ECG monitoring, 5 respiratory strain sensors, 1 accelerometer, a digital pulse oximeter) was used. Monitoring was carried out for at least 7 days and comprehended a two-hour monitoring period a day during rest and a short exercise (6 minutes of brisk walking) and an overnight sleep monitoring on the last day.

Results. Seventeen COVID-19 patients (male 8; age 54.4 ± 15.3 year old; BMI 25.1 ± 3.1) were enrolled at hospital discharge. They underwent 12.5 ± 2.5 (7-17) days of monitoring. Clinical characteristics of the population and data monitoring are shown in Table 1. Twelve patients (70.6%) performed the nighttime monitoring. Among them, one showed an apnea-hypopnea index (AHI) of 20, suggestive of moderate sleep apnea syndrome.

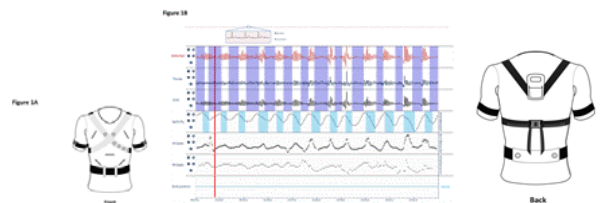


Table 1. Clinical characteristics and monitoring data of post-recovery COVID-19 patients

		Baseline (1 st Day)	Last Day of monitoring	p value
Clinical characteristics	Male sex	8 (47%)	-	-
	Age (years)	64.8 ± 13.8	-	-
	Weight (kg)	72.4 ± 13.2	-	-
	Height (cm)	169.1 ± 7.6	-	-
	BMI (kg/m ²)	25.0 ± 3.1	-	-
Rest parameters	Heart rate (bpm)	65.8 ± 12.8	65.8 ± 12.8	-
	HRV (ms)	64.4 ± 9.8	64.4 ± 9.8	-
	SpO ₂ (%)	97.1 ± 1.1	97.1 ± 1.1	-
	Respiratory rate (breath/min)	12.8 ± 2.3	12.8 ± 2.3	-
	Tidal volume (L/min)	0.71 ± 0.1	0.71 ± 0.1	-
	Ventilation (L/min)	12.9 ± 1.5	12.9 ± 1.5	-
	MIP (cmH ₂ O)	81.8 ± 18.2	81.8 ± 18.2	-
	MEP (cmH ₂ O)	82.6 ± 26.3	82.6 ± 26.3	-
	Heart rate (bpm)	170 ± 14	168 ± 16	0.349
	SpO ₂ (%)	97 ± 1	97 ± 1	0.132
Peak exercise parameters	VO ₂ (ml/min)	355.3 ± 54.2	320.9 ± 77.8	0.023
	VCO ₂ (ml/min)	298.5 ± 52.1	255.5 ± 72.3	0.017
	Respiratory rate (breath/min)	18.5 ± 3.2	15.2 ± 3.1	0.008
	Tidal volume (L/min)	0.71 ± 0.1	0.71 ± 0.2	0.918
	Ventilation (L/min)	12.9 ± 1.5	10.4 ± 1.8	0.001
	MIP (cmH ₂ O)	81.8 ± 18.2	83.3 ± 16.6	0.223
	MEP (cmH ₂ O)	82.6 ± 26.3	83.0 ± 23.8	0.915
	Heart rate (bpm)	170 ± 14	168 ± 16	0.349
	SpO ₂ (%)	97 ± 1	97 ± 1	0.132
	VO ₂ (ml/min/kg)	31.6 ± 7.1	27.5 ± 6.6	0.001
VCO ₂ (ml/min)	257.8 ± 75.6	221.7 ± 69.0	0.016	
VE/VCO ₂ slope	27.5 ± 3.7	28.1 ± 3.7	0.388	
Respiratory rate (breath/min)	45.5 ± 8.0	37.7 ± 5.5	0.041	
Tidal volume (L/min)	2.28 ± 0.7	2.05 ± 0.6	0.001	
Ventilation (L/min)	92.3 ± 26.0	76.2 ± 21.6	0.003	
MIP (cmH ₂ O)	80.6 ± 26.3	82.5 ± 23.0	0.457	
MEP (cmH ₂ O)	75.9 ± 18.2	81.0 ± 29.1	0.614	
RER	1.2 ± 0.1	1.2 ± 0.1	0.665	
Power (watt)	194 ± 37	187 ± 52	0.002	

Conclusions. Our study demonstrated that a post-discharge home monitoring program for COVID-19 patients is feasible and safe. The L.I.F.E. T-Shirt device was able to collect a full set of cardiorespiratory parameters (i.e. heart rate, a full ECG, respiratory rate, SpO₂), both at rest and during a brief exercise. Finally, we were able to identify only one patient without any previous disease who presented post-COVID sleep apnea syndrome. Further studies are certainly needed to assess the prevalence and the clinical impact of this complication in post-COVID-19 patients.

A277: "YOU CAN LEAVE YOUR MASK ON": EFFECTS ON CARDIOPULMONARY PARAMETERS OF DIFFERENT AIRWAY PROTECTION MASKS

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Background and aim. In December 2019, in the city of Wuhan (China), a potential new causative agent of pneumonia, called the new coronavirus 2019 (nCoV-2019) was identified. Since then, the need to contain the global spread of the infection has become urgent through specific social distancing procedures and through the use of individual protection devices (i.e. airway protection masks). In the media doubts were raised about the impact of different types of masks on daily physical activity, in particular for those who perform physical exercise. In this context, we aimed to evaluate cardiorespiratory parameters, assessable through a cardiopulmonary exercise test (CPET), to highlight any differences with the use of surgical mask or filtering facepiece particles class 2 (FFP2) mask compared to the test performed under normal conditions.

Methods. 12 healthy subjects, enrolled in July 2020, performed three consecutive CPETs at least 24 hours apart, but within 2 weeks, without wearing airway protection mask, with surgical mask and with FFP2 mask. The execution order of the CPETs was assigned in order to cover all possible combinations. During the CPETs, the consumption of Watts reached will be obscured to the subject. Before the start and immediately after the end of each CPET, maximum inspiratory pressure (MIP) and the maximum expiratory pressure (MEP) was also assessed.

Results. Comparing the three conditions, we observed a progressive significant reduction in oxygen intake, carbon dioxide output, ventilation and respiratory rate at rest as well as at peak exercise (Table 1). The workload also decreased. We did not notice differences in blood oxygen saturation nor adverse events such as arrhythmias or ischemic events. MIP/MEP comparison did not reveal significant respiratory muscles fatigue.

Discussion and Conclusions. The use of airway protection masks during pandemics (e.g. nCoV-2019) is a key safeguard to contain viral transmission. In healthy subjects it reduces, both at rest and during exercise, ventilation values (mainly due to reduction of respiratory rate) without detectable alteration of arterial saturation, heart rate, respiratory muscle fatigue and/or adverse events even during a maximum effort. Our speculative hypothesis is that the effect is likely to be related to the presence of a mechanical obstacle to ventilation. Our data show that the use of masks is still compatible with the execution of physical activity even

if the maximum workload is slightly reduced. In conclusion airway protection masks (both surgical mask and FFP2) can be safely used in daily life despite a slight impact on ventilation and metabolic parameters.

		Standard CPET	Surgical mask	FFP2 mask	p value ANOVA
Rest parameters	Heart rate (bpm)	73 ± 13	77 ± 14	75 ± 15	0.670
	SpO ₂ (%)	97 ± 1	97 ± 1	97 ± 1	0.675
	VO ₂ (ml/min)	355.3 ± 54.2	320.9 ± 77.8	275.9 ± 89.6	0.023
	VCO ₂ (ml/min)	298.5 ± 52.1	255.5 ± 72.3	220.2 ± 68.2	0.017
	Respiratory rate (breath/min)	18.5 ± 3.2	15.2 ± 3.1	14.3 ± 3.6	0.008
	Tidal volume (L/min)	0.71 ± 0.1	0.71 ± 0.2	0.69 ± 0.2	0.918
	Ventilation (L/min)	12.9 ± 1.5	10.4 ± 1.8	9.8 ± 2.4	0.001
	MIP (cmH ₂ O)	81.8 ± 18.2	83.3 ± 16.6	85.2 ± 16.2	0.223
	MEP (cmH ₂ O)	82.6 ± 26.3	83.0 ± 23.8	80.8 ± 24.0	0.915
	Heart rate (bpm)	170 ± 14	168 ± 16	167 ± 16	0.349
Peak exercise parameters	SpO ₂ (%)	97 ± 1	97 ± 1	95 ± 3	0.132
	VO ₂ (ml/min/kg)	31.6 ± 7.1	27.5 ± 6.6	28.2 ± 8.8	0.001
	VCO ₂ (ml/min)	257.8 ± 75.6	221.7 ± 69.0	226.8 ± 79.4	0.016
	VE/VCO ₂ slope	27.5 ± 3.7	28.1 ± 3.7	26.6 ± 5.0	0.388
	Respiratory rate (breath/min)	45.5 ± 8.0	37.7 ± 5.5	37.1 ± 4.5	0.041
	Tidal volume (L/min)	2.28 ± 0.7	2.05 ± 0.6	1.96 ± 0.6	0.001
	Ventilation (L/min)	92.3 ± 26.0	76.2 ± 21.6	71.6 ± 21.2	0.003
	MIP (cmH ₂ O)	80.6 ± 26.3	82.5 ± 23.0	84.9 ± 24.7	0.457
	MEP (cmH ₂ O)	75.9 ± 18.2	81.0 ± 29.1	79.3 ± 24.3	0.614
	RER	1.2 ± 0.1	1.2 ± 0.1	1.2 ± 0.1	0.665
Power (watt)	194 ± 37	187 ± 52	184 ± 54	0.002	

A278: TELEMEDICINE AND REMOTE HOME MONITORING IN THE COVID-19 ERA: A VALUABLE SURVEILLANCE TOOL FOR PATIENTS WITH CARDIAC DEVICES

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Background. In-hospital management of patients with cardiac implantable electronic device (CIEDs) has been a critical challenge since the early stages of COVID-19 outbreak. In order to safeguard public health, routine in-hospital controls of CIEDs were converted into remote home monitoring (HM). The aim of our study is to investigate the impact of lockdown period on CIEDs patients and its influence on in hospital admissions through the analysis of HM data.

Methods. We analysed data recorded from 312 patients by HM during the national state of emergency related to COVID-19 and then we compared data from the same period of 2019. Emphasis has been given to heart failure alarms and arrhythmia alarms.

Results. We observed a significant reduction of remote monitoring events in 2020, when compared to 2019. Non-sustained ventricular tachycardia episodes decreased (18,3 vs 9,9% p= 0,002) as well as those for atrial fibrillation (29,2% vs 22,4% p= 0,019). In contrast, heart failure alarm activation was lower in 2019 than in 2020 (17% vs 25,3% p=0,012). Nevertheless, hospital admissions for critical events recorded with CIEDs dropped in 2020, including those for heart failure.

Conclusions. HM has ensured the surveillance of patients with cardiac devices even when outpatient visits were not possible. Arrhythmic events decreased significantly compared to those observed in 2019. Similarly, hospital admissions have also decreased dramatically, including those for heart failure, despite the increased exacerbations of heart failure shown by HM.

A279: COVID-19: UN'INFEZIONE GENDER RELATED?

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L'esistenza di differenze tra i due sessi nella suscettibilità, nella manifestazione clinica e nella risposta alle cure di molte malattie, è nota da tempo, seppur continui a essere spesso misconosciuta e sottovalutata da molti professionisti. L'analisi epidemiologica dei dati nazionali ed internazionali relativi alla recente pandemia da COVID-19 sta fornendo un'ulteriore prova tangibile dell'importanza della medicina di genere. Se è infatti vero che tutti gli individui si sono dimostrati essere possibili target di infezione da SARS-CoV-2, è altrettanto vero che vi sono diversi fattori che possono influenzarne la suscettibilità all'infezione, tra i quali anche il genere. L'infezione da SARS-CoV-2 sembrerebbe avere effetti diversi negli uomini rispetto alle donne, con scenari spesso più infausti per gli uomini, sia in termini di complicanze che in termini di mortalità. I dati cinesi hanno evidenziato che il tasso di letalità da COVID-19 negli uomini è circa il doppio rispetto alle donne (4.7% vs 2.8%), dato in seguito confermato anche da altri paesi, ivi inclusa l'Italia. Meno chiara è la situazione sulle differenze di

genere per quanto riguarda i tassi di infezione. I dati oggi disponibili sono discordanti tra i vari paesi e, talora, anche all'interno dello stesso paese nei diversi momenti. Per quanto riguarda l'Italia, dopo un'iniziale maggior prevalenza di casi maschili diagnosticati, gli uomini sembrano essersi ammalati leggermente meno rispetto alle donne, pur mostrando manifestazioni cliniche tendenzialmente più severe qualora infetti.

Alla base di suddette differenze epidemiologico-cliniche sembra esserci una pleora di fattori ambientali, individuali e virali, che si intersecano andando a disegnare i diversi scenari clinici nei due sessi. La presenza di differenze socio-comportamentali associate al genere, come una maggior tendenza alla abitudine tabagica ed al consumo di alcolici degli uomini e la maggior tendenza del sesso femminile alla cura personale ed al rispetto delle regole, potrebbe in parte giustificare le differenze documentate; tuttavia, è altrettanto vero che le donne sono più spesso caregiver e ricoprono la quota maggiore dei professionisti nel settore sanitario, risultando quindi ampiamente esposte al contagio. Dunque, qualcosa deve ipotizzarsi a protezione delle donne, per questa maggior potenziale esposizione virale in assenza di corrispondenza in termini di incidenza di malattia e mortalità. In generale, le donne presentano risposte immunitarie innate e adattative più intense ed efficaci rispetto agli uomini. Questo le rende più protette da possibili infezioni, come evidenziato dalle precedenti epidemie SARS (2003) e MERS (2012). Vi sono poi anche fattori legati al virus ed alla sua interazione con l'enzima ACE2 per infettare le cellule ospite, meccanismo su cui gli ormoni sessuali sembrano esercitare un ruolo condizionante.

Dunque, anche nel contesto della pandemia da COVID-19, un approccio clinico di genere risulta fondamentale, in quanto può contribuire notevolmente all'efficacia degli applicativi diagnostici e/o terapeutici, con importanti benefici per i malati e per la sostenibilità del Servizio Sanitario Nazionale.

A280: IMPACT OF CORONAVIRUS PANDEMIA IN THE MANAGEMENT OF PATIENTS WITH SEVERE CARDIOVASCULAR DISEASE: THE EXPERIENCE OF A CARDIOLOGY OUTPATIENT CLINIC IN THE LOMBARDY REGION

Francesco Fioretti (a), Giuliana Cimino (a), Antonio Milidoni (a), Angelica Cersosimo (a), Andrea Dell'Aquila (a), Mariangela Piazzani (a), Alberto Madureri (c), Laura Lupi (c), Savina Nodari (b) (a) UNIVERSITY OF BRESCIA, ITALY; (b) ASST SPEDALI CIVILI HOSPITAL AND UNIVERSITY OF BRESCIA, ITALY; (c) ASST SPEDALI CIVILI HOSPITAL OF BRESCIA, ITALY

Background. During the lockdown period in Italy, from March 11th to May 4th 2020, a progressive increase in COVID-19 cases occurred in all Italian regions, in particular in the Lombardy Region. The current rise in COVID-19 cases has led to an increasing involvement of hospitals, in order to face the Coronavirus outbreak, shifting healthcare resources towards the management of COVID+ patients. This has led, on the other hand, to a progressive decrease in hospital admissions due to conditions not associated with SARS-CoV2 infection. At the same time, the regional governments have provided for the suspension of all outpatient activities, with the exception of the non-deferrable one. It was decided to postpone any elective intervention, referring to COVID free hospitals any urgent or emergency intervention.

Purpose. We aimed to verify the impact of coronavirus outbreak in the management of patients with high risk of morbidity and mortality, followed at the Cardiology Outpatient Clinic of our hospital, that was a Hub center for COVID patients.

Materials and method. We compared the total number of Day Hospital (DH) visits for worsening heart failure (WHF), severe aortic stenosis waiting for Transcatheter Aortic Valve Implantation (TAVI) and atrial fibrillation (AF) requiring electrical cardioversion (ECV) between March 4th and May 4th of 2019 with those that refer to the same period in 2020. Then, we evaluated the same data in the 30 days following the end of the lockdown (May-June 2020).

Results. As reported in Figure 1, the number of DH visits during March-May 2019 was approximately double compared to the ones in the same interval time in 2020 (81 vs 34 patients). Instead, in just one month (18/05-18/06/2020) there was a significant increase in the number of accesses for WHF (globally 22), if compared with those (21 in total) during the entire lockdown (lasting three months, from 04/03 to 04/05/2020).

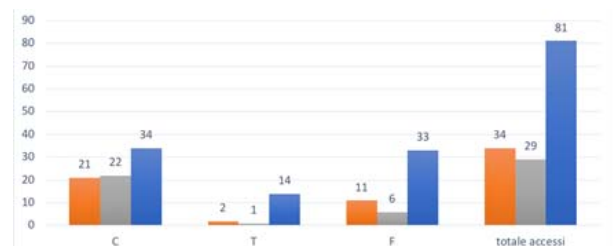


Figure 1. Number of MAC accesses in the indicated periods. C = heart failure; T = TAVI; F = atrial fibrillation.

Legend: March-May 2019 (orange), March-May 2020 (grey), May-June 2020 (blue)

Conclusion. These data confirm how the COVID outbreak impacted negatively on the appropriate management and timing of therapeutic intervention for severe cardiovascular disease, in particular those with high risk of events and mortality, especially in the regions with highest number of hospitalizations and deaths for SARS-CoV-2.

A281: ARRHYTHMIC BURDEN IN COVID-19 PATIENTS OUTSIDE THE ICU - EXPERIENCE OF A THIRD-LEVEL CENTER

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Background. No studies investigated the prevalence of arrhythmias among clinically stable patients affected by COVID-19.

Methods. We assessed prevalence, type, and burden of arrhythmias, by a single-day snapshot in seven non-intensive COVID Units at a third-level center.

Results. We enrolled 132 in-hospital patients (mean age 65±14y; 66% males) diagnosed with COVID-19 infection. Arrhythmic episodes were detected in 12 patients (9%). In detail, 8 had atrial fibrillation, and 4 self-limiting supraventricular tachyarrhythmias. There were no cases of ventricular arrhythmias or new-onset atrioventricular blocks. In addition, we report no patients with QTc interval >450 ms.

Conclusion. Our single-day snapshot survey suggests that the prevalence of arrhythmias among clinically stable COVID-19 patients is low. In particular, no life-threatening arrhythmic events occurred.

A282: PANDEMIA COVID-19: NON SOLTANTO INSUFFICIENZA RESPIRATORIA; AUMENTANO LE COMPLICANZE POST-INFARTO MIocardico

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Introduzione. Durante la pandemia da SARS-CoV-2 (definita COVID-19), a partire dal mese di Febbraio 2020, la percezione degli operatori sanitari, comprovata da numerosi studi scientifici, è stata di una drastica riduzione numerica dei ricoveri ospedalieri per problematiche di interesse cardiologico e, al contempo, di un aumento significativo della mortalità correlata alle sindromi coronariche acute, passando da un 4,1% nei mesi di Marzo e Aprile del 2019 al 13,7% nel 2020. La riduzione dei ricoveri ospedalieri ha trovato ragion d'essere nella paura del contagio, invece, l'aumento della mortalità è stata spiegata sia dall'arrivo più tardivo in Ospedale da parte dei pazienti rispetto al momento di insorgenza della sintomatologia cardine sia dal prolungamento dei tempi di cura attribuibile all'attesa del tampone.

Caso clinico. In data 27 Marzo 2020, un uomo di 59 anni, iperteso e fumatore, faceva accesso c/o il nostro PS per comparsa di dolore toracico nei 4 giorni antecedenti il ricovero, modifiche ECGrafiche a sede laterale e lieve rialzo della troponina. In anamnesi presentava una severa broncopneumopatia cronica ostruttiva ed esiti di talcaggio pleurico per versamento pleurico recidivante. Il paziente, dopo aver eseguito la coronarografia con riscontro di una occlusione cronica della coronaria destra e una stenosi critica del I diagonale (trattata con angioplastica e stenting), ha sviluppato uno stato di shock con notevole incremento degli indici di flogosi, quadro di sospetta polmonite interstiziale bilaterale alla radiografia del torace, per cui ha eseguito, nonostante tampone Covid-19 all'ingresso negativo, una TC polmonare caratterizzata da multipli addensamenti ai campi polmonari superiori e peri-ilari di destra e peri-ilari e apicali a sinistra. Pertanto si è ritenuto necessario eseguire ricerca di antigene Covid-19 su BAL (liquido di lavaggio bronco alveolare) che ha effettivamente escluso la diagnosi. L'ecocardiogramma ripetuto contestualmente ha mostrato un'insufficienza mitralica severa funzionale secondaria a rottura di muscolo papillare (contestuale a una riacutizzazione di BPCO). Grazie al supporto inotropo, alla ventilazione meccanica non invasiva, ad una doppia terapia antibiotica e ad alte dosi di diuretici, il paziente è stato dimesso in discreto compenso emodinamico. In data 30 Aprile, dopo risoluzione di una recidiva di shock cardiogeno, la correzione cardiocirurgica del vizio valvolare mitralico (con conferma di rottura di muscolo papillare!), ha consentito il raggiungimento del benessere psico-fisico del paziente, ad oggi mantenutosi.

Conclusioni. L'insufficienza funzionale da rottura di muscolo papillare si osserva in circa il 35% dei pazienti con infarto miocardico, è responsabile di un brusco deterioramento emodinamico e, soprattutto, si osserva più frequentemente nelle presentazioni tardive delle sindromi coronariche. Il nostro caso clinico è un esempio di come la pandemia COVID-19 abbia avuto un impatto sulla mortalità nazionale, non soltanto per i quadri di insufficienza respiratoria virus relati, ma, anche e soprattutto, per il ritardo nella richiesta di aiuto dei pazienti cardiologici e, quindi, nell'aumento delle complicanze.

A283: SEGMENTAL AND GLOBAL LONGITUDINAL STRAIN DIFFERENCES BETWEEN CHILDREN WITH PAEDIATRIC INFLAMMATORY MULTISYSTEMIC SYNDROME TEMPORALLY ASSOCIATED WITH SARS-CoV-2 PANDEMIC AND KAWASAKI DISEASE: PRELIMINARY DATA FROM AN ONGOING STUDY

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Introduction. The paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) and Kawasaki disease (KD) have overlapping features. This study aimed to describe the strain segmental analysis among both entities.

Methods. Retrospective review of strain segmental analysis within 4 weeks of presentation of symptoms among children diagnosed with PIMS-TS between April and June 2020 and a historic cohort of typical KD from the Royal Brompton Hospital, London.

Results. We included 33 PIMS-TS patients (23 males, 69.7%) at a mean age of 5.8 ± 4.5 years old and 45 KD patients (31 males, 68.9%) at a mean age of 8 ± 4.9 years old. Left ventricle ejection fraction (LVEF) was normal in both groups (63.3% vs 63.5%; $p = 0.89$), 4/33 PIMS-TS children (12.1%) had coronary arteries abnormalities (CAA), whereas 100% of KD cohort had CAA. Both groups had a normal global longitudinal strain (GLS), but in KD it was significantly reduced compared to the PIMS-TS group (-20% vs -22%; $p = 0.008$). Basal segments were the most affected in KD with significant difference in the basal anterior and anterolateral strain compared to PIMS-TS (respectively -18.2% vs -23.4%; $p < 0.001$ and -16.7% vs -22.7%; $p < 0.001$). KD had a greater anterior, anterolateral and posterior segments involvement with a significant reduction in the anterolateral mid-wall longitudinal strain (-18.3% vs -22%; $p = 0.002$). Apical segments were less involved, with significant difference only in the septal and inferior apical strain (respectively $p = 0.001$ and $p = 0.032$).

Conclusions. These preliminary data showed that after 4 weeks from the onset of symptoms, all PIMS-TS patients had a normal LVEF and GLS and different segmental involvement compared to KD cohort. We hypothesize that these findings may be related to direct myocardial damage in PIMS-TS rather than caused by coronaries perfusion abnormalities.

A284: THE VALUE OF ECG CHANGES IN RISK STRATIFICATION OF COVID-19 PATIENTS

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Background. There is growing evidence of cardiac injury in COVID-19. Our purpose was to assess the prognostic value of serial electrocardiograms in COVID-19 patients.

Methods. We evaluated 269 consecutive patients admitted to our Centre, with confirmed SARS-CoV-2 infection. ECGs available at admission and after one week from hospitalization were assessed. We evaluated the correlation between ECGs findings and major adverse events (MAE) as the composite of intra-hospital all-cause mortality or need for invasive mechanical ventilation. Abnormal ECGs were defined if primary ST-T segment alterations, left ventricular hypertrophy, tachy or bradyarrhythmias and any new AV, bundle blocks or significant morphology alterations (e.g. new Q pathological waves) were present.

Results. Abnormal ECG at admission (106/216) and elevated baseline troponin values were more common in patients who developed MAE ($p = 0.04$ and $p = 0.02$, respectively). Concerning ECGs recorded after 7 days (159), abnormal findings were reported in 53.5% of patients and they were significantly more frequent in those with MAE, as shown in Figure 1. Among abnormal ECGs, ischemic alterations and left ventricular hypertrophy were significantly associated with a higher rate of MAE. The multivariable analysis showed that the presence of abnormal ECG at 7 days of hospitalization was an independent predictor of MAE (HR 3.2; 95% CI 1.2–8.7; $p = 0.02$). Furthermore, patients with abnormal ECG at 7 days more often required transfer to intensive care unit ($p = 0.01$) or renal replacement therapy ($p = 0.04$).

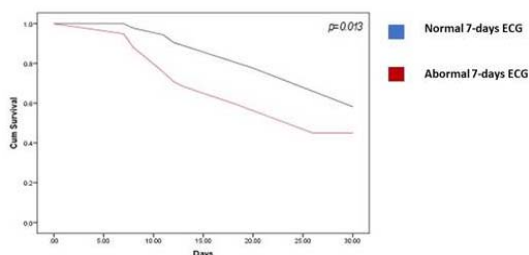


Figure 1. Kaplan-Meier curves for primary outcome of MAE.

Conclusions. Patients with COVID-19 should receive ECG at admission but also during their hospital stay. Indeed, electrocardiographic alterations during hospitalization are associated with MAE and infection severity.

A285: ENDOTHELIAL DYSFUNCTION IN COVID-19 PATIENTS ASSESSED WITH ENDO-PAT2000

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Background. It has been widely reported that SARS-CoV-2 attaches human cells by using the ACE2 receptor, which is expressed in several organs, including the endothelial cells. Whether vascular impairment described during COVID-19 infection is primarily due to the direct involvement of the endothelial cells by the virus or secondarily to the inflammatory host response is currently unknown, but there is evidence that SARS-CoV-2 can directly infect human blood vessel. We therefore aimed to demonstrate in vivo the presence of endothelial dysfunction in COVID-19 patients without cardiovascular risk factors or pre-existing cardiac conditions.

Methods. We used the Endo-PAT 2000, a device able to measure endothelial vasodilation function in a rapid and noninvasive way. The device records endothelium-mediated changes in the digital pulse waveform known as the Peripheral Arterial Tone (PAT) signal, measured with a pair of plethysmographic probes situated on the index finger of both patient's hands. Endothelium mediated changes in the PAT signal are elicited by creating a downstream hyperemic response, induced by blood flow occlusion in the brachial artery for 5 minutes using an inflatable cuff on one arm. The response to reactive hyperemia is evaluated automatically by the device, and a PAT ratio is calculated using the post- and pre-occlusion PAT values relative to the occluded arm (compared to the measurements from the contralateral arm, which serves as control for non endothelial dependent systemic effects). The Reactive Hyperemia Index (RHI) is then calculated as the ratio of Pulse Wave Amplitude (PWA) measured during the 60-second period after cuff deflation divided by the average PWA measured before cuff inflation; RHI values below 1.67 are suggestive of endothelial dysfunction.

Results. We evaluated six patients with laboratory-confirmed SARS-CoV-2 infection with a mean age of 75.8 years. Five of them were female (83.3%); the average mean arterial pressure was 87 mmHg (normal values 70-110 mmHg). Blood sample tests revealed an inflammatory state in all patients, with high plasma levels of C-reactive protein, fibrinogen, ferritin, LDH, and D-dimer. Overall, four patients were positive for endothelial dysfunction, with RHI values between 1.13-1.56 (average value 1.32, normal values >1.67); in one of the two negative patients the reported RHI value was slightly above the cutoff (1.72).

Conclusions. Our findings confirm that COVID-19 patients are at higher risk of developing endothelial dysfunction. In addition, our results demonstrate that endothelial impairment may occur even in the absence of cardiovascular risk factors. Endothelial dysfunction may play a pivotal role in the pathophysiology of the infection process and may identify a subset of patient at a higher risk of worse outcome. In a small series of patients who died from COVID-19, severe endothelial injury associated with intracellular virus detection, disruption of endothelial cell membranes, widespread pulmonary vascular thrombosis and occlusion of alveolar capillaries with significant new vessel growth, was observed. Early recognition of endothelial impairment at an early stage of the disease appears critical. Whether the evidence of endothelial dysfunction, through noninvasive approaches, can predict worse clinical outcomes or higher risk of thromboembolic events needs to be proven by recruiting a larger number of affected patients. Nevertheless, our results contribute to the knowledge of the pathophysiological mechanisms related to COVID-19 infection.

A286: REMOTE CARDIAC CARE IN COVID-19 EPOCH: OUR EXPERIENCE WITH V-LAP DEVICE IN ADVANCED HEART FAILURE PATIENTS

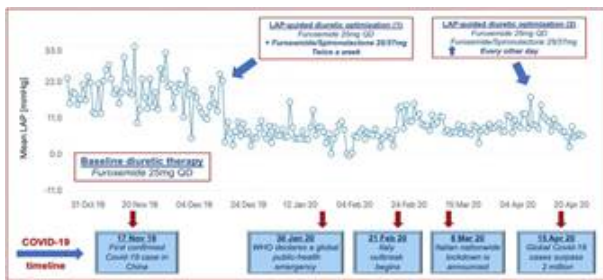
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The outbreak of COVID-19 has imposed disruptive changes in cardiovascular care worldwide: the usual modalities of care delivery for HF patients have been implemented, promoting preventive measures, minimizing in-person contacts, reducing patients' and health care providers' risk of exposure. This unprecedented scenario has accelerated the transition towards telemedicine as a way to provide safe, accountable, and effective care in HF. A paradigmatic example is the chronic HF management through remote telemonitoring of left atrial pressure (LAP) using the V-LAP™ device (Vectorious Medical Technologies), currently tested at our center under the VECTOR-HF first-in-man clinical study.

The study population consists of patients in NYHA functional class III who have a history of hospitalization for worsening HF or elevated ambulatory levels of BNP/N-terminal pro BNP. The device is implanted under fluoroscopy and TEE-guidance in a trans-septal fashion. Once implanted, the battery-free interatrial device captures the LAP, that is collected by means of an external belt, sending data to the cardiologist via a cloud-based system. After 90 days, right heart catheterization confirms the accuracy of LAP measurements as compared to pulmonary capillary wedge pressure. Once the reliability is confirmed, LAP can be used to guide optimization of medical therapy.

In our center, three patients have been enrolled so far: 1) The first V-LAP™ was implanted in Jun 2019 in a 75yo patient with severely reduced LVEF (25%), and frequent HF hospitalizations. At 16 months, NYHA functional class improved (from III to II) along with an amelioration of both the 6-minute walking test and the perceived quality of life, according to KCCQ questionnaire. 2) The second patient is a 70yo patient suffering from HFrEF in dilated ischemic cardiopathy, LVEF 30%, NYHA III, with multiple readmissions for HF worsening. He underwent implantation in Feb 2020. At 8 months, NYHA functional class improved (from III to II). 3) The third patient was implanted in Sep 2020. He is a 65yo patient with non-obstructive hypertrophic cardiomyopathy, LVEF 28%, NYHA III, with several HF related hospitalizations. We eagerly wait for his data to be available after 3-months-right heart catheterization. However, he had no clinical worsening to date.

During the course of COVID-19 pandemic, remote analysis of LAP curves led to earlier detection of underlying disease progression preventing clinical decompensation: when a rise in mean LAP was observed, diuretic therapy was modified accordingly (see example below from first patient). Among our patients, no hospital readmissions occurred over COVID-19 era, avoiding medical contacts and in-hospital exposure. Moreover, the V-LAP™ system showed remarkable reliability and easiness of use, encouraging patients to adhere with a high compliance rate (>99%).



A287: MORTALITY RISK ASSESSMENT USING CHA₂DS₂-VASc SCORES IN PATIENTS HOSPITALIZED WITH COVID-19 INFECTION

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Background. Early risk stratification is needed for complications and death related to COVID-19 infection. Because many patients with COVID-19 who developed acute respiratory distress syndrome have diffuse alveolar inflammatory damage associated with microvessel thrombosis, we aimed to investigate a common clinimetric tool the CHA₂DS₂-VASc in the prognostication of outcomes in COVID-19 patients.

Methods. We analyzed consecutive patients from a multicenter observational registry, CORACLE, which contains data of patients hospitalized for COVID-19 infection in 4 regions of Italy, according to data-driven tertiles of admission CHA₂DS₂-VASc score. The primary outcomes were inpatient death and a composite of inpatient death or invasive ventilation.

Results. Of 1045 patients in the registry, 864(82.7%) had data available to calculate CHA₂DS₂-VASc score and were included in the analysis. Of these, 167(19.3%) died, 123(14.2%) received invasive ventilation, and 249(28.8%) had the composite outcome. Stratification by CHA₂DS₂-VASc tertiles (T1: ≤1; T2: 2-3; T3: ≥4) revealed increases in both death (8.1%, 24.3%, 33.3%, respectively; p<0.001) and the composite endpoint (18.6%, 31.9%, 43.5%, respectively; p<0.001). The odds ratios(ORs) for mortality

and the composite endpoint for T2 patients versus T1 CHA₂DS₂-VASc score were 3.62 (95% CI:2.29-5.73, p<0.001) and 2.04 (95% CI:1.42-2.93, p<0.001), respectively. Similarly, the ORs for mortality and the composite endpoint for T3 patients versus T1 were 5.65 (95% CI:3.54-9.01, p<0.001) and 3.36 (95% CI:2.30-4.90, p<0.001), respectively.

Conclusions. Among patients hospitalized for COVID-19 infection, the CHA₂DS₂-VASc risk score for thromboembolic events was able to prognosticate both inpatient mortality and the composite of inpatient mortality or the requirement of invasive ventilation. Whether this score may be extensively used in other population with different clinical risk profile is a challenge for future researches.

A288: QTc INTERVAL PROLONGATION AND LIFE-THREATENING ARRHYTHMIAS IN PATIENTS WITH COVID-19. RESULTS FROM A MULTI-CENTER PROSPECTIVE REGISTRY

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Background. Prolonged QTc interval and life-threatening arrhythmias (LTA) are potential drug induced complications previously reported with antimarialar, antivirals and antibiotics.

Objectives. To evaluate prevalence and predictors of QTc interval prolongation and incidence of LTA during hospitalization for COVID-19.

Methods. 154 consecutive patients were enrolled in a multicenter international registry. 12-lead ECG was performed at admission, after 7 and 14 days; QTc values were analyzed.

Results. Fifteen (14%) patients developed a prolonged-QTc (pQT) after 7 days (mean QTc increase 66±20msec, +16%, p<0.001); these patients were older, had higher basal heart rates, higher rates of paroxysmal atrial fibrillation, lower platelet count. QTc increase was inversely proportional to baseline QTc levels and leukocyte count and directly to basal heart rates (p<0.01). At multivariate stepwise analysis including age, male gender, paroxysmal atrial fibrillation, basal QTc values, basal heart rate and dual antiviral therapy, age (OR 1.06, 95% CI 1.00-1.13, p<0.05), basal heart rate (OR 1.07, 95% CI 1.02-1.13, p<0.01) and dual antiviral therapy (OR 12.46, 95% CI 2.09-74.20, p<0.1) were independent predictors of QT-prolongation. Incidence of LTA during hospitalization was 3.9%. Three pts experienced cardiac arrest and three non-sustained VT. LTAs were recorded after 14±7 days from hospitalization and were associated with poor outcome with 66% of mortality rate.

Conclusions. After 7 days of hospitalization, 14% of patients with Covid-19 developed pQTc; age, basal heart rate and dual antiviral therapy were found as independent predictor of pQTc. Life threatening arrhythmias had an incidence of 3.9% and were associated with poor outcome.

A289: ANTICOAGULATION THERAPY IN PATIENTS WITH COVID-19. RESULTS FROM A MULTI-CENTER INTERNATIONAL PROSPECTIVE REGISTRY (HOPE-COVID19)

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Background. No standard therapy is currently recommended for coronavirus-19 disease (COVID-19). Several drug approaches, including anticoagulation (AC), have been proposed in small case series. Aim of the study was to evaluate the efficacy of AC in COVID-19 hospitalized patients and its impact on survival.

Methods. 5838 patients were enrolled in a multicenter-international prospective registry (HOPE-COVID19). Demographic and clinical data including drug therapy and in-hospital complications were recorded.

Results. 5480 (94%) patients did not receive any AC before hospitalization. In the overall cohort AC therapy during hospitalization was not associated with better survival rate (81 vs 81%, p=0.94), but with higher risk of bleeding (2.7 vs 1.8%, p=0.03). Among patients admitted with respiratory failure (49%, n=2859 pts), AC started during hospitalization was associated with lower mortality rates (32 vs 42%, p<0.01) and non-significant higher risk of bleeding (3.4 vs 2.7%, p=0.3). AC therapy was associated with lower mortality rates in patients treated with invasive ventilation (53 vs 64%, p=0.05) without increased rates of bleeding (9 vs 8%, p=0.88), but not in those with non-invasive ventilation (35 vs 38%, p=0.40). At multivariate Cox analysis mortality relative risk with AC was 0.58 (95% CI 0.49-0.67) in patients admitted with respiratory failure, 0.50 (95% CI 0.49-0.67) in those requiring invasive ventilation, 0.72 (95% CI 0.51-1.01) in non-invasive ventilation.

Conclusions. AC therapy in general population with COVID-19 is not associated with better survival rates but with higher bleeding risk. Better results can be observed in patients admitted with respiratory failure and requiring invasive ventilation.

A290: EXOSOMAL MICRORNAS DRIVE PULMONARY THROMBOEMBOLISM IN COVID-19

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Introduction. Thromboembolic events have been shown to play a key role in the outcome of COVID-19. The analysis of the exosomal cargo, including microRNAs (miRNAs), may provide a unique view into relevant diseases or define new diagnostic/prognostic potential. Emerging evidence has shown that exosomal miRNAs are involved in a number of physiologic and pathologic processes. However, neither exosomes nor miRNAs have been hitherto investigated in COVID-19.

Methods and Results. To test the hypothesis that exosomal miRNAs are a key determinant of pulmonary thromboembolism (PTE) in COVID-19, we enrolled COVID-19 patients with signs and symptoms suggestive of PTE. The study was approved by the local Ethical Committee and informed consent was obtained. Circulating exosomes were isolated from these patients on admission following established protocols and levels of the top three exosomal miRNAs from a panel to profile human miRNAs were validated by RT-qPCR. Patients were divided in two groups based on the confirmed or non-confirmed diagnosis of PTE, obtained by high-resolution computed tomography and/or angiogram, in order to verify the presence of pulmonary micro/macrotrombi. When comparing patients with confirmed PTE vs patients without PTE, we found that D-dimer, age, and diabetes mellitus were different ($P < 0.05$), corroborating the key role of these factors in the pathogenesis of PTE; we also found that levels of exosomal miR-103a, miR-145, and miR-885 were significantly different between these populations. Mechanistically, Tissue Factor has been identified as a direct target of miR-145, while miR-885 targets the von Willebrand Factor. Equally important, low levels of miR-103a have been observed in deep vein thrombosis, although a precise mechanism explaining such a relationship has not been fully defined. An inverse correlation between exosomal miR-145 and D-dimer was also evident ($R^2: 0.4458$, $P = 0.0002$). Strikingly, using a stepwise multiple regression analysis, correcting for age, diabetes, hypertension, and D-dimer, exosomal miR-145 was confirmed as an independent predictor of PTE [B: -3.140, Wald: 6.047, 95% CI for EXP(B): 0.004-0.529; $P = 0.014$]. To our knowledge, this is the first study showing an association between exosomal non-coding RNA and PTE in COVID-19 patients. Since endothelial dysfunction has been shown to be a prominent hallmark of COVID-19 and to contribute to the pro-thrombotic and pro-inflammatory state of the vasculature, we speculate that a main source could be represented by endothelial cells and/or platelets, which are known to express miR-145, miR-103a, and miR-885 in normal conditions. Moreover, endothelial cells express the main co-factors required by SARS-CoV-2 to enter the host cells, including angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2).

Conclusions. We identified an unprecedented significant association between exosomal miRNAs and PTE, which could be helpful to better understand the molecular mechanisms underlying PTE pathophysiology, as well as to identify patients who are at risk of developing PTE. Consistent with our findings, in a series of COVID-19 autopsies, PTE has been shown to be a fundamental feature, strongly indicating that thrombosis plays a crucial role in the disease process and in its outcome. Further analyses are warranted to ratify our results and prospectively evaluate their prognostic value.

A291: IMPACT OF COVID-19 ON VENTRICULAR ARRHYTHMIAS

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Background. The COVID-19 pandemic has affected the hospital management of many diseases. The rapid spread of the virus and the serious clinical conditions of patients requiring intensive care have caused a reorganization of activities in hospital facilities: in the electrophysiology (EP) laboratory, interventional procedures have been postponed in elective cases, giving priority to clinical emergencies, such as catheter ablation (CA) for electrical storm (ES). As of today, there has been no clear scientific evidence correlating the SARS-CoV-2 infection with fatal or near-fatal arrhythmias, such as ventricular tachycardia (VT) and electrical storm (ES).

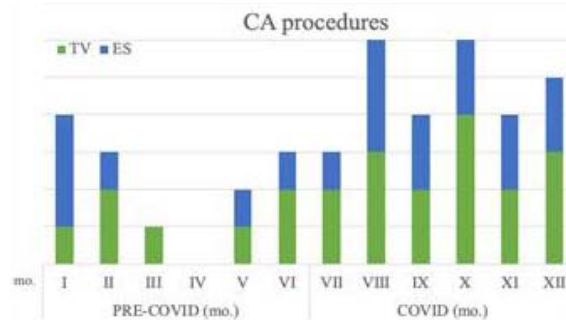
Objective. We sought to evaluate how the numbers of CA for ES and VT have changed in the COVID-19 period, as compared to the pre-COVID-19 era.

Methods. We conducted a single-center, retrospective, observational study. We enrolled two groups of patients undergoing EP procedures of CA for ES and VT at the University Hospital "Ospedale Riuniti" in Ancona, Italy, a tertiary-level referral center. The first group includes patients undergoing CA for ES and VT in the six months preceding the COVID-19 pandemic (September 9, 2019-March 8, 2020). The second group includes patients undergoing the same procedures in the first six months of the COVID-19 emergency (March 9, 2020-September 9, 2020). March 9, 2020 was chosen to mark the beginning of the COVID-19 era because

this was the day when novel health care measures were taken in the cardiology department of our hospital. Each subject in Group B was evaluated with polymerase chain reaction (PCR) tests for SARS-Cov-2 on throat swabs before CA procedures.

Results. We enrolled 40 patients undergoing CA procedures for ES and VT. More CA procedures were performed during the COVID-19 period, as compared to the pre-COVID-19 period (27 vs 13 patients). This difference was mainly driven by an increase in CA for ES during the COVID-19 period (16 vs 7). Furthermore, PCR tests for SARS-Cov-2 on throat swabs were negative in all patients.

Conclusions. Our data suggest that during the COVID-19 emergency, there was an increase of non-deferrable EP procedures, such as CA for ES. We suppose two possible explanations. Firstly, the COVID-19 emergency may have worsened the assistance to patients with chronic diseases, both due to the channeling of resources in the COVID-19 emergency and to the need to minimize interpersonal contacts, including non-urgent visits; this may have indirectly facilitated the development of ES. Secondly, despite the negative results of SARS-Cov-2 throat swabs, a previous COVID-19 cannot be completely ruled out, raising the possibility that the virus may have also acted directly, setting the stage for ES. Further studies are needed in order to examine in depth the multiple possible relationships between COVID-19 and arrhythmogenesis.



A292: SEVERE COVID-19 IN A PATIENT WITH LATE PRESENTATION STEMI: A DOUBLE-EDGED SWORD

Giorgio Solfanelli (a), Massimo Volpe (a), Allegra Battistoni (a), Simone Reale (a), Sara Corradetti (a), Enrico Rathina Raj (a) (a) UNIVERSITÀ LA SAPIENZA DI ROMA, FACOLTÀ DI MEDICINA E PSICOLOGIA. Although the emergent COVID-19 is usually dominated by respiratory symptoms, COVID-19 patients may also develop cardiovascular complications, which may even become the ultimate cause of death. Indeed, several studies have been reported a strict correlation between SARS-CoV-2 infection and the increase of mortality and morbidity in cardiovascular patients. Moreover, the late presentation and management of acute coronary syndromes due to the fear of being infected in healthcare structures during this pandemic have led to worse cardiovascular outcomes.

A 62-year-old man with no previous disease, admitted with respiratory failure caused by SARS-CoV-2 interstitial pneumonia (Fig. 1), incurred in a cardiogenic shock due to a severe left ventricular dysfunction with several episodes of sustained ventricular tachycardia.

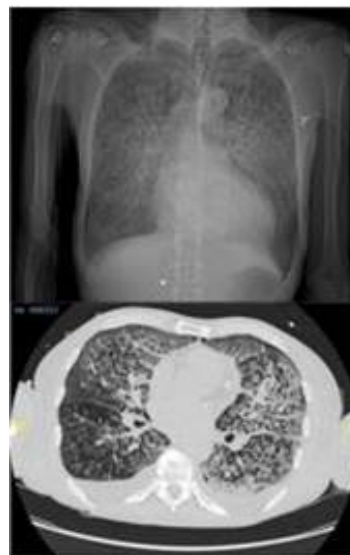


Figure 1

The ECG showed Q-waves with ST-segment elevation as for a late presentation STEMI (Fig. 2) and the echocardiogram confirmed left ventricle dysfunction and septal-apical aneurism (Fig. 3). As soon as the patients could speak, he referred an episode of angina a couple of weeks before the admission to the hospital, but he avoided seeking help because afraid of being exposed to SARS-CoV-2 in healthcare structures. The in-hospital management of this patient has been challenging. Despite a complete coronary revascularization of the left anterior descending artery, the patient had to undergo a defibrillator implantation in secondary prevention and his prognosis remained poor due to the several impairment of left ventricular ejection fraction and the lung interstitial fibrosis.

From this single case, two major lessons can be learned: (1) the course of COVID-19 may be complicated by concomitant critical cardiovascular conditions, such as a recent acute myocardial infarction; (2) late presentation and management of acute myocardial infarction may be the consequence of the fear of the contagion during a pandemic. Therefore there is need for a specific health protocol for acute condition in the perspective of a new pandemic phase.



Figure 2

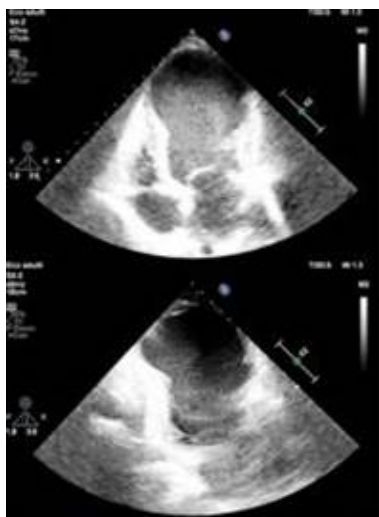


Figure 3

A293: FUTURE PERSPECTIVES OF ITALIAN CARDIOLOGISTS IN TRAINING: A NATIONWIDE SURVEY

Antonio Strangio (a), Isabella Leo (a), Carmen Anna Maria Spaccarotella (a), Francesco Barillà (b), Cristina Basso (c), Maria Pia Calabrò (d), Antonio Curcio (a), Pasquale Perrone Filardi (e), Massimo Mancone (f), Giuseppe Mercurio (g), Saverio Muscoli (h), Savina Nodari (i), Roberto Pedrinelli (j), Francesco Romeo (k), Gianfranco Sinagra (l), Ciro Indolfi (a)
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MESSINA, MESSINA, ITALY; (e) DEPARTMENT OF ADVANCED BIOMEDICAL SCIENCES, FEDERICO II UNIVERSITY; (f) SAPIENZA UNIVERSITY OF ROME, ROME, ITALY; (g) DEPARTMENT OF MEDICAL SCIENCES AND PUBLIC HEALTH, UNIVERSITY OF CAGLIARI, CAGLIARI, ITALY; (h) DEPARTMENT OF MEDICINE, TOR VERGATA UNIVERSITY OF ROME, ROME, ITALY; (i) DEPARTMENT OF CARDIOLOGY, UNIVERSITY OF BRESCIA AND ASST SPEDALI CIVILI DI BRESCIA, BRESCIA, ITALY; (j) CARDIAC, THORACIC AND VASCULAR DEPARTMENT, UNIVERSITY OF PISA, PISA, ITALY; (k) DEPARTMENT OF CARDIOVASCULAR DISEASE, TOR VERGATA UNIVERSITY OF ROME, ROME ITALY; (l) CARDIOVASCULAR DEPARTMENT, UNIVERSITY OF TRIESTE, TRIESTE, ITALY

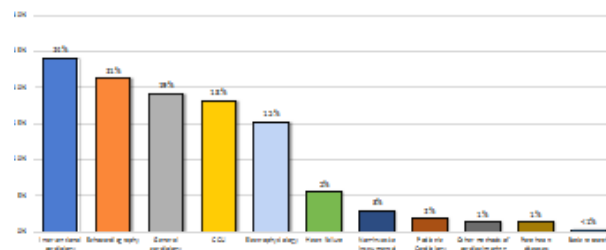
Background. Adequate specialist training is the basis of a health system capable of supporting the continuous expansion of the population's demand for assistance. The continuous scientific advances, technological innovations, and the recent outbreak of a pandemic lead to a reshaping of training courses in order to guarantee a high standard of quality of care.

Aims. Evaluating the feedback provided by Italian cardiologists in training about the current educational program and analyzing their perspectives about the future.

Methods. We performed a 23-item national survey that has been delivered to 1443 Italian Fellow in Training (FITs), registered in the database of the Italian Society of Cardiology (ISC). The survey has been available online for 33 days (from 12 of June to 15 of July 2020). The impact of COVID-19 on medical education has been the original principal topic of the questionnaire, but we took advantage of this opportunity to investigate the perception of the trainees about their future work and training.

Results. 633 cardiologists in training (44% of the FITs) participated to the survey. 45% of the participants affirmed to be completely satisfied by the current training program. 24% of respondents affirmed to have a totally inadequate or inadequate expertise on treating cardiovascular emergencies. 83% claimed to be interested in a working experience abroad but only 24% would remain lifelong in another Country. We asked the future cardiologists an opinion about the possibility of an early access to the world of work, starting from the third year of residency, provided from two recent Italian decrees ("Calabria" and "Milleproroghe"). 63% of the respondents believe that this chance does not represent an overall advantage and for 83% of them the early abandonment of the Universities could jeopardize a thorough cardiologistical training. Sub-specializations such as interventional cardiology and echocardiography emerged as the main topics of interest for the future careers of the FITs; however, general cardiology has been indicated as the third most requested area of interest, in contrast to the increasing tendency to sub-specializations. Only a few numbers of participants (<1%) expressed their interest in dedicating their future in the research field.

Conclusions. Universities and politicians should make a great effort in the organization and re-organization of the teaching programs, taking into account the opinions of the cardiologists of tomorrow.



A294: TELE-HEALTH MONITORING FOR HYPERTROPHIC CARDIOMYOPATHY AND AMYLOID CARDIOMYOPATHY PATIENTS: LESSONS FROM THE COVID-19 LOCKDOWN IN ITALY

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 (a) CARDIOLOGIA, OSPEDALE POLICLINICO SAN MARTINO IRCCS, UNIVERSITÀ DI GENOVA

Introduction. Italy has been profoundly hit by the SARS-CoV-2 pandemic. As a result, governative measures were required to slow virus spread, with a lockdown imposed beginning from March to June 2020. Such measures involved also in-hospital outpatient visits, and clinicians were urged to postpone or even halt visits deemed as non-urgent.

Methods. At the beginning of COVID-19 lockdown (from March 9th throughout May 15th) the already existing tele-health monitoring programme of the Hypertrophic Cardiomyopathy (HCM) Outpatient Clinic at the Ospedale Policlinico San Martino, in Genova, Italy, was implemented. HCM and cardiac amyloid (CA) patients with a scheduled visit were contacted by a medical trainee to assess urgency related to her/his medical evaluation. According to information collected via the tele-medical contact, patients were divided in 'stable' (group A) and 'potentially unstable' (group B). Patients were deemed as 'potentially unstable' if one or more of the following were present: signs and/or symptoms of heart failure (HF), in particular if worsening relatively to the baseline condition; known end-stage HCM; HF hospitalization(s) or multiple (>3) outpatient evaluations in the prior 6 months. Those in group B received weekly tele-

medical contact to monitor their conditions and evaluate the need for in-hospital in-person visits, whereas those in group A were scheduled to be contacted after 1 month.

Results. In the observation period, 40 patients (median age: 62 years, 28 HCM and 12 CA patients) received a tele-contact. In 15 cases the tele-medical contact was pursued via email. Nineteen patients were deemed as 'potentially unstable' (10 CA and 9 HCM). The main reason for inclusion in group-B was a recent HF hospitalization. No 'stable' patients sought medical attention outside the planned tele-medical contacts. Eight 'potentially unstable' patients needed unplanned medical attention. In 4 instances, their needs were managed via tele-contact without the need for in-person evaluations: 2 CA patients needed optimization of diuretic therapy; 2 obstructive HCM patients needed optimization of therapy for relief of obstruction. In 3 other instances, a medical outpatient evaluation was required: 2 CA patients presented worsening HF symptoms, and 1 severely obese HCM patient presented a new-onset atrial fibrillation with high ventricular response. Finally, 1 CA patient required hospitalization due to acute decompensated HF.

Discussion. Tele-health monitoring strategies have never been specifically assessed in cardiomyopathy patients. In our experience, a short-term tele-health monitoring programme was feasible and effective. In current COVID-19 times, tele-medicine served as an emergency tool, yet lessons from its beneficial impact on healthcare practice may be exploited for the future.

A295: PROGNOSTIC UTILITY OF QUANTITATIVE OFFLINE 2D-ECHOCARDIOGRAPHY IN HOSPITALIZED PATIENTS WITH COVID-19 DISEASE

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(b) DIVISION OF CARDIOLOGY, DEPARTMENT OF DIAGNOSTICS, CLINICAL AND PUBLIC HEALTH MEDICINE, POLICLINICO UNIVERSITY HOSPITAL OF MODENA, UNIVERSITY OF MODENA AND REGGIO EMILIA

Purpose. To assess the prognostic utility of quantitative 2D-echocardiography, including strain, in patients with confirmed COVID-19 disease.

Methods. COVID-19 patients admitted to the San Paolo University Hospital of Milan, that underwent a clinically indicated echocardiographic exam were included in the study. To limit contamination all measurements were performed offline. Quantitative measurements were obtained by an operator blinded to the clinical data.

Results. Among the 49 patients, non-survivors (33%) had worse respiratory parameters, index of multiorgan failure and worse markers of severity of lung involvement. Right Ventricular (RV) dysfunction (as assessed by conventional and 2-dimensional speckle tracking) was a common finding and a powerful independent predictor of mortality. At the ROC curve analyses, RV free-wall longitudinal strain (LS) showed an AUC 0.77 ± 0.08 in predicting death, $p=0.008$, and global RV LS (RV-GLS) showed an AUC 0.79 ± 0.04 , $p=0.004$. This association remained significant after correction for age (OR 1.16, 95% CI 1.01-1.34, $p=0.029$ for RV free-wall LS and OR 1.20, 95% CI 1.01-1.42, $p=0.033$ for RV-GLS), for oxygen partial pressure at arterial gas analysis/fraction of inspired oxygen (OR 1.28, 95% CI 1.04-1.57, $p=0.021$ for RV free wall-LS and OR 1.30, 95% CI 1.04-1.62, $p=0.020$ for RV-GLS) and for the severity of pulmonary involvement measured by a computed tomography lung score (OR 1.27, 95% CI 1.02-1.19, $p=0.034$ for RV free-wall LS, and OR 1.30, 95% CI 1.04-1.63, $p=0.022$ for RV-GLS).

Conclusions. In patients hospitalized with COVID-19, offline quantitative 2D-echocardiographic assessment of cardiac function is feasible. Parameters of RV function are frequently abnormal and have an independent prognostic value over markers of severity of pulmonary involvement.

A296: IMPATTO DEL COVID-19 SULLA GESTIONE DEL PAZIENTE CON INFARTO MIOCARDICO ACUTO: SECONDA GIOVINEZZA PER LA FIBRINOLISI O TEMPO DI UN APPROCCIO CENTRALIZZATO? ESPERIENZA DI UN CENTRO HUB

Gabriele Tumminello (a), Lucia Barbieri (a), Stefano Lucreziotti (a), Barbara Conconi (a), Domitilla Gentile (a), Matteo Carlà (a), Marco Centola (a), Antonio Mafri (a), Stefano Carugo (a)
(a) ASST SANTI PAOLO E CARLO, CARDIOLOGIA

L'11 marzo 2020 l'Organizzazione Mondiale della Sanità ha dichiarato pandemica l'infezione da SARS-CoV-2 (COVID-19) e l'Italia è stata una delle nazioni più colpite. Il sistema di Emergenze-Urgenze regionale si è trovato a fronteggiare un incremento esponenziale delle ospedalizzazioni con la conseguente crisi del sistema organizzativo. Esperti dalla Cina, Regno Unito e Stati Uniti d'America hanno suggerito di riconsiderare la trombolisi, rispetto all'angioplastica primaria (pPCI), come il miglior trattamento, in termini di bilanciamento tra tempo-speso e sicurezza degli operatori, per l'infarto miocardico acuto con soprallivellamento del tratto ST-T (STEMI). Per fronteggiare l'emergenza è stata messa in atto una

riorganizzazione completa del sistema con centralizzazione della rete per le emergenze: da un totale di 55 ospedali con relativi laboratori di emodinamica distribuiti all'interno della nostra regione e attivi con un servizio 24h/7giorni si è passati a 13 centri HUB e 42 centri SPOKE afferenti. Sono stati altresì allestiti percorsi intraospedalieri dedicati ai pazienti positivi o sospetti per COVID (pCOV+) e negativi per COVID (pCOV-). Nel nostro studio abbiamo valutato tutti i pazienti che sono stati sottoposti a coronarografia urgente per STEMI afferenti al nostro centro HUB dal 14 marzo al 14 aprile 2020 comparando i tempi dei due percorsi intraospedalieri. Abbiamo quindi collezionato 30 pazienti con diagnosi di STEMI avvenuta nella fase pre-ospedaliera nel 73.3%. L'infarto anteriore è stato il più frequente (44.8%). Diciotto pazienti (60%) sono stati trattati nel percorso pCOV-, mentre dodici (40%) nel percorso pCOV+. Nessuna differenza significativa è stata trovata tra i due gruppi a riguardo dei tempi cardine del trattamento dello STEMI, in particolare modo i tempi di "diagnosi di STEMI-angioplastica" (64.6 ± 21.4 min vs 53.59 ± 30.50 min, $p=0.60$) e door-to-balloon (58.25 ± 42.78 min vs 35.35 ± 17.85 min, $p=0.18$) sono risultati sovrapponibili. Doveroso è sottolineare che i tempi "diagnosi di STEMI-angioplastica" si sono mantenuti ben al di sotto del limite dei 120 min stimati indicato come cut-off dalle attuali linee guida per preferire la trombolisi alla pPCI nel caso questa sia eseguibile oltre tale limite temporale. In conclusione, una revisione completa e focalizzata del sistema di Emergenze-Urgenze permette di mantenere la pPCI come il trattamento di scelta per lo STEMI anche durante la pandemia.

DIABETE E MALATTIE DEL METABOLISMO

A297: PREVALENCE, PRESCRIPTIONS, OUTCOMES AND COSTS OF TYPE 2 DIABETIC PATIENTS WITH OR WITHOUT PRIOR CORONARY ARTERY DISEASE OR STROKE. A LONGITUDINAL 5-YEAR CLAIMS-DATA ANALYSIS OF OVER 7 MILLION INHABITANTS

Silvia Calabria (a), Letizia Dondi (a), Felicità Andreotti (b), Giulia Ronconi (a), Carlo Piccinni (a), Anna Capponcelli (a), Antonella Pedrini (a), Imma Esposito (a), Nello Martini (a), Aldo P. Maggioni (a, c)

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Aims. Contemporary, real-world data on type 2 diabetes mellitus (T2DM) are limited. We analysed prevalence, comorbidities, outcomes and costs of T2DM patients with and without coronary artery disease (CAD) or stroke in >7 million inhabitants.

Methods. T2DM patients were identified in 2015 (accrual period) from the Ricerca e Salute (ReS) database linking administrative records to demographics. From 2013-2015 information, four cohorts were considered: #1 with CAD and/or stroke; #2 without CAD and/or stroke; #3 with chronic CAD but no myocardial infarction or stroke; #4 with chronic CAD undergoing percutaneous coronary interventions (PCI). Hospitalizations, drugs and other outpatient care were assessed from 2015 to 2017.

Results. Prevalence of T2DM was 6% (441,085/7,365,954). CAD and/or stroke in the previous 3 years affected 7.5% of T2DM patients (33,153); this cohort was generally older, male, comorbid, with more prescriptions, hospital admissions (50% versus 13.4%) and recurrences compared to cohort #2. Yearly costs were >3-fold for cohort #1 versus #2, main drivers being hospitalizations in the former and drugs in the latter. Unexpectedly, two-year cardiovascular events were significantly higher in cohort #4 compared to any other. Guideline-recommended therapies were suboptimal in all.

Conclusions. The present analysis points to three areas of potential improvement in T2DM management: 1) undertreatment of T2DM patients with recommended drugs; 2) three-fold event rates and costs in T2DM patients with, compared to those without, prior cardiovascular events; 3) highest risk of events in those with chronic CAD and PCI, warranting specific studies aimed at defining more effective preventive strategies.

A298: SINDROME DI MOYA MOYA NEI PAZIENTI CON DIABETE MELLITO DI TIPO 1: REVISIONE DI CASI IN LETTERATURA

Valeria Silvestri (a), Rita Mele (a)
(a) UNIVERSITA LA SAPIENZA DI ROMA

Introduzione. La sindrome di Moya Moya è una patologia dei vasi del circolo epi-aortico caratterizzata dalla stenosi progressive delle carotidi interne nel loro decorso intracranico nonché dei loro rami prossimali, associate con la formazione di una rete di collaterali ectasici visibili mediante esame arteriografico. I sintomi e segni che caratterizzano questa patologia possono essere correlati sia all'ischemia cerebrale che essere secondari ai meccanismi di compenso messi in atto in risposta all'ipo-perfusione cerebrale. L'incidenza della sindrome di Moya Moya risulta essere maggiore nei pazienti con patologie autoimmunitarie, inclusi i pazienti con diabete mellito di tipo 1.

Obiettivi e metodi. Obiettivo del nostro lavoro è stata la descrizione delle manifestazioni cliniche e delle caratteristiche chirurgiche della sindrome di

Moya Moya nei pazienti con diabete mellito di tipo 1, attraverso una revisione di casi clinici pubblicati in letteratura pubblicata in lingua inglese, effettuata utilizzando come parole chiave "Moya Moya syndrome" AND "Diabetes mellitus type 1".

Risultati. Sono stati inclusi nella nostra revisione della letteratura 7 articoli, per un totale di 17 casi. L'età media dei pazienti (la maggior parte, ove specificato, di sesso femminile) è risultata essere pari a 23.3 ± 9.9 anni; con età media alla diagnosi di diabete mellito di tipo 1 di 11.3 ± 6.8 anni e di 23.4 ± 9.5 anni alla diagnosi di sindrome di Moya Moya. L'anamnesi dei pazienti è risultata essere positiva per patologie autoimmunitarie aggiuntive, oltre al diabete mellito di tipo 1, in 11 casi (64.7%). Le principali manifestazioni neurologiche alla diagnosi sono state: afasia (7 casi; 41.2%), ma anche emiparesi, cefalea o emicrania, corea, emiballismo, crisi comiziali, atassia, disturbi della deambulazione, episodi sincopali o perdita di coscienza, cecità o disturbi del visus e attacchi ischemici transitori. Il coinvolgimento arterioso, valutato mediante esami di imaging angio TC o angio RMN ha documentato stenosi/occlusioni bilaterali del circolo carotideo intracranico nella maggior parte dei casi (6 casi; 35.3%), coinvolgimento monolaterale nell' 11.8%; lo sviluppo di circoli collaterali è stato riscontrato in 3 casi (17.6%). Aree ischemiche cerebrali sono state osservate in 2 pazienti (11.8%). In 7 pazienti è stata pianificata o effettuata una procedura di rivascolarizzazione chirurgica, nello specifico bypass tra la arteria temporale superficiale e l'arteria cerebrale media, un bypass indiretto tra il circolo extra-cranico e quello intracranico mediante encefalo-duro-arteriomiosinangioplastica. L'indicazione al trattamento risultava essere differita rispetto alla diagnosi di Moya Moya in 4 casi (23.5%), e fino a un massimo di 6 anni dopo la stessa. Tra le complicanze precoci e tardive della rivascolarizzazione sono occorse emiplegia con infarto acuto della cerebrale media e un ulteriore caso di infarto tardivo nel territorio della cerebrale media causato da occlusione completa del circolo prossimale stenotico della cerebrale media, entrambe con pervietà del precedente graft temporale/cerebrale media precedentemente confezionato. Ulteriori deficit neurologici residui conseguenti alla sindrome di Moya Moya nei pazienti con diabete mellito di tipo 1 sono stati: deficit mnemonici, ipostenia degli arti, disartria e difficoltà nel reperimento dei vocaboli. Non sono stati riportati casi di mortalità tra quelli presi in esame.

Conclusioni. La sindrome di Moya Moya può manifestarsi nei pazienti con diabete mellito di tipo 1. Dal momento che le manifestazioni cliniche del disordine metabolico e quelle neurologiche secondarie alla vasculite cerebrale possono sovrapporsi, confondendo nella diagnosi differenziale, è raccomandabile un forte sospetto clinico che indirizzi verso indagini approfondite un sospetto di vasculopatia cerebrale nei pazienti con diabete mellito di tipo 1 nei quali si manifestino sintomi neurologici, specialmente in assenza di ipoglicemia. I ritardi riportati nel trattamento, l'elevata morbilità nonché l'incidenza dei deficit neurologici residui nei pazienti che presentano questa associazione di patologie, sottolinea l'importanza di approfondire l'argomento mediante ulteriori studi che possano meglio definire questa stessa associazione in termini di fisiopatologia, per migliorare la gestione e la prognosi dei pazienti.

EPIDEMIOLOGIA E POLITICA SANITARIA

A299: IMPACT OF TEMPORARY TRAFFIC BANS ON THE RISK OF ACUTE CORONARY SYNDROMES IN A LARGE METROPOLITAN AREA

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(a) OSPEDALE SANTA MARIA GORETTI; (b) OSPEDALE M. G. VANNINI; (c) OSPEDALE SANT'ANDREA; (d) FONDAZIONE POLICLINICO UNIVERSITARIO AGOSTINO GEMELLI; (e) POLICLINICO CASILINO; (f) OSPEDALE SAN FILIPPO; (g) SAPIENZA UNIVERSITÀ DI ROMA; (h) AURELIA HOSPITAL; (i) ARPA LAZIO

Background. Strong epidemiologic evidence has highlighted the role of pollution, on top of adverse climate features, as a novel cardiovascular risk factor. However, mechanistic proof that reducing pollution may be beneficial to prevent atherothrombotic events is limited. We aimed at appraising the impact of temporary traffic bans in a large metropolitan area on the risk of acute coronary syndromes.

Methods. Aggregate and anonymized data from 15 tertiary cardiac care centers were obtained detailing pre-coronavirus disease 2019 (COVID-19) daily cases of ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI), including those treated with percutaneous coronary intervention (PCI). Data on pollutants and climate were sought for the same days. Mixed level regression was used to compare the week before vs after the traffic ban (Fortnight analysis), the 3 days before vs after (Weekly analysis) and the Sunday before vs after (Sunday analysis).

Results. A total of 8 days of temporary traffic bans were included, occurring between 2017 and 2020, totaling 802 STEMI and 1196 NSTEMI in the Fortnight analysis, 382 STEMI and 585 in the Weekly analysis, and 148 STEMI and 210 NSTEMI in the Sunday analysis. Fortnight and

Sunday analysis did not disclose a significant impact of traffic ban on STEMI or NSTEMI (all $p > 0.05$). Conversely, Weekly analysis showed non-significant changes for STEMI but a significant decrease in daily NSTEMI when comparing the 3 days before the traffic ban with the ban day ($p = 0.043$), as well as the 3 days before vs the 3 days after the ban ($p = 0.025$). No statistically significant effect of traffic ban was found at Fortnight, Weekly or Sunday analyses for daily mean concentrations of benzene, carbon monoxide, nitric oxide, nitrogen dioxide, ozone, sulfur dioxide, particulate matter (PM) $< 2.5 \mu\text{m}$ or PM $< 10 \mu\text{m}$ (all $p > 0.05$). However, minimum daily concentrations showed a significant reduction of ozone during the ban in comparison to the week preceding it ($p = 0.034$), nitric oxide during the ban in comparison to the 3 days preceding it ($p = 0.046$), and an increase in benzene during the ban in comparison to the Sunday before ($p = 0.039$).

Conclusions. Temporary traffic bans may favorably reduce coronary atherothrombotic events, and in particular NSTEMI, even if not globally and immediately impacting on environmental pollution. Further controlled studies are required to confirm and expand this hypothesis-generating results.

A300: EPIDEMIOLOGIA E FABBISOGNO DI CURE PALLIATIVE NELLE MODERNE TERAPIE INTENSIVE CARDIologiche

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(a) AZIENDA OSPEDALIERO-UNIVERSITARIA S. ANNA FERRARA, CONA (FE); (b) AZIENDA USL DI BOLOGNA, OSPEDALE MAGGIORE BOLOGNA

Background. Negli ultimi decenni abbiamo assistito ad un'evoluzione dalla vecchia unità coronarica verso una più moderna concezione di unità di terapia intensiva cardiologica (UTIC), caratterizzata da tecnologie diagnostiche e terapeutiche avanzate, nonché da un maggiore livello di differenziazione delle competenze cardiologiche. A fronte di questa maggiore specializzazione e intensivizzazione delle cure volte al mantenimento delle funzioni vitali e alla riduzione della mortalità, i pazienti che accedono oggi nelle UTIC sono sempre più spesso anziani e con molteplici comorbidità. I dati di letteratura indicano che il 14-20% dei pazienti in UTIC potrebbe possedere i "criteri" per eseguire una consulenza da parte di uno specialista in cure palliative.

Obiettivi. Valutare l'epidemiologia e i pattern di cura delle moderne UTIC con particolare attenzione alle caratteristiche potenzialmente "end-stage" dei pazienti, alle eventuali necessità di cure palliative e alla gestione del dolore.

Metodi. Tra il primo Marzo 2020 e il 15 Maggio 2020, 151 pazienti sono stati ricoverati nella terapia intensiva cardiologica di secondo livello dell'Ospedale Maggiore di Bologna. Durante la degenza in UTIC sono state raccolte informazioni epidemiologiche, riguardo le terapie e le risorse utilizzate, nonché le complicanze verificatesi durante la degenza. Inoltre, ai pazienti veniva chiesto di rispondere ad alcune domande riguardo le loro condizioni socio-culturali, lo stato lavorativo, la percezione del dolore (su scala numerica 0-10), la qualità delle cure e l'intensità delle stesse. La performance fisica prima del ricovero veniva valutata mediante la Palliative Performance Scale (PPS) semplificata e la contemporanea presenza di red-flags validate che potessero identificare il paziente come potenzialmente "end-stage".

Risultati. L'età mediana dei pazienti ammessi in UTIC è risultata di 74 anni (IQR 63-81); nel 68% dei casi il motivo di ammissione era per sindrome coronarica acuta; la maggior parte presentava rilevanti comorbidità croniche (fino al 39% disfunzione renale, il 26% anemia). Il 74% viveva in famiglia, il 22% da solo e il 4% in strutture residenziali. Durante la permanenza in UTIC sono stati somministrati farmaci sedativi (oppioidi e/o benzodiazepine) nel 13% dei pazienti; lo 0.7% ha necessitato di nutrizione parenterale e per l'1% è stato attivato il percorso di cure palliative (tutti pazienti con età ≥ 75 anni). Nel complesso, è stato ottenuto un ottimo controllo del dolore (valore mediano 0/10 (IQR 0-2): tuttavia tra i pazienti che ne hanno avuto molto (punteggi $\geq 5/10$), il 56% aveva livelli di istruzione più alti (scuole superiori o università). Il 7.7% dei pazienti presentava almeno un criterio per identificare lo stato potenzialmente "end-stage" e l'1.4% presentava ≥ 2 criteri. Analizzando la PPS, il 5.6% dei pazienti aveva un punteggio $\leq 50\%$, che è stato dimostrato associarsi ad una maggiore mortalità. La mortalità globale si è attestata al 3.9%, in linea con i dati pubblicati in letteratura.

Conclusioni. Il cambiamento epidemiologico delle UTIC moderne spinge gli specialisti cardiologi ad acquisire sempre più conoscenze e competenze riguardanti aspetti che esulano dalla sfera prettamente intensiva e si spingono verso la gestione del fine vita, le cure palliative e la corretta comunicazione degli obiettivi terapeutici al paziente e ai familiari. L'invecchiamento della popolazione e la necessità di una virtuosa allocazione delle risorse e tecnologie disponibili rappresentano gli aspetti etici a cui la società e gli specialisti cardiologi sono chiamati a rispondere.

A301: THE PARADOX OF LDL CHOLESTEROL MANAGEMENT IN SECONDARY PREVENTION: KEEPING THE GUN IN THE HOLSTER

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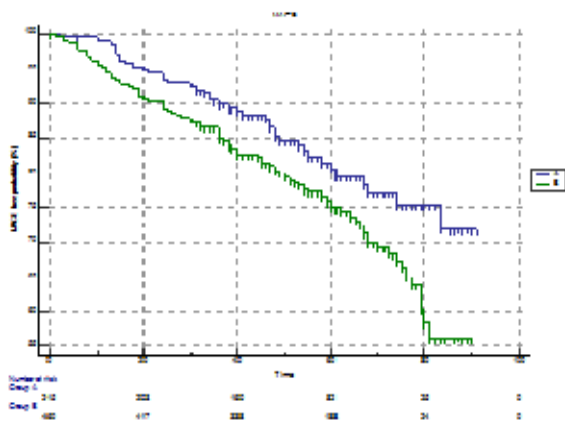
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Background and aim. Current European Society of Cardiology (ESC) guidelines strongly recommend for secondary prevention a combination therapy with a PCSK9 inhibitor for patients at very-high cardiovascular risk not achieving their LDL cholesterol (LDL-C) goals on a maximum tolerated dose of a statin and ezetimibe. Nonetheless, a wide gap exists between the LDL-C target recommended (LDL-C <55 mg/dL) by ESC guidelines and the prescription criteria adopted by the Italian drug regulatory agency (AIFA) (LDL-C ≥100 mg/dL). The aim of the present study was to investigate the prevalence of patients within this gap and their risk of cardiovascular events in a real-world cohort.

Methods. We conducted a retrospective analysis of a monocentric observational registry prospectively enrolling patients admitted to our hospital for ST segment elevation myocardial infarction (STEMI) and followed-up in our dedicated post-myocardial infarction (PMI) ambulatory. We considered the combined endpoint of major adverse cardiovascular events (MACE) defined as a composite of all-cause death, non-fatal MI, non-fatal stroke and unplanned revascularization. LDL-C was collected at baseline and during follow-up; the lower value at follow-up was used to define the achievement of the target. We conducted a Kaplan-Meier analysis and log-rank test comparing patients who achieved LDL-C <55 mg/dL (group A) vs those with LDL-C between 55 and 100 mg/dL (group B). Continue variable are presented as median (interquartile range).

Results. A total of 814 patients (23% female) were included in the analysis. Median age was 63 (55-72) years, 57% had hypertension, 19% diabetes, and 36% were smokers. Median follow-up was 52 (34-66) months. A total of 83.3% of patients were treated with statin therapy alone (73% high intensity), and 15.3% with the addition of ezetimibe. LDL-C <55 mg/dL was achieved in 244 patients (30%), 55 patients had LDL-C >100 mg/dL, while 515 patients (63%) remained in the gap between 55 and 100 mg/dL. High intensity statin and ezetimibe prescription was not significantly different between group A and B (respectively 86% vs 87.9%; P=0.45 and 11.6 vs 17%; P=0.06). The net incidence of MACE was 16.4% in group A vs 23.9% in group B (HR 0.68; 95% CI 0.49-0.94; P log-rank=0.02; Number Needed to Treat=13; see Figure).

Conclusion. The majority of PMI patients, despite high intensity lipid-lowering therapy, fail to reach the recommended LDL-C target in a real-world cohort. Importantly, the prognosis of patients with LDL-C values between 55 and 100 mg/dL was significantly worse than that of patients achieving values <55 mg/dL. A discussion with healthcare authorities is warranted to improve the prescription of PCSK9 inhibitors in this very high-risk cohort of patients in line with current guidelines recommendation.

**A302: CO, NO₂ AND O₃ LEVELS AND OUT-OF-HOSPITAL CARDIAC ARREST IN A LARGE COHORT OF PATIENTS FROM PROGETTO VITA**

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Introduction. Out-of-hospital cardiac arrest (OHCA) is a leading cause of death worldwide. It accounts for up to 50% of all cardiovascular deaths. The incidence of OHCA in Italy is about 1.51 arrests/1000 admission/year. Recent studies have sought to find a link between short-term exposure to air pollutants and OHCA. It is well established that ambient air pollution triggers cardiovascular fatal and nonfatal events. but the results are still

controversial. Most studies on this subject were performed in developed countries with only a paucity of data from Asia, where air pollution is increasingly becoming a major healthcare issue.

Aim. The objective of this study was to investigate the impact of short-term exposure to outdoor air pollutants on the incidence of OHCA in Piacenza, Italy. Outcomes were the incidence of cardiac arrest.

Methods. NO₂ (nitrogen dioxide), CO (carbon monoxide) and O₃ (ozone) levels were extracted from Environmental Protection Agency (ARPA) local monitoring stations; OHCA were extracted from Progetto Vita Database of Cardiac arrest. Conditional logistic regression models estimated odds ratios (OR) with 95% confidence intervals (CI). NO levels exceeded safe threshold recommended by Italian legislation for 46%, CO for 10% and O₃ for 62% of the whole period.

Results. 880 OHCA occurred on 750 days, with 2174 control days. Mean age of OHCA patients was 76 ± 15 years. Concentration of NO₂ and CO were significantly higher on days with occurrence of OHCA (respectively 412 ± 196 µg/m³ vs 442 ± 212 µg/m³ p<0.0001 for NO₂ and 52 ± 31 vs 57 ± 32 for CO). Risk of OHCA presentation was significantly increased by high concentration of CO, OR 1.100 (95% CI 1.001-1.223), and not significantly for NO₂ (OR 1.053, 95% CI 0.948-1.169). No significant differences were found in O₃ levels.

Conclusions. The results of this study confirm the link between OHCA and NO₂ and CO in a large cohort of patients from a high pollution area.

A303: ARRESTO CARDIACO EXTRA-OSPEDALIERO ED INQUINAMENTO ATMOSFERICO. RELAZIONE DOSE-EFFETTO ED INCIDENZA GIORNALIERA

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Introduzione. L'inquinamento atmosferico è stato identificato come uno dei possibili fattori precipitanti l'arresto cardiaco extra-ospedaliero (OHCA), ma l'entità di questa associazione è tutt'oggi oggetto di controversia. Gli studi attualmente disponibili in letteratura su questo argomento sono tuttavia spesso limitati ad aree urbane o ad analisi su un ristretto numero di inquinanti. L'obiettivo del nostro studio è quello di fornire una relazione dose-effetto tra le maggiori componenti dell'inquinamento atmosferico e l'incidenza di OHCA in un'area di 7863 km², eterogenea per grado e tipologia di antropizzazione, comprendente quattro province della Pianura del Po, una delle aree più inquinate d'Europa per alto tasso di industrializzazione e densità di popolazione.

Materiali e metodi. Abbiamo considerato gli OHCA ad eziologia medica classificati secondo lo stile Utstein arruolati nel Registro degli Arresti Cardiaci della Regione Lombardia (Lombardia CARE) dal 01/01/2019 al 31/12/2019 nelle province di Pavia, Lodi, Cremona, e Mantova (7863 km², 1,547,333 abitanti). L'incidenza giornaliera è stata espressa in casi/100,000 abitanti (la popolazione è stata adeguata mensilmente secondo i dati ISTAT). I dati ambientali di PM₁₀, PM_{2.5}, NO₂, CO, benzene, O₃ e SO₂ sono stati registrati da 106 centraline di rilevamento distribuite sul territorio in esame, comprendente aree urbane, suburbane e rurali, e forniti dall'Agenzia Regionale per la Protezione Ambientale (ARPA). È stata calcolata la media giornaliera degli inquinanti, verificandone l'andamento giornaliero nelle quattro province. Infine è stata valutata la relazione dose-effetto con un modello di regressione secondo Probit.

Risultati. nel 2019 nel territorio in esame si sono verificati 1922 OHCA, di cui 1582 ad eziologia medica; l'incidenza giornaliera mediana è stata di 0.3 casi/100,000 abitanti (IQR 0.3-0.5). Nei giorni con un'incidenza di OHCA superiore alla mediana i valori di concentrazione mediana di PM₁₀ [29.1 µg/m³ (IQR 19.5-46) vs 24.9 µg/m³ (IQR 18.7-36.3); p=0.02], PM_{2.5} [21 µg/m³ (IQR 12.6-35.5) vs 15.5 µg/m³ (IQR 10.8-24); p=0.004], NO₂ [27.4 µg/m³ (IQR 18.4-39.6) vs 20.2 µg/m³ (IQR 15.1-27.6); p<0.001], CO [0.5 mg/m³ (IQR 0.4-0.7) vs 0.4 mg/m³ (IQR 0.4-0.5); p<0.001], benzene [0.7 µg/m³ (IQR 0.4-1.2) vs 0.4 µg/m³ (IQR 0.3-0.7); p<0.001] e SO₂ [3.2 µg/m³ (IQR 2.8-3.6) vs 3 µg/m³ (IQR 2.7-3.5); p=0.046] sono risultati significativamente superiori rispetto ai giorni con un'incidenza di OHCA inferiore alla mediana. Al contrario, sono risultati inferiori i valori di concentrazione di O₃ [29.9 µg/m³ (IQR 11-61.7) vs 56 µg/m³ (IQR 25.5-74.1); p<0.001]. È stata inoltre documentata una relazione diretta di dose-effetto statisticamente significativa tra la concentrazione atmosferica di PM₁₀, PM_{2.5}, NO₂, benzene e CO e la probabilità giornaliera di registrare un numero di OHCA superiore alla mediana (p=0.01, p=0.002, p<0.001, p<0.001, p=0.001 rispettivamente). Per SO₂ non è stata raggiunta la significatività statistica (p=0.08), mentre per l'ozono O₃ la relazione è risultata statisticamente significativa, ma inversa (p<0.001).

Conclusioni. Questo studio, oltre ad offrire un chiarimento sul ruolo dell'inquinamento atmosferico nell'incidenza di OHCA, rappresenta la prima dimostrazione di una relazione dose-effetto tra i principali agenti inquinanti e la probabilità di avere un aumentato numero di arresti cardiaci extra-ospedalieri.

FARMACI CARDIOVASCOLARI E NUTRACEUTICI

A304: PROBIOTICI: OSSERVAZIONI NELLA MEDICINA PRATICA

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Background. Diversi sono gli studi, anche recenti, di ricerca di base che hanno dimostrato la carenza del microbiota alla predisposizione e allo sviluppo di disturbi e fattori di rischio degenerativi: patologie cardiovascolari, obesità, sindrome metabolica e diabete. Gli studi, le conoscenze e la comunicazione sui probiotici sono andati e sono sempre più in crescendo, tanto da svilupparsi quasi una "moda" del probiotico. L'importanza di definire il "probiotico" e sviluppare le conoscenze e la ricerca clinica, ovvero valutare i risultati nella pratica clinica reale, è basilare per l'utilizzo appropriato a beneficio della persona. Il medico ha e deve avere un ruolo centrale e primario.

Scopo. Lo studio, che abbiamo condotto nella pratica clinica, è di tipo osservazionale, e ha come outcome primario quello di valutare l'impatto di una integrazione nutriceutica con probiotici sui fattori di rischio markers infiammatori e metabolici e quale outcome secondario la capacità funzionale e la percezione della salute psicofisica.

Metodi. Su 70 pazienti seguiti sono stati selezionati e valutati 50 pazienti per caratteristiche di omogeneità e aderenza. Caratteristiche seguenti di eleggibilità: profilo di rischio, familiarità per malattie cardiovascolari, turbe disendocrine, sovrappeso e obesità, ipertensione, diabete, ipercolesterolemia, ipertrigliceridemia, sindrome da fatica, distonia neurovegetativa. La valutazione della terapia mediante probiotici è stata effettuata in due tempi in base ai seguenti parametri: percezione psicofisica dello stato di salute, tramite Questionario SF-36, capacità funzionale mediante il test di capacità fisica (Six Minute Walking Test 6MWT o Test della Marcia), esami ematici: PCR, Vitamine, profilo lipidico. Lo schema nutriceutico consiste nell'assunzione di 2cps dopo colazione e 2 cps dopo cena di Enterelle, nell'arco della prima settimana. Bifiselle, seconda settimana, Ramnoselle terza settimana Serobrain 1 cps dopo colazione quarta settimana. Serobioma, una compressa al giorno, per 3 mesi: fase di mantenimento.

Risultati e Conclusioni. Lo studio osservazionale nella pratica reale ha indicato un'efficacia del trattamento nutriceutico probiotico sui pazienti riguardo riduzione del profilo di rischio misurabile, miglioramento della percezione della salute compreso livello oggettivo di capacità funzionale, stabilizzazione dei livelli di vitamine (vit B e D).

A305: RELATIVE EFFICACY OF SACUBITRIL/VALSARTAN, DAPAGLIFLOZIN AND VERICIGUAT: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Background. Sacubitril/valsartan, dapagliflozin and vericiguat have shown a prognostic benefit in phase 3 trials on heart failure with reduced ejection fraction (HFrEF). Assessing their relative efficacy is an important goal.

Methods. We assessed the relative efficacy of dapagliflozin, sacubitril/valsartan and vericiguat, by comparing the treatment arms with the respective control arms (standard of care) through a network meta-analysis.

Results. The phase 3 trials (PARADIGM-HF, DAPA-HF, VICTORIA), the HFrEF subgroup of DECLARE-TIMI 58, and a phase 2 trial on vericiguat were evaluated. Dapagliflozin was associated with a non-significant reduction in the risk of cardiovascular (CV) death or HF hospitalization compared to sacubitril/valsartan (hazard ratio [HR] 0.89, 95% confidence interval [CI] 0.64 to 1.22) and vericiguat (HR 0.82, 95% CI 0.6 to 1.12). The risk of CV death did not differ significantly between patients on dapagliflozin or sacubitril/valsartan (HR 0.90, 95% CI 0.51 to 1.58), and between patients on dapagliflozin or vericiguat (HR 0.77, 95% CI 0.44 to 1.37). As for HF hospitalization, dapagliflozin conferred a significant benefit over vericiguat (HR 0.77, 95% CI 0.63 to 0.93), but not over sacubitril/valsartan (HR 0.87, 95% CI 0.72 to 1.06). Dapagliflozin was ranked as the most effective therapy, followed by sacubitril/valsartan and vericiguat.

Conclusions. Based on an indirect comparison, dapagliflozin is not associated with a significantly lower risk of CV death or HF hospitalization or CV death alone compared to sacubitril/valsartan or vericiguat. The risk of HF hospitalization does not differ significantly between patients on dapagliflozin or sacubitril/valsartan, while dapagliflozin is superior to vericiguat.

Registration number: PROSPERO ID 186351.

A306: THE RATIO BETWEEN N-3 AND N-6 POLYUNSATURATED FATTY ACIDS IN THE ADIPOSE TISSUE IS MORE PREDICTIVE OF MYOCARDIAL INFARCTION THAN ABSOLUTE LEVELS OF N-3 FATTY ACIDS: RESULTS FROM THE DANISH DIET, CANCER AND HEALTH COHORT STUDY

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Background. Consumption of dietary n-3 polyunsaturated fatty acids (PUFAs) has been associated with a reduced risk of cardiovascular (CV) events. It is unknown if the total amount of n-3 PUFAs in the diet or the n-3/n-6 ratio are more relevant.

Methods. Subcutaneous adipose biopsies were obtained from participants to the Danish Diet, Cancer and Health population study and no history of myocardial infarction (MI) (n=55,547). Absolute and relative values of n-3 and n-6 PUFAs were determined.

Results. 2,406 participants with an incident diagnosis of MI were compared with 3,165 randomly selected subjects. Three n-3/n-6 ratios (key products of the n-3 and n-6 pathways: eicosapentaenoic acid [EPA]/arachidonic acid [AA]; n-3 final product and the key product of n-6 pathway: docosahexaenoic acid [DHA]/AA; total amount of n-3 PUFAs and key product of n-6 pathway: [EPA+docosapentaenoic acid {DPA}+DHA]/AA) improved risk prediction over age, body mass index, waist circumference, smoking status, physical activity, alcohol intake, educational level, diabetes, hypertension, and hypercholesterolemia (Harrell's C index p=0.026, 0.043, 0.048, respectively), while the total amount of n-3 PUFAs did not (p=0.376).

Conclusions. Subjects from the general population with a higher ratio of EPA/AA, DHA/AA or total marine n-3/AA in the adipose tissue had a lower risk of MI. The same covariates showed to be stronger predictors of MI compared to the total amount of n-3 PUFAs. Increasing the intake of n-3 rich sources and decreasing the dietary intake of n-6 PUFAs could be a more effective strategy than simply increasing the intake of n-3 PUFAs.

A307: ICARIIN PROTECTS H9C2 RAT CARDIOMYOBlasts FROM DOXORUBICIN-INDUCED CARDIOTOXICITY: NEW INSIGHTS ON MOLECULAR MECHANISM

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Background. Doxorubicin (DOXO) is one of the most successfully antineoplastic drugs used to treat different type of malignancies. Furthermore, the chronic administration of DOXO often induces cardiotoxicity which over time causes cardiomyopathy that leads to congestive heart failure. The intramyocardial production of reactive oxygen species (ROS) is the main mechanism by which DOXO injures myocardium. Icaritin (ICA) is a flavonoid isolated from *Epimedium brevicornum maxim* that has been shown promising cardiovascular protective properties. However, less is known about the underlying molecular mechanism of ICA in counteracting DOXO cardiotoxicity. The aim of our study was to assess the protective activities of ICA against DOXO-detrimental effects and to identify, at least in part, the molecular mechanisms involved.

Methods. Rat heart-tissue derived H9c2 embryonic cardiac myoblasts cells were pre-treated with different doses of ICA and after 3h, DOXO was used to treat cells to evaluate the effect of ICA on DOXO cytotoxicity performing an MTT assay. To quantify apoptotic cells, flow cytometry was used. After pre-treatment for 3h with ICA 1µM or 5µM, and treatment with DOXO 1µM for 24h, the cells were stained with 488 Annexin V protein and Propidium Iodide. 2', 7'-dichlorodihydrofluorescein diacetate (H₂DCFDA), a fluorescent probe, was used to detect ROS production. Finally, proteins were separated by western blotting and the membrane were incubated overnight with primary antibody against toll-like receptor 4 (TLR-4), Lectin like ox-LDL receptor-1 (LOX-1), Caveolin-1, NfκB, iNOS, Beclin-1, LC3.

Results. Our results show a dramatic reduction in the viability of the H9c2 cells following 1µM of DOXO exposure which was accompanied by a significant ROS overproduction. Moreover, our data confirmed that *Toll-Like Receptor 4* (TLR4) expression on the surface of cardiomyocytes was involved in the inflammatory and oxidative stress reactions after DOXO treatment, mediating the expression of Caveolin-1 (Cav-1) and Lectin-type Oxidized LDL receptor 1 (LOX-1) which leads to translocation and activation of the pro-inflammatory nuclear transcription factor NF-κB. Finally, the activation of this signalling pathway leads to increased levels of iNOS and activation of pro-inflammatory process, giving rise to dysfunction of the autophagic process and enhanced apoptosis cell death. Intriguingly, pre-treating H9c2 cells with 1 and 5µM of ICA prior to DOXO exposure resulted in increased cell viability and a decreased generation of ROS. Furthermore, for the first time, we identify one feasible molecular mechanism through which ICA could exerts its cardioprotective effects.

Indeed, our results shown a significant reduction of TLR-4, LOX-1 and Cav-1 expression levels as well as a significant reduction in the NF- κ B nuclear translocation and subsequent inhibition of iNOS expression. Besides ICA was found able to prevent apoptosis cell death and to downregulate the main pro-autophagic marker Beclin-1 and LC3 lipidation rate restoring physiological activation levels of the protective autophagic process.

Conclusions. These findings suggest that ICA could have beneficial cardioprotective effects in attenuating cardiotoxicity in patients requiring anthracycline chemotherapy through the inhibition of oxidative stress and inflammation, and more specifically through the modulation of TLR4-Cav-1-LOX-1 pathway, thereby leading to cardiac cell survival.

A308: THE INCREASE IN PEAK ATRIAL LONGITUDINAL STRAIN IN PATIENTS WITH CHRONIC HEART FAILURE IS SIGNIFICANTLY GREATER WITH THE USE OF SACUBITRIL/VALSARTAN. RESULTS FROM A RETROSPECTIVE COHORT STUDY

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Background. The peak atrial longitudinal strain (PALS) is primarily an index of the reservoir function of atrial chambers. The conceptual basis exists to hypothesize that sacubitril/valsartan improves the expandability of atrial chambers in the reservoir phase of the atrial mechanical cycle, as a consequence of its effect of prolonging the half-life of natriuretic peptides. Therefore in this retrospective study we evaluated the repercussions of the administration of sacubitril/valsartan maintained for at least 12 months on the PALS.

Methods. In our retrospective study a cohort of 40 patients treated with sacubitril/valsartan has been compared with a second cohort of 40 patients subjected to the conventional treatment with an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker. A general criterion to be satisfied was the presence of at least one episode of atrial fibrillation (AF) in the history of the enrolled patients. The study population was composed of New York Heart Association (NYHA) class II/III chronic heart failure (CHF) patients, due to the fact that the treating physicians of the patients whose clinical records were used as source of data, complied with the international guidelines that have so far validated sacubitril/valsartan exclusively for the CHF therapy. The aims were to verify whether the 1-year administration of sacubitril/valsartan is effective in improving the PALS, and also ascertain whether the drug is associated with a decreased risk of AF relapses over a mean retrospective observation period of 12 months.

Results. Sacubitril/valsartan cohort was proven to benefit from a significant increase in average values of PALS (median: 26.5%; interquartile range (IQR): 22% - 30%), opposed to the much less pronounced increase in PALS found in the conventional therapy cohort (median: 22.5%; IQR: 18% - 25.5%). Additionally, the comparison made by means of one-way analysis of variance regarding the mean changes of PALS values, outlined clearly that the sacubitril/valsartan users had an increase in PALS after 1 year of therapy significantly greater ($P < 0.001$) compared to the patients taking the conventional drugs. Moreover, a risk significantly higher of AF recurrences ($P = 0.001$) was identified in the conventional therapy group compared to the sacubitril/valsartan group during a 12-month retrospective observation period.

Conclusions. In the present retrospective cohort study a higher increase of PALS has been shown in the cohort treated with sacubitril/valsartan. Moreover, a reduced risk of AF recurrences has been shown in the sacubitril/valsartan users compared to the patients with CHF subjected to conventional treatment.

A309: IDENTIFICATION OF RISK FACTORS FOR AMIODARONE-INDUCED HYPER- AND HYPOTHYROIDISM BY MEANS OF A CASE-CONTROL STUDY: OUR EXPERIENCE ON A SAMPLE OF 314 PATIENTS EXAMINED RETROSPECTIVELY

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Background. Chronic use of amiodarone has been associated with a high risk of iatrogenic hyper- and hypothyroidism. However, risk factors as well as protective determinants regarding the manifestations of amiodarone-induced thyroid toxicity have not been identified yet.

Methods. A retrospective investigation was conducted in order to identify the respective prevalences of hyper- and hypothyroidism related to the chronic use of amiodarone. Furthermore, only patients who had experienced continuous treatment with amiodarone for at least six months were retrospectively enrolled. The demographic characteristics were noted, as well as all the necessary information regarding the patient's clinical status at the beginning and during the treatment. In particular, the underlying pathologies and the results of thyroid function tests performed before and during treatment were considered. Possible predictors of thyroid dysfunction arising during treatment with amiodarone were explored by logistic regression analysis.

Results. 314 patients were enrolled. Among them, there were 31 cases of hyperthyroidism and 60 cases of hypothyroidism. Logistic regression analysis showed that dilated cardiomyopathy ($p < 0.0001$) and duration of treatment ($p = 0.0407$) were able to predict the onset of hyperthyroidism during amiodarone treatment. Moreover, baseline free T4 ($p < 0.0001$) and baseline TSH ($p < 0.0001$) were both recognized as significant predictors of amiodarone-induced hypothyroidism.

Conclusions. By means of a thorough retrospective analysis, the predictors of amiodarone-related thyroid dysfunction can be detected. Thus a more restrictive selection among the candidates to amiodarone therapy should be carried out. Furthermore, where the drug is indispensable, for example in the case of life-threatening hyperkinetic ventricular arrhythmias, a better knowledge of the increased risk of thyroid toxicity in some patient subsets would allow timely implementation of targeted therapeutic measures (replacement therapy with thyroxine in the hypothyroidism, withdrawal of amiodarone plus thionamides and/or glucocorticoids in the hyperthyroidism).

A310: IN THROMBOCYTOPENIC PATIENTS WITH ATRIAL FIBRILLATION REQUIRING ANTITHROMBOTIC PREVENTION, EDOXABAN IS ASSOCIATED WITH A BETTER CLINICAL OUTCOME COMPARED TO ENOXAPARIN SODIUM: A RETROSPECTIVE COHORT STUDY

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Background. Low-dose edoxaban and enoxaparin sodium have been the subject of a retrospective comparison.

Methods. The research has been implemented with the propensity score technique in order to mitigate the effects of the differences in the basal clinical features of the two retrospective cohorts and minimize the risk of bias. Subsequently, with the use of a Cox proportional-hazards model, the association of each type of therapy with the risk of the composite of all-cause death, stroke / transient ischemic attack, hospitalizations and major bleeding events has been assessed. The requirements for inclusion in the retrospective study were: moderate thrombocytopenia, defined by a platelet concentration between 99,000 and 30,000 thrombocytes per mm^3 ; chronic atrial fibrillation (AF), subject to the rate control strategy; absence of newly diagnosed paroxysmal AF. The power and sample size calculations were not made in this study.

Results. In the present retrospective cohort study, which encompassed a median period of 40

months (interquartile range: from 36 to 48 months), a total of 220 patients with AF were included. The therapy with enoxaparin, and the cirrhosis of the liver as causing thrombocytopenia were both associated with an increased risk of the composite endpoint (enoxaparin: hazard ratio (HR): 3.31; 95% CI: 1.54 to 7.13; $p = 0.0023$; cirrhosis of the liver, HR: 1.04; 95% CI: 1.002 to 1.089; $p = 0.0410$). Conversely, edoxaban therapy was significantly associated with a decreased risk of the composite endpoint (HR: 0.071; 95% CI: 0.013 to 0.373; $p = 0.0019$).

Conclusions. Based on this retrospective analysis, edoxaban at low doses would appear as an efficacious and safe pharmacological tool for the prophylaxis of cardio-embolic events in patients with AF and thrombocytopenia.

A311: ANTITHROMBOTIC STRATEGIES AFTER PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH ATRIAL FIBRILLATION - RESULTS OF A SINGLE-CENTER STUDY

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Background. The management of antithrombotic therapy in patients with atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI) is still a matter of debate. The present study aims to evaluate the safety and efficacy of different possible antithrombotic strategies in patients undergoing PCI and requiring long-term oral anticoagulation therapy (OAT).

Methods. This retrospective, observational, single-center study enrolled

patients undergoing PCI requiring long-term OAT, treated with Vitamin K antagonists (VKAs) or with new oral anticoagulants (NOACs), between January 2014 and December 2019. We included consecutive patients undergoing PCI for stable or acute coronary syndromes (ACS) and affected by AF with indication of long-term OAT with VKAs or NOACs. After PCI all patients received a triple antithrombotic treatment including Dual Antiplatelet Therapy (DAPT) with aspirin and clopidogrel, and anticoagulant for at least one month. Patients were divided into three groups based on the type of anticoagulant regimen associated with the DAPT (full-dose NOACs, reduced-dose NOACs, and vitamin K antagonists). The primary endpoint was to evaluate the incidence of bleeding events according to the BARC classification (Bleeding Academic Research Consortium) at 30-days and at long-term follow-up in the three groups of patients. The secondary endpoints were global mortality, MACE in the 30-day and long-term follow-up.

Results. We enrolled 201 patients. All patients were discharged on triple antithrombotic therapy with DAPT and oral anticoagulant. The study population was divided according to anticoagulant treatment: 41 patients were treated with VKAs, 17 with full-dose NOACs and 143 with reduced-dose NOACs. The three groups did not present significant differences in the main clinical features, the thromboembolic risk profile, the hemorrhagic risk profile and the procedural characteristics. The 65% of patients received triple antithrombotic therapy for 1 month, 10% for 3 months, 20% for 6 months and 12 months in 5%. Regarding to the primary endpoint the incidence of bleeding at 30 days was: 1 patient in the VKAs group (2.4%), 2 patients in the full-dose NOACs group (11.8%) and 1 patient in the reduced-dose NOACs group. (0.7% - P = 0.02). At long-term follow-up there were no significant differences in bleeding between the three study groups (6.7% for full-dose NOACs, 16.9% reduced-dose NOACs and 18.4% for VKAs - P = 0.55). After 12 months, the 28.9% of patients was still receiving dual antithrombotic therapy (anticoagulant + aspirin or clopidogrel) with a bleeding rate of 22.7% vs 12.3% of patients in OAT alone (P = 0.09).

Conclusions. Our findings suggest that triple antithrombotic therapy with reduced-dose of NOACs could be a safe and effective strategy in the treatment of patients undergoing PCI with an indication of long-term OAT. Furthermore, the prolongation of antiplatelet therapy beyond 12 months from PCI has been shown to expose patients to an increased risk of long-term bleeding events. These data need to be confirmed in larger and possibly randomized population.

A312: EFFICACY AND SAFETY OF EDOXABAN IN PATIENTS WITH ATRIAL FIBRILLATION (AF) AND SEVERE CHRONIC KIDNEY DISEASE (CKD)

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Background. Atrial fibrillation is an arrhythmia with high prevalence in the. In elderly patients, this arrhythmia is often associated with specific clinical conditions such as CKD. The aim of our observational study is to assess the clinical efficacy and safety of edoxaban 30 mg/die in patients with AF and severe renal impairment, an estimated glomerular filtration rate (eGFR) of 15–29 mL/min.

Methods and Results. We analyzed retrospective data from 30 patients from June 2016 to November 2018 who had documented AF with severe renal impairment (eGFR 15–29 mL/min). Population mean age was 70 years and 20% were female (20 males and 10 females). The inclusion criteria were patients with at least one episode of documented AF of any duration in the preceding 12 months; a CHA₂DS₂-VASc score of ≥ 2; any type of NVAF; age >65 years; and severe renal impairment with an eGFR between 15 and 29 mL/min, calculated using the Cockcroft–Gault formula. Standard two-dimensional transthoracic echocardiographic examination was performed. Left ventricular end-diastolic volume, end-systolic volume, and ejection fraction (LVEF). Follow-up, characterized by clinical examination and blood analysis, was performed at 3, 6, and 12 months. The AF patients were followed for the effectiveness outcome of thromboembolism and bleeding outcomes, as well as bleeding requiring hospitalization. A secondary safety endpoint was total minor bleedings. During follow-up, we observed no major bleedings, systemic embolism, strokes, or cardiovascular deaths. Only three minor hemorrhages (two epistaxis and one hematuria, none of which required blood transfusion or hospital admission) observed. From these three patients with minor hemorrhages, no differences observed in LVEF or left atrial dimension at echocardiography, body mass index, and the thrombotic and hemorrhagic risk profile.

Conclusions. Our observational study confirms the results already present in literature, the AF patients with severe CKD treated with edoxaban 30 mg/die for stroke prevention, no major bleedings or thrombotic events were observed, but only some minor bleedings.

A313: SACUBITRIL/VALSARTAN REDUCES VENTRICULAR ARRHYTHMIAS IN HEART FAILURE WITH REDUCED EJECTION FRACTION

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Background. In the PARADIGM-HF study sacubitril/valsartan has been shown to reduce the rate of sudden cardiac death in patients with heart failure with a reduced ejection fraction. However, it is not clear which mechanism may have led to this result. The aim of our study was to compare the sacubitril-valsartan association and treatment with sartans or ACE-I, on the appearance of ventricular arrhythmias, in patients with heart failure with reduced ejection fraction and equipped with an implantable defibrillator (ICD).

Materials and methods. From March 2016 to December 2018 20 patients M and F were enrolled with an average age of 40-80 years with ejection fraction <35% suffering from post-ischemic dilated cardiomyopathy and with ICD c, in NYHA III class. Patients were declared eligible based on the 2016 ESC criteria (EF 40%, NT-pro-BNP >400 ng/L, target dose of ACE-inhibitor/angiotensin receptor blocker (ARB), GFR >30 ml/h/1.73 m², S-potassium <5.2 mmol/L, treatment with beta blocker and MRA). For 12 months the patients were treated with ACE-I or sartans and beta-blockers and mineralocorticoid antagonists. Subsequently ACE-I or sartan was replaced with the sacubitril-valsartan association for another 12 months. Initially, SV administration was 49/51 mg twice daily until the maximum tolerated dose (one 97/103 mg twice daily tablet) and patients were evaluated at 4-week intervals for two years. The periodic checks of the ICD were assessed: events of unsupported ventricular tachycardia, run ventricular extrasystole, appropriate shocks.

Results. 17 of the 20 patients reached the optimal dose of SV (97/103 mg), 3 reached the dosage of 49/51 mg SV twice a day. There were no side effects in all patients and no changes in the electrolyte pattern and kidney function occurred. The SV determined a reduction in the pro-BNP (from 1500 ± 1030 to 950 ± 800 pg / ml; an improvement in the NYHA class of at least 1; on the echocardiogram, a significant increase in FE was shown: at the follow-up 14 patients reached FE: 45% 4 FE patients: 40%; Regarding arrhythmic events, our data showed during the treatment with SV: reduction of episodes of non-sustained ventricular tachycardia (number of episodes pre: 8.7 ± 10 versus 4.5 ± 5.3); reduction of the pattern of ventricular extrasystoles (pre: 80 ± 15 versus 45 ± 10); finally, no appropriate device (shock) intervention occurred in patients receiving CV. Finally, there is no case of re-hospitalization in patients receiving SV.

Conclusions. Our data shows that the use of SV in patients with heart failure with reduced ejection fraction and with ICD, as well as being well tolerated and improving functional capacity, leads to a reduction in ventricular arrhythmic events and therefore a reduction in events appropriate to the device.

A314: EFFICACY AND SAFETY OF EDOXABAN IN ELDERLY PATIENTS WITH ATRIAL FIBRILLATION (AF)

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(a) AMBULATORIO PER LO SCOMPENSO CARDIACO - CLINICA TRUSSO- OTTAVIANO- NAPOLI

Background. The introduction of direct oral anticoagulants (DOACs) has been the main therapeutic revolution in the last 20 years. Four molecules have been approved for the thromboembolic prophylaxis in patients with non-valvular atrial fibrillation (AF). After the publication of phase 3 clinical trials, many studies evaluating DOAC safety and efficacy in daily clinical practice have been published. Edoxaban is the latest DOAC available on the market, based on the results of the ENGAGE AF-TIMI 48 trial. The phase 4 ETNA-AF (Edoxaban Treatment in Routine Clinical Practice for Patients With Non-Valvular Atrial Fibrillation) observational study was designed with the aim to confirm the results of the pivotal clinical trial in routine care in unselected patients with AF. The ETNA-AF Registry has shown that elderly and frail patients with renal insufficiency in atrial fibrillation treated with edoxaban have a low incidence of bleeding and intracranial haemorrhages. The aim of our study was to describe the use and tolerability of edoxaban in very old patients with heart failure with reduced ejection fraction. The average age of enrolled patients is 75.0 ± 9.4 years with a significant prevalence of the elderly (14.0% with age ≥85 years with a slight male prevalence).

Methods and Results. We analyzed retrospective data from 40 patients from June 2016 to November 2018 and taking edoxaban 30 mg. The average age of enrolled patients was 74 ± 8.2 years and 40% were females. The inclusion criteria were patients with at least one episode of documented AF of any duration in the preceding 12 months; The average CHA₂DS₂-VASc of these subjects is 3.2 ± 1.4, while the haemorrhagic risk expressed by the HAS-BLED appears more contained (2.7 ± 1.1) The risk profile of these patients that receiving edoxaban 30 mg / day was complex as documented by an older age, by a CHA₂DS₂-VASc higher and by the prevalence of comorbidities such as heart failure, valvular disease, peripheral vasculopathy and diabetes mellitus. Follow-up, characterized by clinical examination and blood

analysis, was performed at 3, 6, and 12 months. The AF patients were followed for the effectiveness outcome of thromboembolism (ischemic stroke and/or systemic embolism) and bleeding outcomes (composite of major bleeding, gastrointestinal bleeding, and intracranial hemorrhage), as well as bleeding requiring hospitalization. A secondary safety endpoint was total minor bleedings. Standard two-dimensional transthoracic echocardiographic examination was performed. Left ventricular end-diastolic volume, end-systolic volume, and ejection fraction (LVEF) were measured using the modified Simpson's rule from the apical view. During follow-up, we observed no major bleedings, strokes, or cardiovascular deaths. Only two minor hemorrhages (one epistaxis and one hematuria, none of which required blood transfusion or hospital admission) observed with no differences observed in LVEF or left atrial dimension at echocardiography, body mass index, and the thrombotic and hemorrhagic risk profile.

Conclusions. Such data confirm that the new oral anticoagulants, and in particular edoxaban, are considered safe even in the most population frail and above all elderly, allowing for enlargement the use of anticoagulant therapy. Results are expected of long-term follow-up to confirm the benefits of that therapeutic choice already demonstrated in the registration studies.

A315: DIRECT ORAL ANTICOAGULANTS VERSUS VITAMIN K ANTAGONISTS FOR LEFT VENTRICULAR THROMBOSIS: A META-ANALYSIS

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Introduction. Left ventricular thrombus (LVT) is a frightening complication primarily occurring in patients with LV dysfunction following a large myocardial infarction (MI). It's associated with an increased risk of stroke, systemic embolism and subsequent morbidity and mortality. Reperfusion strategies led to a dramatically reduction of its incidence, which estimates now ranging from 1 to 26% according to the MI location and the diagnostic imaging technique used. International guidelines recommend anticoagulation for at least 3 months, according to thrombus resolution and individualized bleeding risk, with vitamin K antagonists as the first-line therapy. Direct oral anticoagulants (DOACs) have been approved for use in non-valvular atrial fibrillation, venous thromboembolism and other hypercoagulable conditions. Due to their oral bioavailability, predictable pharmacokinetics and safety profile, nowadays are the preferred treatment option for most of the eligible patients, with an off-label extension to patients with LVT. However, prospective, randomized data on the best anticoagulation regimen are lacking. Due to the scarce and contradictory observational data available so far, we conducted an updated systematic literature search and meta-analysis of available studies to evaluate the safety and efficacy of DOACs therapy in LVT compared with VKA.

Methods. We conducted a systematic search for published articles in PubMed, Google Scholar and reference lists of relevant articles from inception to September 10th 2020. The search utilized the following terms: "left ventricular thrombus", "intracardiac thrombus", "intraventricular thrombus", "direct oral anticoagulant", "DOAC", "NOAC", "vitamin K antagonist". Papers describing patients diagnosed with LVT and who were treated with DOACs compared to VKA were examined. Case studies and abstracts were excluded. The primary end-point of this study was thrombus resolution, while other end-points included systemic thromboembolic events and bleeding events. Studies were appraised according to the Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies. Computations were performed with the R statistical software (3.5.2 version), using package "meta".

Results. Of the 671 papers examined, only 5, counting data for 700 patients, were included. We did not observe any difference between DOACs and VKAs in terms of LVT resolution (OR 0.75, CI95% [0.53-1.05], p=0.22), and systemic embolism (OR 1.86, CI95% [0.99-3.50], p=0.05). The incidence of bleeding events, instead, was lower in DOAC arm (OR 0.54, CI95% [0.29-0.99], p=0.04).

Conclusions. This is the first systematic review and meta-analysis comparing VKA and DOACs for the treatment of LVT. DOACs are comparable to VKA in terms of thrombus resolution and systemic embolism events, providing lower bleeding rates. These drugs overcame some of the problems faced with VKA, and in the absence of randomized controlled trials investigating the best anticoagulation strategy in patients with LVT, our findings are encouraging and support their off-label use for thrombus resolution and prevention of embolic events, maintaining a satisfying safety profile.

GENETICA E BIOLOGIA MOLECOLARE

A316: THE CO-EXISTENCE OF KCNQ1 AND TNNI3 GENES MUTATIONS SUPPORTS THE GENETIC ORIGIN OF QTc ABNORMALITIES IN HYPERTROPHIC CARDIOMYOPATHY

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Hypertrophic cardiomyopathy (HCM) and long QT syndrome (LQTS) are inherited diseases characterized by a wide genetic heterogeneity. Based on the separate incidence of these pathologies and on the absence of linkage, the occurrence of both diseases in the same individual has an incidence of about 1/250000. We describe a rare case report of a 24 years-old patient with maternal familiarity for type 1 LQTS (mother carrier of KCNQ1 c.1781G>A) and paternal familiarity for HCM (father carrier of TNNI3 c.592C>G mutation) who inherited both gene mutations and was diagnosed with HCM and LQTS later in adolescence, after clinical and genetic evaluations.

A317: URIC ACID INDUCES EXPRESSION OF TISSUE FACTOR IN HUMAN ENDOTHELIAL CELLS

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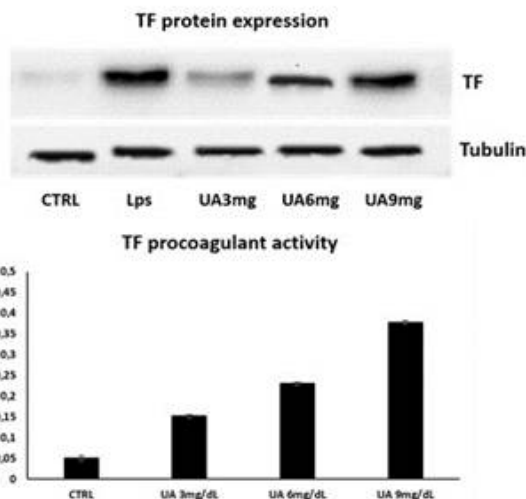
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Background. Epidemiological, experimental and clinical data show that patients with hyperuricemia are at increased risk of developing cardiovascular events. It is well known that hyperuricemia is one of the main risk factors for endothelial dysfunction, mainly mediated by oxidative stress and inflammation. Endothelial dysfunction plays a pivotal role in the pathophysiology of athero-thrombosis since dysfunctional endothelial cells express tissue factor (TF) on their surface, trigger coagulation cascade, finally leading to intravascular thrombosis. To date it remains unknown the link between uric acid and thrombosis, thus the aim of the present study was to investigate whether uric acid might promote a prothrombotic phenotype in endothelial cells by inducing TF expression.

Methods. Human umbilical vein endothelial cells (HUVEC) were incubated with increasing doses of uric acid (3, 6 and 9 mg/dl). TF gene expression and protein levels were assessed at different time points by Real Time PCR and western blot, respectively. TF surface expression and activity were also measured by FACS analysis and coagulation assay. Finally, to evaluate a possible mechanism of action of the uric acid on TF expression, NF-κB translocation assay was investigated.

Results. Uric acid significantly increases TF expression at both gene and protein levels in a dose dependent manner. Surface expression and procoagulant activity were increased as well. This effect seems to related to an increased translocation to the nucleus of NF-κB.

Conclusions. Data of the present study, although in vitro, suggest that high concentrations of UA might cause endothelial dysfunction by shifting them to a pro-thrombotic phenotype via expression of functional TF. This effect may represent a possible link between hyperuricemia and cardiovascular events.

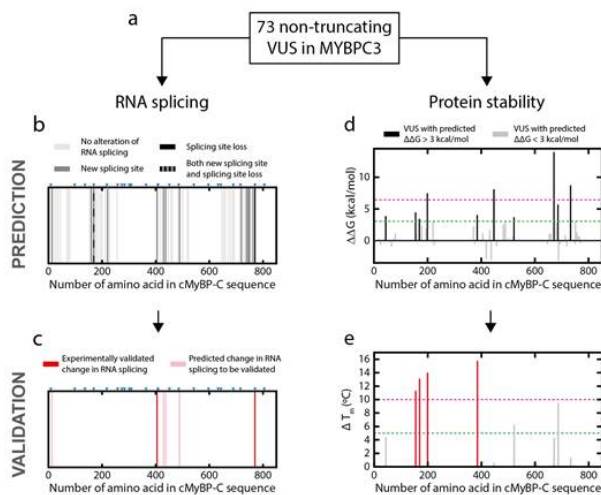


A318: PROTEIN HAPLOINSUFFICIENCY DRIVERS IDENTIFY MYBPC3 MUTATIONS THAT CAUSE HYPERTROPHIC CARDIOMYOPATHY

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Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiac disease. Mutations in MYBPC3, the gene encoding cardiac myosin-binding protein C (cMyBP-C), are a leading cause of HCM. However, it remains challenging to define whether specific gene variants found in patients are pathogenic or not, limiting the reach of cardiovascular genetics in the management of HCM. Here, we examine cMyBP-C haploinsufficiency drivers in 68 clinically annotated non-truncating variants of MYBPC3. We find that 45% of the pathogenic mutations show alterations in RNA splicing or protein stability, which can be linked to pathogenicity with 100% and 94% specificity, respectively. Relevant for variant annotation, we uncover that 9% of non-truncating variants of MYBPC3 currently classified as of uncertain significance induce these molecular phenotypes. We propose that alteration of RNA splicing or protein stability induced by MYBPC3 variants provide strong evidence of their pathogenicity, leading to improved clinical care of HCM patients and their families.



A319: NEXT-GENERATION SEQUENCING GENE PANELS IN INHERITABLE CARDIOMYOPATHIES AND CHANNELOPATHIES: YIELD OF PATHOGENIC VARIANTS AND VARIANTS OF UNKNOWN SIGNIFICANCE IN UNCOMMON GENES

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The knowledge of the molecular bases of cardiomyopathies and channelopathies has increased enormously; actually, causative mutations have been identified in more than 200 genes associated with these diseases, mainly for the diffusion of Next Generation Sequencing (NGS)-based approaches. However, testing for several genes not only increases the detection rate of disease-causing variants, including variants in uncommon genes, but also of uncertain/unknown variants (UCVs). The purpose of this work was to investigate, in patients with cardiomyopathy and channelopathies, the prevalence and the additional diagnostic value of genetic variants found in "minor" genes. To this aim we used a first-level NGS custom panel, including 60 genes, and an enlarged 129 genes panel in patients negative at first-level panel or with familial history of sudden cardiac death (SCD), to screen in the last 2 years, 145 subjects with a cardiomyopathy or a channelopathy. Fifty-five patients (38%) resulted wild type, 27 (19%) carried a known pathogenic mutation, and 63 (43%) bore one or more UCVs. Interestingly, 64% of the UCVs and 30%

of the mutations fall in "minor" genes respect to patients' clinical phenotype. Although small percentages of cases without classic mutations may be explained by pathogenic variants in these genes, the diagnostic value of screening for these genes, and the role of UCVs should be considered.

A320: YIELD AND CLINICAL SIGNIFICANCE OF GENETIC SCREENING IN ELITE AND AMATEUR ATHLETES

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The purpose of this study was to assess the value of genetic testing in addition to a comprehensive clinical evaluation, as part of the diagnostic work-up of elite and/or amateur Italian athletes referred for suspicion of inherited cardiac disease, following a pre-participation screening programme.

Between January 2009-December 2018, of 5892 consecutive participants, 61 athletes were investigated: 30 elite and 31 amateur athletes. Elite and amateur athletes were selected, on the basis of clinical suspicion for inherited cardiac disease, from two experienced centres for a comprehensive cardiovascular evaluation. Furthermore, the elite and amateur athletes were investigated for variants at DNA level up to 138 genes suspected to bear predisposition for possible cardiac arrest or even sudden cardiac death.

Of these 61 selected subjects, six (10%) had diagnosis made possible by a deeper clinical evaluation, while genetic testing allowed a definite diagnosis in eight (13%). The presence of >3 clinical markers (i.e. family history, electrocardiogram and/or echocardiographic abnormalities, exercise-induced ventricular arrhythmias) was associated with a higher probability of positive genetic diagnosis (75%), compared with the presence of two or one clinical markers (14.2%, 8.1%, respectively, p-value. 0.004).

In conclusion, a combined clinical and genetic evaluation, based on the subtle evidence of clinical markers for inherited disease, was able to identify an inherited cardiac disease in about one-quarter of the examined athletes.

A321: INVESTIGATION OF THE MOLECULAR MECHANISMS UNDERLYING CARDIAC HYPERTROPHY IN THE PRESENCE OF MITOCHONDRIAL DYSFUNCTION

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Prolonged hypertrophy of the heart ultimately impairs the cardiac function and results in heart failure, as a consequence of a maladaptive response characterized by mitochondrial dysfunction and disturbed energy metabolism. Several studies have demonstrated that a dysfunction of the mitochondrial Complex I and of the sirtuins pathway is associated with the development of left ventricular hypertrophy (LVH). A deficiency of Ndufc2 (a subunit of NADH dehydrogenase [ubiquinone]) has been previously shown to alter Complex I activity leading to severe mitochondrial dysfunction. Moreover, an impairment of the sirtuins activity, which are critical regulators of many cellular cascades, including stress responses, cell growth, energy metabolism and apoptosis, and are involved in the regulation of multiple mitochondrial metabolic events, such as fatty acid oxidation, tricarboxylic acid cycle, electron transport chain and urea cycle, has been demonstrated as a molecular mechanism involved in the LVH process. The aim of our study was to investigate whether the deficiency of Ndufc2 may cause cardiac hypertrophy and to identify the underlying molecular mechanisms.

We performed Ndufc2 gene silencing in H9c2 cardiomyocytes by using specific siRNA and the nucleic acid transferring agent, Lipofectamine 2000 (Invitrogen). The efficiency of the Ndufc2 silencing has been evaluated with RT-PCR and western blot using specific primers and a Ndufc2-specific antibody. Cellular hypertrophy of the Ndufc2-silenced cells was documented by fluorescence microscopy for the α -actin and by

gene expression analysis of the atrial natriuretic peptide and β -myosin heavy chain. RNA and proteins were extracted from silenced and not silenced cells and used for the assessment of the sirtuins molecular pathway. We found that Ndufc2-silenced cardiomyocytes, compared to not silenced cells, showed a significant degree of hypertrophy by fluorescence microscopy ($p < 0.01$), with a significant increase of both hypertrophy markers ($p < 0.01$). In parallel, sirtuin 3 and its downstream molecules (AMPK, phosphoAMPK, FOXO3a) were significantly reduced ($p < 0.05$), with an increase of the mTOR pathway ($p < 0.05$). Ndufc2-deleted cardiomyocytes were then exposed to nicotinamide in order to evaluate the impact of NAD⁺ supplementation on cellular hypertrophy. In fact, the administration of nicotinamide was able to reduce the cellular volume and the gene expression level of both hypertrophy markers. Our data demonstrate that complex 1-dependent mitochondrial dysfunction plays an important role in the development of cardiac hypertrophy and that the sirtuin3 pathway is involved as a mechanism mediating the effect of Ndufc2 gene deletion in cardiomyocytes. In this context, NAD⁺ supplementation, through the correction of the Complex 1 deficit, represents an efficacious strategy to prevent cardiac hypertrophy.

A322: CIRCULATING LEVELS OF LINC-223 AND ITS LIGAND MIR125A REFLECT PLATELET ACTIVITY IN PATIENTS WITH CORONARY ARTERY DISEASE

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Background. Platelets are key players in the pathophysiology of coronary artery disease (CAD). Platelet-derived circulating microRNA (miRNAs) are emerging biomarkers of platelet activity and clinical prognosis in CAD patients. LincRNAs are long non-coding RNAs transcribed from intergenic DNA segments. Among these molecules, it was recently shown that Linc-223 - co-transcribed with miR-223 - is able to bind to miR-125, known to be enriched in platelets. Our aim was to investigate whether their reciprocal expression levels might reflect the degree of platelet activity.

Methods. RNA was extracted using miRVANA. MiRNAs and lincRNAs were measured by means of quantitative Real Time RT-PCR.

Results. CAD patients (n=30) on antiplatelet treatment had significantly lower Linc-223 ($p < 0.05$) and a significantly higher in miR-125 levels ($p < 0.05$) compared to untreated patients (n=10). The upgrade from ASA+clopidogrel to the higher-intensity antiplatelet treatment with ASA+ticagrelor (n=30) was associated to a further reduction in Linc-223 ($p < 0.05$) and a further increase in miR-125 levels ($p < 0.05$). These results were validated in a cohort of 300 patients from the ATLANTIS study, demonstrating significant modulation of both miR-223 and miR-125 in patients with high on-treatment platelet aggregation levels compared to antiplatelet-responsive patients.

Conclusions. In line with previous evidence from patients with acute myeloid leukemia, we found a reciprocal modulation of Linc-223 and miR-125 upon different levels of platelet activity. These results suggest that plasma levels of Linc-223, miR-125 and miR-223 might be useful as markers of platelet function, to improve risk stratification of CAD patients and to monitor antiplatelet treatments.

A323: A NOVEL CRYOINJURY MODEL TO STUDY CARDIAC REGENERATION IN VITRO

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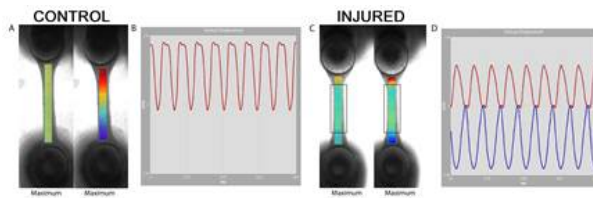
Background. Unlike lower vertebrates, adult mammals, including humans, fail to regenerate the majority of the lost cardiomyocytes (CMs) and instead replace necrotic muscle with scar tissue after cardiac injury. This lack of regenerative response is due to the loss of proliferative capacity of adult CMs which in mice occurs 7 days after birth. Using engineered heart tissues (EHT), a useful model for preclinical drug testing and disease modeling, we have developed an in-vitro injury-like model using a custom-made cryoinjury system that allows to evaluate the regenerative potential of putative factors and drugs.

Methods. rEHT were generated by mixing neonatal rat heart cells with fibrin. For the cryoinjury model, a discrete lesion was produced on the mid-section of mature EHTs using a custom-made system based on liquid nitrogen and a 23G needle.

Results. We set up a cryoinjury protocol that is relatively easy and reproducible. Cryoinjury produces a localized injury without compromising EHT's structural integrity. Indeed, all the EHTs subjected to cryoinjury preserved their contractile activity and did not show any significant

change in shape. As expected, visual observation and video analysis of injured EHTs indicate a break in the functional syncytium which leads to division in sub-regions with different contractile parameters, including beating frequency independent from each other (Figure). Furthermore, EdU administration and staining shows a significant increase of EdU⁺ CM 48 hours after injury without cell division together with an increase of activated fibroblast markers indicating the occurrence in our model of CM DNA synthesis similarly to what has been shown in mice and rats after myocardial infarction.

Discussion. We established that cryoinjury produces a localized and reproducible injury in EHTs, leading to a selective loss of contractile activity accompanied by electrical isolation. The use of a newly developed software that allows a regional evaluation of functional contractile parameters within the EHT will extend the possibility of using this system as a model to evaluate the effect of pro-regenerative therapies. These preliminary results encourage future experiment aimed to evaluate recovery properties of cardiac tissue and to identify, using a high-throughput screening, strategies or factors capable of regenerating the injured myocardium.



A324: MECHANICAL UNLOADING STIMULATES CARDIOMYOCYTE PROLIFERATION BY REVERSING CELL MATURATION

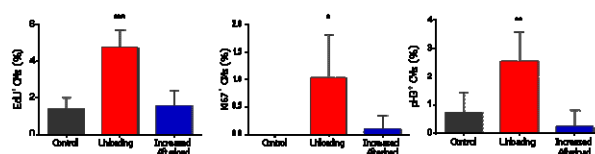
Giulio Ciucci (a, b), Sara Boer (a), Giovanni Cimmino (c), Paolo Golino (c), Gianfranco Sinagra (b), Francesco Loffredo (a, c) (a) MOLECULAR CARDIOLOGY - ICGEB TRIESTE; (b) DIVISIONE DI CARDIOLOGIA - DIPARTIMENTO DI SCIENZE MEDICHE CHIRURGICHE E DELLA SALUTE - UNIVERSITÀ DI TRIESTE - TRIESTE; (c) DIVISIONE DI CARDIOLOGIA - DIPARTIMENTO DI SCIENZE MEDICHE TRASLAZIONALI - UNIVERSITÀ DELLA CAMPANIA L. VANVITELLI - NAPOLI

Introduction. Mammal cardiomyocytes (CMs) lose their proliferative capacity early after birth acquiring an adult phenotype characterized by an organized sarcomeric structure, among others features. Neonatal hearts are subjected to a sudden increase in mechanical loading that may contribute to switch mammal CMs phenotype from neonatal proliferative to adult postmitotic. We show that mechanical unloading of Engineered Heart Tissues (EHTs) leads to a significant increase of EdU positive CMs, suggesting that mechanical loading can regulate the proliferative state of CMs. Furthermore, unloading was associated to reduced expression of genes linked to maturation, suggesting that reduced loading brings CMs back to a more immature phenotype. In this study we will test the hypothesis that variations of mechanical loading may regulate proliferation and maturation of cardiomyocytes in an EHT model.

Methods. EHT were generated using neonatal rat heart cells and initially subjected to a 48h pulse of BrdU between 48 hours and 28 days post-casting, a window that corresponds to EHTs maturation. Mechanical unloading was performed by reducing the distance between silicon posts that anchor the extremities of EHTs while afterload was increased by changing Young's module of posts with modified silicon posts.

Results. After an initial increase in the percentage of BrdU⁺ CMs early after EHT casting, similarly to what is observed in mouse neonatal hearts, CM DNA synthesis progressively decreased becoming negligible at day 28. Interestingly, the decrease of BrdU⁺ CMs was accompanied by a progressive increase of binucleated cardiomyocytes. The increase of binucleated CMs corresponds to the beginning of a coherent and spontaneous contractile activity of EHTs that occurs around day 13, suggesting that the increasing force of contraction required may represent the trigger to switch from a pro-proliferative state to a mature phenotype. In line with our hypothesis, mechanical unloading of developed EHTs significantly increased the percentage of EdU⁺, Ki67⁺ and pH3⁺ mononucleated CM suggesting active CM proliferation while an increase in afterload produced a higher degree of sarcomeric organization and a reduction of proliferating CMs (Figure).

Discussion. Our data indicate that EHTs may represent a valuable model to study post-natal cardiac biology and support the hypothesis that indicate mechanical loading as a master regulator of cardiomyocytes proliferation and maturation. Ongoing experiments are aimed at identifying the mechanisms that regulate this process.



A325: BRAIN-DERIVED NEUROTROPHIC FACTOR IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Introduction. Brain-derived neurotrophic factor (BDNF) is a neurotrophic factor highly expressed in coronary plaques, particularly in macrophages, and in activated platelets. Thus, a possible role for BDNF in the pathogenesis of acute coronary syndrome (ACS) has been suggested.

Objectives. In this study, we evaluated systemic BDNF levels according to the different clinical presentations of ACS. Moreover, we assessed the relationship between BDNF levels and the presence of optical coherence tomography (OCT)-defined macrophage infiltrates (MØI) and healed plaques along the culprit vessel.

Methods. We enrolled consecutive patients presenting with ST-elevation myocardial infarction (STEMI) or non-ST elevation (NSTEMI)-ACS. Serum BDNF levels were assessed by enzyme-linked immunosorbent assay. Plaque characteristics of the culprit vessel were assessed by OCT.

Results. Among 126 ACS patients (median age 68.00, interquartile range [IQR] 59.75-75.25 years, male 74.6%, 71 (56.3%) were NSTEMI-ACS and 55 (43.7%) were STEMI. BDNF levels were higher in STEMI patients compared to NSTEMI-ACS. OCT assessment was performed in 53 (42.1%) patients. Patients with MØI had higher BDNF levels compared to patients without MØI. Furthermore, patients with healed plaques had lower BDNF levels than patients without healed plaques. At multivariate regression analysis BDNF levels independently predicted the presence of MØI (OR 2.579; 95% CI [0.661-10.066], $p=0.024$) and the absence of healed plaques (OR 0.438, 95% CI [0.185-0.992], $p=0.050$).

Conclusions. Among ACS patients, BDNF levels were higher in patients with STEMI. Moreover, BDNF levels were independently associated with MØI and with the absence of healed plaques along the culprit vessel, suggesting a possible role of BDNF in promoting plaque inflammation, destabilization and occlusive thrombosis.

A326: TOWARDS STANDARDIZATION OF ECHOCARDIOGRAPHY FOR EVALUATION OF LEFT VENTRICULAR FUNCTION IN ADULT RODENTS: A POSITION PAPER OF THE ESC WORKING GROUP ON MYOCARDIAL FUNCTION

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Echocardiography is a reliable and reproducible method to assess non-invasively cardiac function in clinical and experimental research. Significant progress in the development of echocardiographic equipment and transducers has led to the successful translation of this methodology from humans to rodents, allowing for the scoring of disease severity and progression, testing of new drugs, and monitoring cardiac function in genetically modified or pharmacologically treated animals. However, as yet, there is no standardization in the procedure to acquire echocardiographic measurements in small animals. This position paper focuses on the appropriate acquisition and analysis of echocardiographic parameters in adult mice and rats, and provides reference values, representative images and videos for the accurate and reproducible quantification of left ventricular function in healthy and pathological conditions.

A327: ATAXIA-TELANGIECTASIA MUTATED PROTEIN PROTECTS CARDIAC CELLS FROM STRESS BY REWIRING GLUCOSE METABOLISM

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Introduction. Pressure overload-induced cardiac hypertrophy is associated with increased reactive oxygen species (ROS), inducing DNA damage and activating the protein kinase ataxia-telangiectasia mutated (ATM). Recently, ATM has been also involved in the regulation of several metabolic processes, but whether and how it affects cardiac metabolism is still poorly understood.

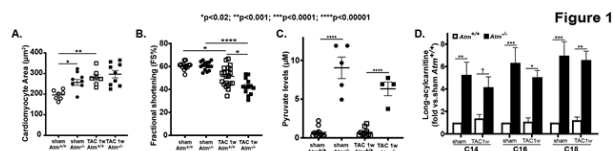
Purpose. We hypothesized that ATM might play crucial roles in the maintenance of cardiomyocyte metabolic homeostasis and in the development of cardiac dysfunction in response to pressure overload.

Methods. *Atm*^{+/+} and *Atm* homozygous mutated mice (*Atm*^{-/-}) underwent transverse aortic constriction (TAC) or sham operation (sham). After one week (1w), sham and TAC mice were anesthetized, cardiac function and morphometry were analyzed, and gene expression reprogramming,

cardiac histology, mitochondrial morphology were performed. Metabolic profiling was carried out through untargeted metabolomics (LC-MS/MS and GC/MS), mRNA and/or protein levels analysis to investigate glycolysis, pyruvate oxidation, Krebs cycle, amino acid synthesis, gluconeogenesis and lipid oxidation.

Results. *Atm* genetic inactivation induced cardiomyocytes hypertrophy and fetal gene reprogramming in sham mice, with normal cardiac function and in the absence of fibrosis or mitochondrial dysfunction (Figure 1A). After TAC 1w, cardiac function was significantly decreased in *Atm*^{-/-} mice, compared to *Atm*^{+/+} (Figure 1B). In both sham and TAC 1w *Atm*^{-/-} mice, significant metabolic abnormalities were identified, including switching of glycolysis, reduction of pyruvate oxidation, activation of amino acid synthesis and accumulation of long and short-chain fatty acid conjugated with carnitine (Figure 1C-D). Pyruvate accumulation was associated to a significant reduction of pyruvate carrier (MPC1-MPC2) and pyruvate dehydrogenase (PDH) levels in sham and TAC 1w *Atm*^{-/-} mice.

Conclusions. ATM regulates gene expression, cardiomyocyte hypertrophy and cardiac responses to pressure overload, modulating cardiac metabolism and the profile of intracellular substrate utilization in the heart. Thus, ATM might represent a novel important player in the development of cardiac dysfunction and a novel therapeutic target.

**A328: VARIABILITÀ FENOTIPICA DELLA MUTAZIONE E258K IN MYBPC3 IN UNA FAMIGLIA CON CARDIOMIOPATIA IPERTROFICA (HCM)**

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Il gene *MYBPC3* codifica per la proteina C legante la miosina C (cMyBP-C), uno dei principali componenti del sarcomero cardiaco. Mutazioni eterozigoti del gene *MYBPC3* sono una delle cause più comuni di cardiomiopatia ipertrofica (HCM).

Un elevato numero di pazienti affetti da HCM è eterozigote per mutazioni troncanti di *MYBPC3*, con aploinsufficienza della proteina. Recentemente mutazioni *missense* di *MYBPC3* sembrano correlate al fenotipo della cardiomiopatia ipertrofica. In questi casi il meccanismo patogenetico proposto è l'effetto dominante negativo, ma esso non è al momento dimostrato.

Le mutazioni *missense* di *MYBPC3* ad oggi note negli affetti da HCM sono prevalentemente private, senza hotspots mutazionali nel gene. Fa eccezione della mutazione *missense* E258K identificata in circa il 15% dei casi italiani, suggerendo un effetto fondatore e la presenza di un hotspot mutazionale.

Riportiamo il caso di una famiglia in cui il probando, 79 enne, presenta fibrillazione atriale cronica e, in seguito ad infarto miocardico acuto, ha sviluppato un fenotipo HCM. L'unico suo figlio, sportivo agonista, ha invece manifestato precocemente un ispessimento del setto interventricolare, circa 20 mm, in assenza al momento di sintomi clinici.

L'analisi genetica su DNA estratto da sangue periferico, eseguita con sequenziamento di nuova generazione (NGS) ha rilevato nel probando la mutazione eterozigote E258K nel gene *MYBPC3*. Tale mutazione è stata ereditata da suo figlio che, sebbene asintomatico, evidenzia un fenotipo compatibile con HCM.

L'esito dei test genetici condotti nel nostro laboratorio giustifica l'ipotesi, sebbene speculativa, che anche varianti *missense* nel gene *MYBPC3* possano essere patologiche, mediante un effetto dominante negativo, come meccanismo d'insorgenza della malattia, accanto all'aploinsufficienza già nota in letteratura.

Nella famiglia in esame, inoltre, l'esordio del fenotipo sembra essere più precoce a causa di un'attività fisica intensa che, predispone di per sé, ad un aumento dello spessore del setto interventricolare. Come suggerito da recenti risultati sperimentali, infatti, la presenza in eterozigosi di E258K può ridurre la compliance del tessuto atriale e ventricolare cardiaco. Nel loro insieme questi dati indicano inoltre che le mutazioni familiari *missense* associate a HCM richiedono una valutazione multidisciplinare (cardiologo, medico genetista, aritmologo, genetista molecolare): il corretto inquadramento clinico, supportato dalla diagnosi molecolare e dal successivo *counselling*, rappresentano il *gold standard* per una presa in carico mirata di questi pazienti.

IMAGING CARDIOVASCOLARE

A329: ECHOCARDIOGRAPHY VERSUS COMPUTED TOMOGRAPHY AND CARDIAC MAGNETIC RESONANCE FOR THE DETECTION OF LEFT HEART THROMBOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background. Accurate and reproducible diagnostic techniques are essential to detect left-sided cardiac thrombi (either in the left ventricle [LV] or in the left atrial appendage [LAA]) and to guide the onset and duration of antithrombotic treatment while minimizing the risk for thromboembolic and hemorrhagic events.

Methods. We conducted a systematic review and meta-analysis aiming to compare the diagnostic performance of transthoracic echocardiography (TTE) vs. cardiac magnetic resonance (CMR) for the detection of LV thrombi, and transesophageal echocardiography (TEE) vs. computed tomography (CT) for the detection of LAA thrombi.

Results. Six studies were included in the first meta-analysis. Pooled sensitivity and specificity values were 62% (95% confidence interval [CI], 37-81%) and 97% (95% CI, 94-99%). The shape of the hierarchical summary receiver operating characteristic (HSROC) curve and the area under the curve (AUC) of 0.96 suggested a high accuracy. Ten studies were included in the meta-analysis of the diagnostic accuracy of CT versus TEE. The pooled values of sensitivity and specificity were 97% (95% CI, 77-100%) and 94% (95% CI, 87-98%). The pooled DOR was 500 (95% CI, 52-4810), and the pooled LR+ and LR- values were 17% (95% CI, 7-40%) and 3% (95% CI, 0-28%). The shape of the HSROC curve and the 0.99 AUC suggested a high accuracy of CT vs. TEE.

Conclusions. TTE is a valid alternative to DE-CMR for the identification of LV thrombi, and CT has a good accuracy compared to TEE for the detection of LAA thrombosis.

A330: STRESS-REST MYOCARDIAL PERFUSION SCINTIGRAPHY FOR OUTCOME PREDICTION IN PATIENTS WITH SEVERE LEFT VENTRICULAR DYSFUNCTION

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Background. It is unclear if viability and ischaemia testing can predict the benefit from revascularization and long-term outcome in patients with coronary artery disease (CAD) and systolic dysfunction. We assessed the prognostic significance of the extent of perfusion deficits at baseline and the severity of inducible ischaemia.

Methods. Consecutive patients referred to stress-rest myocardial perfusion scintigraphy (MPS) from January 2010 and June 2019 (n=1,576) were evaluated. They were stratified in the $\geq 50\%$ (n=1,213, 77%), 36-49% (n=207, 13%) and $\leq 35\%$ (n=156, 10%) left ventricular ejection fraction (LVEF) categories, and revascularized according to current guidelines.

Results. Patients with LVEF $\leq 35\%$ had the highest median age and percentage of males, the lowest frequency of typical angina, and were those most likely to have multivessel CAD. Median summed rest score (SRS) values, reflecting the extent of perfusion deficits at baseline, were 11, 6, and 1 in patients with LVEF $\leq 35\%$, 36-49% and $\geq 50\%$, respectively. Patients with LVEF $\leq 35\%$ had more extensive inducible ischaemia, with higher summed stress score (SSS) than those with LVEF 36-49% and $\geq 50\%$ (15, 12 and 6, respectively). SRS, SSS and summed difference score (SDS) were less predictive of significant CAD in patients with LVEF $\leq 35\%$ than in the other patients. Furthermore, SRS, SSS and SDS were poor predictors of 3 endpoints (cardiovascular [CV] death or non-fatal myocardial infarction [MI], all-cause death, and CV death, non-fatal MI or late revascularization), as demonstrated by very low area under the curve values. The best SRS, SSS and SDS cut-offs identified

extensive perfusion deficits at baseline or at peak stress, or severe inducible ischaemia. Moreover, patients with higher SRS or SSS values or SRS/SSS higher than or equal to the respective cut-offs had a worse outcome regardless of whether patients were revascularized or not and of the number of diseased vessels.

Conclusions. In patients with severe systolic dysfunction (LVEF $\leq 35\%$), the extent of perfusion deficits at baseline or at peak stress and the severity of inducible ischaemia are poor predictors of prognosis. The presence of high SRS, SSS or SDS values portend a worse outcome independent of revascularization and the extent of CAD.

A331: NON INVASIVE VENTILATION AND RIGHT VENTRICLE FUNCTION IN CARDIOGENIC PULMONARY EDEMA: THE IMAGER PERSPECTIVE TO SELECT THE "RIGHT" VENTILATORY SUPPORT

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Background and purpose. High-flow nasal cannulae oxygen therapy (HFNCOT) represents a better tolerated alternative to non-invasive pressure support ventilation (NIPSV) for acute cardiogenic pulmonary edema (ACPE) treatment. However, there are still few data on the effect of HFNCOT on cardiac function and hemodynamic. Our purpose was to assess and compare the effects of NIPSV and HFNCOT in ACPE setting on right ventricular (RV) systolic function and on indices of cardiac filling and output, as measured by echocardiography.

Methods. This is a cross-over controlled study, enrolling 15 consecutive patients admitted to our Cardiovascular Intensive Care Unit for ACPE and hypoxaemic, normo/hypocapnic acute respiratory failure, with P/F ratio < 200 . Each patient received NIPSV, followed by HFNCOT. Full echocardiographic assessment and blood gas analysis (BGA) were performed 40 minutes from onset of each ventilation modality, respectively before NIPSV to HFNCOT switch and before HFNCOT interruption. In particular, RV function parameters, together with RV and atrial strain, were prospectively collected.

Results. In spite of not significant changes in BGA, RV function was significantly improved under HFNCOT, as compared to NIPSV, as assessed by the following parameters: tricuspid annular plane excursion (TAPSE) (P=0.001), RV S' wave (P=0.007), RV fractional area change (RVFAC) (P=0.006). Strain analysis confirmed the significant improvement in RV function, with free wall global longitudinal strain (GLS) and free wall and septum GLS significantly higher under HFNCOT, as compared to NIPSV (-21% vs -18% P<0.001, and -15% vs -19% P=0.008, respectively), and a significant increase in right atrial positive longitudinal strain (P<0.001).

Conclusions. NIPSV significantly affect RV function making more complex the management of patients presenting with ACPE. In this setting, HFNCOT represents a valuable alternative, providing similar respiratory outcomes while preserving good right ventricle performance.

A332: TRANSIENT MYOCARDIAL DYSFUNCTION IN A PATIENT TREATED WITH IMMUNE CHECK-POINT INHIBITOR: INSIGHTS FROM PARAMETRIC CARDIAC MAGNETIC RESONANCE MAPPING

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Case presentation. A 70-year-old man presented to the emergency department because of sudden dyspnea. Past medical history included lung cancer for which therapy with check-point inhibitor atezolizumab had been started a week earlier. At admission, ECG showed mild ST-segment elevation in antero-lateral leads, while focus echocardiography revealed extensive akinesia of left ventricular mid-apical segments, more evident at septum level. Urgent coronary angiography showed patent epicardial coronary arteries. In the following days, ECG showed inversion of T waves more evident in V2-V4 and QTc prolongation, peak hs-Troponin T was 3500 pg/ml. On day 3 from admission we performed cardiac magnetic resonance (CMR) imaging. Cine sequences confirmed echocardiographic findings of abnormal left ventricular kinesis. Native T1 was elevated on mid- (septum 1175 msec, lateral wall 1040 msec) as well as apical-short axis (septum 1284 msec, lateral wall 1143 msec), whereas we detected lower values at more basal segments (1006 msec at basal septum level). T2 mapping showed increased T2 values in areas of increased native T1 (mid-septum 54 msec, mid-lateral wall 47 msec, apical septum 65 msec, apical lateral wall 54 msec). Late gadolinium enhancement (LGE) images revealed no evident replacement fibrosis at septum level. In this case, the parallel increase of native T1 and T2 values at septum level, in the absence of any scar detected by LGE, would suggest myocardial water to be the main driver of their increase. Nearly complete recovery of wall motion abnormalities was detected by echocardiography at discharge on day 8.

Discussion. In this patient, reversible circumferential wall motion abnormalities as well as ECG evolution and CMR findings were consistent with takotsubo syndrome (TTS). Notwithstanding, recent administration of atezolizumab poses differential diagnosis with immune check-point inhibitor myocarditis (ICI-M), an uncommon albeit severe complication of immunotherapy in cancer patients. CMR findings in ICI-M include wide areas of myocardial edema often in the absence of any replacement fibrosis detectable at LGE imaging, though same results could be

commonly found in TTS too. In this case, the relatively large cardiac troponin increase as compared to TTS, as well as the temporal link with ICI administration, would suggest a causative role of the drug in determining the myocardial dysfunction. Interestingly, and in accordance with our CMR mapping findings, interventricular septum appears the most common affected cardiac segment in ICI-M, however, reasons for this putative association have been poorly investigated to date. The relatively high native T1 and T2 values at septum level as well as the marked troponin release, could justify a repeated CMR at follow-up, currently planned, to exclude the late development of replacement fibrosis in areas with broader edema/inflammation during the acute phase.

Conclusion. We reported a case of TTS like myocardial dysfunction following ICI treatment, in which CMR findings and clinical evolution largely overlapped those of more typical TTS. Further studies are needed in order to ascertain whether and to which extent ICI-M might be included in the enlarging spectrum of TTS.

A333: RISONANZA MAGNETICA CARDIACA IN UN PAZIENTE CON MINOCA: L'IMPORTANZA DEL REPERTO EXTRA-CARDIACO

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Introduzione. In circa il 10% dei casi di infarto miocardico acuto non è riscontrabile la presenza di una malattia coronarica responsabile. L'infarto miocardico in assenza di coronaropatia ostruttiva (MINOCA) deve essere considerato come una diagnosi provvisoria, in quanto la sua eziologia rimane largamente eterogenea. Tra le diverse cause sono incluse affezioni ischemiche, miocardite, e sindrome takotsubo, ciascuna delle quali comporta una differente prognosi e può richiedere uno specifico trattamento.

Caso clinico. Presentiamo il caso di un uomo di 57 anni, recatosi in pronto soccorso per un dolore toracico persistente. L'elettrocardiogramma risultava nei limiti della norma, così come la radiografia del torace. Per il protrarsi della sintomatologia, e per il riscontro agli esami ematici di aumento della Troponina T, il paziente è stato sottoposto a coronarografia che tuttavia non ha mostrato rilevanti ostruzioni coronariche, confermando la diagnosi di MINOCA. Una risonanza magnetica cardiaca (RMC) è stata quindi effettuata per approfondimenti diagnostici. Questa ha mostrato una buona funzione globale e segmentaria del ventricolo sinistro. La presenza di edema miocardico in sede antero-laterale medio-distale è stata evidenziata nelle sequenze T2W-STIR, T1 e T2 mapping. Nelle stesse aree, si documentavano foci di potenziamento tardivo, di tipologia non-ischemica e modesta estensione. Come reperto collaterale, veniva evidenziata la presenza di un addensamento polmonare a livello del lobo medio, compatibile con focolaio pneumonico. Successivi esami per chiarire l'eziologia della polmonite mostravano positività per l'antigene urinario di Legionella Pneumophila, con conseguente inizio di terapia mirata (antibiotico macrociclico) risultata efficace.

Conclusioni. Nel nostro caso di MINOCA, attraverso la RMC è stato possibile osservare la presenza di miocardite e contestuale polmonite in un singolo esame, guidando ulteriori test laboratoristici per giungere alla diagnosi definitiva. Il coinvolgimento miocardico in corso di infezione da Legionella è un evento poco comune ma verosimilmente sottostimato, la diagnosi eziologica è fondamentale in quanto permette di effettuare una terapia antibiotica specifica. Il pattern di potenziamento tardivo osservato, relativamente benigno, è risultato informativo nell'ambito della pianificazione del successivo follow-up. In conclusione, la RMC ci ha fornito utili indicazioni diagnostiche e prognostiche in un atipico caso di MINOCA, evidenziando come questa risulti uno degli esami diagnostici cardiaci da effettuarsi in questo eterogeneo contesto clinico.

A334: CARDIAC BIOMARKERS IN CHRONIC KIDNEY DISEASE ARE INDEPENDENTLY ASSOCIATED WITH MYOCARDIAL EDEMA AND DIFFUSE FIBROSIS BY CARDIOVASCULAR MAGNETIC RESONANCE

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Background. Cardiac biomarkers troponin T (hs-TnT) and NT-pro-brain natriuretic peptide (NT-pro-BNP) are often elevated in chronic kidney disease (CKD) and associated with both cardiovascular remodeling and outcome. Relationship between biomarkers and quantitative imaging measures of myocardial fibrosis and edema by T1 and T2 mapping remains unknown.

Methods. Consecutive patients with established CKD and estimated glomerular filtration rate (eGFR) ≤ 59 ml/min/1.73m² (n=276, males 189, age: 58±21 years) were compared to age/sex matched controls with eGFR >60 (n=242, males 145, age: 56±19 years). Comprehensive cardiac magnetic resonance (CMR) with T1 and T2 mapping, myocardial

ischemia and scar imaging was performed with venous sampling immediately prior to the CMR study.

Results. Hs-TnT was associated with imaging markers in the CKD group only (CKD vs. controls, hs-TnT(log-transformed, lg10): native T1 r=0.40 vs. 0.07, native T2 r=0.52 vs 0.10). NT-proBNP was associated with native T1 in both groups, but native T2 in the CKD group only (NT-proBNP(lg10): native T1 r=0.49 vs. 0.27, native T2 r=0.42 vs.0.12). Multivariable analyses (CMR volume, function, mass and scar) revealed independent associations between hs-TnT and native T2 (B=0.516, p<0.001), and NT-proBNP with native T1 (B=0.429, p<0.001) in CKD group. In controls both biomarkers were associated with native T1 only (B= 0.304 and 0.407, p<0.001). A subgroup of patients, re-imaged immediately after hemodialysis, showed reduction of native T2, proportional to the removed volume (n=10, mean difference \pm standard deviation=2.40 \pm 1.53 ms, r=0.71, p<0.001).

Conclusions. We demonstrate independent associations between cardiac biomarkers with imaging marker of myocardial edema and diffuse fibrosis, which are CKD-group specific.

A335: RESOURCES AND OUTCOME IMPACT OF ROUTINE AVAILABILITY OF COMPUTED TOMOGRAPHY PERFUSION

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Background. Stress computed tomography perfusion (Stress-CTP) is a functional technique that can be added to coronary computed tomography angiography (cCTA) to improve the management of patients with suspected coronary artery disease (CAD).

Objectives. To determine the impact of routine availability of Stress-CTP added to cCTA in terms of downstream testing, radiation exposure and outcome in patients with high risk or known CAD.

Methods. Patients symptomatic for chest pain, known for CAD, with previous revascularization or with increased pre-test likelihood of CAD, referred for clinically indicated cCTA with Stress-CTP were prospectively enrolled. Data regarding evaluability, overall radiation exposure, invasive and non-invasive downstream testing, hospitalizations, revascularizations, major adverse cardiac events (MACE) as unstable angina, non-fatal myocardial infarction and cardiovascular death after index test were collected at follow-up.

Results. 263 consecutive patients were prospectively enrolled (mean age: 65 \pm 9 years; male: 79%), of which 162 (62%) had previous revascularization. The mean follow-up was 323 \pm 175 days. cCTA and Stress-CTP were fully evaluable in 95% and 99%, respectively. Obstructive CAD and inducible ischaemia were found in 170 (65%) and 129 (49%) subjects, respectively. No significant difference was found between patients with presence or absence of perfusion defects in terms of downstream non-invasive testing (p: 0.229), while patients with inducible ischaemia had more downstream invasive testing, increased overall radiation exposure, more hospitalizations for cardiovascular reasons and revascularization (all endpoints with p: <0.001). No differences were detected between patients with inducible ischaemia treated with revascularization after index test and patients without inducible ischaemia, even if with obstructive CAD, treated medically in terms of MACE.

Conclusions. Routine implementation of cCTA with Stress-CTP is associated with subsequent low rate of other non-invasive testing, low overall radiation exposure in case of negative Stress-CTP and good prognosis if clinical management is based on combined anatomical and functional information.

A336: MULTIMODALITY CARDIAC IMAGING FOR EVALUATION OF A YOUNG MAN WITH CHEST PAIN: EXPECT THE UNEXPECTED

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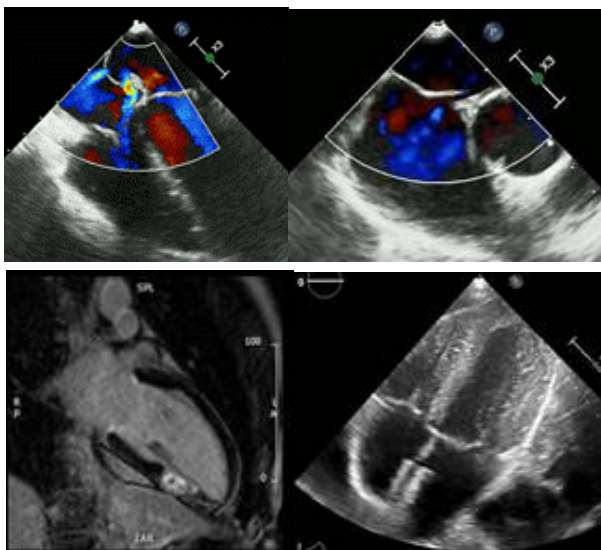
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Background. Coronary embolism is an under-diagnosed cause of Myocardial Infarction with Non-Obstructive Coronary Arteries (MINOCA). In this context, multimodality imaging is the cornerstone for differential diagnosis.

Case report. A 21-year-old male presented to the Emergency Department complaining ongoing typical chest pain, started 2 hours earlier at rest. He had no history of previous cardiac problems, but he suffered from migraines and flu-like symptoms one month ago. At presentation, the electrocardiogram showed mild ST-elevation in the inferior leads. Therefore, the patient underwent urgent percutaneous coronary angiography, which demonstrated normal coronary arteries. Lab test revealed elevated troponin I levels (11800 ng/l). In order to confirm the working diagnosis of MINOCA, we excluded missed obstructions and performed a transthoracic echocardiogram, which showed inferior wall

hypokinesia, normal left ventricle ejection fraction, and an atrial septal aneurysm with left-to-right shunt. Transesophageal echocardiogram confirmed the presence of multiple jets of left-to-right inter-atrial shunt, associated with moderate right-to-left shunt after Valsalva maneuver, due to the presence of an atrial septal aneurysm with multiple fenestrations and a patent foramen ovale (PFO); there was no evidence of thrombosis or embolic sources. The patient started anticoagulation. Two main differential diagnosis were left: coronary embolism versus myocarditis. Therefore, we performed a cardiac magnetic resonance imaging (MRI) which established the presence of inferior wall myocardial infarction in a subacute phase, with right ventricle involvement and no-reflow. Considering the anatomy, we made a diagnosis of MINOCA due to coronary embolism. The Heart Team recommended PFO closure because the probability of a causal link and the risk of recurrence were both high. Although percutaneous closure was challenging, due to the presence of an aneurysmal atrial septum, with excursion of 11 mm and multiple fenestrations, we decided to perform a transcatheter procedure with the new device Flex II UNI Occluder 28.5/28.5 mm, specifically designed as an alternative to surgical approach to close complex cases of atrial septal defects. No complications occurred during the procedure. However, the echocardiogram demonstrated a mild residual shunt, with unknown prognostic significance. The patient was discharged with a program of follow-up, which include thrombophilia testing at 1 month and echocardiogram at 6 months.

Conclusions. Paradoxical embolism in a rare cause of MINOCA. However, the PFO is frequent in the general population and it may only coexist by chance. Closure of the defect should be indicated after understanding the individual probability of a causal link and the risk of recurrence, considering multimodality imaging and case-by-case interdisciplinary discussion.



A337: THE CONUNDRUM OF CLASSIFYING DIASTOLIC FUNCTION IN PRE-CLINICAL HEART FAILURE. A LARGE PRIMARY-CARE ITALIAN STUDY

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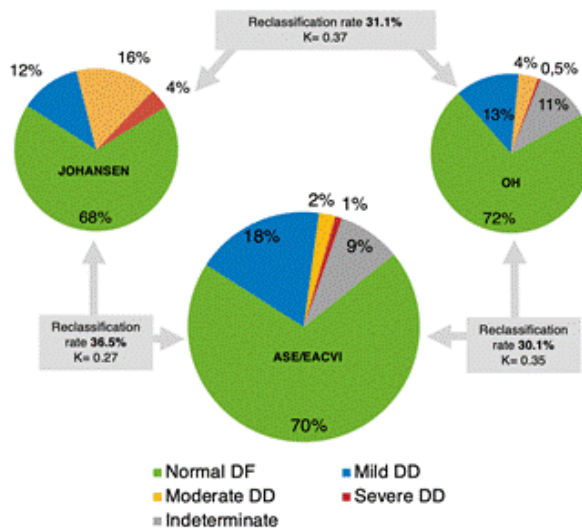
Introduction. Current guidelines on diastolic function (DF) by the American Society of Echocardiography and the European Association of Cardiovascular Imaging (ASE/EACVI) have been disputed and two independent algorithms have been proposed by Johansen et al and Oh et al. We sought (a) to assess the concordance of ASE/EACVI guidelines on DF, with newly proposed alternative approaches; (b) to evaluate the prevalence of indeterminate diastolic dysfunction (DD) by each method, exploring procedures to reduce the number of indeterminate DD.

Methods. We retrospectively analyzed the echocardiographic reports of 1,158 outpatients including subjects at risk of heart failure (HF) without (SAHF, n=644) or with (SBHF, n=241) structural heart disease, and 273 healthy individuals (SOHF). Concordance was calculated using the kappa coefficient and overall proportion of agreement. The effectiveness of pulmonary vein flow (PVF), Valsalva maneuver, and left atrial volume

index/late diastolic a'-ratio (LAVI/a') over indeterminate grading was assessed.

Results. The DD reclassification rate was 30.1% (k=0.35) for ASE/EACVI and OH, 36.5% (k=0.27) for ASE/EACVI and JOHANSEN and 31.1% (k=0.37) for OH and JOHANSEN (p<0.0001 for all comparisons), as shown in the Figure. DF could not be graded in 9% and 11% patients by ASE/EACVI and OH, respectively. The majority of patients (62% and 60%, respectively) could be reclassified using PVF or Valsalva maneuver or LAVI/a', with the latter being the single most effective parameter for this aim.

Conclusions. Inconsistencies between updated guidelines and independent, alternative approaches to assess and grade DF impede their interchangeable utilization. The inconclusive diagnoses can be reconciled by conventional echocardiography in most patients and LAVI/a' emerges as a new and effective approach to this aim.



A338: CLINICAL IMPACT OF LEFT VENTRICULAR MEASUREMENTS IN PATIENTS WITH AORTIC VALVE REGURGITATION. A MULTICENTER ITALIAN STUDY

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Background. Guidelines for the management of aortic valve regurgitation (AR) have been traditionally focused on linear left ventricular dimensions to define the timing for intervention in asymptomatic patients. However, the clinical usefulness of linear dimensions vs. 2D volumes has not been clarified.

Methods. We retrospectively analysed consecutive asymptomatic patients diagnosed with pure chronic moderate or severe AR in two tertiary Italian centres between 2008 and 2019. We assessed 2D-echocardiography quantitative LV remodelling parameters indexed LV end-diastolic volume (LVEDVi), indexed LV end-diastolic diameter (LVEDDi) as per ASE/EACVI recommendations. The endpoint was the combination of cardiac death, hospitalization for acute heart failure, or AVR.

Results. A total of 192 included patients formed the study cohort; mean age 66 ± 17 years 63% women. Overall, there was a poor correlation between LV end-diastolic diameter and volume (r²=0.52, p<0.0001); furthermore, linearity was lost for larger LV diameters. After a median medical follow-up of 4.5±3.6 years, 44 (22.4%) patients died, 20 (10.4%) were hospitalized and 58 (30.2%) underwent aortic valve replacement. Both linear and volumetric end-diastolic measurements were significantly associated with survival after adjusting for age and LV ejection fraction (HR 1.16 [95% CI 1.07-1.26] p<0.001 and HR 1.01 [95% CI 1.0-1.01] p<0.01, respectively). Patients' prognosis was poorer when both diameter and volumes indicated the presence of severe LV enlargement (concordant group) vs. discordant categorization (p=0.001). These findings were confirmed in patients with preserved or reduced LV ejection fraction (p<0.0001), and even after performing a landmark analysis to exclude a possible referral bias (p=0.02).

Conclusions. In large cohort of asymptomatic AR patients, the diagnosis of severe LV dilatation is challenging and there is frequently discordance between linear and volumetric dimensions, especially for enlarged ventricles. The concordance in linear and volumetric measurements helps the identification of patients at higher risk of events during the medical follow-up.

A339: CLINICAL PHENOTYPE OF PATIENTS WITH PROGRESSIVE TRICUSPID REGURGITATION IN AN ITALIAN TERTIARY CENTER

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Introduction. Significant tricuspid regurgitation (TR) is a frequent finding among outpatients assessed by echocardiography, and it is associated with poor prognosis. TR may progress over time, but there are few data on the rate of progression and associated clinical characteristics. The aim of the study is to investigate clinical and echocardiographic features associated with progression to severe TR.

Methods. The study retrospectively analyzed the echocardiography and clinical database of patients with a first diagnosis of moderate TR in an Italian tertiary center. We selected patients with at least two consecutive echocardiographic examinations and complete clinical details. TR severity was graded based on multiparametric evaluation as recommended, and progression was defined as a worsening to severe TR.

Results. Eligible patients with moderate TR were 115 (age 73±9, 60% women), and median time between the two echocardiograms was 20 [95% CI 10-37] months. The majority of patients (N=95, 83%) remained stable, 4 (3%) improved to mild TR, and 16 (14%) progressed to severe TR. At baseline, left ventricular ejection fraction (55±14% vs 51±13%, p=0.4), pulmonary pressure level (47±15% vs 43±7%, p=0.2), ischemic heart disease (26% vs 33%, p=0.6), rate of atrial fibrillation (63% vs 73%, p=0.4), hospitalization for heart failure (19% vs 20%, p=0.7) were similar for progressive-TR vs. stable-TR patients. The distinctive features of patients with progressive-TR (vs. stable-TR) were: frequent concomitant left-side valvular disease (88% vs 62%, p=0.04), particularly of rheumatic etiology (44% vs 18%, p=0.01), previous mitral valve surgery (50% vs 18%, p=0.001) or any cardiac surgery (56% vs 27%, p=0.02), and more cardiac surgical reintervention (19% vs 7%, p= 0.01).

Conclusions. TR progression is predominant, or may occur faster, in patients with previous left heart valve surgery or rheumatic heart disease. Specific studies on the natural history of TR in this clinical context are warranted.

A340: RUOLO DELL'IMAGING NEL CASO DI UNA DONNA CON PONTE INTRAMIocardICO CORONARICO E SOSPETTA RECIDIVA DI SINDROME DI TAKOTSUBO

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(a) AZIENDA OSPEDALIERO-UNIVERSITARIA CAREGGI; (b) UNIVERSITÀ DEGLI STUDI DI FIRENZE

Introduzione. La sindrome Takotsubo (ST) è una forma di insufficienza cardiaca acuta reversibile, caratterizzata da una transitoria acinesia/discinesia segmentaria prevalentemente a carico della regione apicale del ventricolo sinistro (VS). Colpisce solitamente donne in età post-menopausale, spesso in seguito ad eventi stressanti soprattutto a carattere emotivo. Alla base della ST vi sarebbe un danno mediato dal rilascio di catecolamine; l'esatto meccanismo fisiopatologico non è stato tuttavia ancora totalmente chiarito.

Caso clinico. Presentiamo il caso clinico di una donna di 82 anni, ex fumatrice affetta da BPCO, dislipidemia, ipertesa, con sindrome depressiva ed osteoporosi con un pregresso ricovero per ST associata a disfunzione ventricolare sinistra di grado moderato. In tale occasione la coronarografia aveva escluso stenosi critiche e mostrava un'arteria intraventricolare anteriore (IVA) con decorso intramiocardico al tratto medio senza compressioni significative. A distanza di un anno la paziente accede nuovamente al Pronto Soccorso per recidiva di dolore toracico tipico insorto a riposo. L'elettrocardiogramma mostra ritmo sinusale con diffuso soprasslivellamento del tratto ST da V2 a V6 e a sede inferiore. La coronarografia (Figura 1) risulta invariata rispetto alla precedente.



Figura 1. Angiografia coronarica: ponte intramiocardico del III tratto dell'IVA.

L'ecocardiogramma evidenzia un'acinesia apicale ed iper-contrattilità dei segmenti medio-basali con funzione sistolica globale depressa (FE 35%). La paziente ha inizialmente presentato episodi anginosi subentranti e un quadro di instabilità emodinamica per cui è stato eseguito anche un ciclo di levosimendan, con successivo miglioramento clinico-strumentale. Nel sospetto di una possibile ischemia nel territorio del ponte intramiocardico

come causa della sintomatologia, per una sua migliore definizione anatomica è stata eseguita TC coronarografia (Figura 2) con conferma di decorso intramiocardico al terzo tratto dell'IVA di circa 19 mm. A completamento diagnostico una RM cardiaca (Figura 3) ha mostrato edema dei segmenti apicali del VS in assenza di fibrosi, confermando la diagnosi di ST.

Conclusioni. In letteratura vengono riportati casi clinici di ST associata alla presenza un ponte intramiocardico, in particolare del territorio dell'IVA. La RMN cardiaca consente la diagnosi di certezza di ST ed in questo caso ha permesso di escludere come evento causale una possibile ischemia nel territorio del ponte intramiocardico.

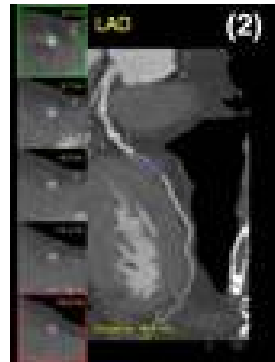


Figura 2. TC coronarografia: decorso intramiocardico superficiale per 19 mm del III tratto dell'IVA.

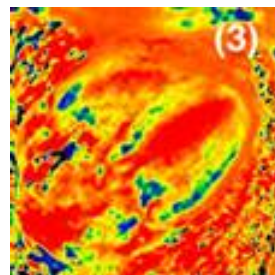


Figura 3. RM cardiaca: incremento dell'ECV (extracellular volume) a sede apicale del VS.

A341: MULTIMODALITY IMAGING IN ICD IMPLANTATION DECISION MAKING IN HEART FAILURE PATIENTS: LGE BY CARDIAC MAGNETIC RESONANCE IS SUPERIOR TO 123I-MIBG TO PREDICT VENTRICULAR ARRHYTHMIAS

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Background. ICD implant in heart failure (HF) patients is currently mainly based on left ventricular ejection fraction (LVEF), despite its well-known limitations. The aim of this study is to determine the impact of the combination of 123-iodine metaiodobenzylguanidine (123I-mIBG) and cardiac magnetic resonance (CMR) for risk stratification in HF patients with reduced LVEF candidates to ICD implant, as these have been tested individually in the past to improve patients selection with not conclusive results.

Methods. 81 patients scheduled for ICD in primary prevention were enrolled. Before ICD implantation, all patients underwent 123I-mIBG scan and CMR. At 48 months follow-up cardiac events (CE, cardiac death and rehospitalization for HF) and major arrhythmic events (ventricular tachycardia, VT and ventricular fibrillation, VF) were evaluated.

Results. Patients were divided into two groups according with CE or VT/VF. CE patients (37%) had higher values of LLS (respectively 42±10 vs 36±10%, p=0.033) and higher rate of LSS>26 (60% vs 43%, p=0.018). Event-free survival rate was lower in LSS >26 patients (p=0.029). CE patients showed a higher rate of LGE (77% vs 60% p=0.048). Event-free survival rate was lower in LGE patients (p=0.048). Event-free survival rate was lower in LSS >26 + LGE patients (p=0.015). Only the presence of LGE resulted to be independently associated with CE [HR 2.1 (CI 95% 1.03-4.4, p=0.037)]. VT/VF patients (41%) had higher values of LSS (46±9vs 37±10%, p=0.003). VT/VF patients showed a higher rate of LGE presence (92% vs 50% p=0.048). Event-free survival rate was lower in LGE patients (p=0.037). LGE was a predictor of VT/VF over 123I-mIBG parameters with HR 2.2 (CI 95% 1.02-4.5), p=0.03.

Conclusions. The present study failed to demonstrate the incremental value of the combination of 123I-mIBG and LGE for risk stratification in patients implanted with ICD for primary prevention. LGE provided added value to select HF patients that will benefit from ICD.

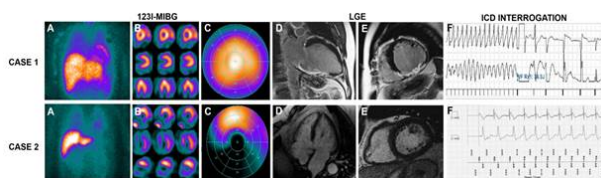


Figure 1. MIBG and CMR cases. Top row shows the case of a patient with negative 123I-mIBG, positive LGE and ventricular fibrillation treated by appropriate ICD shock. MIBG scan showing planar (A), three planes (B) and Bull's eye (C) images; long (D) and short axis (E) LGE images showing transmural LGE in the inferior wall; ICD interrogation showing appropriate ICD shock for VF (F). Bottom row shows the case of a patient with positive 123I-mIBG, negative LGE and no event at ICD interrogation. MIBG scan showing: planar (A), three planes (B) and Bull's eye (C) images; long (D) and short axis (E) LGE images showing no LGE; ICD interrogation showing no arrhythmic event (F).

A342: REDUCED 123I-MIBG UPTAKE IS ASSOCIATED WITH CARDIAC DEATH AND REHOSPITALIZATION IN HFREF IMPLANTED ICD PATIENTS

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Background. Although cardiac sympathetic activity is associated with ventricular arrhythmias (VA), limited data are currently available on the predictive value of 123-iodine metaiodobenzylguanidine (123I-mIBG) imaging on VA occurrence. Aim of the study was to evaluate whether 123I-mIBG scan predicts the occurrence of malignant VA in heart failure (HF) patients with reduced ejection fraction (HFrEF) scheduled for ICD therapy (primary endpoint), and the cumulated occurrence of cardiac death and rehospitalization for HF, summarized as cardiac events (CE) (secondary endpoint).

Methods. 221 HFrEF (EF: 28±5%) patients underwent both echocardiography and 123I-mIBG scan. Early and late 123I-mIBG imaging (Summed Score, SS and heart-to-mediastinum ratio H/M) was performed to assess cardiac innervation. Appropriate ICD therapy or VA occurrence and CE were documented at 48 months.

Results. 221 HFrEF patients were enrolled. VA rate was of 37% and CE was of 34%. Patients were divided into two groups according with CE or VA occurrence. CE group showed a significantly higher rate of SS >26% (60% vs 44%, p<0.001, SE 60%). Survival analysis showed lower event-free rate in SS >26 patients (p log-rank<0.001). No differences in H/M were recorded. Regarding VA occurrence, neither SS and H/M indexes seemed to be related with the endpoint. EF was lower in patients who experienced VA (28±5 vs 26±7%, p=0.048).

Conclusions. Cardiac sympathetic activity failed to demonstrate predictive value for VA occurrence in HFrEF patients. 123I-mIBG scan was still useful in risk stratification for cardiac death and rehospitalization for HF.

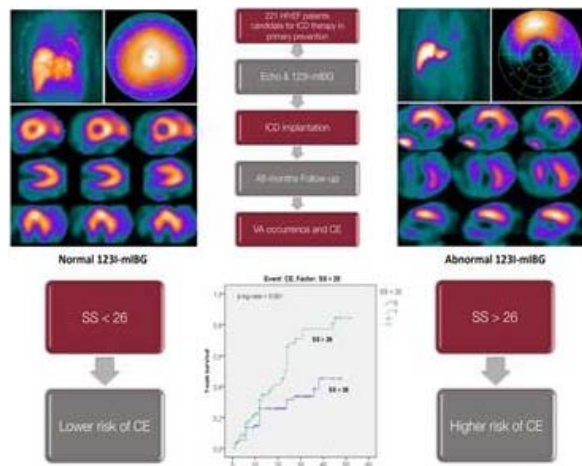


Figure 1. Key figure summarizing study design and findings. On the left a normal 123I-mIBG scan with planar, Bull's eye and three planes images is shown while on the right an abnormal 123I-mIBG scan. SS >26 is associated with cardiac death and rehospitalization for HF.

A343: LEFT ATRIAL STRAIN HIGHLY CORRELATES WITH LEFT VENTRICULAR END-DIASTOLIC PRESSURE IN PAEDIATRIC PATIENTS WITH HEART TRANSPLANT

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Background. Episodes of rejection and graft dysfunction of heart transplant (HT) may occur at different times after surgery. Left-ventricular end-diastolic pressure (LVEDP) is generally invasively obtained through a cardiac catheterization and used to catch early signs of rejection. This study sought to correlate transthoracic echocardiographic parameters to LVEDP at cardiac catheterization in paediatric transplant recipients.

Methods. This is a retrospective study of 50 patients (54% male) with HT who underwent heart transplantation in paediatric age (0-18 years old). The echocardiographic evaluation was performed within three weeks from the left heart cardiac catheterization. From the echocardiographic apical window, we measured: left atrial strain (LAS) indices [atrial contraction (εac), LA filling (reservoir phase, εres), and LA passive emptying (conduit phase, εcon)], mitral Doppler E/A, E/e', global longitudinal strain (LVGLS) and strain rate.

Results. Median LVEDP was 10 mmHg (IQR 8.25-12 mmHg) and had the best correlation with decreased εres (r= -0.56, p<0.0001). The other LAS indices and mitral E/e' correlated less strongly with LVEDP (εac: r= -0.42, p=0.004; εcon: r= -0.55, p= 0.0001; E/e': r=0.28, p=0.04). E/A, LVGLS, and LVGLS rate did not correlate with LVEDP. By ROC analysis, εres ≤ 16.3% was predictive of elevated LVEDP with good sensitivity (86%) and moderate specificity (57%). A multivariate analysis produced εres as the best predictor (p=0.0001) for high LVEDP.

Conclusions. The echocardiographic parameter εres may be used to monitor non-invasively the value of LVEDP. εres may be of value in patients with HT to survey for rejection and graft dysfunction.

A344: GLOBAL LONGITUDINAL STRAIN AT REST PREDICTS SIGNIFICANT CORONARY ARTERY STENOSIS IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

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Background. Critical peripheral artery disease (PAD) is expression of systemic chronic atherosclerosis, it being often associated with cardiovascular events. The assessment of global longitudinal strain (GLS) at rest by speckle tracking echocardiography could be useful to unmask significant coronary artery disease (CAD) in asymptomatic PAD patients.

Purpose. To determine whether resting GLS is able to predict significant coronary artery stenosis in PAD patients selected for peripheral or carotid angiography.

Methods. One-hundred three clinically relevant PAD patients (M/F=76/27, age=66.8±10.2 years, 72 with significant lower limb artery stenosis and 31 with carotid artery stenosis ≥50%), asymptomatic for CAD, underwent standard echo-Doppler exam at rest, comprehensive of GLS analysis, prior peripheral and coronary angiography. Information on cardiovascular (CV) risk factors and comorbidities were collected. Patients with know CAD and previous myocardial infarction, left ventricular (LV) ejection fraction <50% and inadequate echocardiographic imaging were excluded. According to the results of coronary angiography, patients were divided in two groups: with significant coronary artery stenosis (>50% of obstruction. n=73) and without significant coronary artery lesions (n=30).

Results. No intergroup difference in the prevalence of CV risk factors and comorbidities was found. Age, body mass index and blood pressure were comparable between the two groups. LV ejection fraction (59.9±4.2% in patients with significant coronary stenosis vs. 60.2±4.7% in those without coronary stenosis, p=0.75) and wall motion score index (1.02±0.09 vs 1.03±0.09 respectively, p=0.67) did not differ significantly. Conversely, GLS was lower in patients with significant coronary artery stenosis than in those without (21.6±2.7% vs. 22.8±2%, p<0.02). This difference remained significant comparing the carotid subgroup with coronary stenosis vs. those without (p<0.05) whereas it did not achieve the statistical significance in patients with lower limb artery lesions (p=0.42).

Conclusion. In PAD patients, GLS at rest shows the capability in identifying patients at higher probability of significant coronary artery stenosis. This involves in particular patients with carotid artery stenosis. GLS might be helpful to select patients who need to extend the peripheral angiographic evaluation to the coronary tree.

A345: TADALAFIL TREATMENT IMPROVES LEFT VENTRICLE DIASTOLIC PARAMETERS

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Background. Phosphodiesterase type 5 inhibitors (PDE5i) are first-line treatment for erectile dysfunction (ED). Tadalafil, a prolonged half-life PDE5i, has been considered one of the first-line treatment options for ED after nerve-sparing robotic radical prostatectomy (NS-RARP) for prostate cancer. PDE5-inhibitors prevent the breakdown of nitric oxide (NO)-driven cGMP, in vascular smooth muscle cells, and act as potent vasodilators. Since phosphodiesterase 5 inhibitors restore NO signaling, chronic treatment with Tadalafil may enhance plasma NO levels and reduce endothelial and cardiac dysfunction.

Purpose. to determine whether the use of Tadalafil for erectile dysfunction may cause cardiac changes detectable by echocardiogram.

Methods. we enrolled twenty-three patients (age=64.0±7.6 years) who underwent NS-RARP and who were treated with Tadalafil 20 mg on alternate days to promote recovery of sexual function. All patients have been taking Tadalafil for at least 6 months. Participants underwent standard echo-Doppler exam with evaluation of ejection fraction, global longitudinal strain, LA maximum volume index and Doppler-derived LV diastolic parameters (including mitral flow velocities, mitral annular e' velocity, E/e' ratio, peak velocity of Tricuspid regurgitation (TR) jet) at the start of therapy, and after three and six month follow-up. Information about cardiovascular (CV) risk factors was collected. Patients with known coronary artery disease, left ventricular (LV) ejection fraction <53% and inadequate echocardiographic imaging were excluded.

Results. No difference was found at three months. At six month follow-up patients were comparable for body mass index, blood pressure and heart rate. Among echo parameters, LV mass index, relative wall thickness, left atrial volume index, LV ejection fraction and global longitudinal strain were not different between basal and after six months echocardiograms. Of interest E/e' ratio (7.4±2.7 vs. 6.2±1.3, p<0.03) peak velocity of TR jet (2.4±0.2 vs. 2.1±0.2, p<0.001) and PAPs (27.3±3.5 vs. 22.9±5.7, p<0.005) were significantly lower after six months of therapy.

Conclusion. Tadalafil treatment reduced left ventricular end-diastolic pressure and increased left ventricular developed pressure. Our preliminary data, according to what is present in the literature, would show an improvement of diastolic function in the absence of cardiovascular complications detectable by the echocardiogram. Therefore we conclude that the use of Tadalafil for erectile dysfunction is safe and it also brings benefits to cardiac function.

A346: PERIPARTUM CARDIOMYOPATHY IN A PATIENT WITH SITUS VISCERUM INVERSUS AND DEXTROCARDIA

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A 37-year-old woman, with known situs viscerum inversus and dextrocardia, was admitted to the emergency department for shortness of breath one month after the delivery of her first son. Standard cardiac screening as performed during pregnancy was unremarkable. Repeated transthoracic echocardiography showed a dilated left ventricle (LV) with severely reduced ejection fraction (EF). To investigate the aetiology of the LV dysfunction, she was then referred to have a cardiovascular magnetic resonance (CMR) scan. CMR confirmed the situs viscerum inversus with dextrocardia, but no other congenital cardiovascular anomalies were detected. LV was dilated, with diffuse wall thinning and moderate reduction of LV EF. A well-defined pattern of left ventricular non-compaction (LVNC) in the apex was detected. Right ventricular dimensions and function were normal. There were no signs of myocardial oedema on STIR T2-weighted images nor evidence of LV late gadolinium enhancement on post-contrast LGE images. The patient was, therefore, diagnosed with peripartum cardiomyopathy (PPCM) and referred to the physicians for the appropriate treatment.

PPCM is a potentially severe pregnancy-associated disease consisting in LV dysfunction and heart failure occurring over peripartum period. It is widely known that pregnancy could contribute to significant haemodynamic changes and could precipitate pre-existing congenital heart disease (CHD). Situs viscerum inversus with dextrocardia is an uncommon CHD, with the apex of the heart being located on the right side of the chest and with mirror image of major visceral organs. Nevertheless, no cases of PPCM in subjects with this specific congenital condition have been reported so far. Alterations in the process of embryogenesis may constitute a common link between the situs inversus and LVNC, both

observed in these patients. PPCM occurrence with LV dysfunction may be favored by LVNC itself.

We report a unique case of dextrocardia with situs viscerum inversus and PPCM. Being their potential link still unknown, pregnant women with this congenital anomaly, even in absence of overt cardiovascular consequences, should receive careful cardiological checks over the entire peripartum period, as in other form of CHD during pregnancy.

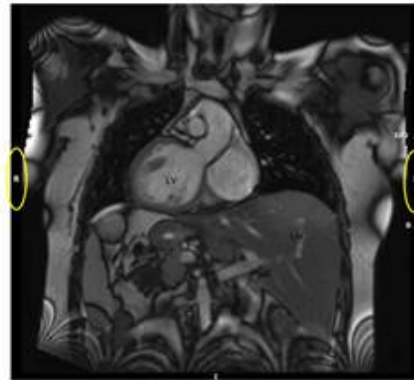


Figure 1. Coronal CMR image showing situs viscerum inversus. LV apex can be observed on the right side of the image while the heart is on the left side. LV=left ventricle; S=stomach; R=right; L=left

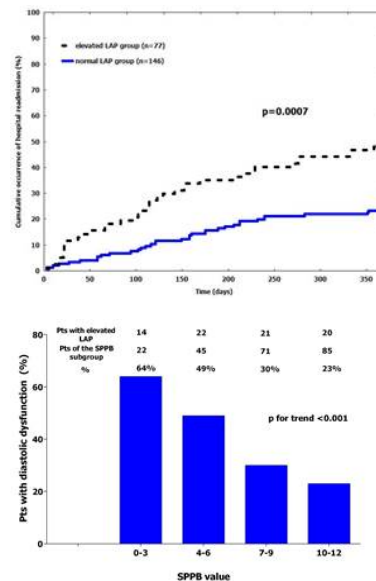
A347: DIASTOLIC DYSFUNCTION IS ASSOCIATED WITH REDUCED PHYSICAL PERFORMANCE AND POOR PROGNOSIS IN OLDER PATIENTS WITH MYOCARDIAL INFARCTION

Laura Sofia Cardelli (a), Anna Piredda (a), Rita Pavasini (a)
 (a) AZIENDA OSPEDALIERO-UNIVERSITARIA DI FERRARA

Aims. In 2016 a new algorithm for the assessment of diastolic dysfunction has been released. No studies investigated the relationship between diastolic dysfunction (DD), physical performance and/or frailty and outcome. The present analysis is carried out to fill this gap in evidence.

Methods and Results. Older (age ≥70 years) patients admitted to hospital for acute coronary syndromes (ACS) were included. Before the discharge a complete transthoracic echocardiogram (baseline TTE) was performed with assessment of DD following the 2016 algorithm. TTE was repeated after 1 year. Clinical follow-up was performed at 1-year. Seven scales of frailty and physical performance were assessed. First, the relationship between DD and tests of frailty and physical performance was investigated. Second, the association with 1-year occurrence of all-cause death and re-hospitalization was valued. Overall 329 patients were included in the analysis. Patients were stratified in two groups: DD grade 0-1 versus 2-3. The mean age of the group was 77±5 vs 79±6 years, respectively. Physical performance and frailty resulted significantly lower in patients with DD grade 2-3 compare to the others. After multivariate Cox logistic regression, DD (degree 2-3 vs. 0-1) remained an independent predictor of the composite endpoint (HR 1.46, 95% CI 1.06-2.02, p=0.02) even if it was not an independent predictor of all-cause mortality, but of one-year re-hospitalization (HR 1.75, 95% CI 1.26-2.44, p<0.001).

Conclusions. In older ACS patients the assessment of diastolic dysfunction with the 2016 algorithm is related to parameters of frailty and physical performance and it is a predictor of one-year re-hospitalization.



A348: "FAST" CMR NEL PLANNING PRE-OPERATORIO DI PAZIENTI CON DIFETTI DEL SENO VENOSO TIPO CAVALE SUPERIORE: ESPERIENZA DI UN SINGOLO CENTRO

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Introduzione. L'approccio chirurgico ai difetti interatriali tipo seno venoso (SVD) è spesso complesso e richiede un accurato planning pre-operatorio. Un imaging diagnostic appropriato permette di coadiuvare il chirurgo nella scelta dell'approccio più indicato, con una migliore prognosi per il paziente.

Obiettivo. Lo scopo di questo studio è di verificare la capacità diagnostica di un protocollo "fast" di risonanza magnetica cardiaca (CMR) nel descrivere correttamente l'anatomia dei pazienti affetti da SVD tipo cavale superiore, che frequentemente si associa a drenaggio venoso anomalo polmonare (APVD) o ad altre anomalie anatomiche. Inoltre, ci proponiamo lo scopo di paragonare la sensibilità diagnostica dell'ecocardiogramma transtoracico (TTE) e della CMR nell'identificare la presenza di APVD in pazienti con shunt sovra-tricuspidalico e di misurare i tempi di acquisizione della CMR.

Materiali e metodi. Questo studio retrospettivo è stato condotto su pazienti trattati all'ospedale di Padova tra marzo 2010 e giugno 2019 che rispondevano ai seguenti criteri di inclusione: (i) diagnosi clinica di sovraccarico volumetrico destro da shunt sovra-tricuspidalico; (ii) TTE effettuato; (iii) CMR programmata; (iv) correzione chirurgica effettuata. I criteri di esclusione sono rappresentati da TTE o CMR eseguiti in altri centri. È stata applicata analisi statistica descrittiva.

Risultati. Sono stati selezionati 32 pazienti che rispondevano ai criteri di inclusione sovradescritti (20 maschi, 12 femmine), età media 8.3 anni (range interquartile 0.4 - 53.8 anni). La CMR ha individuato 16 pazienti affetti da SVD tipo cavale superiore, individuando 57 APVD, con il 100% di concordanza con il reperto operatorio. TEE ha identificato 14 SVD tipo cavale superiore e solamente 18 APVD. Il tempo di scansione mediano del nostro protocollo "fast" è stato di 10 minuti.

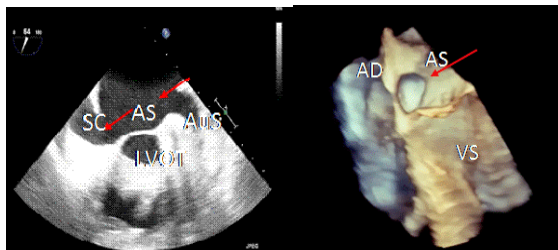
Conclusione. Questo studio dimostra che il protocollo "fast" CMR può essere aggiunto come metodica di imaging di scelta nella valutazione pre-operatoria dei pazienti con SVD, vista la maggiore sensibilità rispetto a TEE nell'identificazione di APVD.

A349: FIBRILLAZIONE ATRIALE CON SORPRESA: UN CASO DI PARTIALLY UNROOFED CORONARY SINUS MISCONOSCIUTO

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Unroofed coronary sinus (URCS) è una rara anomalia cardiaca dovuta alla completa o parziale assenza del tetto del seno coronarico, nella quale è presente una comunicazione tra il seno coronarico e l'atrio sinistro.

Un paziente di 84 anni affetto da ipertensione arteriosa, cardiopatia ischemica cronica, e insufficienza renale, in seguito all'insorgenza di dispnea e cardiopalmo eseguiva visita cardiologica di controllo che evidenziava fibrillazione atriale (FA) di nuova insorgenza. Pertanto, veniva inviato presso il nostro reparto di Cardiologia per gli accertamenti e le cure del caso. Durante la degenza veniva sottoposto ad ecocardiogramma transesofageo che documentava auricola libera da formazioni trombotiche e normali velocità di flusso. Inoltre, si evidenziava la presenza di difetto interatriale tipo "partially unroofed coronary sinus" a livello della porzione prossimale del seno coronarico, che risultava dilatato. Il diametro del difetto del seno coronarico era di circa 1.8 cm x 1.5 cm. Non vi era associata persistenza della vena cava superiore sinistra. Le camere destre risultavano dilatate, con una lieve insufficienza tricuspidale, pressione arteriosa polmonare sistolica di 50 mmHg e un Qp/Qs di 1.3. Le camere cardiache di sinistra e i relativi apparati valvolari risultavano normali. In considerazione del quadro di insufficienza renale si soprassedeva a sottoporre il paziente a TC coronarica o RM cardiaca.



Si iniziava infusione ev di cordarone e si sospendeva terapia antiaggregante con aspirina e ticagrelor sostituendoli con clopidogrel ed apixaban. Per l'evidenza di FA a bassa risposta ventricolare media si

procedeva ad impianto di Pacemaker bicamerale e a tentativo efficace di cardioversione elettrica. Pertanto, in considerazione di tali parametri emodinamici si ottimizzava terapia medica e si poneva indicazione a stretto follow-up clinico strumentale.

A350: L'IMPORTANZA DELL'IMAGING PREPROCEDURALE NELLE VALVULOPATIE: UNA TETROLOGIA DI FALLOT INASPETTATA

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La tetralogia di Fallot è una cardiopatia congenita complessa, il cui difetto principale è rappresentato dalla deviazione antero-superiore del setto infundibolare, da cui risulta un disallineamento con la trabecola setto-marginale. Da ciò derivano le quattro anomalie caratteristiche della patologia: DIV non restrittivo, aorta a cavaliere, ostruzione dell'efflusso ventricolare destro e conseguente ipertrofia ventricolare destra. La sopravvivenza del paziente è correlata al grado di ostruzione all'efflusso ventricolare destro. Nelle ostruzioni di grado medio, a causa dell'aumento del flusso vascolare polmonare si verifica la cosiddetta "tetralogia rosa" (Fallot acianotico); tali pazienti si presentano con grado variabile di dispnea e cianosi minima.

Una paziente di 75 anni affetta da ipertensione arteriosa, diabete mellito, dislipidemia e fibrillazione atriale, accedeva al PS di altro nosocomio per astenia. Veniva posta diagnosi di NSTEMI da discrepanza in un quadro di severa anemia (Hb 6 g/dl) in assenza di lesioni angiografiche sottoponibili a rivascularizzazione percutanea. Per riscontro di stenosi della valvola aortica di grado severo con insufficienza di grado moderato veniva inviata presso il nostro reparto di Cardiologia per essere sottoposta a TAVI. All'ingresso in reparto è stato ripetuto ecocardiogramma che mostrava DIV sotto-aortico con shunt sn-dx (Grad Vsn-Vdx 44 mmHg), aorta anteroposta, ventricolo destro ipertrofico e dilatato con funzione ai limiti bassi, significativa ostruzione sul tratto d'efflusso del Vdx. Inoltre, si riscontrava ventricolo sinistro lievemente dilatato e moderatamente ipertrofico, in assenza di alterazioni della cinesi segmentaria e globale, ostruzione all'efflusso ventricolare sinistro da duplice componente, per membrana sotto-aortica fibrocalcifica e fibrocalcificazione con ipomobilità delle cuspidi aortiche (v max 4.2 m/s, AVA planimetrica 1.2 cm²), insufficienza aortica moderata-severa, insufficienza valvolare tricuspidale moderata, PAPs 50 mmHg, marcata dilatazione biatriale. Tali reperti risultavano compatibili con Tetralogia di Fallot associata a membrana sottovalvolare aortica, diagnosi mai precedentemente sospettata. In seguito, veniva eseguito ecocardiogramma transesofageo che confermava la diagnosi di Tetralogia di Fallot con aorta anteroposta e associato DIV, stenosi infundibolare dx determinante Grad max 60 mmHg, cernice fibrocalcifico sotto-aortico e stenosi valvolare aortica moderata.

In considerazione del quadro anatomico veniva controindicato un trattamento percutaneo e posta indicazione chirurgica, che la paziente comunque rifiutava. Pertanto, in virtù del quadro emodinamico stabile e della sintomatologia anginoso legata a discrepanza, si ottimizzava la terapia medica e si poneva indicazione a stretto follow-up clinico strumentale.

A351: EXPLORING THE GREY ZONE OF E/E' RATIO: DOES LEFT ATRIAL STRAIN HELP?

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Background. The combination of early trans-mitral inflow and mitral annular tissue Doppler velocities (E/e' ratio) is widely applied to noninvasively estimate left ventricular (LV) filling pressures. However E/e' ratio has a significant gray zone that restrict its accuracy and left atrial (LA) deformation analysis by speckle tracking echocardiography (STE) was recently proposed as an alternative approach to estimate LV filling pressures, but the clinical application of LA strain in the subgroup of patients with E/E' between 8 and 14 has been under-investigated.

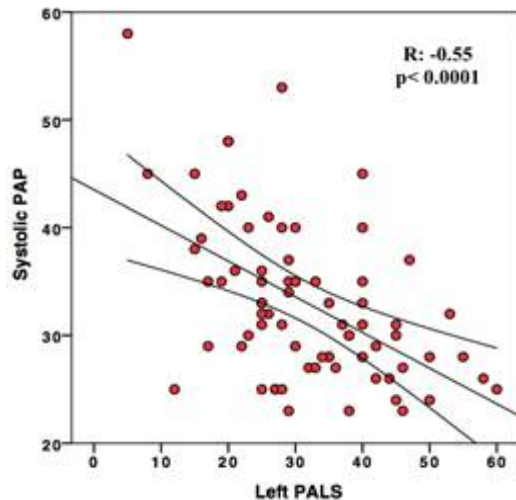
Aims. This study aimed to analyze the role of LA longitudinal function by STE (PALS) to estimate intra-cardiac pressures as assessed by systolic pulmonary artery pressure (sPAP), measured by Doppler, specifically in patients with an E/e' ratio >8 and ≤14.

Methods. We enrolled 142 consecutive, non-selected patients, referred to our echocardiography laboratory for a comprehensive transthoracic echocardiography. Exclusion criteria were: organic mitral valve disease or prosthesis and presence of disease possibly associated with pre-capillary pulmonary hypertension. Particular care was used for accurate measurement of maximal tricuspid regurgitation velocity and of right atrial pressure and consequently sPAP estimation. PALS values were obtained by averaging all segments, and by separately averaging segments measured in the 4-chamber and 2-chamber views.

Results. Seventy-four patients (52% of total) showed an E/e' ratio >8 and

≤ 14, with the following characteristics: mean age 65.5±11.9 years, LVEF 54.5±11.2, E/e' 11.2±1.9, sPAP 33±7 mmHg, PALS 31.6±11.7%. A negative correlation between PALS and sPAP was found ($r = -0.55$, $p < 0.0001$). From receiver operating characteristic (ROC) curves, PALS demonstrated a high diagnostic accuracy [AUC 0.78 (95% CI: 66-90%)]; the cutoff value of 23% showed an excellent specificity of 90% with a sensibility of 60%, to predict sPAP higher than 35 mmHg.

Conclusions. LA function measured by STE is a simple parameter able to predict increased intra-cardiac pressure even in the intermediate E/E' group. These parameters might help in improving the diagnostic algorithm of diastolic function.



A352: LEFT ATRIAL STRAIN IN PATIENTS WITH SEVERE ORGANIC MITRAL REGURGITATION UNDERGOING MITRAL VALVE SURGERY: ASSOCIATION WITH PRE AND POST-SURGICAL FUNCTIONAL CAPACITY

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Background. Left atrial (LA) enlargement in patients with chronic mitral regurgitation (MR) occurs as a part of cardiac remodelling due to volume overload. LA functional impairment evaluated by 2-D speckle tracking echocardiography (STE) has been observed in patients with severe MR, however its role in determining pre and post-surgery heart failure symptoms remain un-explored. Aim of this study was to evaluate the role of LA strain in the occurrence of heart failure symptoms in patients with severe organic MR before and after surgery.

Methods. Patients with severe organic MR underwent to mitral valve surgery were retrospectively enrolled. All patients had a transthoracic echocardiography and a clinical evaluation including New York Heart Association (NYHA) functional classification at baseline and a clinical evaluation after surgery. Peak atrial longitudinal, contraction (PALS, PACS), conduit and global LV longitudinal strain (GLS), were obtained at baseline.

Results. One hundred-twenty patients were enrolled, age 66±11 years, 39% female. Baseline parameters: PALS 29±12%, PACS 12±7%, conduit 19±7%, GLS -21±4%. At baseline there were 30 patients (25%) NYHA I, 40 patients (33%) NYHA II, and 50 patients (42%) NYHA III. At follow-up, excluding patients that were asymptomatic (NYHA I) at baseline, 73 patients (81%) showed an improvement of NYHA class. At univariate analysis, the following parameters were correlated to baseline NYHA: PALS ($R = 0.43$, $p < 0.001$), GLS ($R = 0.37$, $p < 0.001$), PACS ($R = 0.31$, $p = 0.009$), conduit ($R = 0.30$, $p = 0.01$), LV end-diastolic volume ($R = 0.22$, $p = 0.01$). At multivariate analysis baseline PALS was the only parameter ($b = -0.30$, $p = 0.02$) independently associated to baseline NYHA classification. At univariate analysis the following parameters showed to be predictors of NYHA class at follow-up: PALS ($R = 0.43$, $p < 0.001$), PACS ($R = 0.35$, $p = 0.004$), GLS ($R = 0.24$, $p = 0.002$), TAPSE ($R = 0.21$, $p = 0.02$), LVEF ($R = 0.19$, $p = 0.04$). At multivariate analysis, PALS ($b = -0.45$, $p = 0.02$) was the independent predictor of NYHA class at follow-up.

Conclusion. Our study demonstrates that LA strain was independently associated with heart failure symptoms, even after surgery. Also, LA was found to predict AF in these patients. These findings suggest that LA strain is valuable in chronic severe primary MR.

A353: UNVEILING A COMPLEX CONGENITAL DISORDER WITH CARDIOVASCULAR MAGNETIC RESONANCE IN AN ADULT WOMAN WITH SHORTNESS OF BREATH

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A 55-year-old woman was admitted to our emergency department for dyspnea. She had been diagnosed with situs viscerum inversus and dextrocardia with interatrial defect 4 years before during an episode of acute cardiac failure and atrial fibrillation.

ECG showed sinus tachycardia with right axial deviation. Transthoracic echocardiography (TEE) revealed atrial dilation with evident bidirectional shunt through an interatrial septum defect. Moreover, the left and right ventricular systolic function was moderately reduced. She was then referred to have a cardiovascular magnetic resonance (CMR) scan to better characterize the congenital abnormalities. CMR findings included: double superior vena cava (SVC) circulation; completely unroofed coronary sinus, with interatrial defect leading to a significant left-to-right shunt ($Qp/Qs = 2.6$); severely dilated right heart chambers; mildly reduced right ventricular ejection fraction, with preserved left ventricular systolic function.

Coronary sinus atrial septal defects are characterized by the absence of at least a portion of the common wall that separates the coronary sinus from the left atrium, ultimately resulting in left-to-right shunt, and constitute the less common type of atrial septal defect. The combination of abnormal systemic venous drainage from double SVC circulation (usually as a persistent left SVC draining into the left atrium) and unroofed coronary sinus is referred to as Raghb syndrome (or Raghb complex), which is an extremely rare cardiac anomaly, in some cases associated with ventricular septal defects, enlargement of tricuspid annulus and pulmonary stenosis, with potential clinical presentation as heart failure or ischemic stroke.

This case is the first CMR report of a Raghb syndrome in situs viscerum inversus and dextrocardia. CMR, with its high contrast and spatial resolution combined with large field-of-view capability, provided accurate definition of systemic venous return as well as cardiac anatomy and function allowing the full non-invasive depiction of this rare combination of congenital abnormalities. Physicians should always consider performing CMR when handling patients, specially adults, with complex congenital heart disease.

A354: CLINICAL SIGNIFICANCE OF INTRAVENTRICULAR STASIS DETECTED AT CARDIAC MAGNETIC RESONANCE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: A RETROSPECTIVE COHORT STUDY

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Introduction. The relationship between acute myocardial infarction (AMI) and acute cerebrovascular events (CVE) has been widely studied in literature. Sinus rhythm AMI patients, particularly those with left ventricular (LV) systolic dysfunction, carry a 2% risk of CVE in the first 12 months after the cardiac event. Intraventricular stasis (IS) detected at cardiac magnetic resonance (CMR) might have a role in the risk stratification of CVE.

Objectives. To establish the clinical significance of IS in a cohort of AMI patients and to investigate IS as a risk factor for CVE.

Materials and methods. All patients admitted to the Cardiac Intensive Care Unit of Padua University Hospital for AMI between 2013 and 2017, who underwent CMR within 7 days from the event, were included in this retrospective analysis. Patients on treatment with oral anticoagulation therapy at admission or showing ventricular thrombosis at CMR were excluded. IS was defined by the presence of intraventricular signal hyperintensity on T2-weighted images. Patients were followed-up for a median duration of 54 months and predictors of CVE, non-fatal reinfarction and cardiovascular death were determined.

Results. The final population included 214 patients (153 males [71.5%], mean age 61 years), of which 56 (26.2%) showed IS at CMR. Patients with IS had more frequently a transmural AMI (94.4% vs 75.7%, $p = 0.003$), and a lower LV ejection fraction (40.5 ± 8.9 vs 50.9 ± 11.3 , $p < 0.001$). During follow-up, 8 CVE, 6 cardiovascular deaths and 9 non-fatal reinfarction occurred. IS carried an odds ratio (OR) for CVE of 9.36 (95% confidence interval [CI] 1.8-47.9, $p = 0.007$), and for cardiovascular death of 6.0 (95% CI 1.1-33.7, $p = 0.042$).

Conclusions. IS detected at CMR is associated with an increased risk of CVE and cardiovascular death in patients with AMI. Further prospective studies with larger populations are needed to confirm these results, and to explore the possibility of prophylactic low-dose anticoagulation therapy for preventing CVE.

A355: PAC-MAN HEART AND MITRAL VALVE PROLAPSE: AN UNREPORTED LIAISON

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Introduction. Pac-man heart is an extremely rare anomaly consisting with a partial ventricular septal defect. It may be of congenital origin or acquired as a complication of myocardial infarction. Few cases have been already reported in literature including one in patient with parachute mitral valve.

Case presentation. A 50-year-old man accessed the echolab for dyspnea. His past medical history was unremarkable. Transthoracic two-dimensional echocardiogram showed a posterior leaflet of the mitral valve prolapse associated with eccentric regurgitant jet anteriorly directed. Due to the detection of vena contracta width 8 mm; effective regurgitant orifice area 42 mm²; regurgitant volume 65 ml/beat mitral valve regurgitation was considered severe. Mild dilatation of the left atrium and ventricle with ejection fraction 57% were identified. Pulmonary artery systolic pressure derived from a mild tricuspid regurgitation was estimated 42 mmHg. In addition an excavation of the medium interventricular septum with a closure of its mouth during systole and opening during diastole was observed. Of note no evidence of left-right interventricular shunt was observed. Owing to the absence of myocardial infarction in the past medical history, in this case partial ventricular septum defect was considered "Pac-man heart" of congenital origin. After ruling out coronary artery disease by coronary angiography, patient underwent surgical repair of the severe mitral regurgitation by quadrangular resection and posterior leaflet sliding plus annuloplasty. The abnormal cavity of ventricular septum was confirmed by intraoperative evaluation but, taking into account the absence of shunt at colour flow mapping, surgical treatment of Pac-man heart was not indicated. At 3-month follow-up patient was asymptomatic and echocardiography revealed mild residual mitral regurgitation.

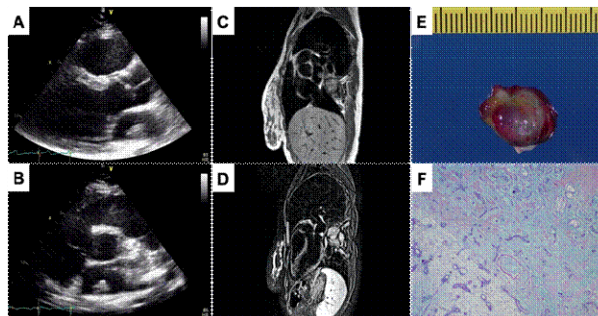
Conclusion. We described a case of Pac-man heart, detected as an incidental finding, in a patient with organic mitral valve regurgitation. A common embryological disorder involving the mesenchymal cells of the cardiac cushions could be hypothesized to explain this previously unreported association of Pac-man heart and mitral valve prolapse.

**A356: ATRIAL MYXOMA: WHAT IS THE BEST MANAGEMENT IN PREGNANCY?**

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Cardiac myxoma during pregnancy is a rare condition with only a few cases described in the literature. Its management is complicated by the absence of specific recommendations and information about the risks related to both mother and fetus. We describe a case of a 37-year-old woman at 22 weeks' gestation presenting with a cardiac mass in the left atrial posterior wall diagnosed by transthoracic echocardiogram (A, B). A cardiac magnetic resonance confirmed the presence of a sessile atrial mass isointense to myocardium on T1-weighted sequences and hyperintense to myocardium on T2-weighted sequences, compatible with a myxoid lesion or a high cellularity tissue (C, D). After multidisciplinary consultation, the decision was to postpone surgery and follow the pregnant woman with serial transthoracic echocardiograms in an outpatient setting until fetal maturity. No changes were registered in the atrial mass characteristics during the follow-up. At 35 weeks of gestation, an elective cesarean delivery was performed without complications. Six weeks later the woman underwent cardiac surgery on cardiopulmonary bypass and the whole tumor was excised. The postoperative course was uneventful, and the patient was discharged on day 5. Histological examination confirmed the diagnosis of a smooth sessile pseudo vascular myxoma of the left atrium (E, F). Short- and long-term follow-up did not show any recurrences of the cardiac mass.

**A357: RUOLO DELLA CARDIO-TC NEL DOLORE TORACICO ACUTO: INIZIALE ESPERIENZA DI UN SINGOLO CENTRO**

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Obiettivo. Descrivere il ruolo e l'impatto clinico della cardio-TC in urgenza come strumento per la diagnosi differenziale del dolore toracico acuto in un DEA di I livello.

Materiali e metodi. Da Agosto 2018 a Luglio 2020 da una popolazione di 9345 con accesso in pronto soccorso per dolore toracico acuto, sono stati selezionati 70 pazienti con indicazione ad esame cardio-TC che presentavano enzimi cardiaci ed ECG non dirimenti e profilo cardiovascolare intermedio. Gli esami sono stati eseguiti con apparecchiatura Dual Source 128 slices e TC 64 slices.

Risultati. All'esame TC sono stati identificati 44 pazienti con stenosi coronarica di grado non significativo e 15 pazienti con lesioni critiche prevalentemente soft ed 11 con patologia coronarica moderata meritevole di valutazione con test d'ischemia inducibile; sono stati inoltre identificati casi di sindrome aortica acuta, embolia polmonare e patologia flogistica polmonare. Dei casi studiati portiamo all'attenzione in particolare 7 casi dirimenti: 1) assenza di patologia coronarica significativa in paziente con successivo riscontro RM di miocardite; 2) paziente con dolore interscapolare e riscontro di dissezione Stanford A coinvolgente l'ostio della coronaria sinistra; 3) paziente con febbre e dolore toracico e riscontro di ascesso del piano valvolare; 4) paziente con riscontro di due pseudoaneurismi e frattura di stent; 5) paziente con nota dissezione di IVA in trattamento conservativo ed accesso in PS per dolore toracico; 6) paziente in triplice terapia antiaggregante e riscontro di stenosi significativa a carico di IVA; 7) embolia polmonare bilaterale e riscontro di associato ritorno venoso anomalo parziale.

Conclusioni. La cardio-TC può essere uno strumento diagnostico utile per la diagnosi accurata di coronaropatia; il suo impiego nei DEA può aiutare nella diagnosi differenziale del dolore toracico fornendo preziose informazioni con la potenzialità di una dimissione rapida in pazienti negativi ed un'ottimizzazione dei tempi di ospedalizzazione nei casi di reale urgenza clinica.

A358: IL RUOLO DELL'ECOCOLOR-DOPPLER TRANSCRANICO NELLA DIAGNOSI DI FORAME OVALE PERVIO (PFO): LA NOSTRA ESPERIENZA

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Obiettivi. In circa il 30% dei pazienti giovani con ictus ischemico non troviamo una causa. Si è visto dagli studi che circa la metà di questi pazienti presenta il forame ovale pervio (PFO) e che tale prevalenza in tali pazienti è superiore a quella della popolazione generale. La chiusura del PFO con un dispositivo percutaneo è spesso consigliata in tali pazienti, ma non è noto se questo intervento riduca realmente il rischio di recidive di ictus. La persistente pervietà del forame ovale (PFO) è considerata una causa di stroke criptogenici ed un fattore di rischio di eventi neurologici in pazienti giovani. La metodica standard per identificare il PFO è il TEE con contrasto. L'obiettivo di questo studio è stato quello di valutare la fattibilità dell'ecodoppler transcranico (TCD) e la sua sensibilità diagnostica comparandolo con il TEE

Metodi. Sono stati studiati 30 pazienti presso il nostro dipartimento (Unità operativa complessa di Cardiologia P.O Sa Luca di vallo della Lucania (sa)) con stroke criptogenici, TIA o sintomi neurologici (diagnosi eseguita dopo valutazione neurologica e TC cranio). Tutti i pazienti sono stati sottoposti a valutazione con TCD e TEE. Il TCD e il TEE sono stati eseguiti secondo una procedura standardizzata: una soluzione salina mista ad aria è stata iniettata nella vena antecubitale destra tre volte,

mentre il segnale Doppler è stato registrato durante la manovra di Valsalva. Durante TCD il passaggio del contrasto nell'arteria cerebrale media di sinistra era registrata 25 secondi dopo la manovra. Abbiamo rilevato un shunt destro-sinistro in 16 pazienti (53,3%) ed assenza di shunt in 10 pazienti (33,3%) sia con TCD e TEE. In 3 (10%) pazienti il TEE non ha rivelato il passaggio di contrasto che è stato poi rilevato dal TCD. La fattibilità di entrambi i metodi è stata del 100%. Il TCD aveva una sensibilità del 95% e una specificità del 92% nella diagnosi di PFO.

Risultati. La persistente pervietà del forame ovale (PFO) è considerata una causa di stroke criptogenici ed un fattore di rischio di eventi neurologici in pazienti giovani. Nei 30 pazienti studiati presso il nostro dipartimento (Unità operativa complessa di Cardiologia P.O. Sa Luca di vallo della Lucania (sa)) con stroke criptogenici, TIA o sintomi neurologici, 16 presentavano uno shunt destro-sinistro al TDC.

Conclusioni. Entrambi, il TCD e il TEE sono test diagnostici complementari per la diagnosi di PFO, ma il TCD dovrebbe essere raccomandato come esame di prima scelta per lo screening, per la sua semplicità, la non invasività, il basso costo e l'elevata fattibilità.

A359: A RARE CASE OF TRICUSPID VALVE LIBMAN-SACKS ENDOCARDITIS IN A PREGNANT WOMAN WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME

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(a) DIPARTIMENTO DI CLINICA MEDICA E CHIRURGIA AOU FEDERICO II NAPOLI; (b) DIPARTIMENTO DI SCIENZE BIOMEDICHE AVANZATE AOU FEDERICO II NAPOLI

A 38-year-old pregnant woman at 17 weeks gestational age of her sixth pregnancy presented to a cardiology clinic. Her obstetric anamnesis was significant for 3 previous pregnancies complicated by fetal growth restriction and for 2 spontaneous pregnancy losses. During her last pregnancy loss, she had a pleuro-pericarditis. In consideration of the previous pleuro-pericarditis, her gynecologist prescribed a cardiological checkup and an echocardiogram. It revealed a large mobile mass with irregular borders, attached to the sub-valvular apparatus of the tricuspid anterior leaflet, presenting heterogeneous echogenicity. Its dimensions, measured by multiplanar 3D echocardiography were 2 cm x 1.5 cm. Urgent cardiac magnetic resonance with gadolinium confirmed the presence of a highly mobile mass with irregular borders attached to the tricuspid valve chordae with low signal intensity and no contrast uptake suggestive of thrombus. A workup was ordered to rule out antiphospholipid syndrome (APS): anticardiolipin antibody IgG and anti-b2 glycoprotein-1 IgG tested positive, while lupus anticoagulant was negative. As there were no features suggestive of connective diseases, the patient received a diagnosis of primary APS, pending confirmation of the positivity of the antiphospholipid antibodies at second sampling after at least 12 weeks. The mass on the tricuspid valve was reinterpreted as vegetation secondary to Libman-Sacks endocarditis. Despite adequate anticoagulant therapy for 3 weeks, guided by the anti-factor Xa assays for dose adjustment, transthoracic three-dimensional echocardiography showed the persistence of the vegetation, without changes in its size. There are no expert suggestions on management strategy for Libman-Sacks endocarditis on the tricuspid valve. Systemic emboli occur in nearly 50% of patients with nonbacterial thrombotic endocarditis. Therapeutic options for our patient included conservative therapy with anticoagulants, thrombolysis, or surgical excision. Enoxaparin did not give appreciable results. The thrombolytic approach was discarded because of potentially harmful side effects for the fetus. A multidisciplinary counseling with obstetricians, cardiologists, anesthesiologists, and cardiac surgeons was requested. Considering the high risk of intracardiac mass detachment, with subsequent massive pulmonary embolism, an early lifesaving surgical thrombectomy was recommended. The patient underwent open-heart surgery with vegetation excision. The removed mass appeared slightly attached to the anterior tricuspid leaflet through an inflammatory process and trapped into a 1-order tendon cord. After 2 days in the Intensive Care Unit, she was transferred for 7 days to the Cardiology Department and then discharged.

Histological findings of the excised vegetation were consistent with Libman-Sacks endocarditis. At 34+3 weeks of gestation, computerized fetal heart rate analysis presented repeated deceleration and abnormal short term variability. Therefore, an emergency cesarean section was performed. A female newborn weighed 1295 grams was born. The newborn was discharged on day 30 after her clinical condition remained stable.

To our knowledge, no case of surgical treatment of isolated tricuspid vegetation, ie not associated with valve regurgitation, has been previously reported. APS should be strongly suspected in any patient with echocardiographic evidence of valvular thickening or valve nodules and history of pregnancy losses and/or thromboses. The indication and timing of the surgical intervention must be decided by a multidisciplinary team.

A360: ASEOUS CALCIFICATION OF THE MITRAL ANNULUS ASSESSED BY THREE-DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY

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Case report. Caseous calcification of the mitral annulus (CCMA) is a rare variant of mitral annulus calcification. Transthoracic echocardiography is the first diagnostic step, but a multi-modality imaging approach can be necessary to differentiate among other intra-cardiac masses. We present a case of CCMA in a 88-year-old woman admitted for acute decompensation of chronic heart failure. Transthoracic echocardiography showed pathognomonic findings of CCMA. Three-dimensional transesophageal echocardiography allowed a better characterizations of the CCMA, avoiding further diagnostic procedures.

A361: MISALIGNMENT OF HEMODYNAMIC FORCES IN THE LEFT VENTRICLE IS ASSOCIATED WITH ADVERSE REMODELING FOLLOWING STEMI

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Background. Infarct size (IS), area at risk (AAR) and microvascular obstruction (MVO) are well known predictors of adverse remodeling (aLvr) following acute myocardial infarction, while the pathogenic role of left ventricular (LV) hemodynamic forces (HDFs) is still unknown. Recent evidence suggests the role of HDFs in positive and negative on remodeling after pathogenic or therapeutic events.

Purpose. The aim of the study was to identify LV HDFs patterns associated with aLvr in reperfused ST-segment elevation MI (STEMI) patients.

Methods. Forty-nine acute STEMI patients underwent CMR at 1 week (baseline) and 4 months (follow-up) after MI. The following parameters were measured: left ventricular end-diastolic and end-systolic volume index for body surface area (BSA) (LVEDVi and LVESVi), left ventricular ejection fraction (LVEF), LV mass index, AAR and IS. LV HDFs were computed at baseline from cine CMR long axis datasets using a novel method based on LV endocardial boundary tracking. LV HDFs were calculated both in apex-base (A-B) and latero-septal (L-S) directions. The distribution of LV HDFs were evaluated by L-S over A-B HDFs ratio (L-S/A-B HDFs ratio %). All HDFs parameters are computed over the entire heartbeat, in systole and diastole. LV adverse remodeling (aLvr) was defined as a relative increase in LVESV of at least 15% from baseline (Δ LV-ESV \geq 15%).

Results. Patients with aLvr (n=18; 37%) had significant greater value of AAR (32 ± 23 vs 22 ± 18 ; p=0.03) and slightly larger IS (23 ± 16 vs 15 ± 11 ; p= 0.07) at baseline. In patients with adverse Lvr at FU, baseline systolic L-S HDF were lower (2.7 ± 0.9 vs 3.6 ± 1 ; p=0.027) while diastolic L-S/A-B HDF ratio was significantly higher (28 ± 14 vs 19 ± 6 ; p=0.03), reflecting higher grade of diastolic HDFs misalignment. At univariate logistic regression analysis, higher IS [Odd ratio (OR) 1.05; 95% confidence interval (95% CI) 1.01-1.1; p= 0.04], lower L-S HDFs (OR 0.41; 95% CI 0.2-0.9; p= 0.04) and higher diastolic L-S/A-B HDFs ratio (OR 1.1; 95% CI 1.01-1.2; p= 0.05) were associated with aLvr at FU. At multivariate logistic regression analysis, L-S/A-B HDF ratio remained the only independent predictor of adverse LV remodeling after correction for other baseline determinants.

Conclusion. Changes in the hemodynamic forces after STEMI are associated with aLvr observed after 4 months. Specifically, after correction for other known determinants of remodeling, L-S/A-B HDF ratio remained the only independent predictor of adverse LV remodeling.

A362: EFFECT OF INFARCT SIZE ON LEFT VENTRICULAR MECHANICS AND INTRAVENTRICULAR HEMODYNAMIC FORCES: A CMR STUDY IN A COHORT OF STEMI PATIENTS

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Background. Infarct size (IS) is a well-known predictor of adverse remodeling (aLvr) following acute myocardial infarction. The influence of IS on left ventricular (LV) mechanics by strain analysis and intraventricular (IV) fluid dynamics by analysis of hemodynamic forces (HDFs) is still under debate.

Purpose. The aim of the study was to compare myocardial deformation and IV hemodynamic forces (HDFs) distribution in patients with different ranges of IS.

Methods. Forty-nine acute STEMI patients underwent CMR at 1 week after the acute event. The following parameters were measured: left ventricular end-diastolic and end-systolic volumes indexed for body surface area (BSA) (LVEDVi and LVESVi), left ventricular ejection fraction (LVEF), LV mass index and infarct size (IS). Large IS was defined as IS>15% of LV mass. LV deformation was evaluated through CMR feature tracking. The following parameters were evaluated: global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS). For GLS and GCS both endocardial and transmural values were computed. LV HDFs were assessed from breath-hold steady-state free-precession cine-CMR long axis datasets using a novel method based on LV endocardial boundary tracking. LV HDFs were calculated both in apex-base (A-B) and latero-septal (L-S) directions. The distribution of LV HDFs were evaluated by L-S over A-B HDFs ratio (L-S/A-B HDFs ratio %).

Results. Patients with large IS showed greater LVESVi (41 ± 12 mL vs 30 ± 10 mL; $p=0.01$) and lower LVEF (44 ± 9 mL vs 54 ± 9 mL; $p=0.02$) compared to smaller IS. No significant differences were found in LVEDVi (72 ± 14 vs 65 ± 12 ; $p=0.14$). With regard to myocardial deformation, larger infarcts showed lower values of endocardial and transmural GLS (GLS-endo $-12 \pm 5\%$ vs $-16 \pm 4\%$; $p=0.008$; GLS-myo $-11 \pm 4\%$ vs $-16 \pm 3\%$; $p=0.004$) and GCS (GCS-endo $-23 \pm 5\%$ vs $-27 \pm 4\%$; $p=0.01$; GCS-myo $-15 \pm 4\%$ vs $-20 \pm 4\%$; $p=0.003$) while GRS did not differ between the two groups (GRS $44 \pm 16\%$ vs $51 \pm 13\%$; $p=0.149$). A-B HDFs were lower among patients with larger infarcts both in systole ($17 \pm 7\%$ vs $23 \pm 5\%$; $p=0.006$) and diastole ($7 \pm 3\%$ vs $11 \pm 8\%$; $p=0.02$). While HDFs distribution did not differ in systole ($17 \pm 4\%$ vs $16 \pm 5\%$; $p=0.494$), patients with larger infarcts had significant misalignment of HDFs in diastole ($26 \pm 11\%$ vs $20 \pm 10\%$; $p=0.032$).

Conclusion. Infarct size significantly affects myocardial mechanics and intraventricular fluid hemodynamic. CMR feature tracking and HDFs estimation may improve physiopathological understanding on wall-fluid mechanic interaction in STEMI patients.

A363: RELATIONSHIP OF INFARCT LOCATION, LEFT VENTRICULAR MECHANICS AND INTRAVENTRICULAR HEMODYNAMIC FORCES: RESULTS FROM A CMR STUDY

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Background.: Patients with acute anterior myocardial infarction (MI) experience more pronounced adverse left ventricular (LV) remodeling and have worse prognosis. Myocardial deformation imaging and intracardiac fluid dynamic hold the potential to add pathophysiological insight, however their relation with infarct location is not known.

Purpose. The aim of the study was to evaluate the effects of infarct location on left ventricular mechanics and intraventricular hemodynamic forces (HDFs).

Methods. Forty-nine acute STEMI patients underwent CMR at 1 week after the acute event. Left ventricular end-diastolic and end-systolic volumes indexed for body surface area (LVEDVi), left ventricular ejection fraction (LVEF), LV mass index, area at risk (AAR) and infarct size (IS) were measured. LV deformation was evaluated through CMR feature tracking. The following parameters were evaluated: global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS). For GLS and GCS both endocardial and transmural values were computed. LV HDFs were assessed from breath-hold steady-state free-precession cine-CMR long axis datasets using a novel method based on LV endocardial boundary tracking. LV HDFs were calculated both in apex-base (A-B) and latero-septal (L-S) directions. HDFs were computed in systole, diastole and over the entire cardiac cycle. The distribution of LV HDFs were evaluated by L-S over A-B HDFs ratio (L-S/A-B HDFs ratio %). STEMI patients were divided on the base of location (anterior versus non-anterior).

Results. Anterior STEMI (63%) had larger IS ($32 \pm 21\%$ vs $14 \pm 13\%$; $p=0.012$) and AAR (22 ± 14 vs 11 ± 10 ; $p=0.016$). Even if LVEF did not differ between two groups, anterior STEMI had lower values of GLS (GLS-endo: $-12 \pm 4\%$ vs $-18 \pm 3\%$; $p=0.001$ and GLS-myo: $-12 \pm 4\%$ vs $-13 \pm 5\%$; $p=0.02$) while no significant differences in GCS and GRS were detected. Patients with anterior STEMI had slightly lower systolic and diastolic A-B HDFs (respectively $18 \pm 6\%$ vs $22 \pm 6\%$; $p=0.08$, $7 \pm 4\%$ vs $11 \pm 9\%$, $p=0.08$), but without reaching significant statistical difference. On the other side, systolic but not diastolic L-S HDFs were significantly lower in anterior STEMI (respectively $2.8 \pm 0.9\%$ vs $3.9 \pm 1\%$, $p=0.01$; $1.6 \pm 0.6\%$ vs $2 \pm 1.4\%$, $p=0.782$). HDFs distribution, assessed by L-S/A-B HDFs ratio was not affected by infarct location (systolic L-S/A-B HDFs ratio: $16 \pm 5\%$ vs $18 \pm 4\%$, $p=0.494$; diastolic L-S/A-B HDFs ratio: $24 \pm 10\%$ vs $20 \pm 12\%$, $p=0.075$).

Conclusion. Patients with anterior STEMI had larger MI and area at risk, significantly reduced longitudinal strain and systolic L-S HDFs. The clinical impact of these observations should be further assessed in larger cohort.

A364: RIGHT ATRIAL THREE-DIMENSIONAL VOLUME IS A MAJOR DETERMINANT OF TRICUSPID ANNULUS AREA IN FUNCTIONAL TRICUSPID REGURGITATION

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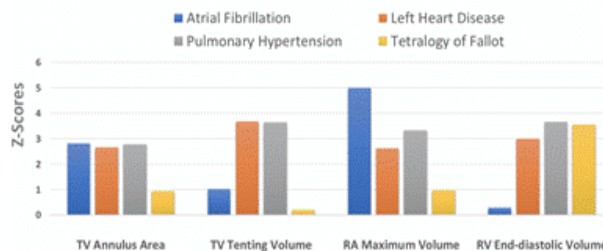
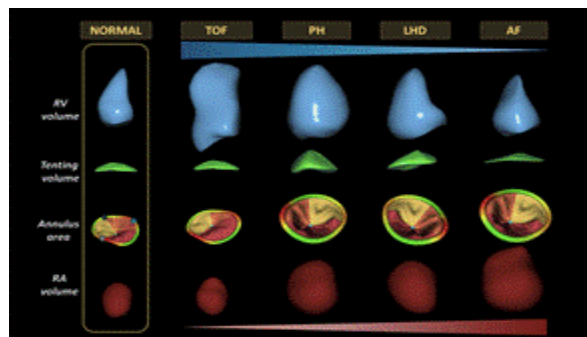
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Aims. Tricuspid annulus (TA) dilation and functional tricuspid regurgitation (FTR) are generally considered to be secondary to right ventricular (RV) remodeling. Our aim was to assess the relationship of TA area (TAA) with right atrial maximal volume (RAVmax) and RV end-diastolic volume (RVEDV) in FTR patients and healthy subjects.

Methods and Results. We enrolled 280 patients (median age 66 years, 59% women) with FTR due to left heart disease (LHD), pulmonary hypertension (PH), corrected tetralogy of Fallot (TOF), chronic atrial fibrillation (AF), and 210 healthy volunteers (45 years, 53% women). We measured TAA at mid-systole and end-diastole, tricuspid tenting volume, RAVmax and RVEDV by 3D echocardiography.

Irrespective of TA measurement timing, TAA correlated more closely with RAVmax than with RVEDV in both controls and FTR patients. On multivariable analysis, RAVmax was the most important determinant of TAA, accounting for 41% (normals) and 56% (FTR) of TAA variance. In FTR patients, age, RVEDV and left ventricular ejection fraction were also independently correlated with TAA. RAVmax (AUC=0.81) and TAA (AUC=0.78) had a greater ability than RVEDV (AUC=0.72) to predict severe FTR ($p<0.05$). Among FTR patients, those with AF had the largest RAVmax and smallest RVEDV. RAVmax and TA were significantly dilated in all FTR groups, except TOF. PH and TOF had largest RVEDV, yet tenting volume was increased only in PH and LHD.

Conclusion. RA volume is a major determinant of TAA, and RA enlargement is an important mechanism of TA dilation in FTR irrespective of cardiac rhythm and RV loading conditions.



A365: ADDITIONAL PROGNOSTIC ROLE OF STRAIN WITH STRESS CARDIAC MAGNETIC RESONANCE (PROGRESS STUDY)

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Background. Stress cardiovascular magnetic resonance (S-CMR) has been recognized as a reliable technique for the diagnosis and prognostic

stratification of patients with known or suspected coronary artery disease (CAD). Recently, the novel technique of feature-tracking (FT) strain has been applied to S-CMR in order to improve the risk stratification of patients. However, no data are available on the prognostic role of FT strain in patients undergoing a S-CMR with dipyridamole. Aim of this study is to assess the additional role of FT strain in the long-term risk stratification of a large population of patients with known or suspected CAD undergoing a S-CMR with dipyridamole.

Methods. 731 consecutive patients (age: 63 ± 10 y, male 84%) with stable typical or atypical symptoms suggesting possible cardiac ischemia underwent dipyridamole S-CMR. The patients were followed up for 5.8 ± 1.2 years. CMR-FT analysis of steady state free precession (SSFP) short and long axis cine images obtained in rest and stress conditions was performed in each patient to obtain 2D global peak systolic rest and stress longitudinal (GLS), circumferential (GCS) and radial strains (GRS). Major adverse cardiac events (MACE) were defined as myocardial infarction and cardiac death.

Results. MACE occurred in 64 (8.7%) patients. Patients experiencing MACE showed higher indexed left ventricular (LV) end-diastolic (EDVi), end-systolic (ESVi) volumes and lower LV ejection fraction (LVEF), higher late-gadolinium enhancement (LGE) presence and reduced both rest and stress GLS, GCS and GRS. At multivariable analysis, LVEDVi (HR 1.01 [95% CI 1.001-1.022]) and LGE (HR 2.399 [95% CI 1.322-4.355]) were independently associated with MACE ($p=0.027$ and $p=0.04$ respectively). By Kaplan-Meier analysis, patients with stress GLS $\geq -15.35\%$ had significantly reduced event-free survival compared with those with stress GLS $< -15.35\%$ (log-rank $p=0.001$). A model based on stress GCS $> -15.3\%$ plus LVEDVi showed a similar prognostic value of a model made of LVEDVi plus LGE.

Conclusions. In patients with known or suspected CAD undergoing S-CMR with dipyridamole, a model based on LVEDVi plus stress GCS owns a prognostic value similar to LVEDVi plus LGE.

A366: COMPUTED TOMOGRAPHY FOR THE PREDICTION OF STRUCTURAL VALVE DETERIORATION IN PATIENTS UNDERGOING TRANSCATHETER AORTIC VALVE IMPLANTATION

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Background. Computed tomography (CT) provides excellent anatomy assessment of the aortic annulus (AoA) and is currently routinely utilized for pre-procedural planning of transcatheter aortic valve implantation (TAVI). This study sought to investigate if geometrical characteristics of the AoA determined by CT may represent predictors of structural valve deterioration (SVD) in patients undergoing transcatheter aortic implantation (TAVI) with balloon-expandable valves.

Methods. AoA maximum diameter (Dmax), minimum diameter (Dmin), and area were assessed using preprocedural CT in patients undergoing TAVI in our Institution. SVD was identified with transthoracic echocardiography at 5.9 ± 1.7 follow-up years.

Results. 124 consecutive patients (mean age: 79 ± 7 years old; female: 61%) were retrospectively enrolled. AoA Dmax, Dmin and area were significantly smaller in patients with SVD compared to patients without SVD (27.1 ± 2.8 mm vs 25.6 ± 2.2 mm, $p=0.012$; 21.8 ± 2.1 mm vs 20.5 ± 2.1 mm, $p=0.001$ and 467 ± 88 mm² vs 419 ± 77 mm², $p=0.002$, respectively). At univariate analysis, female sex, body surface area, the use of a -23 mm prosthetic valve a Dmax < 27.1 mm and a Dmin < 19.9 mm were all variables independently associated with SVD whereas at multivariate analysis, only Dmin < 19.9 mm (OR 2.873, 95% CI 1.191-6.929, $p=0.019$) and female sex (OR 2.659, 95% CI 1.095-6.458, $p=0.031$) were independent predictors of SVD.

Conclusions. Female sex and AoA Dmin < 19.9 mm are associated to SVD in patients undergoing TAVI with balloon expandable valves.

A367: EVALUATION OF AORTIC REGURGITATION SEVERITY GRADE IN BICUSPID VALVE PATIENTS: DIFFERENCES BETWEEN ECHOCARDIOGRAPHY AND CMR

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Background. EACVI recommends the use of an "integrative approach", using several parameters, in aortic regurgitation (AR) quantification. This approach is easily achieved by echocardiography, although cardiovascular magnetic resonance (CMR) remains the gold standard for the quantification of regurgitant fraction (RF).

Purpose. The aim of the study was to analyze the accuracy of AR

grading by CMR (using RF) compared to the "integrative approach" of echocardiography in Bicuspid Valve (BAV) patients.

Methods. 96 BAV patients (33% female, 54.6 ± 15.6 years) with different severity grades of chronic AR were enrolled. All patients underwent CMR and echocardiography studies. AR by CMR was considered as absent ($\leq 1\%$), mild ($\leq 15\%$), moderate ($> 15\%$ and $< 30\%$) or severe ($\geq 30\%$) depending on RF value at valve level. AR was graded by echocardiography as absent, mild, moderate or severe, according to current recommendations. Furthermore, AR was divided by regurgitant jet type in central (41.2%) and eccentric (58.8%). AR was quantified by the same qualified cardiologist in both methods.

Results. Cohen's K was run to determine if there was agreement between echocardiography and CMR: poor concordance was found ($k=0.202$, $p < 0.0005$). Fair agreement was found only on absent ($k=0.368$) and severe AR ($k=0.290$), $p < 0.005$. More than mild AR was found in 47 (49%) patients by echocardiography, versus 19 (19.8%) by CMR (Table 1). 60 patients (62.5%), almost all with mild or moderate AR, showed different severity grades in the two imaging methods. In this class of patients, the disagreement does not depend on the jet type (chi-square = 0.43, $p=0.51$), neither on age ($p=0.672$) or aortic sinus diameter ($p=0.747$)

Conclusions. In BAV patients, the quantification of AR severity by CMR has a poor concordance with the severity grade by the echocardiography. No influence seems to derive from the regurgitant jet type, age or aortic diameter. Nowadays echocardiography remains the gold standard for AR quantification. It is necessary to validate the assessment of chronic AR severity by CMR identifying additional parameters.

AR severity grade by echo	AR severity grade by CMR				Total
	Absent	Mild	Moderate	Severe	
Absent	10	18	0	0	28
Mild	2	19	0	0	21
Moderate	0	27	6	3	36
Severe	0	1	7	3	11
Total	12	65	13	6	96

A368: NORMAL REFERENCE RANGES OF NON-INVASIVE LEFT VENTRICULAR MYOCARDIAL WORK IN PAEDIATRIC AGE

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Background. Myocardial work (MW) estimation by pressure-strain loops (PSL) allows a non-invasive evaluation of myocardial performance, as recently demonstrated in adult patients. Aim of this study is to provide the reference values for global myocardial work index (MWI), constructive work (MCW), wasted work (MWW), and work efficiency (MWE) in a group of healthy children.

Methods. Assessment of MW was performed using a commercially available software package (Echopac, GE). MW was measured from PSLs areas, derived from non-invasive LVP curves combined with strain acquired speckle tracking echocardiography (STE). After calculating GLS, values of brachial blood pressure were inserted and the time of valvular events by echocardiography were indicated, then the software was able to measure non-invasive PSLs.

Results. Two-dimensional (2D) standard and speckle-tracking echocardiography were performed in 90 healthy children (mean age 9.9 ± 4.9 [1-17] years, females: 57%) together with the assessment of MW by means of PSLs. Mean \pm standard deviation, 5th and 95th percentile values for global MWI, MCW, MWW, and MWE in the whole population were 1769 ± 254 mm Hg, (1354-2193); 2201 ± 290 mm Hg, (1657-2658); 78 ± 47 (29-163) mm Hg%; 96 ± 1.8 (92-99)%, respectively.

Conclusions. The assessment of MW is feasible in healthy children. This study provides useful 2-dimensional echocardiographic reference ranges for novel indices of non-invasive MW.

A369: ANTHRACYCLINE THERAPY AND REGIONAL MYOCARDIAL DAMAGE IN BREAST CANCER PATIENTS: HOW, WHEN AND WHERE?

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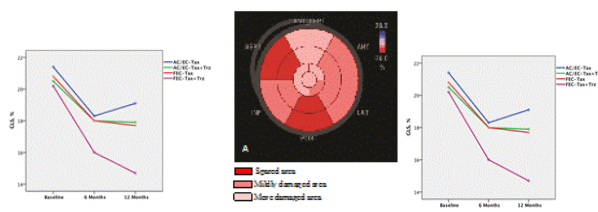
Objectives. In breast cancer (BC) patients treated with anthracyclines-based therapies we aim at assessing whether adjuvant drugs impact cardiac function differently, and whether their cardiotoxicity has a regional pattern.

Background. Cardiotoxicity is a leading cause of morbidity and mortality in cancer survivors. Cardiac dysfunction related to chemotherapy treatment is the main manifestation (Cancer Therapeutics Related - Cardiac Dysfunction CTR-CD).

Methods. In a multicenter study, 146 BC patients with anthracycline-naïve breast cancer (mean age 56 ± 11 years) were prospectively enrolled and divided into 3 groups according to the received treatments: AC/EC (doxorubicin or epirubicin + cyclophosphamide)-Group (n=30), AC/EC/Tax (AC/EC + taxanes)-Group (n=69), FEC/Tax (AC/EC/Tax + fluorouracil)-Group (n=47). Fifty-six patients of the total cohort also received trastuzumab. Left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS) were calculated before starting chemotherapy (T0), at 3 months (T3), at 6 (T6) and 12 months (T12). We defined cardiotoxicity as a ≥10% reduction in the ejection fraction (EF) of the left ventricle between pre- and post-chemotherapy. A relative reduction of ≥15% in GLS values between pre- and post-chemotherapy was considered clinically significant for the definition of cardiac dysfunction related to chemotherapy treatment.

Results. The calculated mean duration of the overall follow-up was 309 ± 109 days. A 310% drop of EF, while remaining within the normal range, was reached at T6 in 25.3% of patients from the whole cohort with an early decrease only in FEC/Tax-Group (p=0.04). A 315% GLS reduction was observed in many more (61.6%) patients. GLS decreased early both in the whole population (p <0.001) and in the subgroups. The FEC-Tax Group showed the worst GLS at T6 (Figure 3). Trastuzumab further worsened GLS at T12 (p=0.031, Figure 2). A significant decrease in LS was observed in all segments of the left ventricle, but greater impairment was found in the (basal-mid-apical) segments of the anterior septum (mean value after chemotherapy = -14.8 ± 2.3%; D-LS 3 4%) and at the apex (mean value after chemotherapy = -16.5 ± 2.6%; D-LS 3 4%) (Figure 1).

Conclusions. The decrease of GLS is more precocious and pronounced in BC patients who received FEC + taxanes. Cardiac function further worsens after 6-months of adjuvant trastuzumab. All LV segments are damaged, with the anterior septum and the apex showing the greatest impairments.



A370: USEFULNESS OF MYOCARDIAL WORK ASSESSMENT FOR THE UNDERSTANDING OF MECHANISMS UNDERLYING SACUBITRIL/VALSARTAN EFFICACY IN PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION

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Background. Sacubitril/valsartan has shown the ability in reducing the risk of death and of hospitalization in patients with HF (heart failure) and is recommended in patients with heart failure with reduced ejection fraction (HFrEF) who remain symptomatic despite conventional therapies. Strain imaging derived myocardial work (MW) is an emerging tool for the evaluation of left ventricular (LV) mechanics by incorporating both systolic deformation and afterload burden in the analysis.

Aim. To evaluate in a prospective fashion the impact of sacubitril/valsartan therapy in HF patients on MW derived parameters in relation with standard echocardiographic indices.

Methods. We recruited thirteen HF patients with indication to sacubitril/valsartan therapy according to current guidelines. Sacubitril/valsartan therapy titrated at the maximum tolerated dose. A comprehensive echo-Doppler exam, including speckle tracking derived assessment of global longitudinal strain (GLS) (in absolute value), was performed before and after a three months therapy with sacubitril/valsartan. Parameters of MW such as global work index (GWI),

global constructive work (GCW) global wasted work (GWW) and global work efficiency (GWE) were calculated according to standardized procedures. Patients with more than mild aortic and mitral stenosis and/or regurgitation were excluded. Other exclusion criteria included permanent and/or persistent atrial fibrillation and inadequate echo images.

Results. The 13 patients (M/F=11/2, age: 57±8.2 years, aetiology: idiopathic in 3 patients, ischaemic in 7 patients and chemotherapy related cardiotoxicity in 3 patients, NYHA Class: II in 7 and III in 6 patients). All patients tolerated sacubitril/valsartan therapy. After the three months therapy an improvement of LVEF (from 32.3±2% to 36.2± 6%, p=0.015), GLS (from 9.8±1% to 11.6±2%, p=0.019), GWI (from 845.0±175.0 mmHg% to 1091.6±336.8 mmHg%, p=0.003), GCW (from 993.4± 211.6 mmHg% to 1262.7±404 mmHg%, p=0.002) and GWE (from 77±11% to 81 ± 10%, p=0.002) was observed, without significant changes in GWW (from 190±121 mmHg% to 211 ± 145 mmHg%, p=0.307). We also found a positive correlation between the magnitude of LVEF improvement and the baseline values of GCW (r=0.66, p=0.014). This relation remained significant even after adjusting for the extent of systolic blood pressure reduction (r=0.54, p=0.033).

Conclusion. Three months sacubitril/valsartan therapy significantly improves standard and advanced indices of LV systolic function. This improvement is due to the increase of constructive work more than to the reduction of wasted work and the increase of LVEF can be predicted by the global constructive work levels at baseline. MW assessment may help to understand the mechanisms underlying the sacubitril/valsartan therapy efficacy in HF patients.

A371: AFFIDABILITÀ DEL RAPPORTO E/E' PER STIMARE LA PRESSIONE DI INCUNEAMENTO DEI CAPILLARI NEI PAZIENTI CON SCOMPENSO CARDIACO AVANZATO SELEZIONATI PER TRAPIANTO DI CUORE

Lorenzo Luschi (a), Filippo Pirrotta (a), Alberto Palazzuoli (a), Stefania Bernazzali (b), Gianfranco Montesi (b)

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Introduzione. La valutazione non invasiva del riempimento diastolico mediante ecocardiografia Doppler fornisce importanti informazioni prognostiche ed è considerato un indice attendibile di misurazione non invasiva delle pressioni intracavitarie del ventricolo sinistro (LV). Tuttavia, la reale accuratezza del rapporto E/e' nel prevedere la pressione di incuneamento e il confronto simultaneo con altre misurazioni ottenute mediante studio invasivo non sono state sufficientemente validate.

Obiettivi. Questo studio è stato progettato per valutare l'accuratezza di una analisi completa PW e TDI rispetto alle misure invasive ottenute durante il cateterismo cardiaco. Abbiamo inoltre analizzato quale parametro Doppler fosse il miglior predittore di aumento delle pressioni polmonari in pazienti affetti da scompenso cardiaco cronico avanzato.

Metodi. 45 pazienti sono stati sottoposti simultaneamente a cateterismo e studio Ecodoppler cardiaco. Il cateterismo del cuore destro è stato realizzato con cateteri a punta micromanometrica ed è stato eseguito come screening diagnostico per l'inserimento dei pazienti in lista dei trapianti di cuore. Tutti i pazienti sono stati preventivamente sottoposti a screening secondo i seguenti criteri: rapporto E/e' >8, E/A >1, pressione polmonare >35 mmHg e frazione di eiezione <35%. Sono state eseguite contemporaneamente misurazioni invasive ed ecocardiografiche della pressione polmonare sistolica (PAPS). La pressione polmonare media (PAPM), la pressione di incuneamento (PAW) e la pressione atriale destra (RAP) sono state tutte misurate mediante Cateterismo; sono state misurate, inoltre, le velocità dell'onda E, onda A, tempo di decelerazione (DT), tempo di rilasciamento isovolumetrico (IVRT), doppler tissutale e' a livello settale basale mitrale e laterale. Infine sono stati misurate le velocità di picco sistolico del rigurgito tricuspidalico e del rigurgito protodiastolico polmonare.

Risultati. La PAW era ben correlata ai valori di E/e' laterali e un cut-off >16 identificava con precisione una PAW >15 mmHg. (r=0.76) Mentre il rapporto E/e' settale ha avuto una modesta correlazione con la PAW. (r=0.60) Il rapporto di E/A >1 non ha mostrato correlazione significativa con tutte le misurazioni invasive. Al contrario, un accorciamento DT <130 msec ha rivelato una buona correlazione con la PAW, mentre RAP e IVRT <70 msec erano inversamente correlati con PAW. Inoltre, la velocità di rigurgito tricuspidalico ha dimostrato una buona correlazione con la stima invasiva delle PAPS (r=0.78). Sebbene i pazienti con E / E' compreso tra 8 e 15 abbiano mostrato una più ampia variabilità la contemporanea analisi di DT e IVRT sono stati in grado di identificare quelli con valori PAW più elevati.

Conclusioni. La combinazione dell'imaging Doppler tissutale dell'anulus mitralico e della velocità di riempimento mitralico stima i pazienti con PAW elevato con buona precisione. Tra i parametri TDI, l'aumento dell'E/e' laterale >16 si è dimostrato il miglior predittore di aumento di PAP. DT <130 e velocità di rigurgito tricuspidalico erano i migliori predittori di ipertensione polmonare e dovrebbero essere le prime 2 variabili da stimare in pazienti con insufficienza cardiaca avanzata.

A372: SIGNIFICATO PROGNOSTICO DEL MYOCARDIAL WORK NEL POSTINFARTO: STUDIO OSSERVAZIONALE

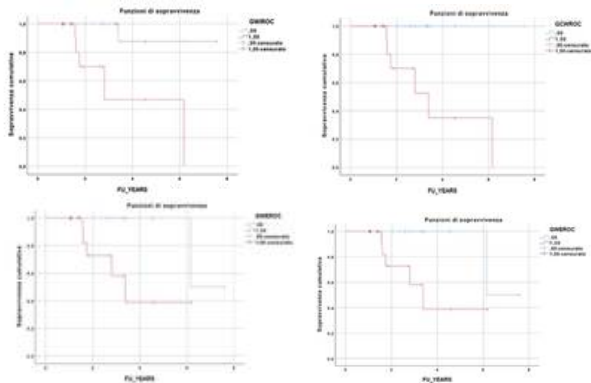
Filippo Mancuso (a), Nicolò Pellegrino (a), Francesca Frecentese (a), Roberto Licordari (a), Maurizio Cusmà Piccione (a), Olimpia Trio (a), Roberta Manganaro (a), Scipione Carerj (a), Concetta Zito (a)
(a) AZIENDA OSPEDALIERA POLICLINICO UNIVERSITARIO G. MARTINO MESSINA

Obiettivi. Valutare se i parametri non invasivi di myocardial work derivati dai loop pressione-strain sono capaci di predire l'outcome nei pazienti con pregresso infarto miocardico acuto (IMA).

Materiale e metodi. Sono stati arruolati 99 pazienti (61 ± 12 anni, 84% uomini, 57% ipertesi) a distanza di almeno un anno dall'evento acuto (STEMI=24 pz; NSTEMI=75 pz) tutti trattati con PTCA primaria. Ogni paziente è stato inserito in un programma di follow-up della durata massima di 8 anni (range 1-8) al fine di individuare l'insorgenza di eventi predefiniti: morte, angina, scompenso cardiaco, aritmie ventricolari, re-IMA, impianto di ICD/CRT-D. Tutti i pazienti al momento della dimissione sono stati sottoposti a misura della pressione arteriosa e a ecocardiogramma transtoracico completo. È stata inoltre effettuata l'analisi speckle-tracking per il calcolo di: strain longitudinale globale (GLS, %), dispersione meccanica (MD) e myocardial work [lavoro costruttivo (GCW mmHg%), lavoro inefficace (GWW, mmHg%), indice di myocardial work (GWI, mmHg%) ed efficienza (GWE, %)].

Risultati. Su un totale di 99, hanno completato il FU 57 pazienti. Questi sono stati suddivisi in 2 gruppi sulla base della comparsa o meno di eventi: gruppo 0 (n=50) pazienti senza eventi e gruppo 1 (n=43) pazienti con eventi che erano così distribuiti: morte= 3.5%; angina= 21%; scompenso cardiaco= 19%; aritmie ventricolari=14%, re-IMA=12% impianto di ICD=5.3%. Non vi erano differenze significative tra i due gruppi per quanto concerne FE (p=0.04), volumi del ventricolo sinistro (p=0.05), GLS (p=0.065) e MD (p=0.021). Al contrario, nel gruppo 0 si osservavano valori di GWI, GWE e GCW (1729 ± 452; 92±9; 1919 ± 493) significativamente maggiori rispetto al gruppo 1 (1276± 378; 83±7.5; 1362±371) con valori di p rispettivamente di: 0.002, 0.003 e <0.001 tra i due gruppi. Al contrario, i valori di GWW risultavano maggiori nel gruppo 1 (164±51) rispetto al gruppo 0 (120± 87.6, p =0.022). All'analisi di regressione di Cox, gli indici di MW erano predittori di outcome: GWI (HR 0.99; IC 0.994-0.998, p<0.001); GWE (HR:0.77; IC 0.685-0.880, p<0.001); GCW (HR: 0.996: IC 0.994-0.998, p<0.001); GWW (HR 1.009; IC 1.002-1.016, p=0.014), insieme al rapporto E/E' (p=0.002). Nei grafici in basso sono rappresentate da sinistra a destra le curve di sopravvivenza libera da eventi in relazione ai cut-off di GWE ≥90.5%, GWI ≥1622 mmHg/%, e GCW ≥1731 mmHg/%, identificati alle curve ROC come quelli con migliore sensibilità e specificità.

Conclusioni. Tale studio ha messo in evidenza la superiorità degli indici di MW, rispetto ai parametri ecocardiografici convenzionali e al GLS nel predire l'outcome nel post-infarto.



GWE, % ≥90.5 (blu); <90.5 (rosso) GWI, mmHg/ % ≥1622 (blu); <1622 (rosso) GCW, mmHg/ % ≥1731 (blu); <1731 (rosso).

A373: DETECTION OF CORONARY ALLOGRAFT VASCULOPATHY BY MULTI-LAYER LEFT VENTRICULAR LONGITUDINAL STRAIN IN HEART TRANSPLANT RECIPIENTS

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Background. Cardiac allograft vasculopathy (CAV) is an obliterative coronaropathy that develops in the transplanted human heart, representing a major cause of graft failure and mortality. Non-invasive CAV detection, especially in the early stages of the disease, is still

challenging, and coronary angiography remains the gold standard. The aim of our study was to investigate the role of speckle tracking echocardiography (STE), in particular three-layer STE, in predicting CAV at early stages, and if other traditional echocardiographic, clinical or biochemical parameters could relate to CAV.

Methods. A total of 33 heart transplanted patients were enrolled and subsequently divided accordingly to the presence or absence of CAV (12 CAV+, 22 CAV-). All subjects underwent a complete transthoracic echocardiographic examination on the same day of the CA, and all conventional parameters of myocardial function were obtained, including strain values assessed by STE.

Results. Strain values were significantly reduced in presence of CAV, at each myocardial layer but in particular the endocardial-epicardial gradient (-4.15±1.6 vs -1.7±0.4% <0.0001) that was also highly predictive of CAV (AUC at ROC curve 0.97). Among diastolic parameters, the E wave deceleration time (DT) and the mean E/e' ratio were strongly positively associated with CAV (Figures 1 and 2).

Conclusions. In our population, left ventricular global longitudinal strain (GLS), layer-specific GLS and the endocardial-epicardial LS gradient, E wave DT and E/e' ratio were the best independent non-invasive predictors of CAV.

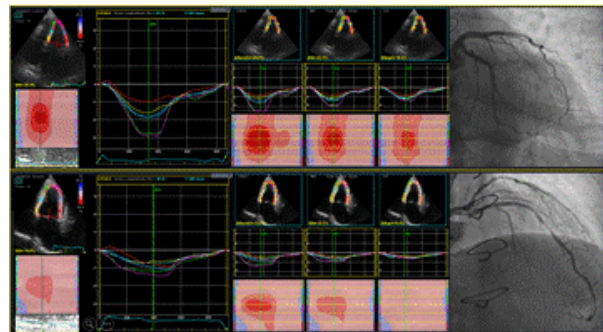


Figure 1

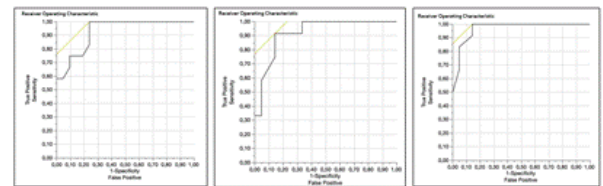


Figure 2

A374: HEART TRANSPLANT AND ANTIBODY-MEDIATED REJECTION: THE ROLE OF MYOCARDIAL STRAIN AS AN EARLY MARKER OF CARDIAC DYSFUNCTION IN PATIENTS WITH ANTI-HLA ANTIBODIES

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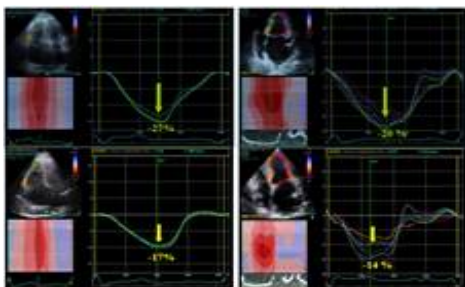
Background. Antibody-mediated rejection of the transplanted heart is diagnosed through endomyocardial biopsy, which represents the gold standard, whereas clinical elements, antibody anti-human leukocyte antigens (HLA) and graft dysfunction are supplementary components. The aim of the study was to identify through a non-invasive technique, such as transthoracic echocardiography, early signs of impaired cardiac function in heart transplanted patients, in presence of anti-HLA antibodies but without any histological sign of antibody-mediated rejection, assessed through endomyocardial biopsy.

Methods. A total of 117 heart transplanted patients were enrolled, and they were divided into two groups 'HLA+' (45 patients) and 'HLA-' (72 patients), based on the presence and the absence of circulating anti-HLA antibodies, respectively. Patients were excluded in presence of coronary allograft vasculopathy or antibody-mediated rejection, attested by endomyocardial biopsy. Each patient underwent an echocardiographic exam, within one month from the biopsy, analysing standard parameters of both systolic and diastolic function, together with strain analysis of right and left ventricle (RV and LV) and left atrium (LA).

Results. Clinical and demographic characteristics did not differ significantly between the two groups, and neither did standard echocardiographic parameters. The only significant parameter that showed a statistically significant difference was deceleration time of E

wave (DT), which resulted to be lower in the 'HLA+' group ($165 \pm 39,5$ vs $196,5 \pm 25$; $p < 0,005$). Regarding strain analysis, the study attested a strong difference of both LV global longitudinal strain ($-16,0 \pm 3,4$ vs $-19,8 \pm 2,0$; $p < 0,005$) and RV strain between the two analysed subsets ($-17,2 \pm 3,6$ vs $-20,6 \pm 3,9$ $p < 0,005$), whereas left atrial strain did not differ significantly (Figure).

Conclusion. The presence of circulating anti-HLA antibodies might be correlated with a mild cardiac dysfunction, even in the absence of antibody-mediated rejection. Standard echocardiographic parameters might not completely reveal this subclinical impairment, whereas strain analysis has showed promising results since it revealed more clearly an impaired function of both ventricles in heart transplanted patients HLA+, with potentially important clinical repercussions.



A375: WHY LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IS NOT STEADILY ASSOCIATED WITH INCREASED PULMONARY PRESSURE? THE BUFFER EFFECT OF LEFT ATRIUM UNMASKED BY ATRIAL STRAIN

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The backward transmission of the increase in left ventricular (LV) filling pressure is not always associated to an increase in pulmonary pressure. To what extent a preserved left atrium (LA) function may modulate the consequences of the increase of LV filling pressure on the pulmonary circulation in terms of hemodynamics and symptoms has not been yet investigated.

Methods and Results. We retrospectively studied 300 patients with available data of diastolic function, systolic pulmonary artery pressure (PAP-S) and LA function analyzed with two-dimensional speckle-tracking echocardiography. 28 patients (9.3%) had $E/e' > 14$, considered the threshold of elevated LV filling pressure; 30 (10%) had $PAP-S > 35$ mmHg; 114 (38%) had LA dysfunction; 68 (23%) were symptomatic for dyspnea and, notably, 87 (29%) with $E/e' > 14$ were asymptomatic. We found a positive association between E/e' and $PAP-S$ ($p < 0,001$); however, $PAP-S$ was significantly higher among patients with impaired LA function ($p < 0,0001$). In a multivariate analysis including clinical and echocardiographic values, only $E/e' > 14$ was significantly associated with $PAP-S$ ($p = 0,006$) exclusively in the group of patients with LA dysfunction. The overall relationship between E/e' and $PAP-S$ was significantly modified by LA function ($p = 0,01$). In a univariate analysis including clinical and echocardiographic predictors of dyspnea, $E/e' > 14$ was a significant predictor exclusively in patients with LA dysfunction ($p = 0,001$) but not in patients with normal LA function.

Conclusion. A preserved LA function may modulate the consequences of elevated LV filling pressure on the pulmonary circulation representing a potential protective factor for the presence and intensity of cardio-pulmonary symptoms.

A376: LEFT VENTRICULAR FORCE ADAPTATION AND CARDIAC DEFORMATION IN THE PROGRESSION OF AORTIC STENOSIS

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Introduction. Aortic stenosis (AS) is one of the most common valvular heart diseases; however, the association between left ventricular (LV) myocardial deformation and hemodynamic forces (HDFs) is still mostly unexplored.

Purpose. This study aimed to assess the differences in LV myocardial deformation and HDFs in a large cohort of patients with aortic stenosis retrospectively.

Methods. Two-hundred fifty-four subjects (median age 77 years, 50% women) with preserved LV ejection fraction (LVEF), and mild ($n = 87$), moderate ($n = 92$) or severe ($n = 75$) AS, were included in the study. The

2D LV global longitudinal strain (GLS), circumferential strain (GCS), and HDFs were measured with new software that allowed us to calculate all these values and parameters from the three apical views.

Results. When comparing severe AS to mild AS, LV mass appeared increased while the LV hypertrophy phenotype was concentric ($p < 0,0001$). Along with the progression of the AS, LVEF was decreased. All GLS, GCS, and HDFs parameters were uniformly reduced in severe AS compared to mild AS ($p < 0,0001$), in the same way, LV longitudinal force, LV longitudinal systolic force, and LV impulse have proven to be accurate on ROC curves (AUC 70%, 73%, and 73% respectively).

Conclusion. The integrated approach of deformation and cardiac mechanics allows the description of pathophysiological changes during the progression of mild to severe aortic stenosis.

A377: IMPROVEMENT OF LEFT VENTRICULAR SYSTOLIC PERFORMANCE DURING SACUBITRIL/VALSARTAN IN A COHORT OF PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION

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(a) SAPIENZA UNIVERSITA DI ROMA

Background. Sacubitril/valsartan is a well-established therapeutic option for patients with heart failure with reduced ejection fraction (HFrEF). While it was clearly demonstrated to improve patients' clinical conditions, its potential role in inducing left ventricle (LV) reverse remodeling is still under investigation.

Purpose. To evaluate clinical and echocardiographic effect of sacubitril/valsartan on a cohort of patients with HFrEF after six months of therapy.

Methods. 36 patients with HFrEF eligible to start a therapy with sacubitril/valsartan were enrolled. A standard and advanced echocardiographic evaluation was performed before starting the therapy and after six months of follow-up (FU). Off-line analysis of left ventricle global longitudinal strain (GLS), longitudinal strain of the free wall of the right ventricle (RVFWSL) and left atrial strain (LAS) was conducted. Clinical and biochemical parameters were evaluated as well.

Results. At six months of FU NYHA class improved in the vast majority of patients (NYHA class III at baseline vs FU: 56% vs 5%, $p = 0,001$). We observed a significant reduction in LV end-diastolic (100 ± 33 vs 92 ± 33 , $p = 0,043$) and end-systolic (70 ± 26 vs 59 ± 25 , $p = 0,001$) volumes and an improvement of LV ejection fraction ($30 \pm 5\%$ vs $37 \pm 6\%$, $p < 0,001$). After six months of therapy, GLS significantly improved ($-9,7 \pm 2,9$ vs $-13,0 \pm 3,1$, $p < 0,001$). No differences in left and right atrial volumes (57 ± 29 vs 54 ± 30 , $p = 0,349$; and 54 ± 24 vs 48 ± 19 , $p = 0,157$, respectively), RVFWSL ($-16,5 \pm 5,4$ vs $-16,8 \pm 1,5$) and LAS (14 ± 6 vs 19 ± 8 , $p = 0,197$) were found at FU.

Conclusion. Left ventricular function evaluated with standard and advanced echocardiographic parameters improved after six months of therapy with sacubitril/valsartan in HFrEF patients. Reduction in LV volumes was found as well.

A378: LEFT VENTRICULAR HEMODYNAMIC FORCES EVALUATION IN PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION TREATED WITH SACUBITRIL/VALSARTAN

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(a) SAPIENZA UNIVERSITA DI ROMA; (b) UNIVERSITA DI TRIESTE; (c) UNIVERSITA DEGLI STUDI G. D'ANNUNZIO CHIETI E PESCARA

Background. Hemodynamic forces (HDFs) represent the forces exchanged between the blood and the myocardium. Recently, HDFs estimation by echocardiography, using the tracking of the endocardial border with dedicated software, permitted their study in different clinical contexts.

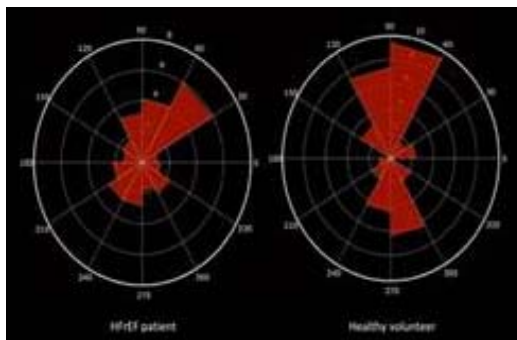
Purpose. To describe left ventricular (LV) HDFs in patients with heart failure with reduced ejection fraction (HFrEF) and to evaluate their possible change after six months of therapy with sacubitril/valsartan.

Methods. 20 patients with HFrEF undergoing therapy with sacubitril/valsartan were enrolled. Echocardiography was performed at baseline and after six months of follow-up. Off-line HDFs estimation using dedicated software was conducted. In order to compare ventricles of different sizes, HDFs were normalized for the LV volume and expressed as a percentage of the force of gravity. HDFs were assessed over the entire cardiac cycle, in systole and diastole by calculating the mean square value over the selected time period. LV HDFs were calculated both in apex-base (A-B) and latero-septal (L-S) directions. The distribution of LV HDFs was evaluated by L-S over A-B HDFs ratio (L-S/A-B HDFs ratio %). 13 healthy volunteers were enrolled as a control group.

Results. Comparing healthy and HFrEF subjects, the latter showed smaller values of A-B HDFs during the entire cardiac cycle ($5,8 \pm 0,83\%$ vs $12,37 \pm 3,7\%$, $p = 0,001$), in systole ($8,47 \pm 1,49\%$ vs $16,6 \pm 6,5\%$,

$p=0.001$) and diastole ($3.2 \pm 0.6\%$ vs $7.1 \pm 3.7\%$, $p=0.001$). While systolic L-S HDFs were lower in HFREF subjects ($1.56 \pm 0.66\%$ vs $2.29 \pm 0.81\%$, $p=0.005$), we observed an inappropriately high value of diastolic L-S HDFs ($1.88 \pm 0.68\%$ vs $1.81 \pm 0.91\%$, $p=0.837$), compared with healthy volunteers. Consequently, L-S/A-B ratio in HFREF patients was higher during the entire cardiac cycle ($29.24 \pm 7.60\%$ vs $15.5 \pm 7.95\%$, $p=0.001$), in systole ($19.14 \pm 8.64\%$ vs $14.76 \pm 4.32\%$, $p=0.006$), but particularly in diastole ($58.24 \pm 14.63\%$ vs $28.54 \pm 13.92\%$, $p=0.001$). At six month follow-up we observed a trend in amelioration of HDFs distribution, but the reduction of L-S/A-B ratios did not reach statistical significance (diastolic L-S/A-B HDFs ratio: baseline 58.24 ± 14.63 vs 6 months FU 44.57 ± 18.8 , $p=0.222$).

Conclusion. Our cohort of HFREF patients presented low A-B HDFs values and a significant misalignment of HDFs, especially in diastole. Those fluid alterations partially improved at 6 months FU but a larger cohort of patients is needed to confirm these initial observations.



A379: LEFT VENTRICULAR DIASTOLIC FUNCTION AND ATRIAL FUNCTION IN MIDDLE-AGED ENDURANCE ATHLETES: DIFFERENCES WITH AGE-MATCHED HYPERTENSIVE PATIENTS

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Introduction and purpose. There is an ongoing debate on whether endurance training, like hypertension (HTN), may in the long run create atrial fibrosis and thus affect left atrial (LA) function, promoting incidental atrial fibrillation (AF). Our aim was to compare left ventricular (LV) diastolic function and LA function between two cohorts of amateur master endurance athletes and age-matched hypertensive patients.

Design of the study. 240 subjects aged 40 through 66 years were enrolled in this study: 120 hypertensive patients with a sedentary lifestyle [mean duration of HTN: 10 (5 to 15) years] and 120 healthy age-matched amateur athletes, without a history or evidence of HTN, who had undergone intensive endurance training over many years [mean years of training: 34 (24.5 to 40)], with an average of 8 hours of training per week [mean lifetime training hours: 10.924 (6.195 to 15.150)].

Methods. All patients underwent a comprehensive two-dimensional echocardiography (2DE) with Doppler and Tissue Doppler study (TD) to assess LV systolic and diastolic function and speckle-tracking echocardiography (STE) and three-dimensional echocardiography (3DE) to assess LA volumes and function according to current guidelines.

Results. Mean age of the pooled population was 54.55 ± 6.71 year old, 65% males. The two groups were comparable for age ($P=0.195$). LV ejection fraction was not significantly different among the two groups ($P=0.978$), while LV mass index was higher in athletes ($P=0.014$). None of the 120 athletes had diastolic dysfunction, 4 athletes had indeterminate diastolic pattern. In the group of hypertensive patients, 5 of them had diastolic dysfunction, 16 had indeterminate diastolic function, while the remaining 99 patients had normal diastolic function. 99 athletes (82.5%) had dilated LA (>34 mL/m²), whereas only 34 (28.3%) hypertensive patients had dilated LA. Early diastolic transmitral flow velocity (E) was similar in the two cohorts ($P=0.441$), but athletes had significantly decreased A velocities ($P<0.001$) with increased E/A ratios ($P<0.001$), compared to hypertensive patients. Athletes showed higher TD-derived septal ($P<0.001$) and lateral ($P<0.001$) e' velocities and lower septal ($P=0.247$) and lateral ($P<0.001$) a' velocities, compared to hypertensive patients. Speckle-tracking analysis of the LA showed in athletes significant lower strain values of the contractile function ($P=0.015$), higher strain values of the conduit function ($P<0.001$) and higher strain values of the reservoir function ($P<0.001$) compared to hypertensive patients. 3DE was in line with the results obtained from the STE, confirming in athletes a better LA total emptying fraction ($P=0.047$) and a better passive atrial EF ($P<0.001$).

Conclusions. Master athletes showed less diastolic dysfunction and more preserved atrial function as compared to age-matched hypertensive

patients. Hence, a reduction in LA conduit or reservoir function in an athlete should raise the suspicion of a cardiac disorder. LA was more dilated in athletes than in hypertensive patients, therefore LA volume seems not to be a useful tool for the differential diagnosis between these populations.

A380: ARTERIAL STIFFNESS IN ASYMPTOMATIC TYPE 2 DIABETIC NORMOTENSIVE POSTMENOPAUSAL WOMEN

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Background. Arterial stiffness is a marker of cardiovascular disease useful to identify, at an early stage, subjects with higher cardiovascular risk.

Aims. The goal of our study was to assess the prevalence of arterial stiffness, assessed by global Pulse Wave Velocity (gPWV), among diabetic normotensive postmenopausal women (DPMW) and its correlation with glycosylated hemoglobin (HbA1c) levels.

Patients and methods. We enrolled 641 consecutive DPMW affected by type 2 diabetes, diagnosed over five years. 300 normotensive normoglycemic postmenopausal women were included as control group (CG). We assessed arterial stiffness by gPWV, performed by pulsed Doppler (3.5 MHz probe) using 2-dimensional guidance and ECG trigger. Philips Epiq 7 was used which is an echo-Doppler system equipped with a multifrequency transducer. The gPWV was assessed as normal for a velocity equal or lower than 7.1 m/s.

Results. 29 (4.5%) women had an increased gPWV among 641 DPMW, and 4 (1.3%) among 300 women of CG, $p<0.01$. There was no difference for mean age between the two groups: 57 ± 12 and 56 ± 4 respectively, $p=0.2$. DPMW with HbA1c $>7.5\%$ were 228 (35.6%), 205 (32%) had an increased gPWV, 23 (3.6%) a normal gPWV. Women with HbA1c $<7.5\%$ were 413 (64.4%), 6 had an increased gPWV (0.9%), $p<0.0000$. DPMW with abnormal ECG were 207 (32.3%), 11 of them had an increased gPWV (5.3%), $p=0.5$ versus women with an increased gPWV and normal ECG, 18 (4.1%).

Conclusions. We found a high prevalence of increased gPWV in asymptomatic normotensive DPMW; there is a statistically significant correlation between increased gPWV and HbA1c high levels, but there is not between increased gPWV and abnormal ECG rate, however ECG is the unique cardiologic test recommended by current Guidelines in all diabetic patients. We conclude that early detection of high level of HbA1c and increased PWV may identify asymptomatic DPMW with higher risk to develop organ damages; while a simple ECG, when normal, is not enough to assess the cardiovascular risk in our population.

A381: STRESS ECHOCARDIOGRAPHY AND DIAGNOSIS OF CORONARY ARTERY DISEASE: NEW ECHOCARDIOGRAPHIC PARAMETERS

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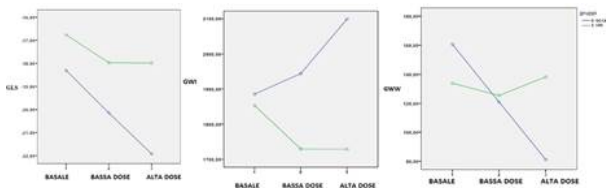
Aims. Myocardial work (MW) is a new interesting non-invasive tool to study left ventricle (LV) performance by pressure-strain loops. We proposed to investigate the role of global longitudinal strain (GLS) and MW, during dipyrindamole stress echocardiography (DSE), in identifying coronary artery disease (CAD) detected at coronary angiography.

Methods. Forty-eight patients, (mean age 65.3 ± 8.7 years) undergone DSE and subsequent coronary angiography, were retrospectively enrolled. The study population was divided in two groups according to the presence of CAD: group 1, patients without CAD ($n=18$, mean age 63.3 ± 6.4 years); group 2, patients with CAD ($n=30$, mean age 67.2 ± 5.9 years). Multilayer longitudinal strain and MW indices, namely global work index (GWI), global constructive work (GCW), global work efficiency (GWE), global work waste (GWE), were obtained at basal, low-dose and peak-dose of DSE. The percentage change between basal and peak-dose was calculated for every parameter.

Results. No significant differences were observed between the two groups of patients about all traditional and advanced echocardiographic parameters at basal stage. GLS, endocardial longitudinal strain (endoGLS) and epicardial longitudinal strain (epiGLS) increased at every step in both groups, even if the trend was more evident for group 2 (Figure). GWI, GCW and GWE increased from basal to peak dose, while GWW decreased, in group 1; the opposite was observed in group 2 (Figure). GWI change ($13.6 \pm 1.6\%$ vs $4.8 \pm 1.1\%$, $p=0.001$), GWE change ($2.4 \pm 1.28\%$ vs $0.7 \pm 4.6\%$, $p=0.001$) and GWW change ($-51.1 \pm 2.8\%$ vs $31.5 \pm 1.1\%$, $p<0.001$) were significantly different between group 1 and group 2. The reduction of every entity or no increment of GWI showed a 85% sensitivity and 55% specificity in predicting CAD. A GWE increase $>44\%$ had a 85% sensitivity and 68% specificity. The association of both

endoGLS increase >16% and GLS increase >18% showed a 73% sensitivity and 75% specificity in identifying significant CAD. The only evaluation of LV segmental kinesis had lower sensitivity and specificity (67% and 33%, respectively).

Conclusions. Myocardial strain and even more the non-invasive evaluation of MW, overcoming the subjective evaluation of LV segmental kinetics, lead to an improvement in the diagnostic accuracy of DSE in the identification of myocardial ischemia.



A382: RIGHT VENTRICULAR BASAL DIAMETER, BUT NOT VOLUME, CAN PREDICT SEVERE TRICUSPID REGURGITATION

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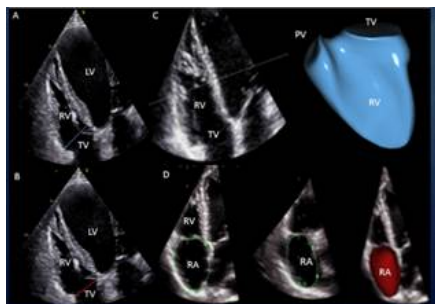
Background. According to current EACVI guidelines, right ventricle (RV), tricuspid annulus (TA) and right atrium (RA) dilatation are supportive signs to identify severe functional tricuspid regurgitation (TR) by echocardiography. However, the ranking by which those parameters should be considered to identify severe TR remains to be clarified.

Purpose. Accordingly, the aim of this study is to compare RV, RA and TA association with severe TR and to rank them in order of importance to predict severe TR.

Methods. 302 patients (59 ± 13 years, 54% women) with functional TR underwent two and three-dimensional echocardiography. Using the nonparametric Variable Importance (VIMP) software package, we assessed the relative importance of 6 different parameters (indexed by body surface area) to identify severe TR: 3D RV end diastolic volume (RVEDVi), 3D RV end systolic volume (RVESVi), 3D RA max volume (3DRAi), 2D RA systolic volume (2DRAi), 2D RV basal diameter (2DRVdi) and 2D TAI measured in the apical 4chamber view.

Results. According to EACVI multiparametric approach, 50/302 pts (17%) were found to have severe TR. 3DRAi (VIMP = 0.075) was the most important predictor of severe TR. 2DRVdi (VIMP = 0.005) was the second most important parameter and was the only parameter of RV dilation (RVEDVi = 0.0011 and RVESVi = 0.0012) associated with severe TR. Also, 2DRAi (VIMP = 0.023), and 2D TAI (VIMP = 0.004) showed good predictive ability.

Conclusions. Among the various right heart structures undergoing remodeling in patients with functional TR, RA dilation was the most important predictor of severe TR. Also the RV basal diameter, but not the volumes, was a predictor of severe TR. This underlines the importance of the shape, more than the volume of the RV as a predictor of severe TR.



A383: CARDIAC MAGNETIC RESONANCE IMAGING IN DIFFERENTIAL DIAGNOSIS OF CARDIAC MASSES

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Background. Differential diagnosis of cardiac masses represents a challenging diagnostic issue with important implications for therapeutic

management and patient's prognosis. Cardiac Magnetic Resonance (CMR) is a no-invasive imaging technique used to describe morphologic and functional features of masses. Integration of these information can lead to correct diagnosis near to histological certain.

Purpose. To evaluate the diagnostic role of CMR in defining the nature of cardiac masses.

Methods. One-hundred-fourteen patients with cardiac masses evaluated with CMR were enrolled. All masses had histological certain, obtained with biopsy and/or surgical samples or, in cases of cardiac thrombi, throughout radiological evidence of thrombus resolution after adequate anticoagulant treatment. CMR sequences allowed a qualitative morphologic description as well as tissue characterization. Evaluation of masses morphology included localization, size and borders assessment, detection of potential multiple lesions and pericardial effusion; tissue characterization resulted from an estimation of contrast enhancement-including early gadolinium enhancement (EGE), late gadolinium enhancement (LGE), sequences-and tissue homogeneity in T1 and T2 weighted acquisitions. The descriptive analysis was carried out by comparing benign vs malignant lesions as well as dividing patients into 4 subgroups: primitive benign tumours, primitive malignant tumours, metastatic tumours and pseudotumours.

Results. The descriptive analysis of the morphologic features showed that diameter >50mm, invasion of surrounding planes, irregular margins and presence of pericardial effusion were able to predict malignancy (p <0.001), as for tissue characteristics heterogeneous signal intensity, independently from T1 and T2 weighted acquisitions, and EGE were more common in malignant lesions (p <0.001). Two blinded expert radiologists were able to correctly diagnose malignancy with a kappa coefficient of 0.9. Subgroup analysis confirmed two-group analysis, but features described cannot discriminate among malignant tumor; instead hyperintensity signal and EGE is able to distinguish benign primitive lesions from pseudotumor (p=0.002). Moreover, left ventricle dilatation (p<0.01) and reduced ejection fraction (p=0.04) were associated to pseudotumors, due to presence in this group of thrombi which often underlie structural heart diseases. Furthermore, using CART analysis, we developed an algorithm to differentiate masses: invasion of surrounding planes identifies malignant tumors; if invasion is not present, we evaluate gadolinium enhancement: presence of contrast uptake is able to identify malignant lesions; in conclusion, in case of absence of invasion and contrast uptake, the last step of decision three includes reduced ejection fraction which increases probability of pseudotumors and reduce probability of primary benign tumor.

Conclusions. Cardiac magnetic resonance is a very useful diagnostic tool for differential diagnosis of cardiac masses in particular to discriminate among benign and malignant heart lesions, throughout morphologic and tissues features.

A384: LEFT VENTRICULAR TWIST PREDICTS PROGNOSIS IN CHILDREN WITH NON-COMPACTION CARDIOMYOPATHY

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Background. Left ventricular non-compaction cardiomyopathy (LVNC) is associated with poor clinical outcome in childhood, with heart failure, arrhythmias, and embolic events as main clinical manifestations. LV twist has recently been demonstrated having good predictive value in diagnosing LVNC in young patients. However, how LV twist may influence long-term clinical outcome of LVNC children and adolescents is still unknown. The aim of this study was to analyse a set of echocardiographic parameters to find imaging predictors of worse clinical outcomes in a long-term follow-up of LVNC children and young patients.

Methods. Children and adolescents, followed from May 2012 to June 2020, were enrolled in a retrospective study. All patients underwent 2-dimensional speckle tracking echocardiography and cardiovascular magnetic resonance imaging (1.5 Tesla) at our Institution's first evaluation. Death, heart failure hospitalization, aborted sudden cardiac death, ventricular arrhythmias (sustained and non-sustained ventricular tachycardia), and embolisms (i.e. stroke, peripheral arterial embolism and/or pulmonary thromboembolism) were registered and referred to as major adverse cardiovascular events (MACEs).

Results. Recruited for the study were 47 children (mean age: 11.1 ± 5; age range: 0–18 years). Twenty-three patients fulfilled the cardiovascular magnetic resonance imaging diagnostic criteria for LVNC (LVNC group), while the remaining 24 did not and were included in the LV hypertrabeculation group (LVHT).

They were followed for 4.9 ± 1.0 years, and MACEs were registered. Thirteen children (56% of LVNC, 28% of total) had at least one MACE. Global longitudinal, circumferential and radial strains (GLS, GCS, GRS), LV twist and LVEF resulted being significantly reduced in children with MACEs at follow-up. A multivariable analysis was performed by combining four parameters: LV ejection fraction, GLS, GCS, LV twist. These independent variables were chosen according to univariable

analyses and clinical relevance. The results from the analysis demonstrated that LV twist was the only independent predictor ($P = 0.033$, coeff. B 0.726) of worse clinical outcomes in young patients with LVNC.

Conclusions. LV twist is a promising tool to stratify and predict prognosis in LVNC young patients. Our findings show the importance of LV twist assessment to detect the severity of LVNC and to plan for early clinical intervention.

A385: ASSESSMENT OF INTRACARDIAC FLOW DYNAMICS FOR THE EVALUATION OF PATIENTS WITH AORTIC STENOSIS

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Background. Assessment of intracardiac flows and turbulence, has acquired rising significance in the past few years, due to the development and introduction of technologies for non-invasive cardiovascular imaging. Recent studies have shown that alterations in intracardiac fluid dynamics can be helpful to identify abnormalities in cardiac function. This study investigates the additional information provided by the quantitative assessment of intracardiac flow dynamics for the evaluation of patients with aortic stenosis (AS), by using an advanced echocardiography vortex-based approach.

Methods. Ten patients with severe AS (5 females) and 10 healthy sex- and BSA-matched controls (CTRL) (5 females) were prospectively included and underwent echocardiographic assessment of intracardiac flow dynamics. Echocardiographic measurements were performed on apical three chamber views recorded by means of MyLab™ X8 Platform. The HyperDoppler software adapted to an Esaote echo-scanner without contrast injection was used to assess intracardiac vortex properties. The endocardial border was manually contoured in one still frame and, then, automatically tracked during the whole cardiac cycle. The following parameters were obtained: vortex area (VA) (the ratio between the total vortex area and the left ventricular (LV) area); vortex length (VL) (the longitudinal length of the vortex relative to the total LV length); vortex depth (VD) (the distance of the vortex center from the LV base relative to the total LV long axis). Inter-rater variability was measured using intraclass correlation coefficients (ICCs) between two independent operators.

Results. Patients with severe AS (mean gradient: 50.1 ± 10 mmHg; aortic valve area: 0.7 ± 0.2 cm²; ejection fraction: $53 \pm 7\%$) had increased LV wall thickness ($p < 0.001$) and mass index ($p < 0.001$) compared with controls. Greater indexed left atrial volume ($p < 0.001$), E/e' ($p < 0.001$) and trans-cuspid gradient ($p < 0.001$) were also observed in the AS group. The assessment of VA, VL and VD was feasible in the whole population. Their calculation was reliable, as ICCs were very good for VA (0.878, $p = 0.033$), VL (0.960, $p = 0.004$) and VD (0.905, $p = 0.021$). Mean VA was significantly larger in patients with severe aortic stenosis compared with CTRL ($p = 0.031$). VL and VD ($p = 0.001$ and $p = 0.001$, respectively) were significantly higher in AS patients compared with CTRL.

Conclusions. The newly defined VA, VL and VD, quantitative indices of vortical flow, were significantly increased in the LV cavity of patients with severe AS compared to normal subjects. These indices, whose measurement was feasible and reliable, might provide complementary information to standard echocardiography, useful for the further diagnostic and prognostic characterization of the heterogeneous population of patients with severe AS.

A386: LEFT ATRIAL STRAIN PREDICTS PROGNOSIS IN PATIENTS WITH AORTIC STENOSIS AFTER TAVI

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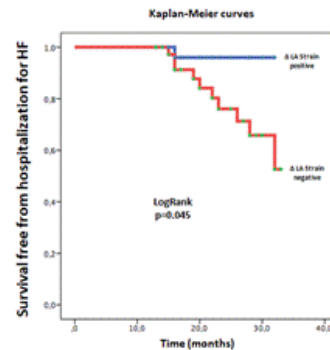
Background. Altered left atrial (LA) function is associated with a poor prognosis in a number of cardiovascular conditions. Our aim was to test the relationship between LA strain (LAS) and prognosis in patients with severe aortic stenosis (AS) undergoing TAVI.

Methods. We retrospectively collected 80 patients with severe AS (mean age 80.9 years) undergoing TAVI. LA volume was calculated by the area-length method in apical four- and two-chamber views before and 3 months after TAVI. LAS was measured using a dedicated software package before and three months after TAVI. The difference, or delta (Δ), between LAS after TAVI – LAS before TAVI (Δ LAS) was then calculated. The outcome selected for the study was a composite endpoint comprising hospitalization for heart failure and death from any cause.

Results. At baseline, LAS was significantly correlated with LV diastolic parameters, and PASP (all, $P < 0.05$). At a median follow-up of 21 months, 9 patients had events. LAS 3 months after TAVI and Δ LAS were

associated with events ($P < 0.05$) at Cox hazard analysis. The Kaplan-Meier survival curve (Figure 1) showed a significant difference of survival between patients with negative and positive Δ LAS ($P = 0.045$).

Conclusion. In patients with severe AS undergoing TAVI, left atrial strain after TAVI and Δ LAS are independently linked to events.



A387: EFFECTS OF IVABRADINE ON CORONARY FLOW RESERVE AND LEFT VENTRICULAR CONTRACTILE RESERVE IN PATIENTS WITH CORONARY MICROVASCULAR DISEASE

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Background. Coronary microvascular dysfunction (CMD) is a potential cause of myocardial ischemia and may affect myocardial function at rest and during stress. Transthoracic Doppler-derived coronary flow reserve (CFR), as an index of coronary arterial reactivity, can be impaired in both obstructive coronary artery disease (CAD) and CMD, and have demonstrated prognostic importance in these patients. Otherwise, left ventricular contractile reserve (LVCR), which assesses contractile reserve independently from preload and afterload changes, have demonstrated to be prognostically powerful in identifying patients at higher risk. The aim of our study was to assess the combined effect of ivabradine on CFR and LVCR in patients with CMD.

Methods. 158 patients (94 M, 64 F; mean age 66 ± 5 years) without obstructive CAD, assessed by invasive coronary angiogram, underwent Doppler-derived CFR. 41 of them (25 M, 16 F; mean age 62 ± 2 years), with CMD (defined as $CFR < 2$) were enrolled in the study. Coronary flow was assessed in the left anterior descending coronary artery (LAD) and was identified as the colour signal directed from the base to the apex of the left ventricle, containing the characteristic biphasic pulsed-Doppler flow signals. CFR were determined as the ratio of hyperaemic, induced by intravenous dipyridamole administration, to baseline diastolic coronary flow velocity. LVCR was defined as the stress/rest ratio of force, calculated as the ratio between systolic pressure and left ventricular end-systolic volume index. Patients were randomly assigned to ivabradine or placebo for one month (after up-titration phase). Doppler echocardiography, CFR and LVCR assessment were performed again at the end of treatment period.

Results. There were no significant differences in baseline characteristics between ivabradine and placebo group. Baseline CFR and LVCR were not significantly different in both groups. After treatment, in ivabradine group both CFR and LVCR significantly increased (2.78 ± 0.36 vs. 1.84 ± 0.12 - $p < 0.01$ and 1.34 ± 0.33 vs. 1.18 ± 0.24 - $p < 0.01$), while in placebo group they did not significantly change. There was a weak correlation between CFR and LVCR in study group.

Conclusions. In patients with CMD, ivabradine is able to improve both CFR and LVCR. Improvement of both parameters suggest a significant effect on the prognosis of these patients. Larger studies could confirm our data.

A388: MULTI-PARAMETRIC VS. INFERIOR VENA CAVA-BASED ESTIMATION OF RIGHT ATRIAL PRESSURE BY ECHOCARDIOGRAPHY

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(a) CARDIOVASCULAR DISEASE UNIT, IRCCS OSPEDALE POLICLINICO SAN MARTINO; (b) DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY OF GENOVA

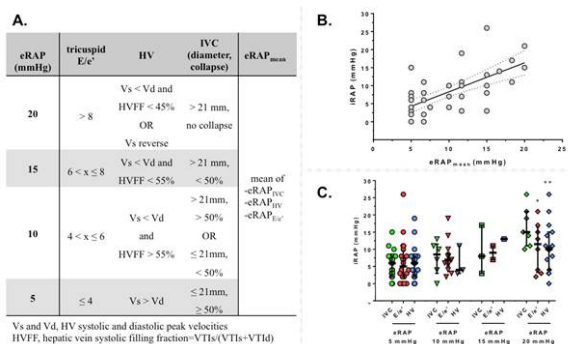
Aim. To evaluate an echocardiographic multiparametric approach for right atrial pressure (RAP) estimation in a general population undergoing right heart catheterization (RHC).

Methods. We prospectively enrolled patients undergoing RHC between September 2018 and January 2020. A trans-thoracic echocardiogram was

performed on the same day by cardiologists blinded to the haemodynamic results. RAP was estimated by evaluation of inferior vena cava (eRAP_{IVC}), hepatic vein pulsed wave Doppler spectra (eRAP_{HV}), tricuspid E/e' ratio (eRAP_{E/e'}) and by the mean of the aforementioned parameters (eRAP_{mean}), according to a pre-specified protocol (Figure panel A). The relationship between invasive RAP (iRAP), eRAP_{mean} and its components was analyzed by Spearman correlation or Wilcoxon signed-rank test. ROC area under the curves (AUC) were used to test eRAP thresholds against the same thresholds as obtained by RHC.

Results. 43 patients were included in the analysis (69 (58-75) year-old, 49% males). There was a positive correlation between eRAP_{mean} and iRAP (r=0.66, P<0.001, Figure panel B). There was also a trend for decreased concordance between eRAP_{IVC}, eRAP_{E/e'}, eRAP_{HV} and iRAP across 5- to 20-mmHg categories, and iRAP was significantly different from eRAP_{E/e'} and eRAP_{HV} for the 20-mmHg category (Figure panel C, * and ** are for P<0.05 and P<0.001 respectively). The area under the curve in predicting iRAP were non-significantly better for eRAP_{mean} than for eRAP_{IVC} at both 5-mmHg (0.64, 95% CI 0.49-0.80 vs. 0.70, 95% CI 0.53-0.87; Wald test P=0.41) and 10-mmHg (0.76, 95% CI 0.60-0.92 vs. 0.81, 95% CI 0.67-0.96; P=0.43) thresholds.

Conclusions. Our data suggest that multi-parametric eRAP_{mean} does not provide a clear-cut advantage over eRAP_{IVC}, despite being more complex and time-consuming.



A389: IL RUOLO DEL MYOCARDIAL WORK NELLA VALUTAZIONE DELLA MECCANICA CARDIACA NEL BLOCCO DI BRANCA SINISTRA

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Il blocco di branca sinistra (BBS) determina un'alterazione delle sequenze di attivazione del ventricolo sinistro (VS), con conseguenti alterazioni di meccanica, perfusione e funzione del VS. La valutazione non invasiva del lavoro cardiaco (myocardial work-MW), un nuovo indice che impiega l'ecocardiografia speckle tracking in combinazione con la stima non invasiva della pressione del VS, è in grado di offrire una valutazione quantitativa della meccanica VS. Abbiamo utilizzato questo nuovo indice per valutare la meccanica del VS per uno studio pilota "proof of concept" in pazienti con BBS, coronarie indenni e frazione d'iezione (FE) ridotta o conservata.

A parità di FE, nei pazienti con BBS si osserva una netta riduzione del lavoro cardiaco, inversamente proporzionale all'incremento del ritardo di conduzione interventricolare.

La misura non invasiva del lavoro cardiaco consente, rispetto ai convenzionali parametri ecocardiografici di funzione di pompa, di avere una valutazione più accurata della funzione VS.

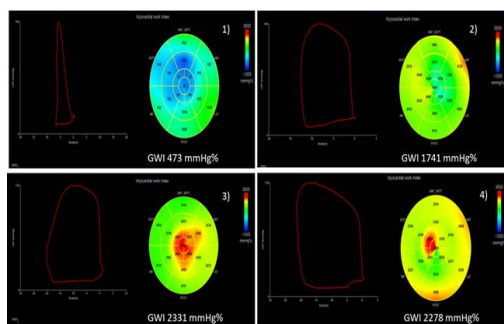


Figura 1. (1) Donna di 67 anni, BBS completo (170 msec), FE 35%, GLS -7%. (2) Uomo di 45 normale conduzione interventricolare. FE 35%, GLS -12%. (3) Uomo di 50 anni, BBS completo (120 msec), FE 60%, GLS -20%. (4) Uomo di 21 anni, normale conduzione intraventricolare, FE 60%, GLS -21%.

A390: CAMBIAMENTI DEI PARAMETRI ECOCARDIOGRAFICI NELL'ANORESSIA NERVOSA: UN ADATTAMENTO FISIOPATOLOGICO O UNA PATOLOGIA?

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Introduzione. L'anoressia nervosa (AN) è una delle forme più comuni di disturbi del comportamento alimentare e costituisce una patologia potenzialmente fatale con elevati tassi di morbilità e mortalità, in modo particolare nella fascia di popolazione compresa tra i 15 ed i 25 anni. Il coinvolgimento cardiaco si ha approssimativamente nell'80% dei pazienti con AN. Le complicanze cardiovascolari includono variazioni nella regolazione autonoma (incremento del tono vagale, bradicardia, ipotensione ortostatica, sincope), aritmie, insufficienza cardiaca e morte cardiaca improvvisa. Sono pochi gli studi che hanno descritto, in un contenuto numero di casi, una varietà di anomalie ecocardiografiche, tra cui la riduzione della massa cardiaca, il prolusso della valvola mitralica, il versamento pericardico e la riduzione delle dimensioni del ventricolo sinistro (VS). Nessuno di questi, però, ha analizzato un possibile cambiamento di questi parametri con le fluttuazioni del peso corporeo nei singoli individui.

Obiettivo. Descrivere i parametri ecocardiografici riscontrati in uomini e donne affetti da AN ed esaminare gli effetti dell'aumento di peso sulle variabili cliniche ed ecocardiografiche.

Metodi. Abbiamo condotto uno studio monocentrico retrospettivo in pazienti con diagnosi di AN (secondo i criteri del DSM-5). I dati clinici, di laboratorio ed ECG sono stati ottenuti analizzando le cartelle cliniche di ogni singolo paziente. I parametri ecocardiografici sono stati misurati off-line.

Risultati. La popolazione oggetto dello studio ha compreso 81 pazienti con età media di 24.5 ± 11.6 anni, il 92.6% donne. Il 75% presentava un grado severo di AN. Il BMI medio era 15.2 ± 2.1 kg/m², la frequenza cardiaca media 57.2 ± 12.7 battiti/minuto. Alcuni pazienti presentavano blocco di branca destra (il 7.4%) o intervallo QTc Lungo (14.8%). I pazienti con BMI al di sotto del valore medio hanno mostrato più frequentemente la presenza di versamento pericardico, una massa cardiaca minore, un inferior volume telediastolico del VS ed un minor spessore del setto interventricolare (p < 0.05 per tutti i parametri citati). Quando indicizzati per superficie corporea, tuttavia, la massa cardiaca ed i volumi ventricolari rientravano nel range di normalità nel 90% della popolazione. Sono state anche riscontrate alterazioni dell'apparato valvolare mitralico e bassi valori di globuli bianchi e piastrine. La presenza di versamento pericardico non è risultata correlata a parametri di laboratorio e quindi risulta difficilmente legata a processi infiammatori o deficit proteici.

In 39 pazienti è stato possibile analizzare l'esame ecocardiografico eseguito in corrispondenza dei valori di peso corporeo più alto e più basso registrati. Con l'aumento di peso è stato evidenziato un incremento dei valori di massa cardiaca, di spessore del setto interventricolare, di globuli bianchi e piastrine, ed una riduzione del versamento pericardico.

Conclusioni. Il nostro studio ha mostrato che i pazienti con AN hanno uno specifico pattern ecocardiografico che appare essere proporzionale alla superficie corporea suggerendo un meccanismo fisiopatologico di adattamento alla riduzione di substrato, ipotesi confermata dalla regressione di tale meccanismo con l'aumento del peso corporeo. È possibile, quindi, che il versamento pericardico riempia il vuoto lasciato dalla perdita di massa cardiaca.

A391: SEX, BODY SIZE, RIGHT ATRIAL AND RIGHT VENTRICULAR VOLUMES ARE THE MAIN DETERMINANTS OF TRICUSPID ANNULUS GEOMETRY IN HEALTHY VOLUNTEERS. A 3D ECHO STUDY USING A NOVEL, COMMERCIALLY-AVAILABLE DEDICATED SOFTWARE PACKAGE

Serena Vaghi (a), Diana Mihalcea (b), Andrada C. Guta (b), Sergio Caravita (a), Denisa Muraru (a), Luigi Badano (a), Gianfranco Parati (a)
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Background. Tricuspid annulus (TA) sizing is essential for planning percutaneous or surgical tricuspid procedures. By current guidelines, TA dimensions are assessed using 2D echocardiography (2DE). However, TA is a complex 3D structure.

Aim. To characterize TA geometry, dynamics and its physiological determinants using 3D echocardiography (3DE) and a novel dedicated software package in healthy volunteers.

Methods. 254 healthy volunteers (113 men; mean age 47±11 years) were enrolled and evaluated using both 2DE and 3DE. 3D TA analysis was feasible in 228 of them (feasibility=90%). 3D TA area, perimeter, diameters, sphericity index and coaptation were assessed at mid-systole, early-diastole and end-diastole using a dedicated software package (4D Auto TVQ, GE Healthcare, Horten, N). Right atrial (RA) and right ventricular (RV) volumes were measured using 3DE.

Results. 3D TA area, perimeter and diameters were largest and smallest

in end-diastole and mid-systole, respectively. Normal TA metrics in end-diastole were $9.6 \pm 2.1 \text{ cm}^2$ for area, $11.2 \pm 1.2 \text{ cm}$ for perimeter, $38 \pm 4 \text{ mm}$, $31 \pm 4 \text{ mm}$, $33 \pm 4 \text{ mm}$ and $34 \pm 5 \text{ mm}$ for major, minor, 4-ch and 2-ch diameters, respectively, and $81 \pm 11\%$ for sphericity index. All TA parameters assessed correlated with BSA ($r=0.42$ to $r=0.58$, $p<0.001$). Except for excursion and sphericity index, TA parameters were significantly larger in men than in women, independently of BSA ($p<0.0001$). Conversely, there were no age-related changes in TA parameters ($r<0.25$, $p<0.001$). 2D TA diameters measured in 4ch and RV focused views were significantly smaller than the corresponding 3D 4ch diameter ($29 \pm 5 \text{ mm}$ and $30 \pm 5 \text{ mm}$ vs $33 \pm 4 \text{ mm}$, respectively, $p<0.0001$). RA minimum volumes had the strongest correlation with 3D TA area ($r=0.74$, $p<0.0001$), compared with RV end-diastolic ($r=0.61$, $p<0.0001$) and end-systolic ($r=0.57$, $p<0.0001$) volumes. At multivariable linear regression analysis, RA minimum volume, RV end-diastolic volume, BSA and sex were independent predictors of 3D TA area ($R^2=0.56$, $p<0.0001$). **Conclusions.** During cardiac cycle TA changes in size, reaching minimum dimensions during mid-systole and largest dimensions during end-diastole. Reference values for TA metrics should be sex-specific and indexed to BSA. 2DE underestimates actual 3D TA dimensions. RA minimum volume, and not the maximum volume, together with RV end-diastolic volume, BSA and sex were the only independent predictors for TA size.

A392: VALORE DEL GLOBAL LONGITUDINAL STRAIN NELLA PREDIZIONE DI MALATTIA CORONARICA E DISFUNZIONE MIOCARDICA SEGMENTARIA

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Introduzione. Il global longitudinal strain sembra essere un parametro molto promettente nell'ambito della diagnostica non invasiva per la diagnosi precoce di malattia coronarica e della disfunzione miocardica segmentaria. Tuttavia ad oggi risulta ampiamente sottoutilizzato.

Metodi. Sono stati arruolati 127 pazienti candidati ad esecuzione di studio coronarografico per la presenza di sintomatologia suggestiva o per l'evidenza strumentale di ischemia miocardica ad una prova funzionale. I pazienti con pregressa storia di cardiopatia ischemica, patologie valvolari moderato-severe o cardiomiopatia sono stati esclusi dallo studio. Prima della coronarografia è stato eseguito un esame ecocardiografico standard includendo l'analisi del global longitudinal strain. I dati di strain "segmentario" sono stati ottenuti sommando i valori dei singoli segmenti facenti parte di un territorio di perfusione coronarica secondo le linee guida dell'American Heart Association.

Risultati. La coronarografia è stata eseguita in tutti i pazienti arruolati (127) portando al riscontro di 80 casi di cardiopatia ischemica e 47 di coronarie epicardiche indenni da stenosi significative. L'analisi statistica ha evidenziato la presenza di differenze tra i gruppi considerati in termini di GLS medio. I pazienti con malattia monovasale avevano un valore di GLS medio (GLS-AVG) minore rispetto ai pazienti con malattia trivasale; i pazienti con malattia trivasale mostravano valori di GLS-AVG maggiori rispetto ai pazienti con assenza di malattia coronarica. Il valore di GLS-AVG nei pazienti con malattia coronarica ha mostrato una differenza significativa tra il gruppo di pazienti con malattia monovasale rispetto al gruppo con malattia trivasale. È presente inoltre una moderata relazione tra la severità della stenosi dell'arteria circonflessa (%) e lo strain segmentario della parete laterale ($r=0.334$, $p<0.01$) e tra la severità della stenosi dell'arteria discendente anteriore e lo strain segmentario della parete anteriore ($r=0.357$, $p<0.01$). Inoltre, lo strain segmentario della parete laterale ha una relazione positiva con la stenosi dell'arteria circonflessa ($\chi^2(1) = 6.58$, $p=0.01$) mentre lo strain segmentario della parete anteriore risulta essere in relazione alla % di stenosi dell'arteria discendente anteriore, pur non raggiungendo la significatività statistica ($\chi^2(1) = 3.58$, $p=0.07$).

Conclusioni. Il global longitudinal strain è un parametro di diagnostica non invasiva di facile e rapida esecuzione che potrebbe permettere di individuare precocemente la presenza di malattia coronarica sia in termini di estensione che di alterazione della funzione contrattile segmentaria. Il suo utilizzo ha la possibilità di accrescere l'appropriatezza diagnostica degli esami invasivi e, conseguentemente, di migliorare la pianificazione della strategia terapeutica.

A393: DOES THE ASSESSMENT OF THE PROPORTIONALITY AND DISPROPORTIONALITY OF SECONDARY TRICUSPID REGURGITATION TO RIGHT VENTRICULAR DILATION IMPROVE THE PROGNOSTIC STRATIFICATION OF PATIENTS OVER THE CONVENTIONAL SEVERITY GRADING?

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Introduction. Proportionate or disproportionate severity of valvular regurgitation to ventricular dilation is a new concept firstly introduced to

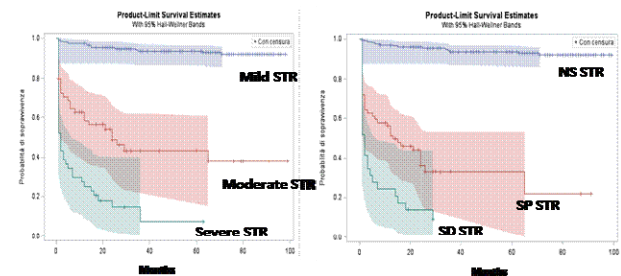
describe the functional impact of secondary mitral regurgitation. Theoretically, the same conceptual framework could be extended to secondary tricuspid regurgitation (STR) to stratify the prognosis of these patients.

Purpose. To evaluate the added prognostic value of classifying tricuspid regurgitation in proportionate/disproportionate STR compared to the classical grading in mild, moderate, or severe.

Methods. 294 patients with STR underwent 2D and 3D echocardiography and were followed for 48 (IQR=17-80) months. The end-point was a composite event of death ($n=32$) and hospitalization for right heart failure ($n=72$). Conventional grading of STR and measured regurgitant volume (mRegVol) were obtained as recommended by ESC/EACVI guidelines. Then, we assessed the proportionality of severe STR establishing a theoretical threshold of regurgitant volume (tRegVol) by defining severe STR as an STR with a regurgitant fraction $>50\%$. According to RV end-diastolic volume and ejection fraction, $t\text{RegVol} = 50\% \times \text{RVEF} \times \text{RVEDV}$. Then, for each patient we compared mRegVol with tRegVol to define STR as: Non severe (NS): mRegVol was significantly lower than tRegVol. Severe proportionate (SP): mRegVol was similar to tRegVol ($\pm 5 \text{ mL}$). Severe disproportionate (SD): mRegVol was significantly higher than tRegVol.

Results. Using the new classification, 8% of patients (16/196) with mild TR were reclassified as SP TR; 66.6% of patients (36/54) with moderate TR were reclassified as SP TR and 9% ($n=5$) as SD TR; 2% of patients (1/44) with severe TR, were reclassified as NS TR, 22% ($n=10$) as SP, and 75% ($n=33$) as SD. The Kaplan-Meier curves are shown in the Figure. The predictive power of both classifications was similar (C-statistics= 0.92, 95% CI 0.89-0.94 vs 0.91, 95% CI 0.88-0.93)

Conclusion. The new system reclassified 53/294 (18%) patients, but it did not significantly improve the prognostic power of the classical grading system in mild, moderate, severe.



IPERTENSIONE ARTERIOSA

A394: RISPOSTA PRESSORIA ESAGERATA AL TEST ERGOMETRICO NELLA POPOLAZIONE GENERALE: RISULTATI DEL REGISTRO MULTICENTRICO HYPERTEST

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Obiettivo. L'obiettivo di questo registro multicentrico è stato quello di valutare la risposta pressoria durante test ergometrico (TE) in un'ampia popolazione di soggetti che si sottoponevano al test per varie ragioni, indipendentemente dal fatto che fossero normotesi, ipertesi o cardiopatici. Abbiamo verificato la presenza di una risposta pressoria esagerata (RPE) all'esercizio fisico, sulla scorta delle indicazioni presenti in letteratura.

Metodi. Sono stati inclusi tutti i soggetti che effettuavano un TE per screening di cardiopatia ischemica e/o rivalutazione in follow-up, in un arco temporale di circa 12 mesi. Sono stati esclusi i test interrotti per esaurimento muscolare precoce, i pazienti con età <18 aa, e coloro con eventi aritmici potenzialmente pericolosi e/o eventi ischemici miocardici/cerebrali/periferici nei 3 mesi precedenti il TE. Tutti i soggetti hanno effettuato il test su tapis roulant o al cicloergometro utilizzando protocolli sovrapponibili nei vari centri, monitorando costantemente frequenza cardiaca, pressione arteriosa e traccia elettrocardiografica. Sulla scorta dei dati della letteratura, abbiamo definito RPE un incremento della PA sistolica $>60 \text{ mmHg}$ (M) o $>50 \text{ mmHg}$ (F) rispetto al valore basale pre-esercizio, ma anche un valore assoluto >210 o $>190 \text{ mmHg}$, rispettivamente nei due sessi.

Risultati. 454 soggetti di età media 60 ± 11 aa sono stati inseriti nel registro. Il TE è stato svolto al tapis roulant nel 61% di soggetti, ed è risultato massimale nel 70% dei casi. I soggetti con RPE sono stati 162 (36%) vs 292 che hanno avuto una normale risposta pressoria (gruppo controllo). Il gruppo RPE includeva circa il 70% di uomini, spesso in eccesso ponderale, con una prevalenza del 30% di diabetici vs 20% nel

gruppo controllo ($p < 0.01$). Una ipertensione arteriosa definita è stata osservata nella metà dei casi. La sospensione pre-esercizio della terapia beta-bloccante o calcio-antagonista non è risultata significativamente diversa tra i due gruppi. Così come sostanzialmente sovrapponibile è risultata la risposta miocardica ischemica indotta dall'esercizio nei due gruppi.

Conclusioni. I risultati di questo registro multicentrico, seppur retrospettivo, hanno evidenziato una RPE durante esercizio in oltre un terzo dei soggetti sottoposti a TE per varie ragioni, spesso per screening di cardiopatia ischemica. Una percentuale non irrilevante di individui era composta da maschi ipertesi già in trattamento, spesso in sovrappeso o diabetici. In linea con studi del passato, i nostri dati sottolineano la necessità di una maggiore attenzione al problema della RPE all'esercizio, il cui significato clinico ed impatto prognostico restano comunque da chiarire attraverso ampi studi osservazionali.

A395: ASSOCIATION BETWEEN ABNORMAL BLOOD PRESSURE RESPONSE TO EXERCISE AND INCIDENT CARDIOVASCULAR EVENTS

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Objective. The aim of this multicentre registry was to verify the association between an exaggerated blood pressure response (EBPR) to exercise stress test (EST) and evidence of previous myocardial and/or brain ischemic events in the general population.

Methods. All subjects who underwent EST for screening of ischemic heart disease and/or follow-up and re-evaluation of heart disease were included in the registry. Patients who discontinued EST due to early muscle exhaustion, younger individuals (<18 years), patients with potentially dangerous channelopathies or ventricular arrhythmias, as well as those with disabling chronic diseases or experiencing cardiovascular events in the 3 months prior to TE. Everyone performed EST on a treadmill or cycle ergometer using similar protocols in the various centres. Based on some study in the literature, we identified the EBPR to exercise for a systolic BP rise >60 mmHg (men) or >50 mmHg (women) compared to pre-exercise baseline measurement, but also an absolute value >210 or >190 mmHg, respectively. Retrospectively, we verified the presence of non-disabling ischemic cardiac and cerebrovascular events over the past 10 years.

Results. 503 subjects of mean age 61 ± 11 years were included in the registry. EST was performed on a treadmill in 65% of subjects and maximal workload was achieved by 75% of them. Subjects with EBPR were 170 (34%) vs 333 (66%) who had normal response (controls). EBPR group included most male subjects, often overweight and with a higher prevalence of diabetes (31% vs 20% in the control group, $p < 0.01$), and with already diagnosed arterial hypertension in a half of cases. Previous ischemic myocardial events were found in 35% of EBPR subjects vs 36% of controls ($p = NS$), while cerebrovascular disease in 20% vs 10%, respectively ($p < 0.005$).

Conclusions. Albeit retrospectively performed, this multicentre registry highlighted an association between EBPR to exercise (present in more than one third of the subjects examined, especially males) and history of cerebrovascular ischemic events within 10 years prior to enrolment. In line with previous studies, present data confirmed a clinical impact of EBPR on exercise. However, the precise pathophysiological mechanism(s) need to be clarified yet, also in terms of therapies against such exaggerated functional response and its possible prognostic impact over time.

A396: METABOLIC EFFECTS OF LOW-DOSE THIAZIDE DIURETIC IN HYPERTENSIVE PATIENTS

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Background. Thiazide diuretics still represent a first-line treatment for essential hypertension. The negative impact of high-dose thiazides on glucose tolerance has been documented. In this study we evaluated the impact of low-dose thiazides on glucose metabolism.

Methods. We analyzed clinical notes of hypertensive outpatients attending our clinic from 01/01/2014 to 14/02/2020. Patients who had low-dose thiazide therapy withdrawn and had measured glucose, HbA1c, insulin and HOMA index (HOMA-I) within 15 days and after six-months from thiazide discontinuation were recruited.

Results. Overall, 120 (mean age 70.77 ± 9.01 , 66 females) patients on hydrochlorothiazide (dose of 17.29 ± 7.77 mg) were recruited. Within the whole sample, 58 patients had normal fasting glucose and 62 patients had impaired fasting glucose. At 6 months after thiazide discontinuation,

glucose decreased by 4.6% ($p < 0.0001$), HbA1c by 3.3% ($p = 0.0475$), insulin by 16.7% ($p < 0.0001$) and HOMA-I by 22.6% ($p < 0.0001$). The improvement was more evident in patients with impaired fasting glucose, where glucose declined by 6.5% ($p < 0.0001$), insulin by 21.6% ($p < 0.0001$) and HOMA-I by 26.8% ($p < 0.0001$).

Conclusion. Discontinuation of low-dose thiazides improves insulin sensitivity in hypertensive patients. Considering that insulin resistance represents an established major independent cardiovascular risk factor, agents such as thiazide diuretics yielding glucose metabolism abnormalities should be a primary concern for cardiovascular specialists, especially in patients with impaired fasting glucose.

A397: SERUM URIC ACID, BLOOD PRESSURE AND GLICO-METABOLIC FACTORS IN A POPULATION OF ADOLESCENTS. THE MACISTE STUDY

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Introduction. Hyperuricemia in adolescents is a predictor for the development of hypertension. Moreover, hyperuricemia treatment seems to associate with a reduction of blood pressure values. It is unknown whether the relationship between hyperuricemia and blood pressure is mediated to concurrent glyco-metabolic alterations that could affect serum uric acid levels and blood pressure levels.

Materials and methods. 414 adolescents (241 males, 173 females), between 14 and 20 years of age (average age 17 ± 1 years old), attending the school "Liceo Scientifico R. Donatelli" in Terni, underwent a complete hemodynamic and glyco-metabolic assessment. BP and BMI were transformed in percentiles by age, height and sex by following CDC charts. A diagnosis of hypertension was made in subjects whose BP was ≥ 1.96 standard deviation, corresponding to 95th percentile, in accordance with the "Second National Task Force on High Blood Pressure in Children and Adolescents" nomograms. The glomerular filtration rate (eGFR) was calculated by using the Schwartz Formula. The HOMA Index was calculated as follows: ((serum glucose/18)+ plasma insulin)/22.5. Metabolic syndrome was diagnosed by using the IDF criteria for adolescents.

Results. 15% of adolescents had hypertension. Only 2 subjects met the IDF criteria for metabolic syndrome. Serum uric acid levels were linearly and continuously related to systolic blood pressure ($R = 0.41$; $p < 0.01$) and diastolic blood pressure ($R = 0.16$; $p < 0.01$). In the group of subjects with hypertension the average serum uric acid level was 6.1 mg/dL, whereas in the group of adolescents with normal blood pressure the average serum uric acid level was 5.5 mg/dL ($p = 0.02$). The relationship between serum uric acid and systolic blood pressure was statistically significant in males, but not in females, whereas there were no significant differences between the two sexes regarding the relationship between serum uric acid and diastolic BP. At the multivariate analysis, the relationship between serum uric acid and blood pressure was not affected by BMI Z-Score, sex, eGFR, HDL-cholesterol, age and other common factors that could affect serum uric acid levels, such as glycemia, triglycerides, HOMA Index and waist-to-height ratio that resulted not significant in the model.

Conclusions. In healthy adolescents, serum uric acid levels showed a linear and continuous relationship with systolic and diastolic BP. The association between SBP and serum uric acid was stronger in males and appeared to be unrelated to clinical and laboratory biomarkers of altered metabolic status. Prospective studies are needed to confirm this association and to evaluate the hypotensive effect of serum uric acid-lowering treatments.

MALATTIE DEI VASI

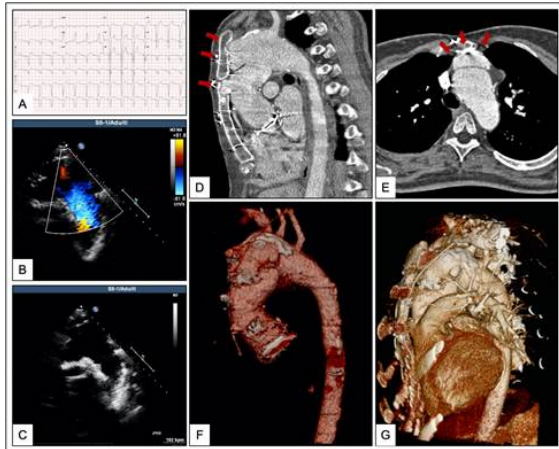
A398: UNEVENTFUL PSEUDOANEURYSM OF THE ASCENDING AORTA WITH STERNAL EROSION IN PREGNANCY

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A 36-year-old woman at 31 weeks' gestation presented with exertional dyspnea and palpitations. She had a history of bicuspid aortic valve treated with surgical aortic valvotomy for severe stenosis, followed by ascending aorta replacement for type A acute aortic dissection and Bentall operation with a mechanical valve for severe aortic regurgitation. Eight years after the last surgery, magnetic resonance angiography showed aortic arch aneurysm (49 mm) with a small intimal flap. Thereafter, the patient was lost to follow-up until the current admission. She was hemodynamically stable on presentation and physical

examination was unremarkable apart from a mechanical second heart sound. The electrocardiogram showed sinus rhythm with left bundle branch block (Panel A). Transthoracic echocardiography revealed severe left ventricular dilation (EDV 90 ml/m²) with mild dysfunction (EF 50%), normal prosthetic aortic valve function, and aortic arch dilation (50 mm) (Panel B and C). After a multidisciplinary evaluation, elective cesarean section was performed at 34 weeks' gestation. A post-delivery aortic computed tomography angiography revealed aortic arch aneurysm (52 mm) with intimal flap and two pseudoaneurysms of the anterior aortic wall causing sternal erosion (Panel D, E, F and G). Subsequently, the patient underwent ascending aorta and aortic arch replacement by Frozen Elephant Trunk technique with a 24 x130 mm prosthesis between the aortic root and the descending aorta. The postoperative course was uneventful, and the patient was discharged to a cardiac rehabilitation center.



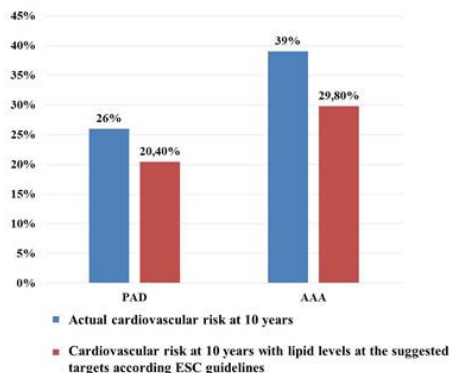
A399: REAL WORLD LIPID MANAGEMENT OF PATIENTS WITH PERIPHERAL ARTERY DISEASE AND ABDOMINAL AORTIC ANEURYSM: AN UNMET CARDIOVASCULAR NEED? RESULTS FROM AN OBSERVATIONAL STUDY

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Background. It is well established that patients with peripheral artery disease (PAD) as well abdominal aortic aneurysm (AAA) are at increased risk for cardiovascular mortality. Previous studies have shown a strong association between PAD and AAA in aging patients, thus further increasing the global cardiovascular risk. Despite this higher risk, PAD and AAA population are suboptimally treated. This study assesses the cardiovascular profiles of PAD and AAA patients quantifying the survival benefits of target-based risk factor modification.

Methods. Patients with PAD and AAA admitted to the Vascular Unit at Monaldi Hospital from 2016 to 2019 were retrospectively analyzed. Biochemical and cardiovascular profile as well as the ongoing medical therapy was assessed. Benefits of risk factor control were estimated using the SMART-REACH model.

Results. A total of 669 patients (mean age 72±9; 21% women) were included. Of these, 190 showed AAA (28.4%) and 479 PAD (71.6%) at any stage. Hypertension was the main risk factor in both, PAD (87%) and AAA (89%); ischemic heart disease was similarly detected in PAD (26%) and AAA (27%). Hypertensive therapy was uniformly distributed in both groups. Only 54% of PAD and 41% of AAA patients were on lipid-lowering



drugs with suboptimal levels for most. A better control of all modifiable cardiovascular risk factors based on current ESC guidelines (LDL-cholesterol <70 mg/dl, systolic BP <140mmHg, smoking cessation, antiplatelet therapy) would offer an absolute risk reduction of the 10-year cardiovascular risk by 5.3% in PAD e 9.2% in AAA.

Conclusion. The biochemical profile of PAD and AAA patients was far from guideline-based targets and medical management was suboptimal. A stronger surveillance of modifiable risk factors and maintenance of biochemical guidelines-based profile would confer additional significant benefits.

A400: ATHEROSCLEROTIC DISEASE OF CORONARY ARTERIES, LEFT CAROTID AND SUBCLAVIAN ARTERIES: THREE SIDES OF THE SAME MEDAL CALLED AORTA?

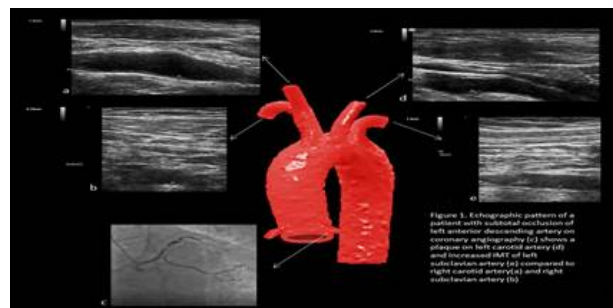
Nertila Kola (a), Gaetana Ferro (a), Agnese Bevilacqua (a), Claudia Vicidomini (a), Lorenzo Iuliano (a), Luigi Tedesco (a)
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Background. The subtle correlation between Carotid Atherosclerosis (CA), Carotid Plaque (CP) and Coronary Artery Disease (CAD) is widely known and the exact mechanism at the base of this relationship is a remarkable object of investigation for the important perspective of obtaining information about the coronary status through an easy-employable tool. With our study we aimed to explore the correlation between the side of carotid plaque and presence of CAD and if, accordingly to the different anatomy of the left and right vessels originating from aorta, a common finding could be detected also in the subclavian arteries.

Methods. We enrolled 180 patients which undergone carotid ultrasound with evidence of carotid plaque. 120 patients (Group A) had one or more cardiovascular risk factors and performed the exam with preventive aim since they resulted as symptoms free and had a negative provocative stress test. 60 patients performed the exam during the hospitalization for Acute Coronary Syndrome (ACS) (Group B). Then we performed a subclavian artery ultrasound in Group B to assess the intima-media thickness (IMT).

Results. In Group A 20 patients had bilateral carotid plaque (17%), 80 patients had right side plaque, mostly calcific, 20 patients had left side plaque, mostly calcific (67% versus 16%). Degree of stenosis did not significantly differ. In Group B 15 patients presented bilateral carotid plaque (25%), 35 presented left side plaque mostly fibrotic, and 10 patients had right sided plaque mostly calcific (58,3% versus 16,7%). Moreover in Group B patients with right carotid plaque, mean left subclavian artery IMT was 0,6 mm ± 0,2 mm and did not significantly differ from mean right subclavian artery IMT (0,7 mm ± 0,2 mm). In patients with left carotid plaque, mean left subclavian artery IMT was interestingly increased (1,4 mm ± 0,3 mm) compared to right subclavian artery (0,7mm ± 0,2 mm).

Conclusions. Our data suggest a correlation between left CP side and composition, and CAD. Moreover the evidence of an increased thickness of left subclavian artery in population with ACS and left CP suggests a common mechanism at the base of the atherogenic process. These mechanisms are still unknown but the anatomical origin of the left epiaortic vessels and coronary arteries, which arise directly from the aorta, may play a key role. Recent studies, indeed, reported the evidence that a low shear stress, as in the aorta, may be linked to an increased atherogenesis.



A401: REFRACTORY VASOSPASTIC ANGINA AS AN EPIPHENOMENON OF FIBROMUSCULAR DYSPLASIA: A CASE REPORT

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The case is about a 49-year-old woman admitted to the emergency department of our institution due to severe and worsening episodes of typical chest pain. She had no cardiovascular risk factors, except for previous smoking habits. Despite the young age, she had a complex past medical history. She experienced two transient ischemic attacks (TIA) at the

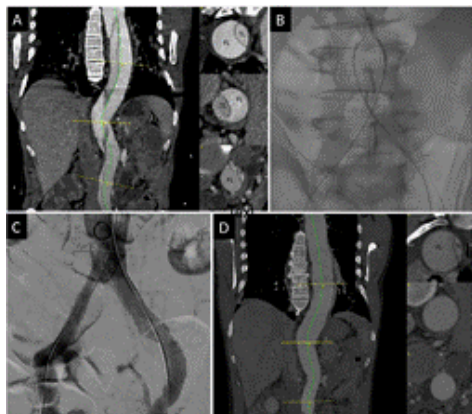
age of thirty, characterized by slurred speech and weakness of both arms. In 2015 she was admitted to her hometown hospital for chest pain, with both negative electrocardiogram (ECG), coronary angiography (CA) and a clinical presentation suggestive for vasospastic angina. Moreover she was hospitalized for epileptic seizure in 2017. Chronic medical therapy included acetylsalicylic acid, statins, beta-blockers and oral nitrates. The patient also assumed of sublingual nitrate twice a month, for episodic anginal pain. At the admission, the blood tests showed a slight elevation of troponin T (peak 156 ng/L) and the echocardiogram revealed a focal hypokinesis of the anterior distal septal region of the left ventricle with a slightly depressed ejection fraction (LVEF 50%). During the examination, the patient complained of an intense episode of chest pain associated with profuse sweating and nausea. The ECG showed a concomitant significant ST elevation in the anterior precordial leads, which led to an urgent CA showing severe spasm of the proximal left anterior descending (LAD) coronary artery, resolved after intracoronary nitrates infusion. Distally, the LAD artery presented with a tortuous path. Intravascular ultrasound virtual histology (IVUS/VH) was performed confirming the absence of dissections or vulnerable atherosclerotic plaque. On top, it was detected a hypo-echogenic plaque compatible with pathological fibrous intimal thickening (800 µm) at VH analysis, and a plaque burden of 42%. Despite aggressive medical therapy with calcium channel blockers (CCB; verapamil 360 mg/daily) and nitrate infusion, the patient presented daily episodes of angina with ST-elevation. The addition of a second CCB (Amlodipine) led to complete resolution of the symptoms and the contractility impairment in a few days. The woman had no family history of vasculopathy, thrombophilia, autoimmune panel tests and total body positron emission tomography were negative. Finally, the patient underwent computed tomography angiography (CTA) of the carotid artery that revealed patent internal carotid arteries with a bilateral "mouse tail" aspect consistent with a diagnosis of fibromuscular dysplasia (FMD). The patient was then safely discharged and reported no recurrence of angina at the five-months clinical follow-up. In conclusion, our case suggests that refractory vasospasm represents a potential coronary involvement of FMD. Moreover, in this setting should be encouraged a global evaluation of several vascular districts. With regard of the coronary involvement, the use of intravascular imaging may play an important role in the study of coronary vasospasm and in the decision-making process. In the present case, the IVUS evaluation ruled-out the presence of significant atherosclerotic plaque, preventing the operator from performing PCI which may have led to subsequent local complications and worsening of the coronary spasm, due to an impairment of vasomotion. Interestingly also vessel's elasticity alterations due to FMD alone have been reported to adversely affect the lesion's response to balloon dilatation and stenting.

A402: THE GROWING ROLE OF TRANSCATHETER ELECTROSURGERY: PERIPHERAL PROCEDURES

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A 54-year-old male presented with progressing Stanford Type B aortic dissection and gradual reduction of true lumen perfusion and symptomatic right kidney and celiac trunk hypoperfusion.

After careful CT scan evaluation (Figure 1A), bilateral femoral artery access to both true and false lumen was achieved through echographic and angiographic guidance. A 0.018" wire mounted on a vertebral 4 Fr catheter crossed the flap just proximally to renal arteries and was snared from contralateral access. Prolonged inflations of large balloons failed to consistently restore flow between lumens; therefore, guidewire was exchanged with a 0.014" coronary wire (300 cm BHW, Abbott, USA) with a "Flying V" configuration. Wire isolation was achieved with 4 Fr catheters, and tissue vaporization throughout the dissection was attained by delivering radiofrequency via an electric scalpel set to pure cut at 70W while gently pulling both catheters (Figure 1B). Optimal flap laceration and



splanchnic blood flow were obtained and subsequent iliac stenting (Epic, Boston Scientific, USA) was performed in order to "seal" the flap and to optimize blood flow below the aortic carrefour (Figure 1C). Hypoperfusion symptoms resolved in the following hours, while follow-up CT scan (Figure 1D) showed good result of the fenestration and of subsequent iliac stenting. At 6 months follow-up, patient was clinically stable and Doppler examination confirmed good perfusion of renal and visceral arteries as well as patency of ilio-femoral axes.

Intimal flap puncture and serial balloon dilation has a reported technical success of 90%. While alternative procedures utilizing drilling devices and stents have been described, transcatheter fenestration for Type B aortic dissection represents another field of application of guidewire-mediated tissue laceration in the panorama of radiofrequency-mediated transcatheter electrosurgery.

A403: ISOLATED EXERCISE-INDUCED PULMONARY HYPERTENSION ASSOCIATES WITH HIGHER CARDIOVASCULAR RISK IN SCLERODERMA PATIENTS

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Background and aim. Isolated exercise-induced pulmonary hypertension (ExPH) associates with cardiovascular (CV) events in patients with left heart disease. We investigated its prognostic significance in scleroderma patients at risk for pulmonary arterial hypertension (PAH).

Methods. In 26 consecutive scleroderma female patients with either low (n=13) or intermediate probability (n=13) of PH at rest, we evaluated – at time 0 and 1 year – prognostic determinants of CV risk: onset or progression of heart failure/syncope; worsening of functional class; functional performance at the 6-Minute Walking Test and at cardiopulmonary exercise test; right atrial area; and pericardial effusion. We assigned a severity score 1-3 to each prognostic determinant, derived an overall CV risk score, and its 0-1 year change. Isolated ExPH at CPET was defined as absence of PH at rest, reduced peak VO₂, VE/VCO₂ >30 at anaerobic threshold, reduced O₂ pulse, and DVO₂/DW <9 mL/min/W. We then correlated ExPH at time 0 with clinical worsening (risk score increase >20% after 1 year).

Results. ExPH was strongly associated with clinical worsening compared to patients without ExPH (p=0.005). In patients without ExPH, none had >20% increased CV risk score after 1 year. Conversely, about 50% of patients with ExPH had such increase, suggesting a worsening of prognosis.

Conclusions. Isolated ExPH associates with higher cardiovascular risk and thus clinical worsening in scleroderma patients. The assessment of ExPH by CPET can thus contribute to a better risk stratification and the planning of a more adequate follow-up.

A404: ANEURISMI NON CORONARICI NEI PAZIENTI CON VASCULITE DI KAWASAKI: CARATTERISTICHE CLINICHE E CHIRURGICHE. REVISIONE DEI CASI IN LETTERATURA

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Introduzione. La sindrome di Kawasaki è la patologia cardiaca acquisita più frequente in età pediatrica nelle nazioni sviluppate, con incidenza di 5–10 per 100.000. Alla fase acuta, caratterizzata da febbre, esantema, linfadenopatia, edema degli arti e congiuntivite, può seguire la formazione di aneurismi coronarici (la complicità si manifesta fino al 30% dei casi). Anche se meno frequentemente, il circolo periferico arterioso può essere coinvolto dalla formazione di lesioni aneurismatiche.

Obiettivi e Metodi. Abbiamo effettuato una revisione della letteratura, nello specifico dei casi clinici pubblicati su PubMed in lingua inglese utilizzando come parole chiave " non-coronary OR peripheral vascular aneurysms AND Kawasaki disease", allo scopo di meglio definire caratteristiche cliniche e chirurgiche della patologia aneurismatica non coronarica nei pazienti affetti da vasculite di Kawasaki.

Risultati. Sono stati inclusi nella revisione 24 casi clinici (20 pazienti di sesso maschile, 4 di sesso femminile). L'età media alla diagnosi di sindrome di Kawasaki è risultata pari a 0.3 anni, mentre quella alla diagnosi di patologia aneurismatica coronarica è stata di 0.8 anni. L'età media alla diagnosi di patologia aneurismatica delle arterie periferiche non coronariche è risultata essere più tardiva, pari a 3.3 anni. La presenza di una massa pulsante è stata descritta come manifestazione clinica più frequente nei pazienti con aneurismi del circolo periferico (29.2%), seguita da infarto del miocardio, shock cardiogeno, dolore addominale e claudicatio periferica. Sono stati segnalati altresì casi di lesioni asintomatiche. Gli aneurismi sono stati diagnosticati in diversi distretti del circolo periferico, quali quello iliaco (33.3%), aorta (20.8%), le arterie brachiali(20.8%), ma anche il circolo viscerale e le arterie degli arti. Il 70.8% dei pazienti ha presentato un coinvolgimento multi-distrettuale. Un approccio chirurgico tradizionale mediante rivascolarizzazione open è

stato proposto ed eseguito nel 58.3% dei casi, nell'8.3% è stata eseguita rivascularizzazione endovascolare, mentre un trattamento farmacologico e conservativo è stato indicato nel 33.3% dei pazienti. La mortalità totale nella casistica è stata del 21.1%, quella relativa ai pazienti sottoposti a chirurgia tradizionale del 9.1%, mentre è stata 0% nei pazienti trattati con approccio endovascolare e del 50% nei pazienti con gestione conservativa.

Conclusioni. Gli aneurismi del circolo periferico si possono manifestare nei pazienti con vasculite di Kawasaki, sia alla diagnosi che dopo anni dalla stessa. Le lesioni possono essere asintomatiche. La giovane età alla diagnosi, la presenza di un processo vasculitico a eziologia della formazione delle lesioni aneurismatiche, l'associata patologia cardiaca nonché l'assenza di linee guida rendono la gestione chirurgica e il follow-up di questi pazienti particolarmente difficile e suggeriscono la necessità di ulteriori studi che approfondiscano la tematica dal punto di vista fisiopatologico e gestionale medico/chirurgico, al fine di migliorare la prognosi di questa specifica categoria di pazienti.

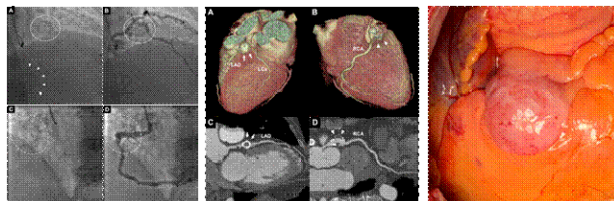
A405: MULTIMODALITY IMAGING FOR DEFINITION AND TREATMENT SELECTION OF MULTIPLE CORONARY ANEURYSMS

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Case report. A 59-year-old woman, smoker, hypertensive, without previous history of CAD referred several episodes of epigastric pain unrelated to physical activity. After exercise ECG and considering the risk profile, coronary angiography was indicated. It revealed extensive coronary calcification, with a nodular calcific structure adjacent to the proximal, sub-occluded, left anterior descending (LAD) and a calcified aneurysm of the right coronary artery (RCA), partially filled with thrombus, causing sub-critical stenosis. Coronary-CT showed aneurysmal saccular dilatation of the proximal LAD (15x13x13 mm) entirely thrombosed with sub-occlusion; and a fusiform aneurysm in the proximal RCA (25x22x24mm), partially thrombosed, with stenosis at the distal portion. The patient was referred for surgical treatment to receive arterial graft with left internal mammary artery to LAD.

Discussion. In our case, congenital aetiology of the aneurysms was unlikely, since the patient did not present congenital heart disease or known genetically inherited disorders. Among acquired aneurysms, the most common cause is represented by atherosclerosis. Other potential causes are Connective tissue disorders, trauma, infections, iatrogenic and Kawasaki syndrome. The latter represents, with atherosclerosis, the most likely causes of aneurysmal disease in our patient. Multiple CAAs, mural calcification and luminal thrombosis are typical of both Kawasaki disease and atherosclerosis. Evidence of coronary stenosis and atherosclerotic plaque (even in other vessels) is an additional helpful finding for atheroaneurysmal disease. Usual complications include myocardial ischemia and infarction, embolism, rupture, fistulization and thrombosis (clearly represented in our case). Current recommendations about management strategies of CAAs are focused on small case series and based on aneurysm's location and morphology, patient's characteristics, and clinical presentation. Medical treatment strategies include antiplatelet therapy, or anticoagulant (in selected Kawasaki patients with large or rapidly expanding CAA). Other therapeutical options are PCI and CABG. The decision to intervene on CAA in patients without acute coronary syndrome is rather complex, due to the lack of supportive data; also in the context of acute myocardial infarction PCI is associated with lower procedural success due to the high frequency of no-reflow and embolization phenomena. In our case the heart team opted for surgical treatment due to the subocclusion of the proximal LAD and considering stable angina as admitting diagnosis, instead of acute coronary syndrome. Moreover the CAAs were placed in proximal segments, with large amount of thrombus, so related with high risk for complications if PCI was performed.

Conclusion. CAAs represent a challenge for both interventional cardiologist and cardiac surgeon. A thorough multidisciplinary diagnostic classification, by means of Multimodality Imaging techniques is crucial to select the correct strategy of management and to ensure the best procedural and long-term result, avoiding unnecessary high-risk procedures.



MALATTIE DEL MIOCARDIO E DEL PERICARDIO

A406: DEEP LEARNING TO DIAGNOSE CARDIAC AMYLOIDOSIS FROM CARDIAC MAGNETIC RESONANCE FINDINGS

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Background. Cardiac magnetic resonance (CMR) is part of the diagnostic work-up for cardiac amyloidosis (CA). Deep learning (DL) is an application of artificial intelligence that may allow to automatically analyze CMR findings and establish the likelihood of CA.

Methods. 1.5 T CMR was performed in 187 subjects with suspected CA (n=92, 49% with unexplained left ventricular – LV – hypertrophy; n=95, 51% with blood dyscrasia and suspected light-chain amyloidosis). Patients were randomly assigned to the training (n=121, 65%), validation (n=28, 15%), and testing subgroups (n=38, 20%). Short axis (SA), 2-chamber (2C), 4-chamber (4C) late gadolinium enhancement (LGE) images were evaluated by 3 networks (DL algorithms). The tags "amyloidosis present" or "absent" were attributed when the average probability of CA from the 3 networks was $\geq 50\%$ or $< 50\%$, respectively. The DL strategy was compared to a machine learning (ML) algorithm considering all manually extracted features (LV volumes, mass and function, LGE pattern, early blood-pool darkening, pericardial and pleural effusion, etc.), to reproduce exam reading by an experienced operator.

Results. The DL strategy displayed good diagnostic accuracy (84%), with an area under the curve (AUC) of 0.96. The precision (positive predictive value), recall score (sensitivity), and F1 score (a measure of test accuracy) were 78%, 94%, and 86% respectively. A ML algorithm considering all CMR features had a similar diagnostic yield to DL strategy (AUC 0.93 vs. 0.96; p=0.45).

Conclusions. A DL approach evaluating LGE acquisitions displayed a similar diagnostic performance for CA to a ML-based approach, which simulates CMR reading by experienced operators.

A407: ASSESSING EXTRACELLULAR VOLUME IN CARDIAC AMYLOIDOSIS BY LEFT VENTRICULAR BIOPSY: HISTOLOGICAL CHARACTERIZATION AND CLINICAL-PATHOLOGICAL CORRELATES

Angela Pucci (a), Alberto Aimo (a), Veronica Musetti (b), Andrea Barison (b), Silvia Masotti (b), Concetta Prontera (b), Michele Coceani (b), Cataldo Palmieri (b), Giampaolo Merlini (d), Chiara Arzilli (a), Claudio Rapezzi (c), Claudio Passino (b), Michele Emdin (b)
(a) UNIVERSITÀ DI PISA; (b) FTGM; (c) UNIVERSITÀ DI FERRARA E MARIA CECILIA HOSPITAL; (d) UNIVERSITÀ DI PAVIA

Background. Findings from endomyocardial biopsy (EMB) could help explain pathophysiological mechanisms as well as many clinical and imaging findings in patients with cardiac amyloidosis (CA), but this possible application of EMB has been basically overlooked so far.

Methods. All patients with LV EMB-proven diagnosis of amyloid light-chain or transthyretin (AL/ATTR) CA between 2014 to 2020 observed in our referral center were retrospectively identified.

Results. Patients (n=37) were more often men (92%), with a median age of 72 years (68-81). By immunohistochemistry, lambda+ AL was found in 14/19 AL (74%) and kappa+ in 5/19 AL cases. TTR was detected in the remaining 18 cases. Amyloid deposits accounted for 15% (interquartile interval 10-30%) of tissue sample area, and fibrosis for another 15% (10-23%), without significant differences between AL and ATTR. The combined extent of amyloid and fibrosis displayed a closer correlation with extracellular volume (ECV) at cardiovascular magnetic resonance than amyloid alone (r=0.661, p=0.001, vs. 0.566, p=0.009, respectively). The combined extent of amyloid and fibrosis also correlated with high-sensitivity troponin T (hs-TnT) and N-terminal fraction of pro-B-type natriuretic peptide (NT-proBNP), which in turn predicted death for HF progression independently from age and etiologic diagnosis: hs-TnT, hazard ratio (HR) 2.23, 95% confidence interval 1.18-4.23, p=0.014; NT-proBNP, HR 1.71 (1.03-2.82), p=0.037.

Conclusions. This first systematic analysis of LV EMBs in CA show that extracellular spaces are expanded by fibrosis, and not just amyloid deposits, and that this combination can better explain myocardial tissue characterization at CMR, and circulating levels of biomarkers of cardiac damage.

A408: SAFETY AND EFFICACY OF LEVOSIMENDAN IN PATIENTS WITH CARDIAC AMYLOIDOSIS

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(a) FTGM; (b) UNIVERSITÀ DI PISA; (c) UNIVERSITÀ DI FERRARA E MARIA CECILIA HOSPITAL

Background. The safety and efficacy of levosimendan in patients with worsening chronic heart failure (HF) related to cardiac amyloidosis (CA) have never been specifically evaluated.

Methods. Data of all patients with CA receiving levosimendan infusion (0.1 mcg/kg/min) at a tertiary referral center for CA were retrieved.

Results. The 25 patients (60% men, age 74 years [68-80]) had either amyloid light-chain (AL) (72%), or transthyretin (ATTR) amyloidosis (28%). Left ventricular ejection fraction (LVEF) at admission was 46% (33-52); 9 patients (38%) had LVEF <40%. Systolic and diastolic arterial pressures were 110 mmHg (100-115) and 70 mmHg (60-75), respectively, and serum potassium was 3.9 mEq/L (3.7-4.5). Two patients died during index hospitalization (8%). Among discharged patients (n=23), the median change in N-terminal fraction of pro-B-type natriuretic peptide (NT-proBNP) from admission to discharge was -3.73% (-31.84/+14.73), with no significant differences between patients with AL vs. ATTR amyloidosis (p=0.056), or those with LVEF <40% vs. ≥40% (p=0.503). Six patients (26%) died for HF progression over a 5.7-month follow-up (1.4-11.1). Nine patients (39%) underwent at least one hospitalization for worsening HF after a median of 1.8 months (1.1-5.4). Among them, 7 (78%) required at least another inotropic infusion. Follow-up duration was significantly longer in patients with any decrease in NT-proBNP during index hospitalization (8.9 months [4.1-11.7] vs. 1.4 [0.1-8.6], p=0.045).

Conclusions. In patients with CA and worsening chronic HF requiring inotropic support, levosimendan therapy is safe and well tolerated. Nonetheless, levosimendan seems to have a limited impact on in-hospital and post-discharge outcome.

A409: INCIDENTAL DIAGNOSIS OF AN EXCEPTIONAL CONDITION: "SAW-TOOTH" CARDIOMYOPATHY

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A 46-year-old man with an unremarkable clinical history was admitted to the Emergency Department because of fever and sharp chest pain exacerbated by lying down or breathing deeply, lasting for 3 days. The electrocardiogram (ECG) showed sinus tachycardia (heart rate 105 b.p.m.) with concave 1-mm ST-segment elevation in V5 and V6 leads. The patient had increased white blood cell count ($14 \times 10^9/\text{mL}$, reference value [r.v.] $<10 \times 10^9$) and C-reactive protein (15 ng/L, r.v. <5) and slightly raised high-sensitivity troponin T (40 ng/L, r.v. <14). On transthoracic echocardiogram (TTE), increased left ventricular (LV) wall thickness (14 mm in the interventricular septum [ISV] and 13 mm in the posterior wall), normal LV volumes and systolic function (LV ejection fraction 55%), no significant wall motion abnormalities, and no pericardial effusion were found. The TTE also raised the suspicion of an area of non-compaction in the mid-cavity portion of the interventricular septum (IVS). The patient then underwent a cardiac magnetic resonance (CMR) showing increased T2 signal in the pericardial layers surrounding the basal portions of the inferior and lateral LV walls, suggesting localized pericarditis, but no regions of increased T2 signal within the myocardium, suggestive of myocardial edema. Thick myocardial protrusions were visualized in the anterior and inferior portions of the mid-cavity IVS, and a myocardial crypt in the distal portion of the IVS. Normal LV volumes (LV end-diastolic volume index 74 ml/m², r.v. 61-106), LV mass index (69 g/m², r.v. 53-94), and right ventricular volumes and function were also found. The patient was therefore diagnosed with pericarditis and "saw-tooth" cardiomyopathy. Whole blood sampling to search for gene mutations associated with LV non compaction (LVNC) or hypertrophic cardiomyopathy (HCM), and possibly next generation sequencing, was performed; at the time of writing, results are still pending. The only living relative was a 42-year-old brother, who did not show any LV morphological or functional abnormalities at TTE. The patient was discharged on standard therapy for pericarditis with colchicine and ibuprofen. ECG Holter monitoring and a 6-month follow-up CMR were scheduled.

Only five cases of "saw-tooth" cardiomyopathy have been reported worldwide so far. Differently from LVNC, which is characterized by fine trabeculations, deep intertrabecular recesses communicating with the LV cavity, and a thin and compacted epicardial layer, "saw-tooth" cardiomyopathy is primarily characterized by a well-developed compact layer with several well-defined protrusions into the LV cavity, a pattern that reminds to a localized form of HCM. Further studies are needed to clarify the genetic bases of "saw-tooth" cardiomyopathy, as well as its clinical manifestations and prognosis.

A410: HIGH SERUM D-DIMER LEVELS AND DISEASE SEVERITY IN PATIENTS WITH TAKOTSUBO SYNDROME

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Background. Takotsubo syndrome (TTS) was initially described as an acute reversible left ventricular (LV) dysfunction associated with emotional trigger and good prognosis. However, several clinical conditions and physical stresses have recently been reported to favor episodes of TTS. Although all episodes of TTS are characterized by similar phenotypes of

LV dysfunction, different pathophysiological aspects seem to be involved, each of them probably associated with different prognoses. Besides myocardial stunning and endothelial dysfunction, a pro-inflammatory status represents a critical point in TTS patients. D-dimer, a specific metabolite of cross-linked fibrin, has recently been proposed as a prognostic tool in critical patients for its connection to proinflammatory and coagulation state. The aim of our study was to evaluate whether high D-dimer levels at admission were related to disease severity and worse outcomes in TTS patients.

Methods. We retrospectively analysed clinical, laboratory, echocardiographic and angiographic characteristics of 25 consecutive cases of TTS admitted to our department from January 2016 to August 2020. Elevated circulating D-dimer level (defined as >550 µg/l) were correlated with characteristics of patients and in-hospital major adverse cardiac events (MACE, defined as the composite of acute pulmonary oedema, cardiogenic shock, ventricular tachycardia, ventricular fibrillation, cardiac arrest and death).

Results. All patients were women, with a mean age of 64.8 ± 13.8 years. 36.0% had hypertension and 20% diabetes. High D-Dimer level was detected in 13 patients (52%, Group A), while 12 patients (Group B) had normal levels of D-Dimer. Similar age, history of classic cardiovascular risk factors, angiographic findings, c-reactive protein, and hs-cardiac troponin serum levels were similar between two groups. Patients with normal D-Dimer levels were more frequently associated with an emotional trigger (58,3% vs 18,2%, p=0.04) and less frequently with reduced ejection fraction (EF ≤40%; 33,3% vs 84,6%, p=0,01). High D-Dimer levels were significantly associated with a higher incidence of MACE during hospitalization (84,6% in Group A vs 33,3% in Group B, p=0.015).

Conclusions. In TTS patients, elevated circulating D-Dimer levels are associated with a reduced ejection fraction (EF ≤40%) at admission and a higher incidence of MACE during hospitalization. Additionally, patients with high D-Dimer levels less often reported an emotional trigger associated with the event. These results support the hypothesis that different pathophysiological mechanisms may be implicated in different triggered LV dysfunction in TTS, leading to different prognosis. Larger studies are needed but early D-dimer detection could represent an early and useful prognostic tool and a guide for targeted therapy in TTS patients, indicating those patients with a high risk of complications.

A411: DIAGNOSTIC AND PROGNOSTIC ROLE OF INVASIVE AND NON-INVASIVE HEMODYNAMIC PARAMETERS IN AMYLOIDOTIC CARDIOMYOPATHY

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MATER STUDIURUM BOLOGNA; (b) POLICLINICO S. ORSOLA-MALPIGHI

BOLOGNA, UO MEDICINA NUCLEARE, ALMA MATER STUDIURUM BOLOGNA;

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NEUROLOGICA RETE METROPOLITANA NEUROMET, BOLOGNA

Background. In cardiac amyloidosis (CA) several echocardiographic

indicators of systolic and diastolic function have been reported to carry a

prognostic role. However, few studies have provided a full instrumental

evaluation of CA including invasive measurements derived from right

heart catheterization.

Objectives. We aimed to assess the hemodynamic profile and outcome

of patients at the time of first evaluation, according to etiology (light-chain

(AL), hereditary transthyretin-related (h-ATTR) and non-mutant

transthyretin-related (wt-ATTR)), to NYHA class (I-II vs III-IV) and to left

ventricular ejection fraction (LVEF ≥50% vs <50%).

Methods. We analyzed 224 patients diagnosed with AC (93 AL, 66 h-

ATTR, 65 wt-ATTR) at our Centre between 1990-2019. The whole cohort

underwent to a comprehensive cardiologic evaluation including central

hemodynamic, echo, ECG, laboratory, clinical and follow-up data.

Results. According to etiology, wt-ATTR patients were mostly elderly

male (94%; median age at diagnosis 77 years) with highest values of

septum wall thickness (18 mm) and a more frequent evidence of atrial

fibrillation (40%) and pacemaker rhythm (14%). In AL, lower systemic

blood pressures, higher heart rate and low QRS voltages (56%) were

reported. Considering all instrumental indicators of systolic function and

the hemodynamic parameters derived from right heart catheterization,

there were no significant differences among the etiologies except for a

slightly lower cardiac index (2,2 L/min/m²) in wt-ATTR. Seventy-five (35%)

and eighty-four (37.5%) patients presented at first evaluation advanced

HF defined as NYHA III-IV and LVEF <50%, respectively. During a

median follow-up of 28 months, 138 (61%) of 224 patients had died. Of

these, 56 (41%) were AL amyloidosis, 39 (28%) m-ATTR and 43 (31%)

wt-ATTR. Interestingly, in a multivariate analysis of the overall population,

only pulmonary wedge pressure and invasive cardiac index were

independently associated with mortality, along with age, AL etiology,

NYHA class and heart rate. Lastly, in patients with class NYHA I-II at

baseline, reduced eGFR and mean pulmonary pressure were

independently associated with hospitalization for heart failure.

Conclusions. In the pathophysiological restrictive model of CA, the

description of invasive hemodynamic profile plays a central role in predicting the natural history of the disease. Reduced cardiac index, pulmonary wedge pressure and mean pulmonary artery pressure are the best predictors of mortality even in comparison with the most important echocardiographic indicators of biventricular systolic and diastolic function.

A412: POTENTIAL CLINICAL ROLE OF ATRIAL UPTAKE ON 99mTc-DPD BONE SCINTIGRAPHY IN PATIENTS WITH CARDIAC AMYLOIDOSIS

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Introduction. 99mTc-DPD scintigraphy is one of the most important diagnostic tools in cardiac amyloidosis (CA). Although bone tracer's ventricular uptake is a typical but non-exclusive expression of transthyretin-related CA, currently there is a lack of knowledge about the clinical and prognostic meaning of atrial uptake (AU) in CA.

Methods. We retrospectively analysed 60 patients with suspected or confirmed CA and cardiac uptake at bone scintigraphy (Bologna score ≥ 1) from 2016 and 2020. All planar and SPECT/CT images (when available) were examined by two experienced different nuclear physicians; diffuse atrial and left ventricular uptake data were collected. Interobserver agreement (IA) analysis was performed (Cohen's κ). Correlation between AU and atrial tachyarrhythmia was evaluated with Pearson's chi square.

Results. Fifty-three patients (88%) were male and seven (22%) were female. Mean age was 77 ± 9.9 years. Twenty-nine (48%) patients had sinus rhythm, while the remaining had different types of atrial rhythm disorders (i.e. permanent and paroxysmal atrial fibrillation 30% and 16.7%, respectively). Mean left antero-posterior atrial diameter was 46 ± 6.3 mm. Twenty-seven patients (45%) had no definite diagnosis about CA etiology, 32 patients (55%) had ATTR and 1 patient had AL amyloidosis. An overall left ventricular cardiac uptake of the tracer at the bone scintigraphy was seen in 60/60 by each two observers, with IA between mild versus moderate/severe uptake of 0.90 ($p < 0.0001$). Atrial uptake was evident in planar images in 36/60 and 42/60 respectively by each two physicians, with an IA of 0.49 ($p < 0.0001$). SPECT/CT was performed in 17/60 pts; AU was observed in 14/17 and 15/17 pts respectively, IA=0.77 ($p = 0.001$). There was no significant correlation between AU and current presence or history of atrial tachyarrhythmias, nor with left atrial enlargement.

Conclusion. Standard planar images of bone scintigraphy are a validated approach for detection and differentiation of CA. Our analysis evidenced limitations of this technique in identifying atrial involvement that can be at least mitigated by adoption of SPECT/CT scan. The association of AU with atrial enlargement and/or arrhythmias was not evidenced by our analysis but larger prospective studies (possibly involving SPET/CT scan) may help to better understand the real meaning of atrial uptake, which still remains uncertain.

A413: SEX-RELATED DIFFERENCES IN CARDIAC WILD-TYPE TRANSTHYRETIN AMYLOIDOSIS

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Background. Cardiac wild-type transthyretin (ATTRwt) amyloidosis is largely more prevalent in males than in females. The reason for this imbalance is not known yet, and there is currently poor data on the differences in clinical presentation of ATTRwt in men vs. women.

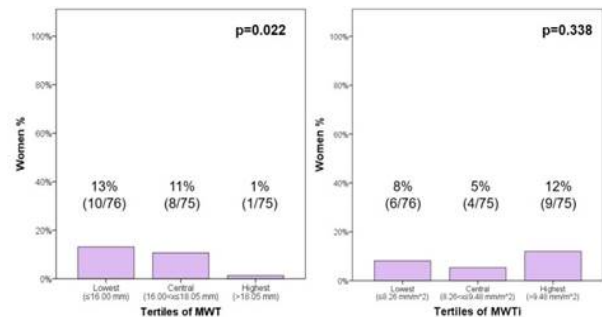
Purpose. We aimed to assess the sex-related differences in terms of clinical, biochemical and echocardiographic parameters in cardiac ATTRwt.

Methods. We analysed 226 patients with cardiac ATTRwt from two tertiary Centers in Italy (n=62) and United Kingdom (n=164). At time of diagnosis, patients underwent a full baseline characterization including N-terminal fraction of pro-B-type natriuretic peptide (NT-proBNP) and high-sensitivity troponin T (hs-TnT) testing as well as a transthoracic echocardiogram.

Results. Female to male ratio was 1:11 (19/207). Mean age at diagnosis was 79 ± 6 years in men and 84 ± 5 in women ($p = 0.070$). There was no

significant difference between females and males in circulating levels of NT-proBNP (2766 [interquartile interval 1871-4237] vs. 2824 [1514-5859] ng/L, $p = 0.776$) and hs-TnT (51.8 [32.8-59.3] vs. 59.0 [39.0-81.0] ng/L, $p = 0.173$). Left ventricular (LV) ejection fraction was also similar in the two groups (53 ± 11 vs. $50 \pm 12\%$, $p = 0.205$). Women had worse diastolic function compared to men (E/e' 20 ± 6 vs. 15 ± 7 , $p = 0.001$), less LV pseudohypertrophy (mean wall thickness - MWT: 15.9 ± 2.2 vs. 17.2 ± 2.5 mm, $p = 0.034$; interventricular septal thickness: 16 ± 3 vs. 18 ± 3 mm, $p = 0.079$; posterior wall thickness: 15 ± 2 vs. 17 ± 3 mm; $p = 0.026$; LV mass: 303 ± 80 vs. 386 ± 97 g, $p = 0.004$) and smaller LV end-diastolic diameter (42 ± 4 vs. 46 ± 7 mm, $p = 0.006$). Differences in LV geometry were not confirmed after indexing for body surface area. Accordingly, female prevalence was significantly lower in patients with higher MWT, while no significant difference in female-to-male ratio emerged within tertiles of indexed MWT (Figure).

Conclusions. Women with ATTRwt present at an older age and with a lower degree of pseudohypertrophy compared to men. Clinical suspicion based on echocardiographic findings should be raised in the presence of smaller wall thickness in women vs. men.



A414: CAUSE DI MORTE CARDIACA IMPROVVISA NEI GIOVANI: REVISIONE SISTEMATICA DELLA LETTERATURA E METANALISI

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Introduzione. L'eziologia della morte cardiaca improvvisa (MCI) nei giovani adulti è ancora molto dibattuta. L'obiettivo della nostra metanalisi è quello di identificare le più frequenti cause di MCI in soggetti di età ≤ 35 anni e valutare eventuali differenze tra atleti e non atleti e tra Europa e Stati Uniti.

Metodi. Sono stati inclusi nella ricerca tutti gli studi che valutavano le cause di MCI nei giovani adulti (≤ 35 anni) pubblicati tra il 01/01/1990 e il 01/31/2020. Tutti i soggetti sono stati divisi in due gruppi: atleti e non atleti. Gli studi che non separavano i dati tra atleti e non atleti sono stati esclusi dall'analisi.

Risultati. Alla fine della nostra ricerca, 34 studi soddisfacevano tutti i criteri d'inclusione e la popolazione totale analizzata era di 5,060 vittime per MCI (2,890 atleti e 2,170 non atleti). Le cause di MCI più frequenti negli atleti erano il cuore strutturalmente normale, la cardiomiopatia ipertrofica (CMI), l'ipertrofia ventricolare idiopatica e l'origine anomala delle arterie coronarie; mentre nei non atleti prevalevano la malattia ischemica cardiaca, la cardiomiopatia aritmogena del ventricolo destro (CMA) e le canalopatie. La cicatrice non ischemica del ventricolo sinistro era più frequente negli atleti rispetto ai non atleti (5.1% vs. 1.1, $p = 0.01$); mentre la cardiomiopatia ischemica (19.6% vs. 9.1%, $p = 0.009$), la CMA (11.5% vs. 4.7%) e le canalopatie (8.4% vs. 1.9%, $p = 0.02$) erano le più frequenti nei non atleti. La CMI ($p = 0.01$) e l'origine anomala delle coronarie ($p = 0.004$) erano le cause di MCI più frequenti negli Stati Uniti, la CMA ($p = 0.001$), il cuore strutturalmente normale ($p = 0.02$), e le canalopatie ($p = 0.02$) in Europa.

Conclusioni. La MCI si può verificare sia negli atleti che nei non atleti, seppure con alcune differenze eziologiche tra i due gruppi. Tali differenze si riscontrano anche tra Stati Uniti ed Europa.

A415: PLEUROPERICARDITIS: A RARE MANIFESTATION OF POLYMYALGIA RHEUMATICA

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Acute pericarditis is an inflammatory pericardial syndrome with or without pericardial effusion. Etiology includes infectious causes like viruses (the

most frequent cause in developed countries) and bacteria and non-infectious causes, such as autoimmune, neoplastic and metabolic diseases, drug-related, post-cardiac injury syndrome and other disorders. Recurrences occur in about 30% of patients within 18 months. Acute pericarditis associated with myocardial infarction (MI) include epistemic pericarditis, that typically develops 1-3 days after MI, and Dressler pericarditis, whose onset is typically 1-2 weeks after MI. Clinically, pericarditis can be isolated or as a part of systemic diseases like lupus, rheumatoid arthritis, amyloidosis and polymyalgia rheumatica (PMR). Diagnosis of acute pericarditis requires at least 2 out of 4 criteria including pericardial rub, chest pain, typical ECG modifications and pericardial effusion at transthoracic echocardiogram (TTE). Treatment is based on anti-inflammatory drugs like aspirin, NSAIDs, colchicine or corticosteroids. We report a very rare case of acute pleuropericardial syndrome as manifestation of PMR after a MI.

We present the case of a 74-year-old male, with recent history of anterior STEMI treated with PPCI on LAD and staged PCI on RCA, that presented to our ER 15 days after the MI, referring chest pain exacerbated by deep breathing, fever and asthenia. Physical examination was unremarkable except for friction rubs on auscultation. The patient medications included DAPT (ticagrelor and cardioaspirin), statin, beta-blocker and ACE-inhibitor drugs. ECG showed sinus rhythm with widespread ST elevation. Blood exams documented Hb 14.2 g/dL, WBC 12,000/mL, CRP 282 mg/L, Troponin I hs 427 ng/L, CK 36 U/L. Chest TC scan showed bilateral pleural effusion and pericardial effusion (max 7 mm). TTE documented EF 40%, IVS akinesia and pericardial effusion (max 8 mm). Post-MI pericarditis was suspected. Therapy with aspirin (750 mg daily) plus Colchicine (0.5 mg twice daily) was started, with no clinical improvement after a week. During an interview, the patient's wife revealed that he was affected by PMR, treated in the past with steroids and sulfasalazine, without any clinical manifestations since 10 years. The patient reported that he was in maintenance therapy with low-dose sulfasalazine, that he autonomously suspended after the MI. After a rheumatologist consultation, we introduced sulfasalazine and low-dose prednisone therapy and in a few days we observed a rapid decrease of CRP levels, with resolution of clinical symptoms and reduction of the pericardial effusion. The patient was discharged in good and stable clinical conditions.

PMR is an idiopathic systemic inflammatory disease. There are not specific diagnostic tests available to make a certain diagnosis. In clinical practice PMR diagnosis is based on its clinical manifestations (adults over 50 years old, especially women, with rapid onset of pain and stiffness in proximal muscles, often with fever and malaise; it may be associated with giant cell arteritis), associated with increased values of CRP and ESR with normal CK and rapid response to low-dose glucocorticoids. PMR is rarely associated with serositis like pericarditis and pleuritis. Only 4 cases of pleuropericardial syndrome in patients with PMR have been previously described in literature, of these 3 were women. Physicians should be aware that PMR is a rare cause of pleuropericardial effusion, especially in the elderly, so it has to be considered in the differential diagnosis.

A416: PROGNOSTIC SIGNIFICANCE OF CARDIAC AMYLOIDOSIS IN PATIENTS WITH AORTIC STENOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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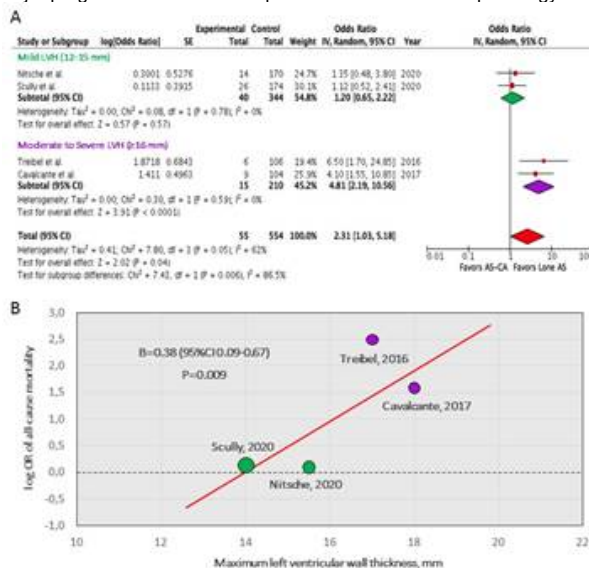
Objectives. We performed a systematic review and meta-analysis to clarify whether concurrent cardiac amyloidosis (CA) portends excess mortality in elderly patients with aortic stenosis (AS).

Background. CA has been increasingly recognized in elderly patients with AS, but with uncertain prognostic significance.

Methods. Our systematic review of the literature published between January 2000 and April 2020, sought observational studies reporting summary-level outcome data of all-cause mortality in AS patients with or without concurrent CA. Pooled estimate of Mantel-Haenszel odds ratio (OR) and 95% confidence intervals (CIs) for all-cause death was assessed as the primary endpoint. We performed subgroup analysis stratified by severity of left ventricular hypertrophy (LVH) and study-level meta-regression analysis to explore the effect of covariates on summary effect size and to address statistical heterogeneity.

Results. We identified 4 studies including 609 AS patients (9% AS-CA; 69% men; age, 84±5 years). The average follow-up was 20±5 months. Compared with lone AS, AS-CA was associated with 2-fold increase in all-cause mortality (pooled OR: 2.30; 95% CI: 1.02-5.18; I² = 62%). When analysed according to LVH severity, pooled ORs (95% CI) for all-cause mortality were 1.20 (0.65-2.22) for mild LVH (<16 mm), and 4.81 (2.19-10.56) for moderate/severe LVH (≥16 mm). Meta-regression analysis confirmed a stronger relationship proportional to the degree of LVH, regardless of age and aortic valve replacement, explaining between-study heterogeneity variance.

Conclusions. Cardiac amyloidosis heralds significantly higher risk of all-cause death in elderly patients with AS. Severity of LVH appears to be a major prognostic determinant in patients with dual AS-CA pathology.



A417: DILATAZIONE E NON COMPATTAZIONE VENTRICOLARE SINISTRA: EFFETTO YO-YO

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Introduzione. Il miocardio non compatto (MNC) è una rara cardiomiopatia congenita secondaria ad arresto intrauterino della normale embriogenesi miocardica, che si caratterizza per le profonde trabecolature del ventricolo sinistro (VS) e i profondi recessi intertrabecolari comunicanti con la camera ventricolare. La dilatazione ventricolare sinistra, indipendentemente dalla causa che la determina, può però accompagnarsi ad un aspetto da non compattezza che è irregolare con la normalizzazione delle dimensioni ventricolari

Caso clinico. Un uomo di 54 anni si ricoverava per dispnea ingravescente di recente insorgenza e segni obiettivi di scompenso cardiaco. Un ecocardiogramma transtoracico evidenziava un VS dilatato (DTD 63 mm) con contrattilità globale ridotta (FE 30%) e trabecolature, in base alle caratteristiche delle quali (rapporto tra strato compatto e strato non compatto in telesistole pari a 2,3, continuità di velocità di flusso tra recessi e cavità ventricolare al color doppler), veniva posto il sospetto di MNC. Veniva inoltre rilevata stenosi aortica di moderata entità, difetto interventricolare perimembranoso restrittivo di scarso rilievo emodinamico e fistola aorto-ventricolare dx con shunt significativo sin-dx (Fig. 1). La diagnosi di MNC era confermata da un ecocardiogramma transesofageo e da una RMN cardiaca. Il paziente veniva sottoposto a intervento di sostituzione valvolare aortica con valvola meccanica, a sutura diretta del difetto del setto interventricolare e a chiusura della fistola aorto-ventricolare destra. Per il riscontro di tachicardia ventricolare sostenuta veniva impiantato defibrillatore. Un ecocardiogramma eseguito dopo 2 anni mostrava normalizzazione delle dimensioni VS e della contrattilità; le trabecole erano diventate meno evidenti e non soddisfacevano più i criteri diagnostici di non compattezza (Fig. 2). Dopo 6 anni il paziente si ricoverava nuovamente per scompenso cardiaco. L'attività elettrica ventricolare era costantemente indotta da pacemaker e l'ecocardiogramma documentava nuovamente FE 35% con dilatazione e ipertrabecolazione del VS (Fig. 3). Tali reperti ricadevano dopo 6 mesi dall'upgrading del defibrillatore a biventricolare (Fig. 4)

Conclusioni. L'ipertrabecolazione può essere direttamente correlata all'indice di sfericità ventricolare sin e le trabecole, che possono divenire manifeste quando il ventricolo modifica la sua geometria e aumenta la sua sfericità, possono tornare a essere meno evidenti o scomparire in caso di rimodellamento inverso. Il caso presentato è, a nostra conoscenza, il primo in cui viene descritta una reiterata

comparsa/scomparsa della trabecolazione in funzione della dilatazione/normalizzazione delle dimensioni del VS, qui definita "effetto yo-yo".

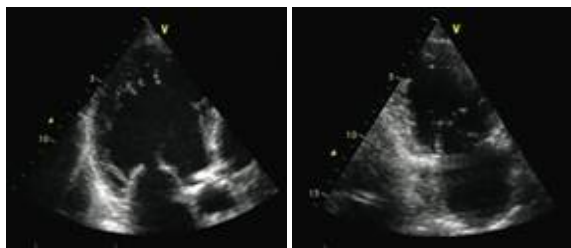


Figura 1

Figura 2

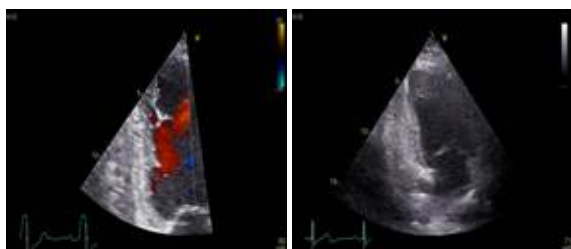


Figura 3

Figura 4

A418: PREVALENCE AND PREDICTIVE VALUE OF CARDIAC BONE TRACER UPTAKE IN PATIENTS UNDERGOING BONE SCINTIGRAPHY FOR ALL CLINICAL INDICATIONS

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Background. Bone scintigraphy (BS) is a nuclear medicine imaging technique, with various clinical applications, ranging from the diagnosis of primary bone diseases (cancer, fractures, inflammation) and staging of different tumors like breast and prostate. In the last decade, BS has assumed also a cardiological application, since it has a central role in the diagnosis of transthyretin (TTR) cardiac amyloidosis (CA). Prevalence and predictive value of cardiac bone tracer uptake in patients undergoing BS for different clinical indications is to date unknown.

Methods. We reviewed all BS scans performed in our nuclear medicine institution in the last 11 years (January 2009-January 2020). Prevalence and predictive role of short- (1 year) and long-term (5-year) mortality of cardiac bone tracer uptake was evaluated.

Results. Among the 9647 BS scans performed, 101 (1.0%) (86% males, mean age 77 years old) showed uptake of bone tracer in the cardiac region. Perugini Score was 1 in n=45 (45%), 2 in n=30 (30%) and 3 in n=26 (26%). Of them, 34 (31%) received appropriate TTR-CA diagnosis and cardiological care for TTR-CA, 7/34 (20%) before 2017. Patients with TTR-CA diagnosis were more frequently on treatment with anticoagulants (66% vs 27%, p<0.001), diuretics (75% vs 43%, p=0.004) and aldosterone-blocking agents (44% vs 12%, p=0.001), compared with patients without appropriate diagnosis. No patients received TTR-targeted therapy. After a 1-year follow-up after BS, we recorded 13 deaths (13%), which raised to 69 (68%) after 5 years. No differences in mortality were found among patients with appropriate TTR-CA diagnosis and care compared with those without (1-year Log Rank p=0.071, 5-year Log Rank p=0.132). By multivariable analysis, age (OR 1.06, 95% CI 1.00-1.13, p=0.037) and Perugini score ≥ 2 (OR 2.63, 95% CI 1.27-5.46, p=0.009) remained independent predictors of long-term mortality.

Conclusions. In patients undergoing BS for different clinical indications, cardiac bone tracer uptake suggestive of TTR-CA is a rare finding. Despite differences in therapy (not TTR-targeted), appropriate diagnosis of TTR-CA do not improve survival. Age and higher cardiac uptake intensity are independent predictors of long-term mortality.

A419: KEARNS-SAYRE SYNDROME: A CASE REPORT

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Introduction. Kearns-Sayre syndrome (KSS) is a rare mitochondrial cytopathy first described in 1958. KSS has been included in a group of

mitochondrial DNA (mtDNA) deletion syndromes and is characterized by the presence of progressive external ophthalmoplegia (PEO), pigmentary retinopathy, and onset age younger than 20 years. Although the diagnosis of KSS is based on clinical criteria, confirmation with muscle biopsy and genetic testing is now routine. Cardiac involvement is variable and reported in approximately 50% of cases and may include dilated cardiomyopathy, conduction defects, QT-prolongation and ventricular arrhythmias. The most frequent ECG abnormality is atrial fibrillation with or without left or right BBB which can progress to high-grade AV block.

Case presentation. A 39-year-old Caucasian woman, was admitted in 2017 to our "Cardiomyopathies Ambulatory". The patient presented eyelid ptosis and complained muscle hypotonia and pain, with history of KSS diagnosed at 25 years old, by muscle biopsy and genetic test in other Institution. Hemodynamic parameters and physical examination were not remarkable. The electrocardiogram (ECG) showed sinus rhythm with left bundle branch block (LBBB), atrium-ventricular block type I and ventricular extrasystole. Echocardiography revealed borderline ejection fraction (55%), absence of areas of regional wall motion abnormalities at rest and intraventricular dyssynchrony related to LBBB. Pre and post contrast tissue characterization by cardiac magnetic resonance (CMR) revealed images of focal, patchy delayed enhancement pattern and non-ischemic late gadolinium enhancement pattern. Subsequently, patient was hospitalized for atrial fibrillation with low heart rate 36/bpm. During hospitalization, Holter ECG monitoring revealed two significant pauses providing indication to pacemaker implantation. Being KSS patients at high risk for life threatening arrhythmias and sudden cardiac death, a bicameral pacing/defibrillation device was implanted. At discharge direct oral anticoagulation therapy with apixaban 5 mg bis in die was recommended and three months later, she underwent trans-esophageal echocardiogram which documented absence of cardioembolic sources, and subsequently electrical cardioversion with restoration of the sinus rhythm. After one month, patient experienced a ventricular tachycardia recognized and treated by device shock. At 1 year follow-up patient is asymptomatic at rest, with stable hemodynamic parameters and in sinus rhythm.

Conclusion. KSS is a challenging condition difficult to recognize and manage, because of the variety of clinical manifestations and the lack of large case series in literature. Since patients with KSS not only develop AV block but also ventricular arrhythmias such as ventricular tachycardia/fibrillation, or torsades des pointe and mortality is often related to sudden cardiac death, cardioverter defibrillator implantation in primary prevention should be considered even in case requiring pacemaker for bradyarrhythmias.

A420: CLINICAL PROFILE AND IN-HOSPITAL COURSE OF PATIENTS WITH PRIMARY AND SECONDARY TAKOTSUBO SYNDROME: SINGLE CENTER EXPERIENCE

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Background. Takotsubo syndrome (TTS) is an acute cardiac disease increasingly recognized in a variety of clinical scenarios. Heart Failure Association of the ESC classified TTS in primary (occurring in the setting of psychological or emotional trigger or without clear identifiable stressors) and secondary (triggered by physical stressors or other critical illnesses). However, the clinical profile and outcome of these different subtypes is still controversial.

Aim of the study: to compare baseline features, clinical presentation and in-hospital outcomes in patients with primary or secondary TTS in a single referral center.

Methods. Overall study population included 210 patients (mean age 66.1±12.2 years, 14 male); 165 and 45 with primary and secondary TTS, respectively; consecutively enrolled from 2012 to 2019 in our center. Clinical, instrumental and laboratory data and in-hospital events were also recorded in both groups.

Results. Compared to patients with primary TTS, patients with secondary form were older (70.6±14.6 vs 64.9±11.2 years; p=0.006) and more frequently man (13.3% vs 4.8%; p=0.043). Several comorbidities such as diabetes (23.8% vs 8.9%; p=0.008); pulmonary (45.2% vs 12.9%; p<0.001); neurologic (23.8% vs 9.7%; p=0.015); nephro-urologic (31% vs 13.5%; p=0.008); psychiatric (42.9% vs 26.5%; p=0.039) and orthopedic (28.6% vs 13.5%; p=0.020) diseases were prevalent in secondary TTS patients. Atypical presentation with higher incidence of dyspnea was significantly prevalent (42.2% vs 19.4%; p=0.002) in secondary group. The number of patients with ST-T elevation on admission was similar (80% vs 77%; p=0.5) in both groups. Prolonged QT interval in a majority of secondary TTS patients (46.3% vs 28.4%; p=0.029) was detected. Peak levels of troponin, creatine-kinase and myoglobin did not differ between the two groups. Echocardiography revealed larger left ventricular end-diastolic and end-systolic volumes (62.7±25.3 vs 50.6±14.3 ml/m²; p=0.024 and 35.1±14.5 vs 28.7±9 ml/m²; p=0.048) at presentation in

secondary TTS, however no differences in baseline left ventricular ejection fraction were detected. Furthermore, the prevalence of apical ballooning was similar between the two groups. Of note, secondary TTS patients experienced more frequently acute heart failure (40.5% vs 23.1%; $p=0.024$), hyperkinetic arrhythmia (9.1% vs 1.9%; $p=0.022$), cardiogenic shock (15.9% vs 3.2%; $p=0.002$), and mechanical ventilation use (9.3% vs 1.3%; $p=0.006$) during the acute phase. In-hospital stay (10.8 ± 6.9 vs 7.4 ± 6.2 days, $p=0.004$) was longer in this cohort.

Conclusions. Our results demonstrate that to classify TTS patients in primary or secondary form is clinically relevant. Secondary form generally is associated to higher rate of comorbidities and to atypical presentation. Owing to the worse in-hospital outcome of the secondary TTS patients a tailored and more intensive treatment should be adopted in this cohort.

A421: TAKOTSUBO SYNDROME COMPLICATED BY ISCHEMIC STROKE: THE CLINICAL DILEMMA OF ANTICOAGULATION

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(a) A.O.U. SAN GIOVANNI DI DIO E RUGGI D'ARAGONA

Background. Takotsubo syndrome (TTS) is an acute and transient heart failure syndrome due to reversible myocardial dysfunction characterized by a wide spectrum of possible clinical scenarios. A stressful event, emotional or physical, usually precede TTS onset, although in one-third of the patients no trigger event can be identified. Although complete recovery of myocardial contractility usually occurs within days or weeks, in about 20% of the patients TTS is associated with adverse in-hospital events including heart failure, cardiogenic shock and life-threatening arrhythmias. Intraventricular thrombosis complicated by ischemic stroke has also been reported, albeit in a minority of cases.

Case summary. A 69-year-old woman presented to our emergency department for dyspnea onset 2 hours before, after a family quarrel. Physical examination, ECG, laboratory exam and transthoracic echocardiography (TTE) were suggestive of anterior STEMI. Urgent coronary angiography was performed showing normal coronary arteries. Based on anamnestic, clinical and instrumental findings, diagnosis of TTS was then hypothesized. On the sixth day of hospitalization, two days after anticoagulation therapy was stopped, the patient developed dysarthria and right hemiparesis. TTE revealed persisting apical akinesia and detected a small apical thrombus attached to the apical segment of lateral left ventricular (LV) wall. Head computed tomography and magnetic resonance imaging (MRI) detected focal areas of ischemic necrosis due to diffuse cardioembolism. Anticoagulation therapy with acenocoumarol was started. Ten days after the hospitalization, left ventricular systolic function was improved and the size of the apical thrombus was reduced. The patient was transferred 3 days later to a neurological rehabilitation institute. At 1-month follow-up (FU), TTE showed normal LV ejection fraction (58%) and no apical thrombus. At 3-months FU, cardiac MRI confirmed the complete recovery of LV systolic function and the absence of thrombi. No area of oedema or late gadolinium enhancement were appreciated. The patient fully recovered speech after five months.

Discussion. The prevalence of intraventricular thrombosis and embolism in TTS patients ranges from 2.2% to 3.3%. Up to date, there is a knowledge gap in literature regarding the appropriate therapeutic strategy to prevent thromboembolic complications in TTS patients. This challenging case reinforces current expert opinion recommendations to adopt anticoagulation therapy in case of extensive apical akinesia and typical apical ballooning pattern, even in presence of sinus rhythm. Such therapy should be prolonged, especially in patients at high-risk for developing thromboembolic events, until complete or near-complete recovery of myocardial function whereas bleeding risk is acceptable. Close echocardiographic monitoring is recommended during the acute phase of TTS in order to both evaluate the recovery of myocardial contractility and to early detect intraventricular thrombi. Future prospective randomized studies should be scheduled to select patients with TTS at higher risk of thromboembolic complications and to establish an appropriate anticoagulation therapy.

A422: RECURRENT PERICARDIAL EFFUSION IN A PATIENT WITH ANKYLOSING SPONDYLITIS

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Ankylosing spondylitis (AS) is a chronic seronegative spondyloarthritis with the major histocompatibility antigen HLA B27 which results in fusion (ankylosis) of the spine and sacroiliac (SI) joints. Heart involvement in AS may be represented by several cardiac manifestations: pericardial, valvular, myocardial and vascular are described with different incidence. We report a case of AS hospitalized for recurrent pericardial and pleural effusion with BAV I and echocardiographic finding of ascending aorta dilatation.

Case presentation. The patient was an 53-year-old man with a history of hypertension and dyslipidemia. The patient was admitted to our Unit for chest pain, fewer and echocardiographic finding of mild pericardial effusion. He also referred low back pain, photophobia and intermittent ocular pain. The patient denied other symptoms, cardiovascular risk factors or previous surgical interventions. His medical history revealed two previous hospitalizations for pleural and pericardial effusion. The patient was in treatment with colchicine. Basal EKG showed sinus rhythm with BAV I degree, no signs of previous necrosis or left ventricular hypertrophy. An echocardiographic exam was performed showing a normal left ventricle endocavitary size and parietal thickness with preserved systolic function (EF 60%), first degree diastolic dysfunction, normal right ventricle dimension and systolic function, mild mitral valve regurgitation, mild tricuspid valve regurgitation, mild dilatation of ascending aorta diameter with aortic root thickening, pericardial effusion less than 10 mm. Chest X Ray showed mild pleural effusion. Antinuclear antibody, rheumatoid factor and anti-double-strand DNA were negative. The axial skeleton X ray showed small erosions at the corners of vertebral bodies with reactive sclerosis, vertebral body squaring, diffuse syndesmophytic ankylosis and subchondral erosions and sclerosis on the iliac side of the sacroiliac joints spine. After the diagnosis of AS was confirmed by a rheumatologist, the patient was addressed to eye examination and an ophthalmologist revealed an anterior uveitis. No arrhythmias were recorder during the hospitalization and colchicine administration was interrupted because of laboratory finding of neutropenia; corticosteroid treatment was started with optimal therapeutic response. The patient was discharged when the pericardial effusion was inferior to 4mm and was thus enrolled for follow-up examination.

Discussion. The AS cardiac involvement ranges around 2-10%. Cardiac complications such as left ventricular dysfunction, aortitis, aortic regurgitation, pericarditis and cardiomegaly are described. A higher risk of CAD and heart failure in AS patients is also reported. Conduction disturbances are observed in 2-25% of AS patients and first-degree AV block is usually the most common electrical abnormality observed, although higher grade block, right and left bundle branch block were also reported. Furthermore several valvular abnormalities are described in AS patients, such as aortic root thickening and dilatation or aortic and mitral regurgitation. Aortic root thickening is more frequent than dilatation (61% vs. 25%). Pericardial effusion has been rarely reported in AS patients, although in the literature are described also cases of cardiac tamponade. In the case we report, an AS patient with several AS-associated cardiac findings (BAV I, ascending aortic dilation) was hospitalized for recurrent pericardial effusion in the setting of polyserositis (pleural and pericardial effusion) with appropriate response to corticosteroid therapy.

A423: EVALUATION OF RIGHT VENTRICULAR DYSFUNCTION USING 3D ECHOCARDIOGRAPHY AND METABOLOMIC ANALYSIS IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction. Systemic lupus erythematosus (SLE) is a chronic inflammatory disease with a multifactorial aetiology and autoimmune pathogenesis. Various studies have suggested a possible early involvement of the right ventricle (RV). In this study, we evaluated the morpho-functional parameters of the right ventricle by 3D echocardiography and the metabolomic profile, correlating both with the severity of the underlying disease.

Materials and methods. We consecutively enrolled 40 patients affected by SLE; among these, we selected patients without cardiovascular disease. All patients underwent clinical evaluation, 12-lead electrocardiogram, conventional echocardiogram and 3D acquisitions for the evaluation of the following parameters relating to the RV: Ejection fraction (RV-EF), Longitudinal strain of the IVS (Septal LS), Longitudinal strain of the free wall (Free-LS) and the Fractional area change (FAC). Furthermore, we carried out a 1H-NMR-based metabolomic analysis on the sera of the patients. Cumulative organ damage was calculated with the Lupus International Collaborating Clinic / American College of Rheumatology (SDI) systemic damage index.

Results. 3D evaluation of right ventricle allowed to detect values in line with those in the literature for patients of the same type. We also carried out a correlation analysis between the M-Mode derived TAPSE values and the RV systolic function parameters evaluated by 3D ultrasound, obtaining a direct correlation with high statistical significance (RV-FE: $r=0.63$, $p<0.001$; FAC: $r=0.56$, $p=0.001$; Septal LS $r=0.49$, $p<0.01$; Free LS: $r=0.64$, $p<0.001$). Subsequently, to evaluate the possible presence of alterations in the RV function due to the underlying disease, we divided the population according to the SDI value in patients with a low degree of cumulative systemic damage (score 0) and patients with the greater impairment (score ≥ 3). Patients with major cumulative damage had

statistically significantly lower RV-EF ($52.4 \pm 4.1\%$ vs $56.9 \pm 2.5\%$, $p=0.007$), Septal LS ($18.9 \pm 2.5\%$ vs $24.4 \pm 3.4\%$, $p=0.004$), Free-LS ($23.9 \pm 3.8\%$ vs $38.8 \pm 4.0\%$, $p=0.003$) and FAC ($46.5 \pm 3.7\%$ vs $53.8 \pm 4.8\%$, $p=0.006$). Moreover, we correlated these parameters with metabolomic data, showing a statistically significant correlation between the metabolic profile and the Septal LS. The model built to verify whether the division into two groups based on SDI values allowed to identify different metabolic profiles related to the degree of RV dysfunction, evaluated with an OPLS-DA, showed good values of R^2 ($R^2X = 0.529$; $R^2Y = 0.926$) and Q^2 (0.635), also confirmed at ANOVA cross-validation ($p=0.04$).

Conclusions. Overall, our results would seem to be the expression of the chronic damage induced at the structural level of the RV by the chronic inflammatory state present in immune-mediated diseases such as SLE. This dysfunction can be detected early with 3D echocardiography, is associated with a specific metabolic fingerprint and its severity appears to be related to systemic organ damage.

A424: TAMPONAMENTO CARDIACO DOPO RIMOZIONE DI ELETTROCATETERE VENTRICOLARE DESTRO: RED FLAG, AGUZZA LA VISTA

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Introduzione. La stimolazione cardiaca temporanea elettrica (PMT), in ventricolo destro collegato ad un generatore, deve essere presa in considerazione in caso di bradiaritmia marcata o blocco atrioventricolare avanzato sintomatici o emodinamicamente instabili, fino a quando si debba avviare una terapia di stimolazione definitiva (PMD). La tecnica di stimolazione cardiaca temporanea può essere eseguita in vari modi, ma quello transvenoso è l'approccio preferito da molti cardiologi nella maggior parte dei pazienti. Tuttavia può comportare delle complicanze, una tra queste è la perforazione del ventricolo destro. Questo evento, pur raro, è potenzialmente letale in quanto può causare un rapido sviluppo di tamponamento cardiaco e richiedere misure di supporto aggressive come la pericardiocentesi in emergenza. Tale incidenza secondo alcuni studi si verifica tra lo 0,1 e 0,8%. In questa percentuale d'incidenza è rientrato il nostro caso clinico.

Caso clinico. Un uomo di 74 anni, ex fumatore, iperteso, dislipidemico e diabetico accede al pronto soccorso di un ospedale periferico per comparsa da alcuni giorni (inizio giugno 2020) di febbre e tosse con escreato rosato. Centralizzato per sospetto di COVID-19 la TC del torace confermava la presenza di polmonite bilaterale associata a lieve versamento pleurico con primo tampone per SARS COV-2 negativo. Visto il rapido deterioramento della dinamica respiratoria il paziente veniva sottoposto a ventilazione non invasiva e poi trasferito presso la Terapia Intensiva per necessità di intubazione orotracheale e ventilazione meccanica. Il successivo decorso clinico è stato caratterizzato da instabilità emodinamica con ipotensione e fasi di blocco atrioventricolare (BAV) completo che hanno richiesto supporto inotropo e posizionamento di pacemaker temporaneo nel ventricolo destro mediante vena femorale destra. Migliorate le condizioni cliniche e del quadro flogistico, per il persistere del BAV, dopo circa 8 gg si è proceduto a impianto di PM definitivo bicamerale per via cefalica sn. Trascorsi circa 15 min dalla rimozione dell'elettrocateterizzatore temporaneo si è assistito comparsa di severa ipotensione con rapida evoluzione in arresto cardiaco da attività elettrica senza polso. All'ecoscopia cardiaca si è evidenziata la presenza di versamento pericardico organizzato attorno alla parete libera del ventricolo destro con aspetto a "focaccia" con progressivo aumento della componente liquida circostante e compressione delle sezioni cardiache destre. Durante le manovre di rianimazione avanzata è stata eseguita in emergenza al letto del paziente una pericardiocentesi con approccio sottocostale con drenaggio di circa 180 cc di liquido ematico e ripresa di circolo e coscienza.

Take home message. L'esecuzione di una semplice ecoscopia cardiaca, fattibile in pochi minuti e al letto del malato prima di rimuovere l'elettrocateterizzatore, avrebbe potuto individuare il versamento pericardico organizzato attorno la parete libera del ventricolo destro e posto il sospetto della complicità potendo quindi anticipare e pianificare gli interventi più appropriati. Noi consigliamo in tutti i pazienti sottoposti a posizionamento di pacemaker temporaneo di effettuare prima della sua rimozione un eco-Doppler focus-oriented. Inoltre occorre che tutti i cardiologi che lavorano in un setting ospedaliero siano adeguatamente formati ad eseguire una pericardiocentesi in emergenza-urgenza, soprattutto se interventisti o intensivisti.

A425: HARD TIME FOR ENDOCARDITIS AND PERICARDITIS DURING THE COVID-19 PANDEMIC: TWO CASE REPORTS

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Case report. We report two clinical cases of fever during the COVID-19 pandemic related to two cardiac clinical entities. A.P. is a 62-year-old patient who arrived to the emergency room for 4 days of fever non-responsive to ceftriaxone 1gr/daily therapy. The patient was in follow-up

for surgical treated colorectal cancer. The patient did not present any relevant symptomatology except for a general malaise related to fever. For this reason a nasopharyngeal swabs was used in polymerase chain reaction (PCR) test to detect SARS-CoV-2. A cardiologic consultation is required for a slight increase in myocardial necrosis enzymes. Despite the clinical suspicion of COVID-19 we still decide to carry out a transthoracic echocardiogram, even if non urgent, which highlights a vegetation on the mitral valve. Through a more detailed examination of the patient, we detected Janeway lesions on his phalanx. These elements lead us to set up an early empirical antibiotic therapy which led to an excellent patient outcome. The second case concerns F.C. a 41-year-old African man, who arrived in Italy a few months earlier by crossing the Mediterranean. He arrives in the emergency room for fever associated with conjunctivitis and is immediately placed in isolation and tested for SARS-CoV-2 viral infection. The patient also reports stabbing chest pain, exacerbated by breathing so a cardiologic evaluation is required. A transthoracic echocardiogram highlights a circumferential pericardial effusion. On physical examination we notice sclerotic nodules on the hands and feet with generalized hardening of the skin. The subsequent rheumatologic screening shows a positivity for scl70 that makes us speculate about a systemic sclerosis with early setting of an adequate therapy. As expected, both patients tested negative for COVID-19. These clinical cases are didactic and lead us to make important assessments. In our experience it is essential to remember that fever, even in a pandemic era, must not make us focus exclusively on the contingent situation, always keeping in mind that fever is also associated with very serious clinical cardiovascular conditions, which treated early can significantly modify their outcome. For this reason we believe that even in the suspicion of COVID-19, it is necessary to apply all the diagnostic and therapeutic protocols without delay trying to use all the individual protective devices adequately.



Fig. 1 Janeway lesion in endocarditis



Fig. 2 Scleroderma in pericarditis

A426: PREGNANCY IS NOT A MODIFIER OF THE NATURAL HISTORY OF HYPERTROPHIC CARDIOMYOPATHY

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Objectives. To determine whether pregnancy is well tolerated in hypertrophic cardiomyopathy (HCM).

Setting. Tertiary care referral clinic for cardiomyopathies.

Design. Records of women consecutively referred to our center from 1969 to 2019 were retrospectively reviewed. Only women with complete information regarding presence or absence of pregnancy and with a follow-up >1 year were included in the study. Overall, of the 647 women followed at our center, 377 (58%) fulfilled our inclusion criteria and constitute our study population. Demographic, clinical and instrumental records were retrieved. The peripartum period was defined as the timeframe from -1 to 6 months after delivery.

Results. There were 432 pregnancies in 238 (63%) women with 132 (62%) having >1 pregnancy. By contrast, 139 (37%) reported no pregnancy or miscarriages: in 6 cases pregnancy was discouraged due to advanced disease stage. Twenty-six (10.9%) women had 38 pregnancies after the diagnosis of HCM and were followed by the obstetrics department: this subset was significantly younger at diagnosis (age at diagnosis: 21 [13-29] vs 56 [47-66] vs 45 [24-62] years, $p<0.001$, in women with a pregnancy after diagnosis vs women diagnosed after the pregnancy vs women with no pregnancy, respectively). Instrumental characteristics were comparable among women. Thirty percent of women presented with obstructive physiology at baseline. Among the 38 pregnancies in women who had a pregnancy after the diagnosis, there were two reported episodes of paroxysmal atrial fibrillation, one sustained ventricular tachycardia with pulse and three episodes of non-sustained ventricular tachycardia in the peripartum period. In this cohort, prevalence of intra-uterine growth delay and miscarriage was 8% in both cases. Only 3 women experienced a worsening clinical profile requiring hospitalization during the peripartum period: 2 were hospitalized for acute heart failure

and 1 was experienced a resuscitated cardiac arrest. Of note, 2/3 of patients were carriers of a (likely)pathogenic troponin mutation. Patients were followed for 5±3 years. Long-term, women who did not have a pregnancy were more symptomatic at last evaluation (NYHA III/IV: 25 vs 17, $p<0.05$), reported a higher incidence of ICD appropriate shocks (26.3 vs 11.8% $p=0.024$) but had similar rates of heart transplant (2.1 vs 0.5%, $p=0.143$) and episodes of acute heart failure (12.3 vs 13.7%, $p=0.193$). Eighteen patients (8.2%) died: incidence of cardiovascular mortality was 4.8%, with a lower rate in patients who reported a pregnancy (0.8%/year vs 2.8%/year, $p=0.01$).

Conclusions. Women with hypertrophic cardiomyopathy tolerate pregnancy well. Rare complications occurred in the peripartum period which were manageable. In the long-term, pregnancy, even when multiple, did not influence the long-term course of the disease nor its outcome. However, appropriate counselling is always mandatory in all patients of fertile age as a selected minority must be discouraged from pregnancy due to advanced disease stage.

A427: RISK STRATIFICATION IN HYPERTROPHIC CARDIOMYOPATHY. INSIGHTS FROM GENETIC ANALYSIS AND CARDIOPULMONARY EXERCISE TESTING

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Aims. Although hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease, the role of genetic testing in the risk stratification over the clinical and functional variables, including data from the cardiopulmonary exercise test (CPET), remains unclear. Accordingly, there is always great interest in investigating approaches potentially able to identify early those HCM patients at high risk of cardiovascular events both in terms of sudden cardiac death (SCD) and heart failure (HF). Our multicenter retrospective study investigated a possible adjunctive role of genetic testing analysis in the HCM patients' management over the main clinical and functional parameters. Particularly, a genotype-phenotype correlation was performed to analyze possible differences between HCM patients with and without pathogenic/likely pathogenic (P/LP) variants with respect to their main clinical and functional features and, mainly, their SCD and HF-related events' rate.

Methods and Results. From an initial study sample of 665 consecutive HCM outpatients, a total of 294 patients (44%) were excluded because they did not undergo genetic testing ($n = 197$), because they were lost at follow-up ($n = 39$), because of the presence of nonsarcomeric variants ($n = 22$) or, eventually, because the genetic analysis was not performed according to the previously described inclusion criteria ($n = 36$). Thus, a total of 371 HCM patients were effectively enrolled and screened at least for the main sarcomeric genes MYBPC3 (myosin binding protein C), MYH7 (β -myosin heavy chain), TNNI3 (cardiac troponin I) and TNNT2 (cardiac troponin T). Two hundred and three (55%) genetic tests were informative as they detected at least a P/LP variant, whereas the percentage of patients with variant of uncertain significance (VUS) was 6% ($n = 23$ patients); 39% ($n = 145$ patients) did not show any P/LP variant or VUS. MYBPC3 and MYH7 resulted in the most mutated genes with 88 P/LP variants (75%). Twenty-four patients resulted to be carriers of multiple variants, considering those with at least one P/LP variant and other P/LP or VUS variants. The P/LP variants group showed a younger age, a slightly higher prevalence of family history of SCD (FH-SCD) and abnormal blood pressure response during exercise and a worse functional capacity in terms of peak oxygen uptake (pVO_2), circulatory power (peak oxygen uptake*peak systolic blood pressure, CP%) and ventilatory efficiency (VE/CO_2 slope). With respect to the other clinical features, at the study run-in, the P/LP variants group had a greater prevalence of patients with end-stage phase (6% vs. 2%, $p=0.011$) and atrial fibrillation (3% vs. 1%, $p=0.032$), whereas no difference in the prevalence of previous myectomy was found (5% for both groups). Median follow-up was 5.4 years (25th–75th centile: 2.3 to 8.1 years) with a total of 2271 patients-year. A total of 14 SCD or SCD-equivalents and of were analyzed. Specifically, SCD occurred in 3 patients; 4 patients experienced

a resuscitated SCD and 7 patients had an appropriate ICD intervention. A total of 52 HF-related events were analyzed. Specifically, HF-related death occurred in 2 patients, 7 patients underwent cardiac transplantation, 20 patients were hospitalized due to HF signs/symptoms, 12 patients were hospitalized for septal reduction procedure due to significant HF signs/symptoms development and 11 patients evolved to end-stage or restrictive phenotype evolution. The Cox proportional univariate survival analysis for both the study end-points showed that, besides a number of clinical, echocardiographic and CPET variables (such as FH-SCD, left atrial diameter, maximal left ventricular outflow tract gradient, VE/CO_2 slope and pVO_2 expressed as percentage of predicted), the P/LP variant presence was significantly associated with the HF but not with the SCD end-point. At multivariate analysis, however, left atrial diameter (LAD), CP% and ventilatory efficiency were the only independent predictors of HF (C-index = 0.839), whereas only LAD and CP% remained independently associated with the SCD end-point (C-index = 0.738).

Conclusions. The P/LP variants were associated with a more aggressive HCM phenotype in terms of early disease onset, high burden of historical risk factor and, for the first time, poor functional status. The present study reaffirmed the pivotal role of the clinical variables and, particularly of those CPET-derived, in the HCM risk stratification.

A428: COINVOLGIMENTO CARDIACO COME ESORDIO DI SINDROME DI CHURG-STRAUSS

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La miocardite è un processo infiammatorio definito dalla presenza di un infiltrato di cellule mononucleari nel tessuto muscolare cardiaco all'analisi istologica. Le manifestazioni cliniche della miocardite sono eterogenee. Nella fase acuta si può manifestare in forma paucisintomatica o esordire con un quadro di insufficienza cardiaca, shock cardiogeno o aritmie maligne. L'infiammazione può essere causata da un ampio spettro di agenti infettivi come virus, batteri, funghi e protozoi. In altri casi la miocardite può essere secondaria a malattie a patogenesi autoimmune quali il LES, la sclerosi sistemica e alcune forme di vasculite. Tra queste, il coinvolgimento miocardico può essere secondario a forme che interessano vasi di medio e piccolo calibro, tra cui la Granulomatosi eosinofila con poliangioite, nota come Sindrome di Churg-Strauss. La presenza di un interessamento multiorgano può indirizzare verso una corretta eziologia in modo da consentire un trattamento terapeutico specifico.

Descriviamo il caso clinico di un paziente di 19 anni senza precedenti cardiologici. In anamnesi storia di asma bronchiale, tonsilliti e sinusiti recidivanti dall'età pediatrica. Il paziente giungeva alla nostra osservazione per astenia marcata associata dolore toracico trafittivo, iperipressia, faringodinia e parestesie a carico delle estremità degli arti. Venivano eseguiti esami ematochimici che mostravano rialzo dei markers di miocardio necrosi (Troponina I hs 4547 ng/L, CK-MB 9.5 ng/ml). All'elettrocardiogramma si evidenziava la presenza di tachicardia sinusale alla FC di 110 bpm con lieve sopraslivellamento diffuso del tratto ST-T. L'ecocardiogramma c/D mostrava lieve riduzione della funzione sistolica globale (FE 50%) in assenza di chiari deficit della cinesi segmentaria, e minima falda di versamento pericardico. Il paziente veniva pertanto ricoverato presso il reparto di Cardiologia con sospetto clinico di perimocardite. Ad una attenta valutazione anamnestica il paziente riferiva il recente riscontro di perforazione spontanea del setto nasale. Nel sospetto di una vasculite autoimmune durante la degenza venivano effettuati esami ematochimici con il riscontro di eosinofilia periferica 20.6%, incremento della PCR, della MR-pro Adrenomedullina (0,6 nmol/L) e delle IgE totali (2305.00 UI/ml). Veniva inoltre dosato il LAC risultato positivo, (168,7 mg/L) e gli ANCA risultati negativi. Lo screening infettivologico per CMV, EBV e Treponema Pallidum risultava negativo per infezioni in atto. Veniva inoltre effettuata biopsia del setto nasale, che evidenziava aspetti di rinosinusite cronica con sparsi eosinofili associata a focali quadri di vasculite dei piccoli vasi capillari. In presenza di 4 dei criteri diagnostici quali storia di asma, eosinofilia $>10\%$ nel sangue periferico, sinusite paranasale ed evidenza istologica di vasculite con eosinofili extravascolari, è stato possibile porre diagnosi di Malattia di Churg-Strauss; veniva impostata terapia con corticosteroidi ad alte dosi con progressivo miglioramento della sintomatologia e del quadro clinico. Durante il follow-up veniva eseguita RMN cuore che riscontrava la presenza di aree di LGE subepicardiche a livello dei segmenti basali della parete infero-laterale del ventricolo sinistro. La causa più comune di miocardite è quella virale. Il coinvolgimento di altri organi e un'attenta indagine clinica ed anamnestica consentono in alcuni casi di individuare un'eziologia specifica che consente un trattamento mirato della malattia. La sindrome di Churg-Strauss si manifesta attraverso tre stadi di malattia: lo stato allergico, quello dell'ipereosinofilia e lo stadio vasculitico. Nel nostro caso un interessamento precoce del tessuto miocardico ha permesso la diagnosi della malattia in stato vasculitico. La miocardite rappresenta inoltre una manifestazione spesso associata a pazienti ANCA-negativi, come nel nostro caso.

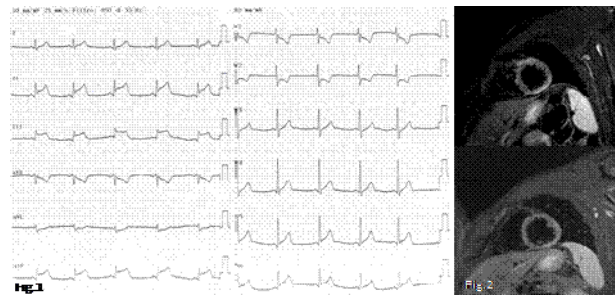
A429: ACUTE MYOCARDITIS: ATYPICAL PRESENTATION AND CMR DIAGNOSIS

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Background. The clinical presentation of myocarditis is very variable, it can start as asymptomatic or it can manifest itself with acute and severe symptoms such as dyspnoea or chest pain. In rare cases, focal myocarditis can mimic acute myocardial infarction.

Case report. We present the case of a 21-year-old man with no relevant medical history admitted at the emergency department (ED) of our hospital with severe chest pain spontaneously regressed after 20 minutes. There was no history of cocaine or other substance abuse, neither of chest wall trauma. The patient reported a gastrointestinal illness with diarrhea and fever two days before the initiation of the chest discomfort. At presentation, the patient was afebrile. His vital signs and ECG were normal. Blood analysis showed mildly increased levels of monocytes, C-reactive protein, lactate dehydrogenase and high levels of troponin I (5274 pg/ml, cut off value 34,2 pg/ml). Transthoracic echocardiography revealed inferior wall motion abnormalities with preserved (57%) ejection fraction and without pericardial effusion. During evaluation in the ED the patient had another episode of acute chest pain, the ECG is shown in Figure 1. The patient underwent urgent coronary angiography, which showed normal epicardial coronary arteries. During the first hours of hospitalization in coronary intensive care unit, the patient had some episodes of intermittent chest pain with transient ST elevation and also some episodes of non sustained ventricular tachycardia; troponin I increased up to 15000 pg/ml. Nonsteroidal anti-inflammatory drugs and non-dihydropyridine calcium channel-blockers were initiated with gradual symptom improvement and laboratory findings. Cardiac magnetic resonance (CMR) showed inferolateral intramyocardial late gadolinium enhancement and oedema as for acute focal myocarditis (Figure 2). The serology for most common cardiotropic viruses was performed and COVID-19 nasopharyngeal swab was negative. During the rest of the hospitalization, the patient remained asymptomatic and troponin I decreased progressively. The patient was discharged after one week and enrolled in our follow-up program. After two weeks the patient was free of symptoms and ECG an TTE echo were improved.

Conclusion. The correct diagnosis of myocardial diseases often requires integrated imaging. In this reported case, CMR led to the correct diagnosis of focal acute myocarditis.

**A430: ARRHYTHMOGENIC CARDIOMYOPATHY: THE ROLE OF CARDIOPULMONARY EXERCISE TESTING IN HEART TRANSPLANTATION REFERRAL**

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We describe the case of a 20-year-old male patient affected by a biventricular form of Arrhythmogenic cardiomyopathy (ACM) who was evaluated for heart transplantation (HTx). The patient was diagnosed with ACM at the age of 12 years, after a syncopal episode during effort. No family history of arrhythmic cardiac disease and/or of sudden death was present. 12-lead ECG showed sinus rhythm, low QRS voltages and localised QRS widening in V1-V3 leads with T wave inversion in V1-V4. Two-D echocardiogram showed severe right ventricular (RV) dilation and dysfunction with presence of kinetic abnormalities. CMR demonstrated the RV dilatation and dysfunction, RV anterior wall fibrosis and preserved left ventricular (LV) dimension and function. Due to the clinical history and the important disease extent, an ICD was implanted. The patient was included in a follow-up program at the Outpatient Clinic of our Department. During the following years a progressive decreasing of LV function was observed, leading to the diagnosis of biventricular ACM. The patient remained asymptomatic until the age of 19, when he presented to Emergency department because of heart failure (HF) symptoms and new-onset atrial fibrillation. No sustained ventricular arrhythmias were recorded. Since then, he persisted symptomatic for asthenia and exercise dyspnoea (NYHA III). Echocardiogram showed a markedly dilated RV with severely reduced RV systolic function, and moderate reduction of systolic function. Because of the worsening of clinical status, the patient

was admitted to the Cardiology ward of our Hospital. The patient underwent a cardiopulmonary exercise testing (CPET), performed on beta blocker therapy but with maximal intensity exercise (respiratory exchange ratio = 1.20, maximum heart rate = 151 bpm). No significant stress-induced arrhythmias were recorded. The test did not show signs of ventilation-perfusion mismatch, with a VE/VO₂ slope (relationship between minute ventilation and carbon dioxide production) value of 26.98. The peak oxygen consumption (pVO₂) was 16.9 mL/Kg/min. The patient also underwent a coronary angiography and cardiac catheterization that showed normal coronary arteries and reduced cardiac index. The patient was then discharged with a follow-up programme. 10 months later the patient presented with relapsing HF and was readmitted to hospital. Another CPET was performed, showing worsening of VE/VO₂ slope (30.54) and pVO₂ (15.1). On the basis of the rapid disease progression, the patient was considered eligible for HTx. ACM is a rare disease, characterized by the presence of RV morphological abnormalities, even if in the last years the LV has been found to be frequently involved. In addition, patients affected with ACM usually show a high degree of electrical instability that can lead to sudden death. In a significant number of cases ventricular dysfunction can progress causing HF symptoms that require HTx. Due to the predominant RV involvement, the management of these patients may differ from other HF patients. In addition, CPET parameters, which have an important role in the evaluation of prognosis of patients with HF and in possible indication to advanced HF therapies (ventricular assistance devices and HTx), need to be adjusted in ACM patients, as ventilatory efficiency (VE/VO₂ slope) rather than pVO₂ has been found to have a predictive role in risk stratification. Moreover, specific recommendations on indication for listing ACM patients for HTx are lacking. Finally, according to literature, young age at first symptoms (<35 years old) independently predicts HTx, as well as VE/VO₂ slope >34.

A431: A RARE LIFE-THREATENING COMPLICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background. Systemic lupus erythematosus (SLE) is a systemic autoimmune disease, known to involve different organs including the heart. Cardiac involvement in SLE is represented by pericarditis (12-48%), myocarditis (10-40%), Libman-Sacks endocarditis (13-74%), rhythm and conduction disturbances (5%-10%) and coronary arteries disease (25-45%).

Case description. A 49-year-old woman was admitted to the hospital due to fever, nausea and vomit which she had for 3 days. Her medical history was characterized only by arterial hypertension well controlled with medical therapy. In the Emergency Room vital signs and clinical exam were normal except body temperature (37.8°C). Lab tests showed normocytic normochromic anemia (hemoglobin 10 g/dL) with leukopenia (White Blood Cells 2700/mmc with normal form). Electrocardiogram, echocardiogram and chest X ray didn't exhibit significant abnormalities, so she was admitted to the Medicine Division. During hospitalization other clinical and laboratory alterations appeared: oral ulcers, autoimmune hemolysis, proteinuria, lupus anticoagulant, low C3 and low C4, anti-dsDNA and anti-Smith antibodies. The patient had 24 points of Systemic Lupus Erythematosus' criteria so anti-inflammatory and immunosuppressive therapy, based on methylprednisolone, intravenous immunoglobulins and cyclophosphamide (CYC), was administered. The patient's clinical conditions worsened after 3 days: she had acute heart failure with severe left ventricular systolic dysfunction and high troponin value (9.5 ng/mL, n.v. <0.04), complicated by cardiogenic shock treated with inotropes and vasopressors. Urgent coronary angiography was performed and didn't reveal critical stenosis; during procedure an intra-aortic balloon pump (IABP) was positioned to assist cardiac circulatory function. Diagnostic hypothesis were 2: CYC-induced cardiomyopathy or lupus myocarditis (LM).

Discussion. Considered the low dosage of CYC used (750 mg/die), it was more probably that the cause of heart failure was LM so it was increased CYC dose and started hydroxychloroquine. This therapy determined clinical improvement and recovery of left ventricular systolic function. LM usually has good long term outcome under specific treatment for SLE and cardiomyopathy, especially regarding cardiac recovery. Its diagnosis is primarily based on clinical suspicion as diagnostic tools are not sensitive. Anatomopathological analysis of endomyocardial biopsy is not necessary in most cases because it has low sensitivity since the myocardial pattern may be focal in many situations.

Conclusion. LM is a rare but serious condition which should be diagnosed and treated promptly to avoid fatal consequences (mortality of 10.3% during acute phase). CYC has been reported as a causal agent of myocarditis but it is generally safe for treating LM if used at right dose.

A432: PREVALENCE AND DIAGNOSTIC VALUE OF EXTRA-VENTRICULAR FINDINGS IN TRANSTHYRETIN-RELATED CARDIAC AMYLOIDOSIS

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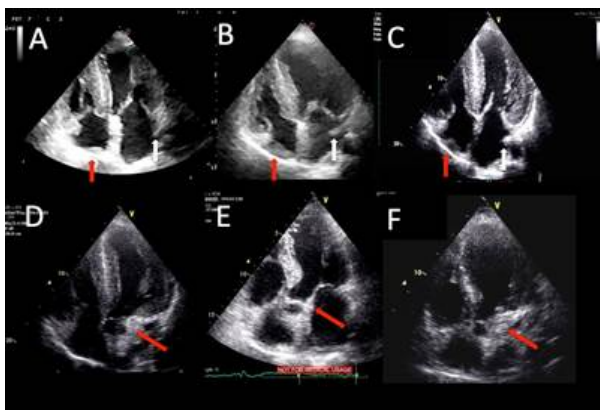
Objectives. To evaluate prevalence and diagnostic value of echocardiographic evidence of non-ventricular localization of amyloid deposition in patients with left ventricular (LV) hypertrophic phenotype.

Background. Cardiac amyloidosis (CA) is a cardiomyopathy characterized by diffuse deposition of anomalous fibrillar proteins in extracellular matrix.

Methods. A group of 134 patients with LV thickness >15 mm including 58 patients who received a definite diagnosis of sarcomeric hypertrophic cardiomyopathy (HCM group) and 76 patients with transthyretin cardiac amyloidosis (CA group) were enrolled. Echocardiography was used for the identification of crista terminalis (CriT), atrio-ventricular plane (AVP), mitro-aortic lamina (MAL), posterior wall of RV outflow, interatrial septum (IAS), Eustachio valve (EusV) and coumadin ridge (CouR).

Results. CA group showed significant higher dimensions of CriT, IAS, CouR, AVP, MAL and IAS compared to HCM group. According to areas under the receiver operating characteristic curves the best cut-off values to determine CA were identified (CR >8 mm², IAS >8 mm², MAL >7 mm, CT >9 mm² and AVP >9 mm). The logistic univariate analysis showed that presence of CT, area CT >9 mm², MAL >7 mm and IAS >8 mm were all predictors of CA (all *P* <0.01). The multivariate analysis selected area CT >9 mm (odds ratio [OR] 4.3), MAL >7 (OR 3.3) and IAS >8 mm (OR 13) as independent predictors of CA. Among these 3 independent predictors, IAS >8 had the best specificity (96%) and positive predictive value (93%) in identifying CA.

Conclusions. Evidence of non-ventricular sites of amyloid deposition is a frequent finding in CA. In the context of hypertrophic phenocopies, an increased thickness of IAS, and/or CT and/or MAL should suggest a diagnosis of transthyretin CA.

**A433: SUPRAVENTRICULAR PERSISTENT TACHYARRHYTHMIA REVEALING A SCAR OF A PROBABLE PREVIOUS MYOCARDITIS: UN UNUSUAL PRESENTATION FOR AN ATYPICAL LOCATION**

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A 59-year-old man was admitted to our emergency department (ED) for palpitations (started five hours earlier), asthenia, and absence of chest pain. Past medical history: heavy smoker, chronic gastritis, and surgery for benign salivary glands neoplasm. At admission, ECG showed atrial 1:1 tachycardia conducted with 2nd degree type 1 atrioventricular (AV) block; heart rate ranged from 110 to 130 beats per minute (bpm); P wave morphology was similar to sinus rhythm.

Physical examination: high blood pressure (systolic blood pressure 170 mmHg, diastolic blood pressure 100 mmHg). Routine lab tests and heart ultrasound (US) were normal. Atrial tachycardia was successfully treated with infusion of amiodarone; during sinus rhythm, heart rate ranged from 50 to 75 beats per minute and AV conduction was still characterized by 2nd degree type 1 AV block, with periods of AV dissociation by active junctional rhythm at 60 bpm. Continuous ECG recording confirmed persistence of sinus rhythm tracked with 2nd degree type 1 AV block, in absence of advanced degree AV block or marked bradycardia.

Intracavitary electrophysiological study: we mapped tachycardia (cycle 530 ms) rising from a focus very close to sinoatrial node with long AH interval (360 ms) and normal HV interval (43 ms). Decremental atrial

stimulation showed Wenckebach point 510 ms (upper limits), very close value to tachycardia cycle. After adenosine infusion (12 mg), atrial fibrillation (AF) was induced with sinus arrest >5 sec. Because of the location of the focus, we did not perform ablation.

We added ivabradine and episodes of "parasinusal" tachycardia were excluded; continuous ECG recording showed sinus rhythm with heart rate ranging from 55 to 65 bpm, and only 1st degree AV block. Cardiac magnetic resonance documented fibrosis of anterior, mid-basal interventricular septum (late-gadolinium enhancement at post-contrast sequences). Such findings were suggestive for a previous myocarditis involving AV node region (explaining the 1st degree AV block, the asymptomatic recent onset of the persistent 2nd degree type 1 AV block). Ivabradine reduced cardiac frequencies with evidence of 2nd degree type 1 AV block regression. Of note, blood antibodies for Borrelia, Tripanosoma Cruzi and Parvovirus B19 were negative. According to the observed response to ivabradine, absence of distal AV conduction disease or symptoms potentially related to 2nd degree type 1 AV block, implantation of a loop recorder system and the use of home monitoring system were indicated.

In conclusion, we documented that a previous, unrecognized, and silent myocarditis may cause fibrosis of the conduction system; such location of the inflammatory process may predispose to the occurrence of clinically significant conduction disorders.

A434: SYSTEMATIC CUTTING OF SECONDARY MITRAL VALVE CHORDAE, IN ASSOCIATION WITH A SHALLOW MYECTOMY, IN A LARGE COHORT OF PATIENTS WITH OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY

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Few centers worldwide have large experience with performing an extended septal myectomy in patients with obstructive hypertrophic cardiomyopathy (HCM). Therefore, many HCM patients eligible for surgical relief of left ventricular (LV) outflow gradient do not have access to treatment. In a previous study, we showed that in patients with obstructive HCM and mild septal hypertrophy, cutting fibrotic anterior mitral leaflet (AML) secondary chordae, in association with only a shallow myectomy, was highly effective in moving the mitral valve (MV) apparatus away from the LV outflow tract and relieving the outflow gradient. This surgical approach simplified the operation because it did not require a deep septal excision.

Purpose of the present investigation was to assess whether chordal cutting, in association with a shallow myectomy (excision of 25 to 35% of absolute septal thickness), was equally effective in relieving LV outflow gradient and heart failure symptoms, and improving MV geometry, in HCM patients with mild (<20 mm) as in those with more marked (≥20 mm) septal hypertrophy.

Surgical outcome and MV geometry and function were assessed in 226 consecutive HCM patients who underwent systematic cutting of fibrotic AML secondary chordae in association with a shallow myectomy at our center from January 2015 to December 2018. Of the 226 patients, 1 died (perioperative mortality 0.4%). None had iatrogenic septal defect. After a mean 9 month follow-up, LV outflow gradient at rest decreased from 70±36 to 10±2 mmHg (*P*<0.001), and was <30 mmHg in 223 (98%) of the 226 patients. NYHA functional class improved significantly (*P*<0.001), with the number of patients in class III-IV decreasing from 178 (79%) to 2 (0.9%). No patient had residual severe MV regurgitation and 4 (1.7%) had moderate-to-severe regurgitation. In the group with mild hypertrophy, the maximal thickness of the excised muscle (measured in the operating room) was 6.9±2.6mm and mean septal thickness (measured with transthoracic echocardiography) decreased 22%, from 18 mm to 14 mm (*P*<0.001). In the group with more marked hypertrophy, maximal thickness of excised muscle was 8.8±2mm and mean septal thickness decreased 32%, from 25 mm to 17 mm.

Quality of the echocardiogram allowed assessment of MV geometry in 212 (94%) of the 226 study patients. In the 62 patients with mild septal hypertrophy, anterior leaflet-annulus ratio increased 27% postoperatively, from 0.43±0.06% to 0.55±0.06% and MV tenting area decreased 34% from 2.9±0.6 to 1.9±0.4 cm² (*P*<0.001), indicating repositioning of MV coaptation away from the outflow tract in a more physiological position toward the LV posterior wall. Similarly, in 150 patients with more marked hypertrophy, anterior leaflet-annulus ratio increased 27% from 0.43±0.05% to 0.55±0.05% and tenting area decreased 28% from 2.9±0.6 to 2.1±0.4 cm² (*P*<0.001).

In conclusion, our results show that cutting fibrotic AML secondary chordae, in association with a shallow myectomy, by moving the MV apparatus away from the LV outflow tract, abolishes or substantially reduces the outflow gradient and MV regurgitation and improves symptoms in most patients with obstructive HCM. This novel operative technique could make septal myectomy more accessible to surgeons and, therefore, increases the availability of surgical treatment for those many patients with obstructive HCM and severe symptoms who are eligible for invasive abolition of the LV outflow gradient.

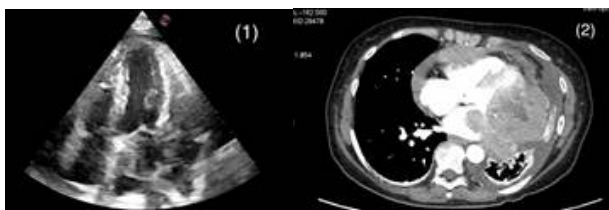
A435: UNA NEOPLASIA RARA CON UNA LOCALIZZAZIONE INSOLITA: UN CASO DI LINFOMA PRIMITIVO CARDIACO DELLE SEZIONI SINISTRE

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Introduzione. Il linfoma primitivo cardiaco è un tumore raro, privo di una definizione univoca che attualmente viene riservata ad un linfoma la cui massa principale risiede a livello cardiaco o pericardico, anche se può essere presente un limitato interessamento extra-cardiaco. I linfomi primitivi cardiaci hanno una spiccata predilezione per il cuore destro (in particolare modo l'atrio destro).

Caso clinico. Descriviamo il caso di una donna di 62 anni presentatasi in Pronto Soccorso per cardiopalmo e dispnea da sforzo di nuova insorgenza. L'unico precedente anamnestico era rappresentato da un ricovero l'anno precedente, sempre per dispnea, in cui era stata sottoposta a drenaggio di un versamento pleurico con citologia negativa per cellule neoplastiche. L'ECG all'ingresso mostrava una tachicardia sinusale con bassi voltaggi; all'ecocardiogramma (Figura 1) era presente una massa a livello dell'atrio sinistro, adesa alla parete laterale, un versamento pericardico lieve ed una struttura iperecogena a livello della giunzione atrio-ventricolare, inizialmente interpretata come apposizione di fibrina. Una successiva TC del torace (Figura 2) ha evidenziato la presenza di una massa con aspetti colliquativi localizzata attorno al cuore, adesa alle sezioni sinistre con infiltrazione dell'atrio sinistro, delle vene polmonari e del bronco lobare inferiore sinistro; un'altra massa, con caratteristiche simili, circondava la porzione antero-superiore del cuore destro. La paziente è stata successivamente sottoposta ad una TC total-body per escludere altre localizzazioni di malattia e ad una RM cardiaca per un'ulteriore caratterizzazione della massa; una biopsia TC guidata ha infine consentito la diagnosi di linfoma diffuso a grandi cellule. Dato il potenziale rischio di rottura di cuore durante chemioterapia, il primo ciclo di R-CHOP (rituximab, ciclofosfamide, doxorubicina, vincristina, prednisolone) è stato effettuato in ambiente ospedaliero con una riduzione del 75% della dose di doxorubicina. Dopo una iniziale buona risposta alla terapia di induzione, al termine del sesto ciclo di R-CHOP è stata evidenziata progressione di malattia per cui è stata intrapresa chemioterapia di salvataggio; la paziente è deceduta per shock settico dieci mesi dopo la diagnosi.

Conclusioni. Il linfoma primitivo cardiaco è una malattia rara, a prognosi infausta, che esordisce solitamente con sintomi aspecifici. Nonostante la localizzazione preferenziale a livello del cuore destro, in questa paziente la neoplasia interessava principalmente le camere sinistre. La chemioterapia è il trattamento di scelta e spesso necessita di approcci individualizzati (in base a caratteristiche e localizzazione del tumore) per minimizzare il rischio, descritto in letteratura, di rottura di cuore.



A436: LATE IMPROVEMENT OF LEFT VENTRICULAR EJECTION FRACTION IN PATIENTS WITH PERSISTENT SEVERE SYSTOLIC DYSFUNCTION UNDER GUIDELINE-DIRECTED MEDICAL THERAPY

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Background. A consistent proportion of patients with dilated cardiomyopathy (DCM) experience left ventricular reverse remodeling (LVRR) during the first 24 months of guideline-directed medical treatment (GDMT). However, important decisions, such as the need for implantable cardioverter defibrillator (ICD), are requested after 3 months of GDMT. The evolution of left ventricular ejection fraction (LVEF) during the first years after GDMT in DCM is unknown. Our study aims to investigate the proportion and characterize DCM patients experiencing late LVEF improvement.

Methods. We analyzed DCM patients consecutively enrolled with short disease duration (≤ 6 months), recent initiation of GDMT (≤ 3 months) and a LVEF $\leq 35\%$ associated with NYHA class I-III at 6-month follow-up evaluation. LVEF $>35\%$ at 24-month was the primary end-point of the study.

Results. Among 131 patients matching inclusion criteria (mean age 53 ± 14 , male sex 74%), 88 (67%) improved their LVEF at 24 months above 35%. A $>10\%$ reduction of the indexed left ventricular end-diastolic diameter (LVEDDi) between enrollment and 6-month evaluation emerged as the only independent predictor of late LVEF improvement. During the subsequent follow-up, the late LVEF improvement was associated with a

lower cumulative incidence of major arrhythmic events, compared to patients with persistent LVEF $\leq 35\%$ ($p=0.010$).

Conclusions. A high proportion of DCM patients improve their LVEF after more than 3-6 months of GDMT, which is associated with lower long-term arrhythmic risk. The early evaluation of dynamic parameters, such as the reduction of LVEDDi could help to identify those patients.

A437: ATRIAL FIBRILLATION IN DILATED CARDIOMYOPATHY: OUTCOME PREDICTION FROM AN OBSERVATIONAL REGISTRY

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Aim. Little is known about the role of different types of atrial fibrillation (AF) in dilated cardiomyopathy (DCM). We investigated epidemiology and prognostic impact of different types of AF in DCM during long-term follow-up.

Methods. We evaluated consecutive DCM patients enrolled in the Trieste Muscle Heart Disease Registry. Uni- and multivariable, extended Kaplan-Meier and propensity score-matching analyses has been performed for a composite outcome including death/heart transplantation/ventricular-assist device.

Results. Out of 1181 DCM patients (71% males, age 49 ± 15 years old, left ventricular ejection fraction $33 \pm 11\%$), 46 (3.9%) had baseline permanent AF (permAF), while 66 (5.6%) had history of paroxysmal/persistent atrial fibrillation (AF). Compared with sinus rhythm (SR), permAF patients were older (48 ± 15 vs. 61 ± 11 respectively, $p=0.001$), were more frequently in NYHA class III-IV (18% vs. 30%, $p=0.002$) and had larger left atrium diameter (40 ± 8 vs. 50 ± 10 mm, respectively). Paroxysmal/persistent AF patients had intermediate characteristics between permAF and SR. During a median follow-up of 135 (75-210) months, 63 patients developed permAF (0.45 new cases/100patients/year). At multivariable analysis, permAF, as time-dependent variable, was an independent outcome predictor (HR 2.45; 95% CI 2.61-3.63, $p<0.001$), together with creatinine, NYHA class, restrictive filling pattern and moderate-severe mitral regurgitation, while history of AF was neutral. Propensity score-matching analysis confirmed the higher rate of primary outcome events in patients with baseline or incident permAF versus patients without permAF during a very long-term follow-up (70% vs. 20%, $p<0.001$).

Conclusions. PermAF in a large DCM cohort had low prevalence and incidence but carried a relevant prognostic role on hard outcomes.

A438: PROGNOSTIC VALUE OF LONGITUDINALLY MEASURED GLOBAL LONGITUDINAL STRAIN IN THE PROGNOSTIC STRATIFICATION OF DCM PATIENTS

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Background. The prognostic value of global longitudinal strain (GLS) measurements is increasingly recognized in heart failure (HF), but its value in patients with non-ischemic, non-valvular dilated cardiomyopathy (DCM) is poorly evaluated.

Objectives. To investigate the predictive value of longitudinal GLS measurements, on top of left ventricular reverse remodeling (LVRR) in the prediction of long-term outcome in DCM patients.

Methods and Results. A total of 323 DCM patients with both baseline and 1-year follow-up (FU) echocardiogram were included (66% men, age 55 ± 14 years, left ventricular ejection fraction (LVEF) at baseline 32 ± 11 , duration of symptoms $2 [0.5-3.5]$ months). GLS was measured based on echocardiographic 2-, 3- and 4-chamber views. Primary outcome was the combination of all-cause mortality, life threatening arrhythmias (LTA), and HF hospitalization. LVRR was defined as an LVEF increase of 10 points or LVEF $>50\%$ and a decrease in indexed left ventricular end-diastolic diameter (LVEDDi) of at least 10% or LVEDDi <33 m² at 1-year FU.

Results. A total of 77 (24%) patients experienced the primary endpoint during a median FU of 6.4 [3.4-9.4] years. Mean GLS values at baseline and 1-year FU were $-12.5 \pm 5\%$ and $-15 \pm 4\%$, respectively. In a multivariable clinical baseline model, adjusting for significant clinical parameters from univariable analysis, GLS was not independently associated with outcome. Meanwhile, in a second FU model, including the same echocardiographic parameters measured at 1-year FU, GLS was the only independent predictor of the occurrence of events after 1-year FU (HR 1.22, CI 1.13-1.31, $p<0.001$).

Conclusions. This study showed that in recently-onset DCM patients, only GLS assessed at 1-year FU evaluation, after optimization of HF therapy, is independently associated with outcome in the prognostic risk stratification.

A439: GENETIC BACKGROUND OF THE LATE ONSET DCM

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Background. Dilated cardiomyopathy (DCM) represents a specific subgroup of non-ischemic cardiomyopathies. Little is known about the genotypic characterization of DCM patients diagnosed over 60 years of age.

Objectives. To investigate prevalence, characterization and prognostic impact of the genetic background of late-onset DCM patients.

Methods: We analyzed a study population of 552 DCM patients from two international referral centers. Genetic background was analyzed and patients were grouped into typical-onset DCM (<60 years of age at diagnosis) or late-onset DCM (>60 years of age at diagnosis).

Results. Approximately 12% of patients (n=68) had late-onset DCM and female sex was significantly more frequent in the late-onset DCM cohort compared to the typical onset DCM (47% vs. 29% respectively, p=0.005). Diagnostic yield of genetic testing was comparable between typical- and late-onset DCM (32% vs. 34%, respectively; p=0.78) whereas the prevalence of T1tn gene truncation variants (TTNtv) was higher in the late-onset DCM group compared to the younger cohort (22% vs. 13% respectively; p<0.05). Notably, patients with late-onset genetic DCM had comparable long-term outcomes to those with typical-onset DCM.

Conclusions. Late-onset DCM patients have more than double the rate of TTNtv mutations and are more likely to be female compared to younger DCM patients. These observed differences in mutational makeup and sex may reveal insights into age and sex dependent mechanisms for TTNtv and should prompt further study. Notably, the increased prevalence of TTNtv and female sex did not translate into noticeable differences in rates of measurable cardiac events.

A440: THE IMPACT OF SEX ON GENETICALLY DETERMINED DCM

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Background. The prognosis of women affected of dilated cardiomyopathy (DCM) appears to be more favourable than males, however, little is known regarding genetic landscape of this subgroup.

Aim. To investigate the genetic landscape of DCM in women and to evaluate the prognostic role of female sex together with sex-specific outcomes in patients with DCM over long-term follow-up.

Methods. A cohort of 566 DCM patients, enrolled in the Familial Cardiomyopathy Registry from two international tertiary referral centers, was analyzed. Patients were divided according to their sex and to their mutation status. The primary outcome was a composite of all-cause mortality or heart transplantation or implantation of a ventricular assist device (VAD).

Results. Approximately two thirds of patients (n=388, 68%) of the patients were male. Positive genetic finding were comparable between females and males (43% vs 49% respectively, p=0.110). Besides a higher prevalence of motor sarcomeric mutations in women, no other differences in genetic background were found between sexes (p=0.101). Non-carriers women had lower incidence of adverse outcomes during follow-up (p=0.040) and this was, more pronounced after 10 years of follow-up (p=0.012). However, no sex differences in the long-term survival were found in the DCM mutation positive patients. At multivariable analysis, female sex was an independent protective factor only in the non-carriers group.

Conclusions. Long-term prognosis of women affected by truly idiopathic DCM is more favorable than men. Noticeably, when a genetic mutation is found, a protective effect of female sex is missing. Awareness of sex differences is important as a first step of clinical evaluation. However, in the era of precision medicine, all the efforts should be directed to identify the underlying causes of the disease.

A441: SEX-SPECIFIC PROGNOSTIC IMPLICATION IN DCM AFTER LEFT VENTRICULAR REVERSE REMODELING

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Background. Women affected by dilated cardiomyopathy (DCM) experience better outcomes compared to men. Whether a more

pronounced left ventricular reverse remodelling (LVRR) might explain this is still unknown.

Aim. Investigating the relationship between LVRR and sex and its long-term outcomes.

Methods. A cohort of 605 DCM patients with available follow-up data was consecutively enrolled. LVRR was defined, at 24-month follow-up evaluation, as an increase in left ventricular ejection fraction (LVEF) $\geq 10\%$ or a LVEF $>50\%$ and a decrease $\geq 10\%$ in indexed left ventricular end-diastolic diameter (LVEDDi) or an LVEDDi ≤ 33 mm/m². Outcome measures were a composite of all-cause mortality/heart transplantation (HTx) or ventricular assist device (VAD) and a composite of sudden cardiac death (SCD) or major ventricular arrhythmias (MVA).

Results. 181 patients (30%) experienced LVRR. The cumulative incidence of LVRR at 24-months evaluation was comparable between sexes (33% vs 29%; p=0.26). During a median follow-up of 149 months, women experiencing LVRR had the lowest rate of main outcome measure (global p=0.03) with a 71% relative risk reduction compared to men with LVRR without significant difference between women without LVRR and males. A trend towards the same results was found regarding SCD/MVA (global p=0.06). Applying a multi-state model, male sex emerged as an independent adverse prognostic factor even after LVRR completion.

Conclusions. Although the rate of LVRR was comparable between sexes, females experiencing LVRR showed the best outcomes in the long term follow-up compared to males and females without LVRR. Further studies are advocated to explain this difference in outcomes between sexes.

A442: CARDIOVASCULAR MAGNETIC RESONANCE CHARACTERIZATION OF ALCOHOL-INDUCED DCM.

A MULTICENTRE STUDY

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Background. Alcoholic cardiomyopathy (ACM) is part of the non-ischaemic dilated cardiomyopathy (NI-DCM) spectrum. Little is known about cardiovascular magnetic resonance (CMR) features in ACM patients. The aim of this study is to describe CMR findings and their prognostic impact in ACM patients.

Methods. Consecutive ACM patients evaluated in five referral CMR centres from January 2005 to December 2018 were enrolled. CMR findings and their prognostic value were compared to idiopathic NI-DCM (iNI-DCM) patients. The main outcome was a composite of death/heart transplantation/life-threatening arrhythmias.

Results. Overall 114 patients (52 with ACM and 62 with iNI-DCM) were included. ACM patients were more often males compared to iNI-DCM (90% vs 64%, p ≤ 0.001) and were characterized by a more pronounced biventricular adverse remodelling than iNI-DCM, i.e. lower LVEF (31 \pm 12% vs 38 \pm 11%, p=0.001) and larger left ventricular end-diastolic volume (116 \pm 40 ml/m² vs 67 \pm 20 ml/m², p<0.001). Similarly to iNI-DCM, late gadolinium enhancement (LGE), mainly midwall, was present in more than 40% of ACM patients but, conversely, it was not associated with adverse outcome (p=0.15). LGE localization was prevalently septal (87%) in ACM vs lateral in iNI-DCM (p<0.05). Over a median follow-up of 42 months [interquartile range 24-68], adverse outcomes were similar in both groups (p=0.67).

Conclusions. ACM represents a specific phenotype of NI-DCM, with severe morpho-functional features at the onset, but similar long-term outcomes compared to iNI-DCM. Despite the presence and pattern of distribution of LGE was comparable, ACM and iNI-DCM showed a different LGE localization, mostly septal in ACM and lateral in iNI-DCM, with different prognostic impact.

A443: ARRHYTHMOGENIC DILATED CARDIOMYOPATHY: PREVALENCE, CLINICAL CHARACTERIZATION AND CLINICAL-INSTRUMENTAL GENOTYPIC CORRELATION

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Background. In patients with DCM, ventricular arrhythmias may occur in the absence of signs and symptoms of overt heart failure and may not be related to the severity of left ventricular (LV) dysfunction, so that

"arrhythmogenic dilated cardiomyopathy" (AR-DCM) is emerging as a new nosological entity; however the prevalence, clinical-instrumental correlation and genotypic characterization of this pathology are still to be determined.

Objectives. In the present analysis, we sought to describe the genetic landscape and to provide genotype-phenotype insight in a large cohort of AR-DCM patients.

Methods. We analyzed 461 patients with a DCM diagnosis and all genotyped using Next Generation Sequencing technique. The AR-DCM phenotype was identified, according to literature data, whether was found positivity to one of the following criteria: history of likely cardiogenic syncope, 24-hour Holter ECG documentation of ≥ 1 non-sustained ventricular tachycardia or ≥ 1000 premature ventricular contractions or ≥ 50 couplets, or experience of sudden cardiac death (SCD) or major ventricular arrhythmia (MVA), in stable NYHA class I-III patients. We grouped the patients who tested positive for AR-DCM criteria into "early" AR-DCM and "late" AR-DCM based on whether there was evidence of diagnostic criteria within or past 12 months from enrollment. Patients with a positive genotype for pathogenic or probably pathogenic variants were divided according to the same gene ontology in the following functional genetic clusters: motor sarcomeric genes, structural cytoskeleton-Z disk genes, desmosomal genes, TTN, LMNA, FLNC, RBM20 and other genes.

Results. Within the 461 patients, 364 (79%) tested positive for the AR-DCM phenotype criteria (57% early AR-DCM, 22% late AR-DCM).

168 patients (36%) out of the 461 reported a positive genotype; of these, 139 (83%) were positive for the AR-DCM criteria (109 [78%] early AR-DCM and 30 [22%] late AR-DCM). Among the genetic landscape: TTN mutations resulted prevalent in all groups (39% of the entire cohort and, respectively: 34%, 53, 41% of early AR-DCM, late AR-DCM and non-AR-DCM with positive genotype, $p=0.059$), followed by mutations in the FLNC (17% of the total and respectively: 21%, 10%, 10% of early AR-DCM, late and non-AR-DCM Global $p=0.2$) and mutations of sarcomeric genes (16%; and 7,30%, 34% of early, late and non-AR-DCM, $p_{Global} < 0.001$, $p_{value\ Early\ vs\ Late\ AR-DCM} = 0.002$). Desmosomal gene mutations were found only in early AR-DCM and LMNA were rarely found in late AR-DCM. Among those 168 patients with positive genotype, mutations in FLNC, desmosomal, and LMNA genes characterized 23%, 17% and 17% of early AR-DCM respectively who experienced SCD/MVA, while they were absent in late AR-DCM; in contrast, mutations of sarcomeric genes were present in 6% of early AR-DCM vs. 57% of the late AR-DCM that developed SCD / MVA ($p < 0.003$). Mutations in FLNC genes were associated with an increased risk of developing the AR-DCM phenotype within one year (OR 2.36 $p=0.08$). Finally, sarcomeric mutations were found in 40% and 33% of late and non-AR-DCM (respectively) with positive genotype that experienced death from heart failure, heart transplant or left ventricular assist device implantation for refractory heart failure [DHF / HTx / LVAD] ($p < 0.003$), against 7% of early AR-DCM.

Conclusion. In this large and well characterized population of DCM patients, the AR-DCM forms constituted a consistent proportion. The early AR-DCM group emerged as a specific entity, representing >50% both of genetic and non-genetic DCM. Conversely, late AR-DCM and non AR-DCM forms appeared to share a similar phenotype. By a genetic standpoint, TTN mutation were confirmed as the most frequent cause of AR-DCM and non AR-DCM. Specifically, LMNA, FLNC, Desmosome genes mutation characterized early AR-DCM and motor sarcomeric genes mutation emerged typical of late and non AR-DCM forms.

A444: GLOBAL LONGITUDINAL STRAIN IS ASSOCIATED WITH MORTALITY IN PATIENTS WITH NON-ISCHEMIC CARDIOMYOPATHY AND RECOVERED LEFT VENTRICULAR EJECTION FRACTION

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Objectives. Test the hypothesis that global longitudinal strain (GLS), assessed by speckle tracking echocardiography, is associated with mortality in patients with non-ischemic cardiomyopathy (NICM) and recovered left ventricular ejection fraction (LVEF).

Background. Patients with NICM may experience a normalization in LVEF. Although this correlates with improved prognosis, it does not correspond with a normalization in the risk of death during follow-up. Currently, there are no tools to risk stratify this patient population.

Methods. We designed a retrospective, international, longitudinal cohort study enrolling NICM patients with echocardiographic evidence of LVEF <40% improved to the normal range (>50%). We studied the relationship between absolute GLS (aGLS) measured at the time of the first recording of a normalized LVEF and all-cause mortality during follow-up. Based on current literature, we identified aGLS >18% as normal and aGLS $\geq 16\%$ as of potential prognostic value.

Results. 206 patients met inclusion criteria. Median age was 53.5 years (IQR: 44.3, 62.8) and 56.6% were males. LVEF at diagnosis was 32.0%,

(IQR: 24.0-38.8). Follow-up LVEF at the time of recovery was 55.0% (IQR: 51.7-60.0). aGLS at the time of LVEF recovery was $13.6 \pm 3.9\%$. 166 (80%) and 141 (68%) patients had aGLS $\leq 18\%$ and $< 16\%$, respectively. At a mean follow-up of 5.5 ± 2.8 years, 35 patients (17%) had died. After adjusting for country of enrollment and LVEF at the time of recovery, aGLS at the time of LVEF recovery was associated with mortality (HR 0.9, 95% CI 0.81-0.99, $p=0.04$). No deaths were observed in patients with recovered aGLS (>18%). In Kaplan-Meier survival analysis, aGLS <16% was associated with increased mortality during follow-up (HR 3.2, 95% CI 1.1-9.0, $p=0.03$).

Conclusions. In patients with NICM and normalized LVEF, an impaired GLS at the time of LVEF recovery is frequent and strongly associated with increased mortality during follow-up.

A445: COMBINED EFFECT OF MEDITERRANEAN DIET AND AEROBIC EXERCISE ON WEIGHT LOSS AND CLINICAL STATUS IN OBESE SYMPTOMATIC PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY

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Objectives. Obesity is an important comorbidity in patients with hypertrophic cardiomyopathy (HCM), and it has been associated with adverse outcomes. We aimed to evaluate the impact of weight loss (WL), on a Mediterranean diet and a mild-to-moderate intensity aerobic exercise program, on clinical status of obese, symptomatic patients with HCM.

Methods. We studied 20 consecutive patients (45.3 \pm 12.1 years; 65% males) with HCM and body mass index (BMI) >30 kg/m². All patients underwent a focused 2-years WL program, including Mediterranean diet and aerobic exercise protocol. WL groups were divided as follows: <10%WL or weight gain (non-responders), $\geq 10\%$ WL (responders).

Results. Compared to non-responders (n=15), responders (n=5) showed a significant reduction of LA antero-posterior (AP) diameter (-4.8 ± 4.3 vs. -0.3 ± 2.2 mm; $p=0.006$), LAVI (-7.0 ± 3.8 vs. -0.6 ± 2.8 ml/m²; $p<0.001$), E/E' average (-3.8 ± 2.9 vs. 0.0 ± 2.6 ; $p=0.014$), pulmonary artery systolic pressure (PASP) (-8.6 ± 7.6 vs. -0.8 ± 3.5 mmHg; $p=0.005$), and a significant increase in $VO_2\max(\%)$ ($+7.4 \pm 2.4\%$ vs. $+1.1 \pm 5.0\%$; $p=0.015$) and peak workload ($+22.6 \pm 12.8$ vs. $+5.3 \pm 5.0$ Watts; $p<0.001$). At multivariate analysis, BMI changes from baseline correlated with reduction in LA AP diameter (beta 0.66; $p=0.005$), LAVI (beta 0.83; $p=0.001$), E/E' average (beta 0.79; $p=0.001$), PASP (beta 0.77; $p<0.001$), and increase of $VO_2\max(\text{mL/kg/min})$ (beta -0.53; $p=0.033$), $VO_2\max(\%)$ (beta -0.68; $p=0.005$), peak workload (beta -0.65; $p=0.030$). Out of 3 patients being considered for myectomy and 3 for heart transplant, 2 and 1, respectively, showed significant improvement of clinical-hemodynamic status, and did not require cardiac surgery.

Conclusions. In obese, symptomatic patients with HCM, WL by a combined protocol of Mediterranean diet and aerobic exercise showed markedly favorable effects on LA remodeling, diastolic function, exercise capacity and clinical status.

A446: PEAK ATRIAL LONGITUDINAL STRAIN AS A PREDICTOR OF CARDIOVASCULAR EVENTS IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY

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Introduzione. La cardiomiopatia ipertrofica si associa ad una elevata incidenza di eventi avversi cardiovascolari (aritmie, scompenso cardiaco, morte). Obiettivo del nostro studio è stato valutare il ruolo predittivo di alcuni parametri ecocardiografici (in particolare lo strain di picco longitudinale dell'atrio sinistro-PALS) e di alcuni parametri alla risonanza magnetica cardiaca (quale estensione del delayed enhancement-DE).

Metodi. Abbiamo arruolato 165 pazienti (64 M, 79 F), età media (54,33 ±15,95) con cardiomiopatia ipertrofica (ostruttiva in 44 pazienti e non ostruttiva in 121 pazienti). Ai pazienti è stato effettuato un ecocardiogramma Color-Doppler con valutazione degli indici di deformazione miocardica (GLS del ventricolo sinistro, PALS), una risonanza magnetica cardiaca con valutazione dell'estensione del DE. Dopo un periodo medio di 2,5 anni sono stati valutati gli eventi avversi cardiovascolari: trapianto cardiaco, numero shock dell'ICD e aritmie ventricolari, scompenso cardiaco, morte, ospedalizzazioni per cause cardiovascolari, aritmie sopraventricolari, trapianto cardiaco.

Risultati. Sono stati registrati i seguenti eventi avversi: 7 pazienti sono stati sottoposti a trapianto cardiaco, 8 sono morti, 29 pazienti hanno sviluppato fibrillazione atriale, 6 pazienti aritmie ventricolari e/o shock ICD, 17 pazienti sono stati ospedalizzati, 16 pazienti hanno sviluppato scompenso cardiaco. I pazienti che andavano incontro a morte presentavano rispetto ai pazienti senza eventi: valori significativamente più bassi di PALS (PALS $4,6 \pm 2,6$ vs $17,5 \pm 3,26$, p -value $<0,0001$) e valori più elevati di volume atriale sinistro- vol asx (179 ± 81 vs 76 ± 37 , p -value $<0,001$); estensione del DE significativamente maggiore (57 ± 20 vs 17 ± 19 , $p=0,0082$), valori significativamente più bassi di GLS (10 ± 3 vs 15 ± 4 , $p=0,0033$) e FE ($p=0,0001$). I pazienti che svilupparono aritmie ventricolari invece non presentavano variazioni significative della FE ($p=0,26$), del vol asx (90 ± 17 , $p=0,36$) e PALS (18 ± 1 , $p=0,7$), ma presentavano valori significativamente più bassi di GLS ($5,7 \pm 12$, $p=0,02$) e una maggiore estensione del DE ($p=0,04$). Nei pazienti con fibrillazione atriale invece il vol asx aumentava significativamente (100 ± 43 , $p=0,0034$) e il PALS ($10,8 \pm 5,9$, $p<0,0001$) era significativamente ridotto rispetto ai pazienti senza eventi; FE, GLS ($-11,8 \pm 8$, $p=0,08$) e DE non erano significativamente ridotti ($14,8 \pm 8$, $p=0,14$). Nei pazienti che svilupparono scompenso cardiaco invece sia la FE, GLS ($p=0,035$), vol asx e PALS ($p<0,0001$) e DE ($65 \pm 22,5$, $p<0,0001$) erano significativamente alterati rispetto ai pazienti senza eventi.

Conclusioni. Nei pazienti con cardiomiopatia ipertrofica lo strain atriale così come il volume atriale sinistro sembrano essere importanti fattori prognostici insieme alla FE, GLS ed estensione del DE. In particolare il PALS e volume atriale sinistro sono predittivi di morte, scompenso cardiaco oltre che di fibrillazione atriale. Lo strain atriale rappresenta un utile parametro aggiuntivo nella stratificazione prognostica dei pazienti con cardiomiopatia ipertrofica.

A447: AN EASTER EGG: A RIGHT VENTRICULAR MYXOMA CONCEALED WITHIN A THROMBUS IN A PATIENT WITH A CROHN'S DISEASE RELAPSE

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Introduction. Cardiac masses often pose great challenges of differential diagnosis and characterization with non-invasive imaging for subsequent medical or surgical management. We here report on a peculiar case of a right ventricle mass with unusual localization and misleading features posing unique diagnostic challenges.

Case summary. A 26-year-old woman presented to the Emergency Department complaining of diarrhea and abdominal pain. She had a history of Crohn's disease, previous i.v. and inhaled drug abuse and a recent miscarriage. The physical examination was unremarkable except for a lower abdomen tenderness. An abdominal computed tomography (CT) imaging indicated the presence of portal and superior mesenteric vein thrombosis, prompting the beginning of s.c. low-molecular weight heparin therapy. Thoracic CT scans, however, also revealed a hypodense right ventricular mass. An echocardiogram then documented a firm, isoechoic mass adherent to the RV free wall. Cardiac magnetic resonance imaging (MRI) confirmed the presence of a 20x24x17 mm right ventricular mass adherent to the moderator band and apparently trapped among papillary muscles insertions and trabeculae. T1 and T2-STIR MRI sequences featured the presence of a hypointense central core surrounded by a hypointense margin. There was no significant enhancement after gadolinium administration at 3 and 5 minutes, with minimum enhancement at 10 minutes. Because of the concomitant presence of atypical location vein thrombosis, a right ventricular thrombus was suspected. Acquired or congenital thrombophilia screening was negative. After a 48-h course of therapeutic enoxaparin, the patient was shifted to unfractionated heparin infusion since no changes in the right ventricular mass size could be documented. UFH was then continued for 14 days with repeated echocardiography examinations documenting no significant changes in mass size, with complete dissolution of the mesenteric and portal vein thrombosis. Given the high embolic risk and the ineffective medical therapy the patient underwent surgical removal via median sternotomy and cardiopulmonary bypass. Postoperative recovery was

uneventful. Pathology examination revealed a small central core of calcitine-positive cardiac myxoma cells surrounded by a thin thrombotic mass.

Conclusion. Right ventricular myxoma is an extremely rare finding. An ineffective antithrombotic therapy after the suspicion of a thrombus should be key to direct diagnosis suspicions in other directions despite the presence of other thromboses. Crohn's disease relapses confer a hypercoagulable state, but in this case the coexistence of two rare occurrences did not allow a correct preoperative diagnosis.

A448: RISK STRATIFICATION OF MYOCARDITIS PATIENTS UNDERGOING VENTRICULAR TACHYCARDIA ABLATION: ROLE OF MYOCARDIAL INFLAMMATION

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Background. Risk stratification of myocarditis patients undergoing ventricular tachycardia (VT) ablation is still unpredictable.

Objective. To describe VT ablation results and identify factors associated with arrhythmia recurrences in a cohort of patients with myocarditis.

Methods. We enrolled 125 consecutive patients with myocarditis, undergoing VT ablation. Before ablation, disease stage was evaluated, to identify active (AM) vs. previous myocarditis (PM). The primary study endpoint was assessment of VT recurrences by 12-month follow-up. Predictors of VT recurrences were retrospectively identified.

Results. All patients (age 51 ± 14 y, 91% males, LVEF $52 \pm 9\%$) had history of myocarditis diagnosed by endomyocardial biopsy (59%) and/or cardiac magnetic resonance (90%). Furthermore, all had multiple episodes of drug-refractory VTs. Multimodal preprocedural staging identified 47 AM (38%) and 78 PM patients (62%). All patients showed low-voltage areas (LVA) at electroanatomical map (97% epicardial or endocardial); of them, 25 (20%) had wide borderzone (WBZ, constituting >50% of the whole LVA). VT recurrences were documented in 25 patients (20%) by 12 months, and in 43 (34%) by last follow-up (median 63 months (IQR 39-87)). At multivariable analysis, AM stage was the only predictor of VT recurrences by 12 months (HR 9.5, 95% CI 2.6-35.3, $p<0,001$), whereas both AM stage and WBZ were associated with arrhythmia recurrences anytime during follow-up. No VT episodes were found after redo ablation performed in 23 patients during PM stage.

Conclusion. Our findings suggest that VT ablation should be avoided during AM, but is often of benefit for recurrent VT after the acute phase of myocarditis.

A449: A CASE OF CONSTRICTIVE PERICARDITIS IN THE PRECISION MEDICINE ERA

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A 73-year-old man without known cardiovascular risk factors was admitted in October 2019 at our Cardiology Ward for fatigue and breathlessness with the echocardiographic suspect of constrictive pericarditis. He had been in hematological follow-up for splenomegaly and monocytosis since 2011. In 2017 he had undergone left pleurodesis for a pleuritis non responsive to pharmacological or invasive treatment. He was also showing relapsing eyelid and thorax xanthelasma after surgery removal despite low LDL levels without being on a lipid-lowering therapy.

At admission, EKG revealed sinus tachycardia, while a chest X-Ray showed right pleural effusion. Blood tests showed anaemia, thrombocytopenia, kidney failure and signs of inflammation.

During the hospital stay, diuretic treatment was started with immediate symptoms relief. Cardiac catheterization showed increased right atrial pressure, with an M/W wave pattern on the pressure curve, dip and plateau pattern in left and right ventricles and end-diastolic pressure equalization in all four cardiac chambers. Cardiac magnetic resonance showed abnormal septal motion and increased ventricular interdependence. Pericardial thickening with nodular lesions was also observed with hyperaemia and oedema in T2-weighted sequences after contrast administration.

Taken together, these aspects further strengthened the hypothesis of constrictive pericarditis. Given the MR findings and multiorgan involvement we suspected a secondary form of pericarditis due to a systemic disease: clinical and instrumental features raised the suspicion of Erdheim Chester Disease (ECD), a rare form of non-Langerhans cell histiocytosis. We performed femoral X-ray and MR scan, which confirmed the presence of proximal metaphysis and diaphysis osteosclerosis, a common feature of ECD. However, the whole-body scintigraphy scan with ^{99m}Tc was negative, and the total-body PET/CT only showed diffuse and intense bone marrow glucose uptake, a finding consistent with a

myeloproliferative disease but not with ECD, which often shows cortical bone uptake. Bone marrow biopsy showed a pattern consistent with chronic myelomonocytic leukemia (CMML), a rare myeloproliferative disorder.

Despite these findings, ECD was still suspected and a skin biopsy from eyelid xanthelasma was performed. The histological and immunophenotype findings were consistent with ECD (CD 68+, CD163+, S100- and CD1a-) and the genetic analysis showed a K-Ras mutation. Consequently, a diagnosis of ECD with concomitant CMML was made. Corticosteroid therapy was then started with an improvement of clinical conditions and radiological findings. We observed the complete resolution of symptoms and the total regression of pleural effusion at the chest x-ray at the three-month follow-up. Cardiac MR showed a complete resolution of pericardial effusion and the disappearance of the nodular lesions without evidence of inflammation in T2-weighted sequences without signs of constrictive pericarditis at 6-month follow-up. Cutaneous lesions showed a progressive reduction with complete resolution after ten months of medical therapy.

Our clinical case demonstrates the importance of precision medicine in the modern era: thanks to a specific diagnosis, a pattern of constrictive pericarditis caused by an inflammatory disease was treated with medical therapy alone, avoiding unnecessary high risk cardiac surgery.

A450: DIAGNOSTIC ECHOCARDIOGRAPHIC MASS SCORE: A MODEL TO PREDICT THE NATURE OF THE CARDIAC MASS

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Background. Cardiac masses (CM) represent a rare and heterogeneous group including benign masses (primary tumors and pseudotumors) and malignant ones (primitive tumors and more frequently metastasis). 2D echocardiography plays a critical role in the diagnosis and the management of CM.

Purpose. To evaluate the diagnostic accuracy of echocardiography, identify the echocardiographic predictors of malignancy and create a multiparametric echocardiographic score capable of suspecting the malignant nature of the mass.

Materials and methods. We evaluated 352 patients, 243 retrospectively and 109 prospectively, referred to our Cardiology Department for suspected CM between 2000 and 2017. In 264 patients, a definitive diagnosis was obtained with histologic examination. In cases of cardiac thrombi, the radiological evidence of thrombus resolution after adequate anticoagulant treatment was considered diagnostic. Normal anatomical variants in pseudotumor group were excluded due to the impossibility of obtaining histological examination. The echo score is between 0 and 9 based on the presence of following parameters: mass diameter >4 cm, irregular margins, non-adhered to interatrial septum, dishomogeneous mass and extension.

Results. In 13 of the 352 patients, a poor acoustic window did not allow an optimal examination and 75 with no histological examination patients were excluded. In the remaining 264 patients, classical 2-D echocardiogram identified 246 masses with a diagnostic accuracy of 73.1%. Benign CM were predominantly localized in left chambers (p<0.001), involving valvular apparatus (p<0.001) and were more frequently pedunculated (p=0.001), mobile (p=0.001) and adhered to interatrial septum (p<0.001). Malignant tumors were instead more isoechoic (p=0.014), dishomogeneous (p<0.001), sessile (p<0.001) and tend to infiltrate the structures (p<0.001). They were associated with pericardial effusion (p<0.001) and showed a greater diameter (p<0.001), extension (p<0.001), irregular margins (p<0.001) and multilobated aspect (p<0.001) compared to the benign masses. Considering these characteristics, echo score was created to predict the nature of the mass. A score ≥ 4 points corresponded to a higher risk of malignancy whereas a score <2 points indicated a lower risk.

Conclusions. 2D echocardiography provides a high diagnostic accuracy in identifying cardiac masses and our multiparametric echocardiographic score could be useful to predict the benign or malignant nature of these ones even if second level instrumental examinations were often required.

A451: SYNCOPE AND ACUTE KIDNEY FAILURE AS FIRST PRESENTATION OF FABRY DISEASE: A MULTIORGAN DISEASE

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Anderson-Fabry disease (FD) is a rare X-linked lysosomal storage disease caused by mutations in the alpha-galactosidase A (GLA) gene, resulting in an inability to catabolize lipids with a-galactosyl terminal residues, mainly GB3, with progressive accumulation of these products within different cells, leading to Zebroid bodies deposits and cellular

dysfunction. FD incidence is 1:117.000 and is higher in patients with end stage renal disease (ESRD). Males are more severely affected; heterozygous females with lyonization can also develop severe forms. FD is a multi-systemic disease with a wide clinical spectrum, that ranges from angiokeratomas, hypo or hyperhidrosis, achroparesthesia, "Fabry crises", proteinuria, ESRD, HCM, arrhythmias, myocardial infarction, stroke, cochleovestibular disorders, GI disorders, obstructive pulmonary disease, asthenia. There is a classic variant of FD with total loss of activity of GLA and an atypical variant with partial residual GLA enzyme function, characterized by later onset and milder symptoms. In the classical form, renal, cardiac and cerebrovascular complications usually appear after the 2nd decade of life. FD is suspected in case of low alpha-GLA enzyme activity, is confirmed by genetic testing - and when a variant of uncertain significance is detected by a biopsy of an affected organ. Enzyme replacement therapy (ERT) is based on recombinant human GLA; a pharmacological chaperone has also been approved in monotherapy.

Case report. A 46-year-old man presented to our ER for asthenia, dysphagia, loss of weight and recent syncope. His maternal uncle was affected by CKD. Physical examination was unremarkable, except for upper limbs tremor, slowed speech and temporal disorientation. BP was 195/100 mmHg. The ECG showed SR at 88 bpm, normal AV conduction and LBBB. Blood tests documented anemia and severe AKI, treated with blood transfusions and an emergency dialytic session, complicated by 2:1 AV block and complete AV block with LBBB, that required temporary PMK implantation. The TTE showed preserved EF with severe LV hypertrophy involving also the RV with ground glass aspect of the IVS. TB CT scan documented cerebral hypodense areas, pulmonary hyperdense pseudonodular areas, iliac bone hypodense areas. A 24-h Holter ECG showed SR, enlarged QRS, rare PVC and PAC. The genetic test resulted negative for Gaucher disease and positive for Anderson Fabry disease (hemizygous mutation in exon 4 of GLA gene c.548G>C), with a depressed production of alphaGLA and accumulation of lyso-Gb3. Peri-umbilical fat biopsy for Amyloid disease was negative. Renal echography documented cortical hyperechogenicity, kidneys volume reduction, diffuse perirenal edema; renal biopsy showed ESRD secondary to glycosphingolipid storage disease ceramid type. Brain MRI-T2 revealed white matter hyperintense confluent areas. Heart MRI confirmed LV myocardial circumferential hypertrophy and myocardial hypointensity area in the Fast Spin Echo sequences. He underwent dialytic sessions, with improvement of renal function, and was later addressed to a reference center to start ERT.

Discussion. FD diagnosis is often delayed due to subtle clinical signs. Our patient had a late onset of FD with the typical manifestations of cardiac and renal involvement, associated with cerebral and gastrointestinal dysfunctions. Differential diagnosis of a young male with AKI and family history of kidney disease must include FD; in case of AKI with cardiac symptoms of uncertain cause, a cardiologic evaluation with an echocardiogram may be helpful in the diagnostic evaluation.

A452: LE ETEROGENEE MANIFESTAZIONI DELLA MALATTIA DI FABRY: SOLO IPERTROFIA VENTRICOLARE SINISTRA?

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Introduzione. La malattia di Anderson-Fabry è causata da un deficit dell'attività lisosomiale dell'alfa-galattosidasi A, responsabile della degradazione del globotriaosylceramide, il cui progressivo accumulo tissutale porta al danno d'organo. Le manifestazioni cliniche sono estremamente eterogenee sia per la modalità di trasmissione che per il progressivo accumulo.

Case report. Un paziente di 37 anni giunge alla nostra osservazione per riscontro di ipertrofia ventricolare sinistra. In anamnesi presentava canale atrio-ventricolare sottoposta correzione cardiocirurgica con patch di pericardio e valvuloplastica in età pediatrica. Inoltre riferisce due episodi di TIA di cui l'ultimo manifestatosi con afasia motoria e ipostenia marcata all'emilato sinistro, al controllo TC non evidenza di lesioni in atto, per cui veniva dimesso in terapia con Warfarin. Al controllo ecocardiografico evidenza di ipertrofia concentrica con spessore parietale massimo di circa 13 mm. Alla risonanza magnetica cardiaca evidenza di severa ipertrofia concentrica e presenza di area di fibrosi miocardica in sede infero-laterale del ventricolo sinistro con valori di T1 ridotti. Posto il sospetto di malattia di Anderson-Fabry viene praticata analisi genetica che conferma la presenza della mutazione

patogenica nel gene GLA p.R356W. Il paziente comincia terapia chaperonica per os, con stabilizzazione del quadro clinico neurologico e cardiologico. In seguito allo screening familiare, tale mutazione viene confermata nelle due sorelle del probando e nella madre (dosaggio LysoGb3 nella sorella maggiore: 2.04 nMol/l, nella madre: 1.78 nMol/l; v.n. <2.3 nMol/l). L'unica a manifestare sintomi è la sorella minore del probando (dosaggio LysoGb3 2.67 nMol/l) che ha presentato due episodi di TIA.

Discussione. L'analisi molecolare e clinica di tale famiglia ha evidenziato un esordio precoce e invalidante nel probando, mentre per il fenotipo femminile il quadro clinico è estremamente variabile, in linea con la letteratura; tuttavia il nostro caso dimostra che l'esordio precoce può essere presente anche nel sesso femminile.

A453: VATTR AMYLOIDOSIS AND ICD THERAPY, A CASE REPORT

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(a) LAZIO; (b) POLICLINICO TOR VERGATA

Transthyretin-related amyloidosis (ATTR) is a type of systemic amyloidosis characterised by extracellular deposition of amyloid fibrils composed of transthyretin (TTR) protein. It includes an acquired form, the so-called "wild type", the "variant" form due to a dominant autosomal inherited mutation and the acquired form after domino liver transplantation. Because of the variability of the clinical manifestations, diagnosis of this condition is challenging; accurate patient's clinical and family history is of great importance. We report the case of a patient affected by variant transthyretin amyloidosis (vATTR) making its first appearance with non-sustained ventricular tachycardia (NSVT) and syncope.

In January 2020, a 72-year-old Caucasian man, was admitted to our hospital for syncope without prodromes. Ten years before he underwent to the implantation of a bicameral Pacemaker (PMK) because of a tri-fascicular block. In the device event's memory, we identified at the time of the syncope, a NSVT. The blood tests reported electrolytes and thyroid hormones in normal range. The man had history of psychiatric disorder regarding sexual sphere and twenty years before he executed endovascular embolization of intracranial arteriovenous malformation. He referred a familiarity for neurological disorders and one of his brothers underwent the implantation of a PMK few years before because of a high grade atrio-ventricular block. The patient suffered of dyspepsia, nausea and constipation. We performed an echocardiography study which showed normal left ventricle ejection fraction (LVEF), moderate increase of LV thickness with granular sparkling pattern, apical sparing of longitudinal strain diastolic dysfunction without relevant valvular diseases. The patient underwent to a coronary angiography but no atheromatic lesions were found. Based on echocardiographic characteristics and clinical and family history, we suspected systemic amyloidosis. Blood tests showed absence of monoclonal protein and bone scintigraphy with PYP revealed grade 3 of Perugini score, compatible with ATTR. We performed a rapid genetic test for vATTR using a buccal test which ascertains TTR variant c.148G>A p.Val50Met. In consideration of the tendency of the patient to develop symptomatic NSVT, we performed device upgrading to cardiac resynchronization therapy-defibrillator (CRT-D) and the family received genetic counselling. Cardiological and neurological follow-up was administered.

Patients with amyloidosis that develop heart failure (HF) symptoms have a median survival of less than one year; this seems to be correlated with NSVT, so it could predict implantable cardioverter-defibrillator (ICD) therapy. Sartiani et Al. demonstrated that in addition to the genesis of the deposits of amyloid which create a barrier to the diffusion of micronutrients and electrical impulses in the myocardium, there could be a direct cytotoxic damage by the fibrils themselves through a receptor-mediated calcium intracellular release with an alteration of the myocyte membrane potential. The growing availability of easy runnable genetic test for identifying ATTR is increasing the number of diagnosis, even in asymptomatic patients. For this reason, identification of patients that could benefit from ICD implantation and the correct timing of intervention are very important, even in order to prevent overtreatment. More studies are needed for the prognosis and therapy of this rare and challenging disease.

A454: A CASE OF PERIPARTUM CARDIOMYOPATHY: WHEN THERE IS NO RECOVERY

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Introduction. Peripartum cardiomyopathy (PPCM) is defined as an idiopathic cardiomyopathy occurring towards the end of pregnancy or in the months following delivery, abortion or miscarriage, without other

causes for heart failure (HF), and with reduced left ventricular ejection fraction (LVEF<45%). The incidence of PPCM has been assessed as 1 in 2,230 births in the United States and as 1 in 1,000 births worldwide. Africans and African Americans are subject to higher risk for the development of PPCM. The prognosis varies from full recovery to persistent reduction of LVEF and to death. Reduced LVEF and fractional shortening are predictors of worse clinical outcome. The recovery can occur after 6 months but in some cases, it may require several years. Given the teratogenic effects of some drugs, the treatment of this condition depends on the status of the patient (pregnancy or not) and it is based on current Guidelines of acute and chronic HF. In literature there is no evidence that the treatment should be guided only by LVEF; the timing of the implantable cardioverter defibrillator (ICD) implant for the prevention of sudden death and of the heart transplant is equally uncertain. Current evidence suggests that ICD implantation should be performed if LVEF does not improve within six months. Therefore, re-assessment of cardiac function with echocardiography is recommended every six-months. Outcomes with heart transplantation in PPCM are worse than in other causes of HF, so delaying heart transplantation as long as possible is essential. We present a case of an African woman suffering from PPCM since 2001, with no recovery of the LVEF, developing refractory HF and heart transplantation indication.

Case report. In May 2020, a 47-year-old African woman affected by PPCM with reduced LVEF since 2001, was admitted to the ER for appendicitis. The patient did not regularly control her clinical status and she had not adherence to medical therapy. Therefore, appendectomy was performed, but during the hospitalization she developed peripheral oedema and dyspnoea. The ECG showed sinus rhythm at 100 bpm with negative T waves. She was transferred to the Cardiology Department where she underwent an echocardiography that showed severe reduction of cardiac global function (LVEF 20%), severe mitral regurgitation and moderate tricuspid regurgitation. She was treated with diuretic, beta-blocker, angiotensin-converting-enzyme inhibitor and mineralocorticoid receptor antagonist with improvement of symptoms and clinical status. Therapy with angiotensin receptor neprilysin inhibitor was contraindicated due to a critical hypotension. Her clinical condition gradually improved during the hospitalization. ICD implantation was performed in primary prevention of sudden cardiac death and she was addressed to the referral heart transplant center.

Conclusions. Improvement of LVEF occurs approximately in 50-70% of women subject to standard medical therapy for HF with reduced LVEF. African American women are more likely to have a worse prognosis of PPCM and they have a lower chance to recover despite an apparently optimal medical therapy. It appears fundamental to establish regular follow-ups, particularly in these cluster of patients, and it is essential to test their adherence to treatment in order to evaluate the best timing for each invasive treatment strategy.

A455: LONG-TERM SURVIVAL IN PATIENTS WITH CARDIAC AMYLOIDOSIS: A MULTICENTRE STUDY

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Background and aims. Cardiac amyloidosis (CA) is usually characterized by a poor outcome in the short-term; clinical and echocardiographic features are heterogeneous and could identify patients with different prognosis. The aim of our study is to describe patients with long survival and to assess predictors of better outcome.

Materials and methods. 344 patients with CA (170 patients with AL, 100 with wild type transthyretin (wtTTR) and 74 with mutated transthyretin (mTTR) amyloidosis) were evaluated between 2003 and 2019 at 2 specialized Italian tertiary centres (Rome and Florence). Patients with a follow-up longer than 60 months (long survival, LS) and less of 12 months (non-long survival, non-LS) were included in the study and analysed. Each patient underwent clinical, and echocardiographic evaluation.

Results. LS patients were 44 (12.7%) and had a mean follow-up of 7.8 ± 2.7 years; while non-LS were 32 and had a mean follow-up of 0.5 ± 0.2 years. Patients with LS were younger at diagnosis (LS 63.9 ± 11 years vs non-LS 69.1 ± 12 years, p=0.06) and predominantly had TTR-CA (29/44 (65%), specifically, 19 mTTR and 10 wtTTR), while non-LS patients more frequently had CA-AL (23/32, 72%, p=0.00). LS patients at baseline, compared to non-LS patients, showed a lower NYHA class (NYHA class I or II, 89% vs 19%, p=0.00), less frequently had atrial fibrillation (18% vs 31%, p=0.2); had significantly lower levels of troponin I and NT-proBNP (0.03 ng/ml and 1729 pg/ml vs 0.15 and 7180 pg/ml, p=0.00 and p=0.08); similar left ventricle ejection fraction (LVEF, 53 vs 52%, p=0.5); smaller left atrial diameter (42.8 ± 6 vs 46.1 ± 7 mm, p=0.07); less frequently had advanced diastolic dysfunction (restrictive pattern, 29 vs 55%, p=0.04) and right ventricle dysfunction

(TAPSE, 18.8 ± 4 vs 15.5 ± 4 mm, $p=0.05$). In all subgroups, at multivariate analysis NYHA class I or II at baseline resulted to be an independent predictor of LS. In AL-CA LVEF and in TTR-CA right ventricle function were also independently associated to LS.

Conclusions. A not so small percentage of patients with CA have a long-term survival. CA-TTR patients more frequently are LS compared to AL patients. NYHA functional class I or II resulted to be the best predictor of LS.

A456: LEVOSIMENDAN ADMINISTRATION DURING THE ACUTE PHASE OF TAKOTSUBO SYNDROME: A PROPENSITY SCORE MATCHED ANALYSIS

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Background. Acute heart failure (AHF) is one of the most common complication related to takotsubo syndrome (TTS) hospitalization. Levosimendan is a non-catecholamine inotrope that does not increase oxygen consumption and an alternative to catecholamines that are contraindicated in TTS. Aim of the study is to evaluate safety, feasibility and potential benefits of levosimendan infusion during hospitalization and at long term follow-up (FU) in TTS patients.

Methods. Three hundred and forty consecutive patients with TTS from a multicenter prospective registry were included in the analysis. After a propensity matching for the use of levosimendan, 28 consecutive high-risk TTS patients (as classified by Mayo Clinic AHF score) who were treated with i.v. infusion of levosimendan within the first 24 hours after admission were compared in a 1:2 ratio with 56 patients similar for principal baseline and bias factors not treated with levosimendan. Clinical course, ecg presentation, left ventricular function, mayor cardiac adverse events (MACE) during hospitalization and at FU were recorded.

Results. Compared to the control group, patients treated with levosimendan had non significantly different length of hospitalization (10.5 ± 4.4 vs 8.7 ± 5.6 days $p=0.17$) and rate of in-hospital complication (75 vs 55% $p=0.08$). No differences were found when evaluating left ventricular ejection fraction after 72 hours from hospitalization (38 vs 39% $p=0.85$) and at discharge (51 vs 48% $p=0.18$). No complications related to drug administration and no differences in terms of ventricular arrhythmias between patients treated with levosimendan and not were observed (11% vs 13% $p=0.78$). At long-term (3-year) FU, similar rates of MACE (29 vs 23% $p=0.56$) and death (21 vs 28% $p=0.57$) were found.

Conclusions. Levosimendan infusion during acute phase of TTS is safe and feasible. However, no benefit in term of length of hospitalization and in and out-of-hospital MACE were found.

A457: INCIDENCE AND PROGNOSTIC IMPLICATION OF CANCER AMONG PATIENTS WITH TAKOTSUBO SYNDROME. RESULTS FROM A PROSPECTIVE REGISTRY

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Background. Takotsubo syndrome (TTS) is a transient ventricular systolic dysfunction mimicking an acute myocardial infarction. Although the global mechanisms inducing the syndrome are still partially unknown, in several cases emotional and physical stressors are involved. Cancer is a comorbidity frequently associated with TTS. Aim of the study is to evaluate incidence of cancer and in and out-of-hospital mayor cardiac events (MACE) among TTS patients.

Methods. Three hundred forty consecutive patients with TTS were enrolled in a prospective multicenter registry from four Italian hospitals from September 2007 to October 2019. Clinical features, laboratory data, ECG, echocardiographic parameters and in and out hospital MACE were recorded.

Results. Forty-three patients out of 340 (13.5%) had a diagnosis of cancer at the moment of hospitalization, while three patients received it during follow-up. Five patients had a hematological cancer (11.6%), while all the others had a solid cancer (colon-rectal (20.9%), breast (18.6%), lung (13.9%), bladder (6.9%), and pheochromocytoma (4.6%). Mean hospital stay of cancer patients was 8.2 ± 5.3 days. Twenty patients (43.4%) experienced in-hospital MACE: cardiogenic shock (45%), acute pulmonary oedema (20%) and death (30%). Additional in-hospital complications were ventricular arrhythmias (25%) and endo-ventricular thrombi (20%). At long-term follow-up eighteen patients (39.1%) died with a median of 166 days from the acute event. Three patients were re-hospitalized for cardiovascular events after one year (6.5%) and one patient experienced a recurrence of TTS (2.1%).

Conclusions. TTS patients with cancer have a high rate of in and out of hospital MACE. Strict cardiological follow-up is needed among this subset of patients.

A458: PROGNOSTIC VALUE OF ACUTE MITRAL INSUFFICIENCY AMONG PATIENTS ADMITTED WITH TAKOTSUBO SYNDROME. PRELIMINARY DATA FROM A PROSPECTIVE MULTICENTER REGISTRY

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Background. Takotsubo syndrome (TTS) is an acute and reversible left ventricular dysfunction, whose pathophysiological mechanisms are not completely known. Aim of the study is to evaluate the incidence and prognostic value of acute mitral insufficiency among TTS patients.

Methods. Three hundred sixteen consecutive patients admitted for TTS were enrolled from July 2007 to December 2019 in a prospective registry among four hospitals. Clinical features, laboratory data, ECG and echocardiographic parameters and in-hospital complications were recorded.

Results. Eighty-five (27%) patients, mean age 76 ± 8 years, presented with moderate/severe mitral insufficiency (msMI). Compared to the control group, patients that presented with msMI were older (76 ± 8 vs 71 ± 12 years, $p<0.01$), had lower LVEF ($34 \pm 7\%$ vs $37 \pm 9\%$ $p=0.02$) and experienced higher rate of in-hospital complications (42 vs 32% $p=0.04$). The incidence of in-hospital adverse events was higher in case of both msMI and LVEF $<35\%$ than in one of the two previous conditions or neither (69%, 42%, 23% respectively, $p<0.05$). Differences remained statistically significant even after correction for age and gender in the multivariate analysis. There was a reduction of mitral insufficiency from moderate/severe into mild in 30 out of 87 (34%) pts after 48h from admission and in 52 out of 87 pts at discharge (60%). Left ventricular outflow tract obstruction (LVOTO) was found in 13 out of 87 (15%) pts with msMI at admission and was transient in 11 out of 13 pts (84%). At long-term follow-up (650 days) patients with msMI when compared to those without, experienced higher rate of mayor cardiovascular events (31.7% vs 20% $p=0.03$).

Conclusions. Patients with TTS and moderate/severe mitral insufficiency at admission have an increased risk of in and out-of-hospital mayor cardiac adverse events.

A459: PREVALENCE, INCIDENCE, RISK FACTORS AND PROGNOSTIC SIGNIFICANCE OF PACEMAKER IMPLANTATION IN AMYLOIDOTIC CARDIOMYOPATHY

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(a) POLICLINICO S. ORSOLA-MALPIGHI BOLOGNA, UO DI CARDIOLOGIA, ALMA MATER STUDIURUM BOLOGNA; (b) POLICLINICO S. ORSOLA-MALPIGHI BOLOGNA, UO DI MEDICINA NUCLEARE, ALMA MATER STUDIURUM BOLOGNA; (c) IRCCS ISTITUTO DELLE SCIENZE NEUROLOGICHE BOLOGNA, UOC CLINICA NEUROLOGICA RETE METROPOLITANA NEUROMET, BOLOGNA

Background. Amyloidotic cardiomyopathy (AC) is traditionally associated with increased risk of conduction abnormalities and arrhythmias, although factors related to pacemaker (PM) implantation are not known yet.

Purpose. We aimed to assess prevalence, incidence, risk factors and prognostic significance of PM implantation in light-chain (AL), hereditary transthyretin-related (m-ATTR) and non-mutant transthyretin-related (wt-ATTR) AC.

Methods. Retrospective study of 477 patients from a single (159 AL, 154 m-ATTR, 164 wt-ATTR). Baseline characteristics of patients with or without PM implantation during follow-up were analyzed.

Results. 40 patients had a PM at the time of diagnosis. During a mean follow-up of 4.1 years, 28 patients underwent PM implantation. PM prevalence at baseline was 8.3% (AL 3.7%, m-ATTR 3.3%, wt-ATTR 17.7%) with an incidence rate of 1.8% person-years. Age, wt-ATTR etiology, mean left ventricular (LV) wall thickness, left atrial diameter and QTc interval, low QRS voltage, presence of right bundle branch block (RBBB) in the first electrocardiogram (ECG) were associated with PM implantation. Multivariate analysis identified presence of right bundle branch block ($p=0.008$), mean LV wall thickness ($p=0.02$), and age at diagnosis ($p=0.015$) as independent predictors of PM implantation. There was no significant difference in terms of survival between the two groups.

Conclusions. Cardiac amyloidosis is associated with conduction abnormalities that lead to PM implantation, whose prevalence varies widely according to etiology with a mean value of 8.3% that reaches 17.7% in wt-ATTR cardiomyopathy. RBBB, LV wall thickness and age at the time of diagnosis were the main independent risk factors. Further analysis could identify other predictors of PM implantation and its impact on the prognosis.

A460: ACUTE MYOCARDITIS: PROGNOSTIC ROLE OF SPECKLE TRACKING ECHOCARDIOGRAPHY AND COMPARISON WITH CARDIAC MAGNETIC RESONANCE FEATURES

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Aims. To evaluate myocardial longitudinal deformation in patients affected myocarditis, its association with cardiac magnetic resonance (CMR) parameters, and its predictive value in functional recovery during follow-up (FU).

Background. A central diagnostic tool in clinical stable patients with acute myocarditis is CMR, which also provides prognostic guidance, through the detection of necrosis/scar. Speckle tracking echocardiography is an emerging, non-invasive, and fast imaging modality which can offer useful information in diagnosis and FU of these patients.

Material and methods. Patients with acute myocarditis, confirmed by CMR criteria, and age- and sex-matched healthy controls were enrolled. Standard 2D transthoracic echocardiography and speckle tracking analysis were performed at admission and after 6 months of FU.

Results. 115 patients with myocarditis (mean age 41 ± 17, 70% males) and 70 controls were enrolled. Global longitudinal strain (GLS) and layer-specific strains were markedly lower in myocarditis group than in healthy subjects (mean GLS %: -14.1 ± 5.1 vs -23.1 ± 3.6, p <0.001). A strong positive correlation between total scar burden and baseline LV GLS was found (r = 0.67, p <0.0001). GLS improved after 6 months of FU in myocarditis on optimized medical therapy (mean GLS %: -14.1 ± 5.1 vs -16.5 ± 4.8, p <0.01). By bivariate correlation analysis, baseline LVEF, GLS, and total scar burden were all associated to LVEF at 6 months of FU. These baseline parameters confirmed to be independent predictors of functional recovery at 6 months, by multivariable linear regression analysis (LVEF b 0.38, p <0.01; GLS b -0.35, p <0.01; total scar burden b -0.52, p <0.0001). Segmental peak systolic strain was significantly different between segments with and without LGE on CMR (-13.2 ± 3.1% vs -18.1 ± 3.5%, p <0.0001). A segmental strain value of -12% identified scar with a sensitivity of 79% and a specificity of 84% (AUC = 0.91; 95% CI 0.73–0.97; p <0.001).

Conclusion. STE-derived parameters are importantly associated to the presence of scar on CMR and are predictors of functional outcome in patients with acute myocarditis. Their assessment during ultrasound examination has to be considered in order to get more information about prognosis and risk stratification of this myocardial disease.

A461: PREVALENCE OF TRANSTHYRETIN AMYLOID CARDIOMYOPATHY IN MALE PATIENTS WHO UNDERWENT BILATERAL CARPAL TUNNEL SURGERY: THE ACTUAL STUDY

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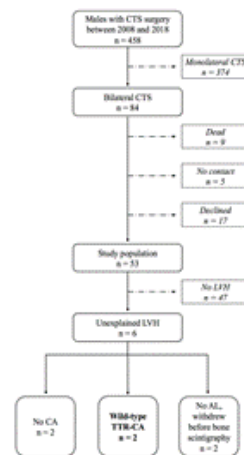
Background. In transthyretin cardiac amyloidosis (TTR-CA) the incidence of bilateral carpal tunnel syndrome (CTS) is known to be higher as compared to the general population. Despite the association of CTS with a subsequent diagnosis of CA has been acknowledged, data regarding prevalence of TTR-CA among individuals with CTS, and timing from CTS occurrence to TTR-CA detection are scarce. The ACTUAL study (Amiloidosi Cardiaca nel Tunnel carpALE) aimed at describing the prevalence of TTR-CA in male patients who underwent bilateral CTS surgery. Objective of the study was to clarify whether screening for TTR-CA in this specific population might be effective.

Methods. Medical records of 1689 CTS surgeries performed at the Ospedale Policlinico San Martino, Genova, Italy between June, 2008 and June, 2018 were reviewed, including 544 procedures in 458 male individuals. Males who underwent bilateral surgery were eligible for the study (n=84, 18%), and were offered enrolment. The study procedure consisted of an electrocardiogram and a transthoracic echocardiography according to current recommendations for all enrolled patients. Those with diastolic interventricular septum thickness >12 mm without other causes for LVH (i.e., unexplained LVH) were considered as possibly affected by TTR-CA and were offered second-line diagnostic testing: serum and urine samples to detect monoclonal gammopathy and bone scintigraphy with 99Tc-hydroxymethylene diphosphonate.

Results. Final study population consisted of 53 bilateral CTS male patients (Fig. 1). Median age at study evaluation was 73 years (min-max range: 42-95) and median age at first CTS surgery was 70 years (40-89). Median time from first and last CTS surgery to study evaluation was respectively 4 (1-11) and 3 years. Six patients (11%) had unexplained LVH (Fig. 1). None of the 6 patients had monoclonal gammopathy. Two patients declined to undergo bone scintigraphy. Of the remaining, 2 had positive bone scintigraphy testing (both Perugini 2 uptake) and tested negative for TTR gene mutations (wild-type TTR-CA). Prevalence of TTR-

CA in the entire study population was 4%, but among bilateral CTS patients with unexplained LVH peaked at 33%.

Conclusions. Despite CTS is an important red flag for TTR-CA, the best screening strategy for detection of this condition remains to be determined. Careful selection of recipients of the screening (males with bilateral CTS) may help optimizing results.



MISCELLANEA

A462: PATHOLOGY OF CONDUCTION TISSUE IN CARDIAC AMYLOID: CORRELATION WITH ARRHYTHMIC MANIFESTATIONS

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Aims. Pathology of conduction tissue (CT) and relative arrhythmic manifestations in living subjects with cardiac amyloid (CA) have never been reported.

Methods. In 17 out of 45 consecutive patients with CA, a left ventricular (LV) endomyocardial biopsy included CT sections. Extensive clinical examination, non-invasive (resting ECG, Holter monitoring, echocardiography), and invasive cardiac studies (selective coronary angiography, LV angiography, and LV endomyocardial biopsy) were performed in all patients. Cardiac magnetic resonance (CMR) was performed in 12 of the 17 patients (70%). CT was identified by Aschoff-Monckeberg histologic criteria associated to positive immunostaining for HCN4. Degree of CT infiltration was defined as mild when ≤30% of CT area was replaced by fibrous tissue and Congo red+ material, moderate in 30-70% CT area involvement and severe in >70% CT cell area replacement. CT infiltration was correlated with ventricular arrhythmias, echocardiographic LV maximal wall thickness (MWT) and type of amyloid protein identified by myocardial immunohistochemistry.

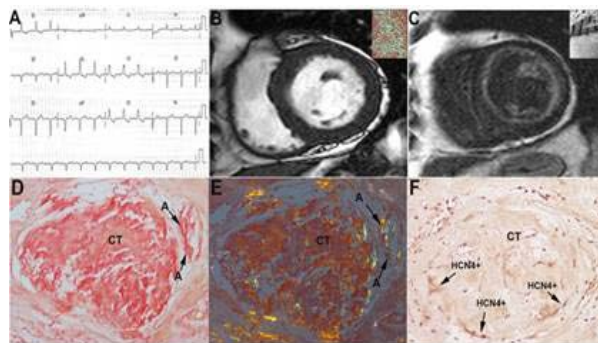


Figure. Severe infiltration of CT in cardiac amyloid. Cardiac amyloid presenting with remarkable conduction abnormalities at ECG (BBDx + BFAS + I degree A-V block (panel A), and mildly thickened LV (panel B, MWT 13 mm) with diffuse "zebroid" LGE at CMR (panel C). Histology with Congo Red staining (panel D and E without and with polarized light) and immunohistochemistry for HCN4 (panel F) show massive infiltration of CT involving CT artery (a). Apple-green birefringent material at polarized light of Congo Red-stained myocardial sections is visible in insert in panel B. Inserts in panel C suggests ultrastructural evidence of CA.

Results. CMR confirmed the presence of cardiac hypertrophy with preserved systolic function in all but one patient. LGE was present in all patients, predominantly with diffuse (5/11) or subendocardial (4/11) pattern compared to focal (2/11). In 7/11 patients T1 mapping sequences have been acquired; nT1 and ECV were increase in all patients (nT1: 1171 ± 61 ms; ECV: $59.9 \pm 7.5\%$). Mild CT involvement was observed in 5 cases; moderate in 3; severe compromise in 9. CT involvement was associated with a parallel infiltration of CT artery. CT infiltration correlated with severity of arrhythmias (Spearman $\rho=0.8$, $p < 0.001$) but not with age, MWT or type of amyloid protein. In particular, major ventricular tachyarrhythmias requiring pharmacologic treatment or ICD implantation occurred in 7 patients with severe, 1 patient with moderate and none with mild CT infiltration. Pacemaker implantation was required in 3 patients with complete CT area replacement.

Conclusion. CA associated arrhythmias correlate with severity of CT infiltration. CT involvement is independent from type and severity of CA suggesting a variable affinity of amyloid protein to CT.

A463: ACETYLCHOLINESTERASE INHIBITORS: EVALUATION OF POTENTIAL POSITIVE CARDIAC EFFECTS IN PATIENTS WITH ALZHEIMER'S DISEASE

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Background. Acetylcholinesterase inhibitors (AChE-Is) are used to improve cognitive functions in patients with Alzheimer's disease (AD). AChE-Is have miscellaneous effects on the cardiovascular system, partly explained by their vagotonic and anti-inflammatory properties. There is little evidence of reduction of cardiovascular diseases (CVDs) in patients chronically treated by AChE-Is. In this study we explored the potential role of AChE-Is in reducing cardiovascular events in patients with AD.

Methods. In this retrospective cohort study we enrolled AD patients treated by AChE-Is referred to the Neurology department of our institution. Patients' caregivers with comparable age acted as control group. The primary outcome was a composite of cardiovascular events (cardiovascular death, acute myocardial infarction, coronary revascularization, stroke and/or transient ischemic attack, hospitalizations for heart failure). Descriptive statistics, Kaplan-Meier time to event and univariate and multivariate Cox regression analysis were performed.

Results. 104 AD patients (Group 1) taking AChE-Is (50 Donepezil, 54 Rivastigmine) and 98 control subjects (Group 2) not taking AChE-Is were analyzed. The median duration of follow-up was 5 years. Baseline characteristics were comparable between the two groups except for: history atrial fibrillation (AF) (4% in Group 1 vs 12% in Group 2, $p=0,032$), family history of CVDs (17% in Group 1 vs 30% in Group 2, $p= 0,038$), use of Aspirin (51% in Group 1 vs 30% in Group 2, $p= 0,002$) and use of psychotropic drugs (significantly major in Group 1). A total of 34 events (9 [9%] in Group 1 and 25 [25%] in Group 2) occurred. Kaplan-Meier survival curves revealed significant higher rate of the composite outcome in Group 2 (log-rank: $p=0,021$). General mortality and hospitalization for non cardiovascular causes were not different between groups. At Cox regression univariate analysis, history of AF [HR 4,086 (95% IC 1,894-8,816)], higher age [HR 1,059 (95% IC 1,005-1,115)] and family history of CVDs [HR 2,045 (95% IC 1,004-4,167)] significantly increased while belonging to Group 1 [HR 0,428 (95% IR 0,198-0,927)] significantly reduced the risk of the composite outcome. Belonging to Group 1 [p-value 0,021 HR 0,335 (95% IC 0,132-0,849) and history of AF [p-value 0,032 HR 2,703 (95% IC 1,092-6,693) remained statistically significant after multivariate adjustment. In Group 1, dosage and type of AChE-I had no impact on the incidence of the composite outcome.

Conclusions. Our data show that the incidence of main cardiovascular events was lower in the group taking AChE-Is, compared to the control one. Therefore, the use of AChE-I appears to have a potential cardiovascular protective role. Further studies are needed to explore this protective role on a wider range of patients.

A464: VASCULITI CORONARICHE: NON SEMPRE CORONARIE INDENNI DA LESIONI SIGNIFICA ESENTI DA MALATTIA. CASE REPORT DI GRANULOMATOSI EOSINOFILA CON POLIANGIOITE CON COINVOLGIMENTO CARDIACO

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La granulomatosi eosinofila con poliangerite (EGPA), precedentemente identificata col nome di sindrome di Churg-Strauss, è una vasculite sistemica dei vasi di piccole e medie dimensioni, che si associa ad autoanticorpi anti-citoplasma dei neutrofili (ANCA) e ipereosinofilia. Si ha interessamento dell'apparato respiratorio, del sistema nervoso periferico e ci può essere un coinvolgimento cardiaco nel 15-60% dei casi. Quest'ultimo comporta una peggiore prognosi, è spesso asintomatico, meno frequentemente associato a positività degli autoanticorpi e si può

manifestare sotto forma di vasculite coronarica, miocardite, pericardite e trombosi endocavitaria.

Si descrive il caso di una paziente di 61 anni, pregressa fumatrice, con storia di asma bronchiale, e senza altri fattori di rischio cardiovascolare, che si è recata al Pronto Soccorso con un quadro clinico di sindrome coronarica acuta, associato ad astenia e mialgie agli arti inferiori. All'elettrocardiogramma viene rilevata una tachicardia sinusale con onde Q in V1-V3 e bassi voltaggi nelle derivazioni periferiche. L'ecocardiogramma ha mostrato una funzione sistolica ventricolare sinistra moderatamente ridotta (FE 40%) con ipocinesia del setto interventricolare medio-apicale e dell'apice e lieve versamento pericardico circonfrenziale. Agli esami ematici viene evidenziato un aumento significativo della troponina T ad alta sensibilità e leucocitosi con spiccata componente eosinofila. Il quadro clinico è stato interpretato come un possibile infarto miocardico acuto recente e la paziente è stata sottoposta a una coronarografia d'urgenza che non ha mostrato stenosi dei vasi epicardici. È stato, quindi, posto il sospetto diagnostico di poliangerite, da granulomatosi eosinofila, corroborato dagli esami di laboratorio, dalla TC del torace ad alta risoluzione, dalla TC dei seni paranasali e dall'elettromiografia dei quattro arti. È stata, pertanto, iniziata una terapia steroidea ad alte dosi con miglioramento dei parametri clinici, laboratoristici e con un lieve incremento della funzione sistolica ventricolare sinistra.

Nella maggior parte dei casi le sindromi coronariche acute sono determinate da aterosclerosi stenotante delle coronarie epicardiche. Quando questa è assente, diventa fondamentale un approccio olistico al paziente considerando anche in diagnosi differenziale cause più rare come vasculiti con coinvolgimento coronarico. Quest'ultimo, quando presente nella granulomatosi eosinofila con poliangerite, comporta una prognosi peggiore, ed è quindi necessaria una corretta identificazione della malattia per impostare rapidamente un'adeguata terapia.



Figura 1. ECG di ingresso.

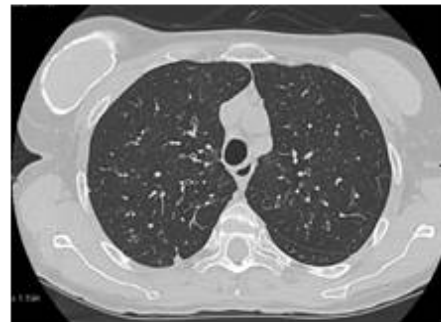


Figura 2. HRCT polmonare.

A465: WHAT BIBLIOMETRIC INDICATORS SHOULD BE USED FOR THE EVALUATION OF INDIVIDUAL RESEARCHERS AND BIOMEDICAL JOURNALS?

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Bibliometric indicators are now the cornerstone of biomedical researchers' assessments in their career progression paths (H-index, in particular, accepted as a yardstick for research output in most universities and research centers). Furthermore, bibliometric indicators are used for the quality and impact ranking of scientific journals (the case of the impact factor). In this review, alternative forms of web-based biomedical bibliometry are also mentioned, such as in particular the score of the Altmetric software, which is important for the assessment at the single article level, which is not ensured by the impact factor, and adopted by important biomedical journals. Ultimately, the criterion of adopting multiple metrics, both citational and non-citational, properly integrating them with each other, would result in an improved assessment of the quality and impact of the individual researcher, as well as biomedical journals.

A466: L'ATTENZIONE ALLA RADIOPROTEZIONE NEL LABORATORIO DI EMODINAMICA

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Obiettivi. Il lavoro presenta una raccolta sistemica ed operativa degli aspetti utili a garantire la migliore radioprotezione nell'attività dei laboratori di emodinamica, anche in seguito all'entrata in vigore del nuovo Decreto Legislativo 101/2020, in vigore dallo scorso luglio.

Metodi. Negli ultimi anni, grazie all'evoluzione tecnologia (sistemi angiografici e di imaging, anche intra-operatorio, materiali e device) ed alla maggiore diffusione di tali metodiche si è osservato un conseguente incremento delle procedure interventistiche cardiologiche, consentendo, inoltre procedure di maggiore complessità procedurale. Questo aumento di complessità ha comportato l'incremento dell'esposizione radiogena dei pazienti e degli operatori, tanto che si ritiene che le procedure di cardiologia interventistica effettuate sotto guida fluoroscopica contribuiscano per circa il 40% alla dose radiante da attività mediche. Per questo diventa fondamentale l'attenzione a tutti gli aspetti che attengono alla radioprotezione ed al corretto utilizzo delle tecnologie e dei DPI. Le figure professionali coinvolte nell'attività di sala, sono differenti, svolgendo compiti diversi che comprendono l'esecuzione della procedura, nel caso dello specialista (primo operatore) oppure l'assistenza al paziente ed al tavolo, nel caso dell'infermiere circolante o infermiere di sala. Altra figura presente è il tecnico sanitario di radiologia, figura chiave nella gestione delle tecnologie radiologiche e nella radioprotezione. La conoscenza di ogni aspetto radioprotezionistico, dell'utilizzo ottimizzato delle tecnologie, una pianificazione dell'esposizione e comportamenti corretti da assumere al tavolo o nei movimenti in sala, l'adozione e l'utilizzo e manutenzione opportuna di tutti i DPI, sono elementi essenziali al fine di garantire concretamente la radioprotezione.

Risultati. Oltre la corretta manutenzione di ogni tecnologia e dpi, la formazione e la simulazione nella nostra esperienza hanno rappresentato un elemento indispensabile per migliorare la protezione e la sicurezza nell'utilizzo delle radiazioni ionizzanti.

Conclusioni. Il rispetto della normativa non può prescindere da una corretta e continua formazione ed informazione del personale, nell'utilizzo consapevole delle tecnologie e di comportamenti idonei a prevenire ogni rischio dall'esposizione a radiazioni ionizzanti. Inoltre, risulta di particolare importanza la presenza, all'interno del laboratorio di emodinamica, del TSRM quale figura individuata come preposto alla radioprotezione, il quale, in questo grado di responsabilità, non può essere sostituito da altre figure in quanto è l'unica che possiede le competenze specifiche, affidatarie delle apparecchiature a raggi X.

A467: RIGHT ENDOVENTRICULAR INVOLVEMENT IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS AND VENTRICULAR ARRHYTHMIA IN A YOUNG PATIENT WITH SYNCOPÉ

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(a) SC CARDIOLOGIA UTIC PO SAN PIO DA PIETRELCINA CASTELLANETA ASL TARANTO

We report a case of a 30-year-old man, with previous hospitalizations for inflammatory sinusopathy and right parotid swelling, with evidence of increased LDH and hypereosinophilia. Due to right otalgia, headache, postural instability, a previous finding of left parietal subarachnoid haematoma and ischemic hypodensities on CT brain scan; he was admitted to the hospital for suspected cerebritis (presence of proteins at lumbar puncture); consequently a diagnosis of vascular encephalopathy from probable primary cerebral vasculitis in the context of undetermined nature connectivity was made. This patient came to our attention complaining chest pain that had radiated to the jugule, which lasted a few minutes, followed by a syncopal episode. Echocardiography showed a formation in the mid-apical portion of the right ventricle inflow tract. During hospitalization, clinicians, performing a CT-scan, excluded pulmonary embolism and expansive/infiltrative lesions; ECG showed negative T waves in D3, aVF, V3-V4 leads. Transesophageal echocardiography confirmed a right ventricle endocavitary mass, right ventricular diastolic dysfunction and patent foramen ovale. Carotid artery Doppler showed a hypochoic non-stenosing parietal apposition at the mid-proximal tract of the common carotid artery; on Doppler examination, the common femoral vein showed a sleeve-like hypochoic parietal apposition, and a probable right subclavian vein obstruction. MRI confirmed the presence of the mass in the right ventricle, as well as biventricular dysfunction and a delayed enhancement at the level of the left ventricular medioapical inferolateral wall and of the posterior papillary muscle. The main autoantibody dosage, rheumatological and infectious disease markers were negative. During hospitalization, there was a single episode of self-

limiting torsade de pointes. After evidence of fast growth of the RV mass it was suspected eosinophilic granulomatosis and patient underwent to biopsy that indicated thrombus with eosinophil infiltration. Therefore prednisone 25 mg and rivaroxaban 20 mg were started. After four months regression of mass on echocardiography was found. The Churg-Strauss syndrome, recently renamed eosinophilic granulomatosis with polyangiitis (EGPA) (in differential diagnosis with Loeffler's endocarditis) is a systemic necrotizing vasculitis with extravascular granulomas in eosinophilia. Cardiac involvement (in 15-60% of cases) can occur with myocarditis, heart failure, pericarditis, arrhythmias, coronary arteritis, valvulopathy and intracavitary thrombosis. In this specific case, the right ventricular mass), associated with arrhythmic episodes, can be related to the clinical manifestations that led to hospitalization.

A468: TAKOTSUBO SYNDROME AND AMYOTROPHIC LATERAL SCLEROSIS

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Background. Takotsubo syndrome (TTS) is a novel syndrome characterized by an acute, transient and reversible left ventricular regional systolic dysfunction, which resemble an acute myocardial infarction at presentation, but atherosclerotic obstruction of epicardial coronary arteries is not detected on angiography. It is triggered by important physical or psychological stressors, with women at post-menopause predominating and with multiple comorbidities, especially neurological ones. Amyotrophic Lateral Sclerosis (ALS) is the most common motor neuron disease and the progressive degeneration of motor neurons leads to their death, usually due to respiratory failure. An autopsy study remarked that heart failure represented the second most common cause of death. This study aimed to evaluate the relationship between TTS and SLA.

Material and methods. We have studied 85 patients admitted in our Coronary Care Unit, between September 2007 to June 2020, with a diagnosis of TTS according both to the Mayo Clinic criteria and the International Expert Consensus Document on TTS.

Results. Over the study period, the incidence of TTS increased from 2.5% in the first half of 2007 to 22.4% in 2019 and 9% in the first semester of 2020. We observed that the mean age at presentation was 70.3 ± 11.7 , range 44-96, and 96.5% of the total patients (83/85) were over 50 years old; women constitute 85.8% of our cohort (73/85). We found various comorbidities: 9 (10.5%) had hypothyroidism secondary to Hashimoto's thyroiditis, 3 (3.5%) hyperthyroidism, 15 (17.6%) psychiatric disorders and 12 (14.1%) neurological diseases, of which 6 (7%) were ALS. On admission, patients with ALS had atypical symptoms ($p=0.003$) and less frequently a typical chest pain (1 vs 53, $p=0.038$). The clinical conditions were more compromised, with greater impairment of overall systolic function ($EF 35.3 \pm 6.8$ vs 47 ± 10.4 , $p=0.007$) and severe systolic dysfunction present in 50% of patients, $p=0.035$. During hospitalization ALS patients had a more complicated course: two (33%) patients presented cardiogenic shock, compared to only 3/79 (3.7%) patients not affected by ALS ($p=0.003$) and ALS patients were treated more frequently with intravenous catecholamines infusion ($p=0.001$). Moreover, ALS patients had a higher incidence of acute respiratory failure and therefore underwent assisted ventilation more often than the other group (2/6, 33% vs 4/79, 5%, $p=0.009$). But we did not find a higher in-hospital mortality rate between the two groups (0% vs 1.2%, $p=0.78$).

Conclusions. Our study shows a high prevalence of ALS in patients with TS suggesting that ALS could be a predisposing condition to TTS, and even more so if associated to precipitating factors both emotional and physical, such as surgery, respiratory distress or infection. These data make us reflect on the need to search carefully for any acute cardiac dysfunction in patients suffering from ALS who manifest sudden worsening of clinical conditions as acute respiratory failure and thoracic discomfort, which may be an expression of TTS and require specific acute therapeutic support.

A469: PREDITTIVITÀ PROGNOSTICA DELLA TROPONINA T CARDIACA ULTRASENSIBILE NEL DEU CARDIOLOGICO IN ASSENZA DI SINDROME CORONARICA ACUTA

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Obiettivi. La troponina cardiaca ultrasensibile ha dimostrato buona efficacia nella stratificazione del rischio nella sindrome coronarica acuta (SCA). Abbiamo quindi voluto studiare il suo ruolo prognostico in pazienti in osservazione nel Dipartimento di Emergenza urgenza (DEU) del nostro ospedale in assenza di diagnosi SCA, impiegando la Troponina T cardiaca ultrasensibile (hs-cTnT).

Metodi. Abbiamo valutato retrospettivamente n.7807 dosaggi consecutivi di hs-cTnT (ove indicato eseguiti in modo seriato) su un tot. di n. 3566 paz. di età >18 anni in osservazione nel DEU da genn. a dic. 2016. È stato considerato valore elevato della hs-cTnT un limite decisionale pari a 14 ng/L. Tutti i valori superiori sono stati definiti positivi, i valori nei limiti negativi. L'analisi è stata condotta escludendo i paz. con diagnosi finale di SCA. Il campione così selezionato di n. 906 paz. è stato suddiviso in n.2 gruppi: A con valori di hs-cTnT positivi e B con valori negativi. L'associazione di elevati livelli di hs-cTnT e prevalenza di mortalità intraospedaliera è stata statisticamente valutata con il test chi quadro.

Risultati. La mortalità complessiva è stata 12.0%. Nel gruppo A (n.712) la mortalità era 14.5%, nel gruppo B (n.194) 3.1%. Le morbidità prevalenti erano nell'ordine: polmonite, scompenso cardiaco avanzato, ictus ischemico o emorragico, sepsi, neoplasie avanzate, aritmie cardiache sostenute. All'analisi statistica la positività di hs-cTnT (gr.A) si correlava in modo significativo con una maggiore mortalità rispetto al gr.B con valori di hs-cTnT normali ($p < 0.0001$).

Conclusioni. La valutazione della hs-cTnT in paz. ricoverati in DEU cardiologico o internistico in condizioni critiche e in cui non si confermi la diagnosi di SCA, è un importante predittore di mortalità e morbidità maggiore.

A470: NON SOLTANTO URGENZE CARDIOLOGICHE: IL DELIRIUM!

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Introduzione. Il delirium è una sindrome ad esordio acuto e decorso fluttuante, spesso reversibile, caratterizzata da alterazioni cognitive, deficit dell'attenzione e della consapevolezza dell'ambiente. È estremamente comune nei pazienti ospedalizzati, raggiungendo un'incidenza di circa il 75% nei pazienti di Terapia Intensiva sottoposti a ventilazione meccanica non invasiva, ove rappresenta uno dei principali fattori di rischio per complicanze e un fattore predisponente il deterioramento cognitivo post-terapia intensiva. Esso risulta, inoltre, correlato a un peggioramento della prognosi del paziente e ad un aumento della mortalità, con dilazionamento dei tempi di ventilazione meccanica, prolungamento della degenza in UTIC e, quindi, dei tempi di ospedalizzazione. Tuttavia, appare ancora oggi, estremamente misconosciuto, sottodiagnosticato e, quindi, non adeguatamente trattato.

Caso clinico. Il paziente OG, di 80 anni, autonomo e autosufficiente, in data 27 Novembre si ricoverava in UTIC per Sindrome coronarica acuta senza soprassollamento del tratto ST (SCA/NSTEMI); in data 28 Novembre eseguiva la coronarografia con evidenza di coronarie angiograficamente indenni. Al rientro dalla sala di Emodinamica si presentava con un'intensa e violenta agitazione psicomotoria che ha motivato il personale medico a sottoporlo a due esami TC encefalo in 24 ore (conclusive per cerebrovasculopatia cronica in assenza di acuzie ischemiche o emorragiche) e ad utilizzare un'elevata dose di benzodiazepine che hanno contribuito all'automantenimento del Delirium stesso. Il paziente, a seguito dello stato di agitazione ha sviluppato gravi complicanze, divenendo pericoloso per se stesso (oltre che per il personale preposto alle sue stesse cure!): imponente macroematemia, infezione delle vie urinarie, tamponamento vescicale (pur in corso di cistoclisti). Soltanto il trasferimento in degenza e l'avvio della mobilitazione hanno contribuito a metter fine al tunnel dell'agitazione psicomotoria.

Conclusioni. Il delirium pur non essendo un'urgenza meramente cardiologica, può diventare un'emergenza di Terapia Intensiva, soprattutto per la complessità di gestione e le possibili complicanze, aspetti ancora oggi misconosciuti e sottostimati. La letteratura descrive numerosi strumenti finalizzati alla prevenzione del Delirium, raccomandando, inoltre, una gestione farmacologica dello stesso obbligatoriamente individualizzata e personalizzata, rimanendo le benzodiazepine controindicate salvo in setting specifici, l'uso degli antipsicotici off-label e la dexmedetomidina il farmaco di scelta in un altissima percentuale di pazienti.

A471: ARRESTO CARDIACO NEI PAZIENTI IN FOLLOW-UP CARDIOLOGICO. PERCEZIONE DEL RISCHIO E SENSO DI ADEGUATEZZA DEI PARENTI

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Introduzione. I pazienti cardiopatici sono a maggior rischio di arresto cardiaco (AC). Poiché questa condizione necessita di un trattamento tempestivo e la stragrande maggioranza dei casi di AC avviene in casa, risulta fondamentale il ruolo dei parenti o caregivers familiari. Lo scopo del seguente studio è quello di indagare la probabilità percepita dai parenti che il loro familiare possa avere un AC e il loro grado di adeguatezza nel riconoscere l'evento e nel mettere in atto la rianimazione cardiopolmonare (RCP).

Materiali e metodi. Sono stati distribuiti questionari ai parenti dei pazienti

durante i follow-up presso gli ambulatori di Cardiologia, chiedendo loro di valutare, in una scala da 0 a 100, la probabilità che il loro parente potesse avere un AC, il loro grado di adeguatezza nel riconoscere l'evento e nell'eseguire RCP da soli o guidati per telefono dalla centrale operativa 118. Attraverso un modello di regressione multivariata è stato valutato se fattori relativi al parente (età, sesso, grado di istruzione e precedente esperienza di corsi di rianimazione), o relativi al paziente (età, classe NYHA, valori di frazione di eiezione del ventricolo sinistro, presenza di dispositivi impiantabili e precedente AC) fossero in grado di influenzare in maniera indipendente la probabilità percepita di AC.

Risultati. Sono stati compilati 208 questionari (88% presso l'Ambulatorio Scompenso Cardiaco; 75% femmine con età media 55.5 ± 12.5 anni; 42% consorte e 35% figlio/a). Alla domanda "quanto ritiene probabile che il suo parente possa avere un AC?" la risposta mediana è stata 50/100 (IQR 10-50). All'analisi multivariata l'età del parente, il suo grado di istruzione, la sua partecipazione a corsi di rianimazione o l'aver già testimoniato un AC non sono risultati in grado di influenzare la probabilità percepita in modo statisticamente significativo. In merito ai dati clinico-strumentali del paziente, l'aver avuto un AC in passato si è dimostrato in grado di influenzare significativamente ed in modo indipendente il rischio percepito (coef. 19.5; $p=0.02$). Il senso di adeguatezza mediano nel riconoscere l'AC, ad eseguire la RCP da soli e guidati telefonicamente dal 118, è risultato rispettivamente di 10/100 (IQR 0-37,5), 0/100 (IQR 0-10) e 20/100 (IQR 0-50) e si è dimostrato significativamente superiore ($p<0.001$) in coloro che avevano frequentato almeno un corso di rianimazione: 50/100 (IQR 30-80), 50/100 (IQR 30-80) e 80/100 (IQR 50-90) rispettivamente.

Conclusioni. Il rischio di arresto cardiaco percepito dai parenti dei pazienti in follow-up ambulatoriale cardiologico è discretamente alto, mentre il loro senso di adeguatezza nel riconoscerlo e trattarlo è risultato piuttosto basso, ma significativamente più alto in coloro i quali avevano partecipato ad almeno un corso di rianimazione. I dati mostrano come sia importante che gli ambulatori di cardiologia promuovano, e se possibile organizzino, un corso di rianimazione cardio-polmonare indirizzato ai parenti dei pazienti cardiopatici.

A472: VALUTAZIONE DEI PARAMETRI BASALI DELL'ELETTROCARDIOGRAMMA A RIPOSO SU 369 PAZIENTI AMBULATORIALI CONSECUTIVI

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Introduzione. In questo studio abbiamo valutato i parametri di base, rilevabili dall'elettrocardiogramma a riposo (intervallo P-Q, durata del QRS, intervallo Q-T corretto), in soggetti che si presentavano per una visita cardiologica ambulatoriale di controllo.

Materiali e metodi. Abbiamo analizzato i dati di 369 pazienti ambulatoriali che si sono presentati consecutivamente alla nostra osservazione per una visita cardiologica di controllo, indipendentemente da qualsiasi altro fattore (compresi, ad es., la motivazione per cui era stata richiesta la visita di controllo, la storia clinica del paziente e l'eventuale terapia in atto). L'età media dei pazienti era di $64,73 \pm 14,26$ anni ed erano 155 pazienti maschi e 214 pazienti femmine. I soggetti diabetici erano 65, i pazienti con pregresso infarto miocardico erano 36, i soggetti dislipidemici in trattamento erano 113, i fumatori attivi erano 40, i soggetti ipertesi 186, i pazienti in terapia emodialitica per un'insufficienza renale cronica erano solo 5 e i pazienti con distiroidismo 19. Al momento della registrazione dell'elettrocardiogramma di base 355 soggetti erano in ritmo sinusale, 14 in fibrillazione atriale. Per la registrazione e l'analisi della traccia elettrocardiografica è stato utilizzato un elettrocardiografo Mortara Rangoni™ Eli 10™ (frequenza di campionamento: 10.000 campioni/sec/canale per il riconoscimento pacemaker; 1.000 campioni/sec/canale per l'analisi).

Risultati. Abbiamo ottenuto i seguenti valori (espressi come media \pm deviazione standard): intervallo P-Q (calcolato nei soli pazienti in ritmo sinusale) 0.16 ± 0.03 sec., durata del QRS 0.089 ± 0.013 sec., intervallo Q-T corretto (calcolato utilizzando la formula di Bazett) 0.397 ± 0.021 sec.

Discussione. I parametri derivati dalla nostra analisi si posizionano assolutamente all'interno dei valori di normalità e possono pertanto essere considerati come un possibile indicatore di base e di facile valutazione delle condizioni generali della popolazione ambulatoriale durante le visite cardiologiche di controllo.

A473: DIFFERENZE UOMO-DONNA NEI DIVERSI PARAMETRI DELL'ELETTROCARDIOGRAMMA DI BASE IN 369 PAZIENTI AMBULATORIALI CONSECUTIVI

Paolo Terranova (a)
(a) CARDIOLOGO LIBERO PROFESSIONISTA

Introduzione. In questo studio abbiamo valutato la presenza di eventuali differenze uomo : donna nei parametri base, rilevabili dall'elettrocardiogramma a riposo (intervallo P-Q, durata del QRS, intervallo Q-T corretto), in soggetti che si presentavano per una visita cardiologica ambulatoriale di controllo. presentavano per una visita cardiologica ambulatoriale di controllo.

Materiali e metodi. Abbiamo analizzato i parametri elettrocardiografici di

base di 369 pazienti ambulatoriali (155 uomini e 214 donne) che si sono presentati consecutivamente alla nostra osservazione per una visita cardiologica di controllo. L'età media dei pazienti era di 64,73±14,26 anni (maschi 63,61±14,01 anni; femmine 65,54±14,45 anni; p=0,0996).

Risultati. Abbiamo ottenuto i seguenti valori dei parametri derivati dall'elettrocardiogramma di base (espressi come media ± deviazione standard):

1. intervallo P-Q (calcolato nei soli pazienti in ritmo sinusale) 0,162±0,027 sec. (maschi) vs 0,159±0,025 sec. (femmine), p=0,135;
2. durata del QRS 0,089±0,013 sec. (maschi) vs 0,088±0,014 sec. (femmine), p=0,197;
3. intervallo Q-T corretto (calcolato utilizzando la Formula di Bazett) 0,398±0,022 sec. (maschi) vs 0,396±0,022 sec. (femmine), p=0,235;
4. frequenza cardiaca : 71,065±12,248 battiti/minuto (maschi) vs 73,921±12,389 battiti/minuto (femmine), p=0,029.

Discussione. I parametri derivati dalla nostra analisi, che si posizionano all'interno dei valori di normalità e possono essere considerati come un possibile indicatore di base e di facile valutazione delle condizioni generali della popolazione ambulatoriale oggetto delle nostre visite cardiologiche di controllo, non presentano significative differenze nel rapporto uomo/donna, ad eccezione della frequenza cardiaca che sembra essere leggermente più elevata nel sesso femminile che in quello maschile, probabilmente a causa anche delle note differenze nella struttura fisica dei due sessi e nelle differenti modalità di attivazione e di oscillazione nel tempo del sistema simpato-vagale.

A474: PROGNOSTIC IMPACT OF ANTIPLATELET THERAPY IN TAKOTSUBO SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE LITERATURE

Francesca Rizzetto (a), Micaela Lia (a), Maddalena Widmann (a), Domenico Tavella (a), Luisa Zanolla (a), Michele Pighi (a), Flavio Luciano Ribichini (a)
(a) AOUI VERONA

Background. Over the past decades the association between single/double antiplatelet therapy use and outcome in Takotsubo Syndrome (TTS) has been widely investigated. While the most recent evidence seems to suggest a lack of benefit, antithrombotic therapy is still extensively prescribed in patients with stress cardiomyopathy.

Rationale and Objectives. To determine whether patients with TTS benefit from aspirin and/or other forms of antiplatelet therapy in terms of either short-term or long-term outcomes (death, myocardial infarction, TTS recurrence, stroke).

Methods. A systematic review with meta-analysis was conducted. A comprehensive search of the literature included MEDLINE, Cochrane Central Register of Controlled Trials, Clinicaltrials.gov, EU Clinical Trial Register, References and contact with the authors. Methodological quality assessment and data extraction were completed in a systematic way. The review adhered to the PRISMA framework guidelines.

Results. A total of 79 citations were identified, of which six studies were eligible for inclusion, for a total 1997 patients. Only one of them considered both short-term and long-term outcome. One reported only major cardiovascular (and cerebrovascular) events during the index event, while the remaining four focused only on long-term potential benefits. They were all retrospective cohort studies. The two only studies analysing the short-term prognostic role of antithrombotic drugs showed no consensus, also due to different follow-up duration. Conversely, based on our data, the long-term use of single or dual antiplatelet therapy led to a significant higher incidence of the composite outcome (OR: 1.54; 95% CI 1.09-2.17; p=0.014) and overall mortality (OR 1.72; 95% CI 1.07-2.77; p=0.027). No other statistically significant results emerged.

Conclusions. The antiplatelet therapy administered after a diagnosis of Takotsubo syndrome had no benefit in improving the long-term outcomes and it may be even detrimental. The study showed conflicting results with regard to the short-term outcomes. The results of the present study should further promote the evaluation of the real impact of aspirin on outcome of Takotsubo patients. Future research on this topic, and in particular the design of adequately powered randomized controlled trials is warranted.

PREVENZIONE E RIABILITAZIONE

A475: UN NEMICO NASCOSTO

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Un uomo di 64 anni con multipli fattori di rischio cardiovascolare (FR-CV) si presentava al nostro ospedale per angina tipica in corso di NSTEMI. In anamnesi, procedura di rivascularizzazione coronarica per via percutanea (PTCA) per angina instabile 18 mesi prima (stenting di arteria interventricolare anteriore) e multiple rivascularizzazioni percutanee ai vasi degli arti inferiori per claudicatio e ulcere trofiche. Il paziente presentava un alto rischio ischemico residuo (TRS-2P=4) e, nonostante

l'aggressiva terapia medica intrapresa dopo la procedura di PTCA (ASA e ticagrelor 90 mg bid per 12 mesi, terapia antidiabetica con SGLT-2i e GLP-1 agonista, sartanico, beta-bloccante e rosuvastatina+EZE) non aveva raggiunto un adeguato controllo dei FR-CV, continuando a fumare e non controllando il peso corporeo (BMI 31). All'ECG di ingresso era presente ritmo sinusale con frequenza cardiaca nei limiti, QS anteriore e diffuse alterazioni della ripolarizzazione ventricolare. Al controllo ecocardiografico: ventricolo sinistro di normali dimensioni e funzione (FE 55%) con ipocinesia dei segmenti apicali (reperti sovrapponibili a un precedente controllo), non presenti valvulopatie o complicanze meccaniche. La curva troponinica mostrava un delta significativo (Troponina T-hs: 43 pg/mL >80 pg/mL >148 pg/mL con valori di normalità <14 pg/mL). Alla coronarografia veniva riscontrata coronaropatia trivasale con coronaria destra diffusamente malata con stenosi critiche al I e II tratto in quadro di dominanza destra, stenosi critica del tronco comune e restenosi critica dell'interventricolare anteriore; l'arteria circonflessa presentava stenosi del 60% al primo ramo marginale e al III tratto. Il nostro paziente presentava un SYNTAX score di 44, a fronte di un basso rischio di mortalità chirurgica a 30 giorni (STS score 1.97%), per cui, dopo discussione collegiale in Heart Team, si optava per rivascularizzazione coronarica chirurgica (Off-pump CABG), eseguita in assenza di complicanze intra- o post-procedurali. Al termine dell'ospedalizzazione, il paziente è stato trasferito in riabilitazione cardiologica e attualmente, circa 10 mesi dopo la dimissione, presenta una buona aderenza alla terapia medica, ha cessato l'abitudine tabagica, ha perso peso ed è in buon compenso clinico.

A nostro parere questo caso clinico, seppur simile a tanti altri riscontrati nella pratica clinica quotidiana, mette in luce due importanti aspetti del management dei pazienti con cardiopatia ischemica cronica: da un lato la necessità di valutare il rischio ischemico residuo nell'ambito della prevenzione secondaria con score validati in questo setting (per esempio TRS-2P score), al fine di prescrivere una terapia più aggressiva e un follow-up più stringente in base al profilo di rischio del singolo paziente. Dall'altro lato, nasce la necessità di rivalutare l'aderenza alla terapia medica e alle prescrizioni comportamentali a ogni contatto con il paziente, rafforzando l'empowerment circa la propria salute. A questo scopo la riabilitazione cardiologica è di estrema importanza già dopo il primo evento ischemico e dovrebbe essere sempre incoraggiata nei pazienti ad alto rischio ischemico residuo, specie se con caratteristiche psico-sociali a rischio di scarsa compliance alla terapia. Infatti, nonostante la ricerca farmacologica abbia determinato un notevole miglioramento nel controllo dei FR-CV e nella prevenzione secondaria, circa il 30% dei pazienti dimessi dopo una sindrome coronarica acuta presenta una scarsa aderenza alla terapia medica e comportamentale, vanificando gli sforzi per ridurre il burden ischemico.

A476: ACHIEVING LDL CHOLESTEROL TARGET IN A REAL-WORLD SECONDARY PREVENTION COHORT: WHEN TWO IS BETTER THAN ONE

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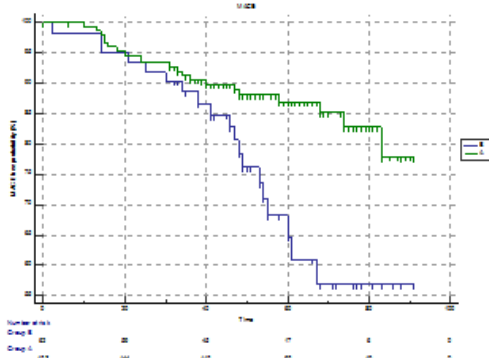
Background and aim. Lipid management plays a key role in secondary prevention after acute coronary syndrome. Current European Society of Cardiology guidelines recommend a dual goal: to achieve LDL cholesterol (LDL-C) <55 mg/dL, and to reduce it ≥50% from baseline. Currently, data on the reduction of cardiovascular events in patients achieving both goals in a real-world population are missing. Accordingly, the objective of this study was to determine the prognosis in post myocardial infarction (PMI) patients and determine the risk of new events according to the achievement of the optimal goals indicated by the guidelines in terms of LDL-C reduction.

Methods. We conducted a retrospective analysis of a monocentric observational registry prospectively enrolling patients admitted to our hospital for ST segment elevation myocardial infarction (STEMI) and followed-up in our dedicated PMI ambulatory. The analysis considered the patients enrolled between 2013 and 2017. Demographical and clinical data were extracted from a dedicated digital database, and the clinical events occurred during follow-up were obtained by telephone interviews or clinical records. We considered a combined endpoint of major adverse cardiovascular events (MACE) of all-cause death, non-fatal MI, non-fatal stroke and unplanned revascularization. LDL-C was collected at baseline and at 1, 6 and 12 months after the event. The lower value collected at follow-up was used to define the achievement of the target goals. We conducted a Kaplan-Meier analysis and log-rank test comparing patients who achieved LDL-C <55 mg/dL and ≤50% from baseline (group A) vs those with only LDL-C <55 mg/dL (group B). Continue variable are presented as median (interquartile range).

Results. A total of 814 patients (23% female) were included in our analysis. Median age was 63 (55-72) years, 57% had hypertension, 19% diabetes, 36% were smoker and 17% obese. Baseline LDL-C was 124

(97-146) mg/dL, the median LDL-C at follow-up was 63 (52-78) mg/dL, significantly reduced from baseline ($P<0.0001$). Between 6 and 12 months 83.3% of patients were treated with statin therapy alone (73% high intensity), 15.3% with the addition of ezetimibe, and 0.5% with ezetimibe alone. LDL-C <55 mg/dl was achieved in 244 patients (30%), while 175 patients (21%) obtained also LDL-C $\leq 50\%$ from baseline. Median follow-up was 52 (34-66) months. The net incidence of MACE was 12% in group A vs 27.5% in group B (HR 0.35; 95% CI 0.17-0.70; P log-rank=0.0032; Number Needed to Treat=6; see Figure).

Conclusion. Our data from a real-world cohort of PMI patients emphasize the importance of achieving both the guideline-recommended secondary prevention goals of LDL-C <55 mg/dl and $\leq 50\%$ from baseline in order to reduce MACE.



A477: NEW DIAGNOSIS OF HYPERGLYCEMIA DURING CARDIAC REHABILITATION: PREVALENCE AND OUTCOMES

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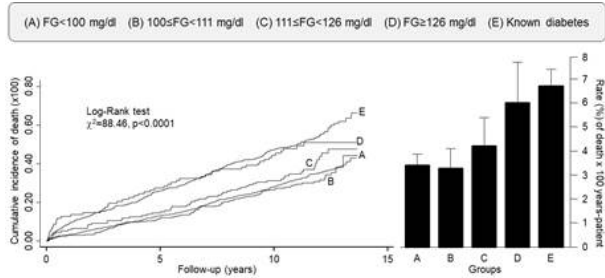
Background. Hospitalized patients with impaired glucose regulation after an acute cardiovascular (CV) event have adverse outcomes when compared with euglycemic patients. Several observational studies and meta-analyses documented that new-onset hyperglycaemia during acute coronary syndromes increases the short and long term risk of complications in patients with and without previously known diabetes mellitus. Conversely, data regarding the role of altered fasting glycemia (FG) in patients during cardiac rehabilitation are scanty.

Aim. The aim of our study was to assess prevalence and long-term prognosis (all-cause death) of new hyperglycaemia documented during cardiac rehabilitation programs.

Methods. We collected data of consecutive patients admitted to an in-hospital cardiac rehabilitation program after an acute CV event.

Five groups of pts were identified according to clinical history and serum glucose levels recorded during cardiac rehabilitation: group A with $FG<100$ mg/dl and without history of diabetes, group B with $100\leq FG<111$ mg/dl and without history of diabetes, group C with $111\leq FG<126$ mg/dl and without history of diabetes, group D with $FG\geq 126$ mg/dl and without history of diabetes, and group E with a clinical history of diabetes (known diabetes).

Results. Overall, 2490 patients were analysed; groups A, B, C, D and E included 1379, 307, 156, 105 and 543 patients, respectively. Prevalence of sex, smoking habits and chronic obstructive pulmonary disease was similar between groups. During a follow-up of 15 years, groups C, D and E showed the highest incidence rates of death (Log-Rank test: $p<0.0001$, Figure). We also modelled a multivariable Cox regression model including age, smoking status, chronic obstructive pulmonary disease, and left ventricular ejection fraction as covariates. Forcing in the model groups of FG, we documented that group D ($FG\geq 126$ mg/dl without history of diabetes), and group E (known diabetes) were associated with an increased risk of all-cause mortality during follow-up (group D: HR 1.41, 95% CI: 1.03-1.94; group E: HR 1.62, 95% CI: 1.38-1.91).



Conclusions. Our data show that new onset hyperglycemia is relatively frequent in patients without clinical history of diabetes and admitted to an in-hospital cardiac rehabilitation. More importantly, new-onset hyperglycemia confers a risk of adverse outcome similar to previously known diabetic patients.

A478: L'INFLUENZA DEI FATTORI PSICOSOCIALI SULL'ADERENZA AI PROGRAMMI DI RIABILITAZIONE CARDIOLOGICA DELLE PERSONE AFFETTE DA INFARTO MIOCARDICO: REVISIONE DELLA LETTERATURA

Estera Iurean (a)

(a) SI

Obiettivo. Le malattie cardiovascolari rappresentano la prima causa di morte in Europa e in Italia. Sopravvivere ad eventi cardiaci gravi come l'infarto del miocardio può comportare ricadute negative sul benessere psicologico e sulle condizioni di salute con la manifestazione di sintomi quali ansia e depressione. La riabilitazione cardiologica può fornire un miglioramento significativo della qualità della vita e facilitare il raggiungimento degli obiettivi terapeutici a lungo termine. Nonostante i benefici riconosciuti l'aderenza ai programmi riabilitativi è molto bassa.

Obiettivi del presente elaborato sono: -identificare l'influenza dei fattori psicosociali sull'aderenza alla riabilitazione cardiologica -valutare i benefici della riabilitazione sul controllo di ansia e depressione - individuare gli interventi per migliorare l'aderenza ai programmi riabilitativi.

Materiali e metodi. È stata realizzata una revisione bibliografica interrogando le banche dati PubMed, Cinhal, Psycinfo, Joanna Briggs, Cochrane, TRIP database. Sono state considerate le pubblicazioni realizzate negli ultimi 10 anni in merito ai temi identificati nell'obiettivo.

Risultati. Sono stati selezionati 24 articoli, di cui 6 revisioni e metanalisi, 3 RCT e 15 studi osservazionali. I fattori correlati ad una bassa aderenza alla riabilitazione cardiologica sono molteplici, i più importanti includono: il genere femminile, l'età avanzata, la comorbidità, il livello basso di istruzione, la disoccupazione e i fattori psicosociali. Ansia e depressione a loro volta sono influenzati da diversi fattori soggettivi o esterni, ritardare l'accesso al programma riabilitativo può aumentarne i livelli. Di 8 studi che trattano dei benefici della riabilitazione cardiologica solo uno studio osservazionale non ha trovato una differenza significativa sul cambiamento di ansia e depressione tra i partecipanti e non alla riabilitazione cardiologica, mentre gli altri studi hanno evidenziato un impatto positivo con ottimi risultati. Interventi che possono migliorare l'aderenza sono: fornire programmi riabilitativi diversi e personalizzati a donne e soggetti vulnerabili, l'utilizzo di applicazioni mobili, e l'intervento infermieristico nell'indagine di percezione della malattia e tramite strategie di apprendimento e coping.

Conclusioni. Merita investire tempo e ricerca sulla riabilitazione cardiologica e investire sulla formazione dell'equipe multidisciplinare, che garantisca continuità nella presa in carico del paziente sia nel momento di acuzie della malattia cardiaca, sia nel momento riabilitativo, al fine di educare e guidare il paziente verso un percorso di riabilitazione cardiologica, con maggior riguardo verso chi manifesta sintomi di ansia e depressione.

A479: EARLY DETECTION OF ATRIAL FIBRILLATION IN A PATIENT WITH AL CARDIAC AMYLOIDOSIS: ROLE OF REMOTE MONITORING

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Introduction. Antibody-light chain (AL) amyloidosis is the most common form of systemic amyloidosis. It is predominantly found in older males and it is characterized by deposits of light chains immunoglobulins produced by bone marrow plasma cells in plasmacytic dyscrasias. AL amyloidosis develops in 10-15% of patients with multiple myeloma (MM). Amyloid deposition can occur virtually in any organ, more often kidneys and heart. Cardiac involvement is found in $>70\%$ of patients and consists in an infiltrative-restrictive cardiomyopathy that leads to progressive heart failure (diastolic> systolic) and arrhythmias.

Case description. A 59-year-old woman diagnosed four years ago with MM and AL amyloidosis with cardiac, renal and bowel involvement treated with a 1st-line chemotherapy with cyclophosphamide-bortezomib-dexametasone and a 2nd-line chemotherapy with lenalidomide-dexametasone, presented to our outpatient clinic with palpitations and presyncope. Physical examination was unremarkable. The ECG documented SR with a rate of 90 bpm, leftward QRS axis, normal AV conduction, low voltages with "pseudoinfarct" pattern, diffuse VR abnormalities. The transthoracic echocardiogram showed normal LV dimensions with severe LV hypertrophy, EF 35%, diastolic dysfunction, atrial dilatation, moderate mitral and tricuspid regurgitation, RV hypertrophy, moderate pulmonary hypertension and minimal pericardial effusion. Because of the palpitations and presyncope complained by the patient, we prescribed a 24Hour-ECG Monitoring, that did not detect any arrhythmias. We started Bisoprolol 1.25 mg o.d. and we titrated it up to 2.5 mg o.d., the maximum dose tolerated. The patient was still

symptomatic. In consideration of the higher risk of atrial fibrillation (AF), ventricular arrhythmias and sudden cardiac death in patients with cardiac Amyloidosis, and the fact that cancer is a prothrombotic state, we decided to implant a loop recorder. During the first month of remote monitoring, we detected several episodes of paroxysmal AF. The patient was quickly called back to our outpatient clinic to start oral anticoagulant therapy with apixaban 5 mg b.d. At the present time, two years after implantation, the patient is clinically stable and no cerebrovascular accidents have occurred. No hospitalization was required. No sustained ventricular arrhythmias were detected on remote monitoring.

Discussion. Cardiac involvement in systemic Amyloidosis is a leading cause of morbidity and mortality. The prognosis is poor, with a median survival time of 6 months for patients that are left untreated and 5-10 years for patients with treatment. AF is a known complication of amyloidotic cardiomyopathy, probably due to amyloid deposition within the left atrium. Prevalence of AF varies according to the etiology of amyloidosis, with a mean value of 9% for AL amyloidosis. When present, AF is associated with a very high incidence of thromboembolism, but in literature it does not seem to impact all-cause mortality. Remote monitoring can identify clinically relevant arrhythmias in symptomatic or asymptomatic patients, allowing earlier hospitalization as well as optimization of therapies to prevent stroke. Remote monitoring can also help us redefine the real incidence and prevalence of AF in patients with AL amyloidosis.

A480: LE CONOSCENZE DEL PAZIENTE AFFETTO DA SINDROME CORONARICA ACUTA DI PATOLOGIA E PREVENZIONE SECONDARIA, QUALE IL LIVELLO RAGGIUNTO ALLA CONCLUSIONE DEL RICOVERO?

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Introduzione. La SCA (Sindrome Coronarica Acuta) è una patologia ad elevato rischio di recidiva nonché causa principale di morte e morbilità nel mondo occidentale. Risulta quindi fondamentale che il paziente, a seguito di diagnosi di SCA e del ricovero associato, sappia riconoscere precocemente la manifestazione di segni e sintomi di recidive, segua stili di vita idonei e aderisca al programma di riabilitazione cardiologica per ridurre in maniera significativa la possibilità che si ripresenti un ulteriore evento cardiovascolare.

Obiettivo. L'obiettivo primario di questo elaborato è quello di indagare il livello di conoscenza raggiunto dal paziente affetto da SCA, a seguito del percorso ospedaliero, in merito al riconoscimento dei fattori di rischio cardiovascolare e di segni e sintomi di manifestazione clinica.

Metodo. Il lavoro di ricerca è stato svolto tramite revisione della letteratura poiché risulta essere il metodo più funzionale per ottenere un campione statisticamente significativo e trasversale a differenti realtà operative. Sono stati consultati documenti reperiti attraverso un iniziale e breve ricerca libera sul motore Google e successivamente ricercati articoli scientifici sul tema attraverso la consultazione di banca dati di letteratura scientifica quali PubMed. Ho poi consultato manuali e libri specialistici per la stesura del quadro teorico.

Risultati. Dalla revisione degli studi si è evidenziato come la maggior parte dei pazienti affetti da SCA, a distanza di sei mesi dall'evento acuto, risulti avere una limitata conoscenza delle manifestazioni cliniche tipiche della patologia in oggetto e dell'importanza dell'aderenza alle pratiche di educazione terapeutica. Il controllo dei fattori di rischio risulta inadeguato con alte prevalenze di fumo persistente, diete malsane, inattività fisica e di conseguenza la maggior parte dei pazienti risulta essere in sovrappeso o obesa con un'alta prevalenza di diabete. Meno della metà dei pazienti coronarici accede a programmi di prevenzione e riabilitazione cardiaca. I risultati non variano modulando l'intervallo di indagine poiché la prevenzione secondaria a lungo termine risulta non ottimale anche a distanza di due anni dall'evento acuto.

Conclusione. L'aderenza ai programmi di prevenzione secondaria: cessazione del fumo; dieta; peso ed esercizio fisico; controllo della pressione arteriosa; controllo del colesterolo e della glicemia, nei pazienti con diagnosi di SCA è risultata scarsa. A tal proposito, è stato sviluppato un breve opuscolo che contenga i punti salienti che il paziente affetto da SCA deve seguire per prendersi cura della propria condizione a domicilio e prevenire l'insorgenza di complicanze o recidive ed è nostra intenzione rendere questo opuscolo fruibile dalle unità operative di cardiologia. Possibili sviluppi per la pratica potrebbero essere indagati con studi successivi che valutino i livelli di conoscenza del paziente nelle unità operative dove l'opuscolo è stato utilizzato.

A481: EFFETTI DI UNA COMBINAZIONE DI NUTRACEUTICI PER IL CONTROLLO DELL'ASSETTO METABOLICO, LIPIDO-GLICEMICO, IN PAZIENTI CON BASSO PROFILO DI RISCHIO CARDIOVASCOLARE, IN PREVENZIONE PRIMARIA

Nicola Bernardi (a), Greta Pascariello (a), Giuliana Cimino (a), Emiliano Calvi (a), Andrea Dell'Aquila (a), Chiara Schiannini (a), Erica Legramanti (a), Paola Belotti (a), Riccardo Raddino (a)
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Obiettivi. La dislipidemia è un fattore di rischio cardiovascolare indipendente (1). Attualmente le statine sono il farmaco di prima linea

nella terapia di questa condizione, sia per il miglioramento del profilo lipidico che per gli effetti pleiotropici associati. Tuttavia, questa terapia non è priva di effetti collaterali. Inoltre, considerato l'elevato costo di una terapia prolungata nel tempo, il SSN pone indicazione all'utilizzo delle statine in prevenzione secondaria oppure in prevenzione primaria solo se il rischio cardiovascolare globale a 10 anni risulti essere pari o superiore al 20%. Si è pertanto valutato l'impatto di una terapia con nutraceutici sul profilo lipidico-metabolico e sulla funzione endoteliale, la rigidità arteriosa e il profilo infiammatorio di una coorte di pazienti con basso profilo di rischio CV (SCORE <1%).

Metodi. L'obiettivo primario di questo studio prospettico è quello di verificare l'effetto di MonacolinaK 10 mg + CoenzimaQ10 10 mg sul profilo lipidico, infiammatorio e sulla funzione endoteliale e la rigidità arteriosa. I criteri di inclusione sono: 1) pazienti con rischio cardiovascolare molto basso (SCORE <1% a 10 anni); 2) nessun trattamento precedente o in atto. Tutti i pazienti sono stati valutati al tempo 0 e dopo 12 settimane di trattamento misurando i livelli di: colesterolo totale, colesterolo LDL, colesterolo HDL, trigliceridi, CPK, hs-PCR, glicemia, funzionalità endoteliale attraverso il calcolo dell'indice di iperemia reattiva (RHI index, ottenuto attraverso il device EndoPAT 2000 che consente la misurazione non invasiva dell'ampiezza e delle variazioni del tono arterioso nei vasi periferici) e la rigidità arteriosa (PWV misurata con metodica SphygmoCOR)(3).

Risultati. In questo studio sono stati inclusi 20 pazienti ambulatoriali, di età compresa tra i 46 e i 75 anni. Il trattamento è stato ben tollerato, nessun soggetto ha riportato effetti collaterali o abbandonato lo studio. Non si è verificato alcun cambiamento significativo in termini di indici di funzionalità epatica (ALT, AST, CK) o glicemia. Dopo 12 settimane di terapia si è verificata una riduzione statisticamente significativa del colesterolo totale e del colesterolo LDL (p<0,001). È stata osservata inoltre una riduzione dei trigliceridi ed un incremento del colesterolo HDL, anche se non statisticamente significativo. Sono stati riscontrati effetti positivi sulla funzionalità endoteliale e sulla rigidità arteriosa dopo 12 settimane di trattamento. È stata evidenziata anche l'associazione tra incremento di RHI e la riduzione di hs-PCR nell'intera coorte di studio.

Conclusioni. I nutraceutici riducono i livelli di lipidi plasmatici, migliorano la funzione endoteliale e la rigidità arteriosa con associato miglioramento del profilo infiammatorio. Questo può suggerire un loro utilizzo in pazienti a basso rischio CV senza indicazione a statine, in pazienti intolleranti a statine in aggiunta ad ezetimibe e in pazienti non a target con terapia massimale con statine.

A482: HYPERTRIGLYCERIDEMIA IN ASYMPTOMATIC OBESE SUBJECTS WITHOUT OTHER COMORBIDITIES IS ASSOCIATED WITH SIGNIFICANT STRUCTURAL AND FUNCTIONAL ABNORMALITIES AS COMPARED WITH CONTROL

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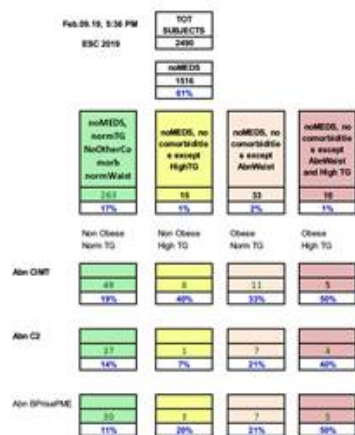
Background. Cardiovascular (CV) risk factors (diabetes, dyslipidemia, hypertension, smoking) contribute to common and destructive mechanisms of disease, including endothelial dysfunction, oxidative stress and inflammation. Early atherosclerosis is characterized by the adhesion of circulating white blood cells (leukocytes) to the dysfunctional endothelium. Triglycerides, among the other lipids, undergo oxidative damage that trigger innate and adaptive inflammatory processes.

Purpose. The aim of this study is to assess whether elevated triglyceridemia or obesity or their simultaneous presence is significantly associated with structural and functional abnormalities in asymptomatic subjects taking no CV medications.

Methods. We screened 2490 asymptomatic subjects, age 20-79, for CVD risk using the Early Cardiovascular Disease Risk Scoring System (ECVDRS), which consists of 10 tests: large (C1) and small (C2) artery stiffness, blood pressure (BP) at rest and post mild exercise (PME), Carotid Intima Media Thickness (CIMT), abdominal aorta and left ventricle ultrasound (LVUS), retinal photography, microalbuminuria, ECG, and pro-BNP. Abnormal blood pressure rise post mild exercise (BPrisePME) was defined as systolic BP rise >30 mmHg post 3-min-walk at 7% elevation, 2.5 mph. Normotension (NT), pre-hypertension (pre-HTN), and hypertension (HTN) were defined according to JCN7 criteria. Hypertriglyceridemia is defined as TG ≥150 mg/dL according to 2011 AHA GLs.

Results. Among the 2490 subjects, 1292 are female and 1198 male. Of these, 1516 (61%) are not taking any CV medication. The subjects are grouped into 4 groups according to the presence or absence of elevated TG and the presence or absence of obesity. Prevalence of abnormal structural and functional abnormalities are shown in Table below.

Conclusions. Based on our data, (1) hypertriglyceridemia in asymptomatic non-obese subjects is very low; (2) hypertriglyceridemia in asymptomatic subjects is associated with early structural and functional abnormalities especially in obesity; (3) hypertriglyceridemia in asymptomatic subjects is an independent early risk factor for CVD. Hence, hypertriglyceridemia in obese subjects needs to be treated aggressively in order to reduce the CVD risk.



A483: EXCESS EPICARDIAL FAT VOLUME AS A NOVEL RISK FACTOR FOR CV STRUCTURAL AND FUNCTIONAL ABNORMALITIES

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Background. Adipose tissue is an important endocrine system in our body. Elevated adipokines have been reported to be atherogenic. We have previously reported that excess abdominal visceral adipose tissue is associated with structural and functional abnormalities. Abdominal visceral adiposity is frequently associated with increased epicardial fat volume. Epicardial fat has a different mRNA than abdominal visceral tissue that belongs to the visceral abdominal adipose tissue.

Purpose. The aim of this study is to assess whether in a 10-year follow-up period abnormal epicardial fat volume has been contributing to structural and functional abnormalities even with normal Calcium Score.

Methods. We screened 2706 asymptomatic subjects, age 20-79, for CVD risk using the Early Cardiovascular Disease Risk Scoring System (ECVDRS), which consists of 10 tests: large (C1) and small (C2) artery stiffness, blood pressure (BP) at rest and post mild exercise (PME), Carotid Intima Media Thickness (CMT), abdominal aorta and left ventricle ultrasound (LVUS), retinal photography, microalbuminuria, ECG, and pro-BNP. Abnormal blood pressure rise post mild exercise (BPrisePME) was defined as systolic BP rise >30mmHg post 3-min-walk at 7% elevation, 2.5mph. Normotension (NT), pre-hypertension (pre-HTN), and hypertension (HTN) were defined according to JCN7 criteria. Hypertriglyceridemia is defined as TG >= 150 mg/dL according to 2011 AHA GLs. 114 Subjects underwent a 10 year follow-up, and 194 subjects underwent additional screening using Siemens Dual CT scan 64x2 to assess epicardial fat volume (ECFV) in millimeters as well as calcium deposits and coronary calcification (Calcium Score, CS, according to the Agatston risk score).

Results. Among the 2706 subjects, 1390 are female and 1316 male. Of these, 1496 (55%) are not taking any CV medication. Results in Table.

Conclusions. Based on our data, (1) normal epicardial fat volume and normal Calcium Score are associated less functional and structural abnormalities; (2) abnormal epicardial fat volume and abnormal Calcium Score are associated with functional and structural abnormalities; (3) abnormal epicardial fat volume even with normal Calcium Score is associated with functional and structural abnormalities. Hence, we conclude that excess epicardial fat volume is a novel CV risk factor and needs to be considered for future management.

TOTAL SUBJECTS 2706				
Subjects w/ F-Up 115 (4%)				
	Normal BP rise PME	Normal => Abnormal BP rise PME	Abnormal BP rise PME	Abnormal => Normal BP rise PME
	22 (19%)	40 (35%)	35 (30%)	18 (16%)
Normal CaS	11 (50%)	15 (38%)	15 (43%)	4 (22%)
Normal CaS and abnormal Epicardial Fat Volume			6 (40%)	
Abnormal CaS	2 (9%)	4 (10%)	11 (31%)	2 (11%)
Abnormal Epicardial Fat Volume	3 (14%)	6 (15%)	11 (31%)	3 (17%)

A484: VALUTAZIONE DEI LIVELLI PLASMATICI DI COLESTEROLO REMNANTS E DEL RAPPORTO MONOCITI/HDL IN PAZIENTI DELL'ASIA DEL SUD AFFETTI DA SINDROME CORONARICA ACUTA

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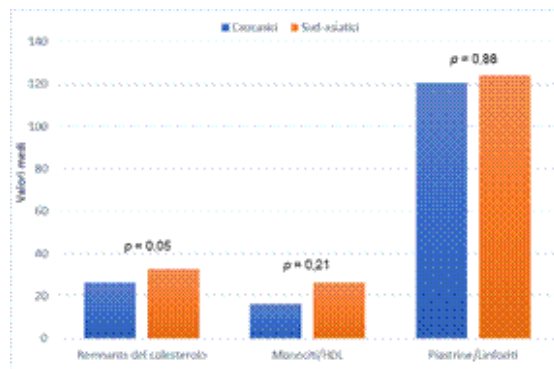
Obiettivi. Nel presente studio, abbiamo voluto confrontare le caratteristiche cliniche e coronarografiche tra pazienti sud-asiatici e

caucasici affetti da sindrome coronarica acuta (SCA). In particolare, abbiamo focalizzato la nostra analisi sulla valutazione di recenti indicatori di rischio cardiovascolare, quali i remnanti del colesterolo, corrispondenti a tutto il colesterolo plasmatico meno quello HDL e LDL, ed il rapporto monociti/HDL. Inoltre, abbiamo confrontato tra i due gruppi anche i valori di vari rapporti lipoproteici e del rapporto piastrine/linfociti, accurati predittori di eventi coronarici e di coronaropatia.

Materiali e metodi. In questo studio osservazionale retrospettivo abbiamo incluso 40 pazienti (34 uomini) provenienti dall'Asia del Sud, ricoverati per SCA presso l'UTIC e la Degenza dell'U.O.C. di Cardiologia tra il 2013 ed il 2018 e sottoposti a procedura di rivascularizzazione coronarica mediante angioplastica coronarica transluminale percutanea (PCI).

Risultati. I pazienti sud-asiatici, rispetto a quelli caucasici, hanno presentato valori medi superiori dei vari parametri analizzati: remnanti del colesterolo (32,6 ± 17 vs 26,5 ± 9,6), rapporto monociti/HDL (26,4 ± 48,7 vs 16,5 ± 8,3), rapporto piastrine/linfociti (124,7 ± 130,7 vs 120,5 ± 58,8). Inoltre, sono stati riscontrati anche valori medi superiori dei vari rapporti lipoproteici nei pazienti sud-asiatici, rispetto al gruppo di controllo.

Conclusioni. Nel nostro studio abbiamo evidenziato valori superiori dei remnanti del colesterolo e del rapporto monociti/HDL in un campione di pazienti provenienti dall'Asia del Sud, confrontati con un gruppo di pazienti caucasici. Inoltre, abbiamo anche osservato valori più elevati dei vari rapporti lipoproteici e del rapporto piastrine/linfociti nei pazienti sud-asiatici, rispetto al gruppo di controllo. La valutazione in maniera routinaria dei parametri analizzati in questo studio potrebbe fornire informazioni più accurate riguardo il rischio cardiometabolico dei pazienti provenienti dal sud dell'Asia.



SCOMPENSO CARDIACO

A485: ROLE OF RIGHT VENTRICLE IN ACUTE HEART FAILURE WITH PRESERVED EJECTION FRACTION: A COMPARISON BETWEEN HYPERTENSIVE PULMONARY EDEMA AND DECOMPENSATED HEART FAILURE

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Background. Limited data are available on the pathophysiological role of the right ventricle (RV) in patients with acute heart failure with preserved ejection fraction (AHF-PEF) and its impact on the main clinical manifestation such as pulmonary edema or peripheral congestion. Mainly through right-to-left stroke volume mismatch and ventricular-arterial decoupling, right chambers size and function may play a key role leading to fluid overload or maldistributed phenotypes.

Methods. In this monocenter, prospective, observational study 80 consecutive patients with AHF-PEF were enrolled. A complete echocardiographic examination was performed within 6 hours from emergency department admission; multiparametric RV function was carefully evaluated in the very acute phase. Focusing on hypertensive pulmonary edema (H-AHF) and decompensated AHF without pulmonary edema (D-AHF) phenotypes, the study aims to analyze the echocardiographic peculiarities of these clinical entities in the early phase of admission and its modification at discharge (D-AHF n=58, H-AHF n=22).

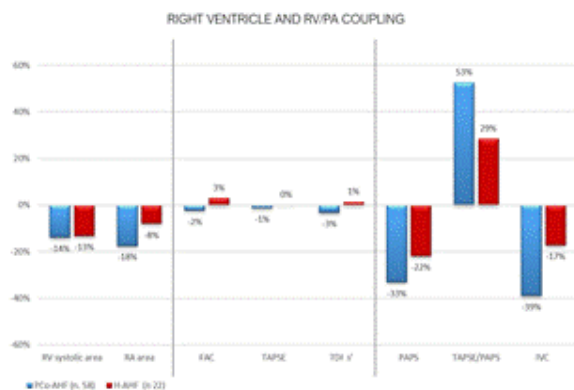
Results. Baseline clinical characteristics were comparable in both groups, except for coronary artery disease more prevalent in H-AHF and atrial fibrillation more prevalent in D-AHF. D-AHF patients showed dilated and dysfunctional right chambers compared to H-AHF. Regarding systolic

function, normal values of fractional area change (FAC) and tricuspid annular plane systolic excursion (TAPSE) were registered in H-AHF at admission and at discharge. D-AHF showed greater systolic pulmonary artery pressure (sPAP) and lower TAPSE/sPAP ratio. Left ventricular dimensions and function were comparable in both groups. Conversely, E/e' ratio was significantly higher in H-AHF at admission. Data are summarized in the Table and Figure below.

Conclusion. D-AHF and H-AHF represent different phenotypes of AHF-PEF. Right heart structure and function and ventricular-arterial coupling could play a crucial role in their pathophysiology. Non dilated RV with preserved systolic function seems to be crucial to develop pulmonary edema without signs of peripheral congestion. Further investigations are needed to corroborate the hypothesis of interventricular stroke volume mismatch in the complex AHF-PEF clinical scenario.

RV structure and function	D-AHF (n: 58)		H-AHF (n: 22)	
	Admission	Discharge	Admission	Discharge
RV diastolic area (cm ²)	20,27 ± 5,16	16,99 ± 4,13 #	14,85 ± 2,84 *	13,24 ± 2,58 *
RV systolic area (cm ²)	12 ± 3,75	10,33 ± 3,6 #	8,25 ± 2,59 *	7,16 ± 1,77 *
Right atrium area (cm ²)	27,29 ± 22,73	22,51 ± 11,53 #	16,13 ± 3,67 *	14,83 ± 5,08 *
RV basal diameter (cm)	3,92 ± 0,66	3,54 ± 0,55 #	3,08 ± 0,58 *	2,78 ± 0,48 *
FAC	41,13 ± 8,97	40,18 ± 9,42	45,02 ± 9,26 (*)	46,37 ± 9,56 *
TAPSE (mm)	18,91 ± 3,27	18,67 ± 3,97	21,28 ± 2,74 *	21,3 ± 2,63 *
PAPs (mmHg)	52,24 ± 11,19	34,96 ± 10,19 #	40,95 ± 12,35 *	32 ± 9,6 #
TAPSE/PAPs (mm/mmHg)	0,38 ± 0,12	0,58 ± 0,19 #	0,56 ± 0,17 *	0,72 ± 0,21 #
RV s' (cm/s)	12,1 ± 2,9	11,7 ± 2,9	12,82 ± 2,08	13 ± 2,87
IVC (mm)	21,4 ± 4,4	13,06 ± 4,1 #	14,65 ± 4,28 *	12,12 ± 3,25

* p < 0,05 admission D-AHF vs admission H-AHF; # p < 0,05 discharge D-AHF versus discharge H-AHF; # p < 0,05 admission vs discharge.



A486: CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN HEART FAILURE: IMPACT ON CIRCULATING LEVELS AND PROGNOSTIC VALUE OF NT-PROBNP, HS-TNT AND SST2

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Background. Chronic obstructive pulmonary disease (COPD) is a frequent comorbidity in patients with heart failure (HF). We assessed the influence of COPD on circulating levels and prognostic value of 3 HF biomarkers: N-terminal pro-B-type natriuretic peptide (NT-proBNP), high-sensitivity troponin T (hs-TnT), and soluble suppression of tumorigenesis-2 (sST2).

Methods. Individual data were analyzed from 14 cohorts of patients with chronic HF, known COPD status and NT-proBNP, hs-TnT, sST2 values.

Results. In the whole population (n=13328), patients with COPD (n=2155, 16%) were older (age 71 years [64-77] vs. 66 [57-75]; p<0.001), were more frequently men (79% vs. 74%; p<0.001), had also severe dyspnea (43% in New York Heart Association [NYHA] class III-IV vs.

31%; p<0.001), and slightly worse renal function (median estimated glomerular filtration rate [eGFR] 58 mL/min/1.73 m² [43-73] vs. 60 [46-77]; p<0.001). They had also higher NT-proBNP (1508 ng/L [650-3363] vs. 1239 ng/L [479-2911]; p<0.001), hs-TnT (22 ng/L [13-38] vs. 17 ng/L [9-30]; p<0.001), and sST2 (31 ng/mL [23-45] vs. 29 [21-43]; p=0.040). In both the COPD and non-COPD subgroups, the best cut-offs of the 3 biomarkers refined the prediction of 1- and 5-year all-cause and cardiovascular mortality and 1- to 12-months HF hospitalization over a prognostic model including age, sex, ischemic etiology, eGFR, HF categories, NYHA III-IV, and the NT-proBNP cut-off alone.

Conclusions. Patients with HF and COPD have higher NT-proBNP, hs-TnT and sST2. Patient classification based on COPD-specific cut-offs refines risk reclassification for 1- and 5-year all-cause and cardiovascular mortality and 1- to 12-months HF hospitalization.

A487: CARDIOMYOPATHY IN DUCHENNE SYNDROME: NEW TOOLS FOR A STANDARDIZATION OF ICD IMPLANTATION

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Duchenne muscular dystrophy is an X-linked recessive disorder characterized by the loss of cardiac tissue, replaced by patchy fibro-fatty biventricular deposition, leading to scar formation and eventually ventricular dysfunction and life-threatening arrhythmias. Currently, there are no specific guidelines on ICD implantation, in primary and secondary prevention in DMD patients. This relevant decision in the natural history of the disease has to be appraised carefully taking into account ethical and practical considerations that should be tailored together with the family and caregivers. Moreover, the current pieces of evidence do not support any genotype-phenotype correlations or cardiac magnetic resonance high-risk pattern able to stratify the risk of ventricular arrhythmias in DMD patients.

Here we report the case report of a DMD patient of 37 years old, having a deletion in exons 3-7 of the dystrophin gene, which determined the complete absence of the protein. He underwent clinical assessment for cardiac dysfunction throughout the years, showing progressive LV dysfunction and dilation and since 2016, he has been followed in our tertiary center. The last CMR was performed in February 2019, showing an extensive late gadolinium enhancement in mid-inferolateral walls with a transmural distribution and subepicardial enhancement in mid-apical SIV, suggesting a high-risk pattern for arrhythmias development. Nevertheless, the LVEF was stable in the last four years. The patient was treated with ACE, MR Antagonist and BB. Importantly, since 2019 continuous EKG monitoring showed NSTV, frequent PVCs, and PACs and the patient started to complain for palpitations. Therefore, the case was discussed in our multidisciplinary team (neurologist, pneumologist, infectious disease specialist) and considering the CMR pattern, the genetic background, (exons 3 to 7: ABD1 domain), the full support of the family, and the optimal disease-related quality of life (the patient is a semi-professional wheelchair hockey player) and life expectancy, after obtaining the consent of the patient, biventricular ICD was implanted. No complications occurred during the hospital phase (infection, bleeding, respiratory failure, access-related events) nor the 6 months after. Importantly, psychological rejection of the device was not referred. Ten months later the implant, the patient complained of palpitations, chest pain, and general malaise. At the device interrogation: An episode of sustained VT at 183 bpm treated with ATP was detected. Other episodes were noted of Non-sustained VT episodes at 185 bpm, in the absence of any modifiable condition.

In the case described, a focused multidisciplinary-based approach was able to make the decision to proceed with the ICD implantation in a DMD patient, without any short and long term complication. The intervention effectively prevents a sudden cardiac death and keeps the patient's and the caregivers' engagement to the clinical pathway very high.

A488: EFFECTS OF SACUBITRIL/VALSARTAN IN A MODEL OF AGE-ASSOCIATED HEART FAILURE

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Background. The majority of elderly patients with heart failure (HF) has a preserved ejection fraction (HFpEF) that constitutes a syndrome characterized by frequent hospitalizations and high mortality. Despite the growing social burden of HFpEF, the comprehension of its pathophysiology is incomplete, and treatment remains largely undefined. As recently highlighted, the mechanisms might involve both cardiovascular and non-cardiovascular components, such as left ventricle hypertrophy and remodeling, microvascular dysfunction, hypertension and

mitochondrial dysfunction that lead to diastolic abnormalities. Moreover, aging itself may contribute independently to deterioration of diastolic function. A recent trial has demonstrated the efficacy of sacubitril/valsartan, first-in-class angiotensin receptor-neprilysin inhibitor, in reducing mortality and morbidity in patients with HF with reduced EF. Additional studies conducted on elderly patients with HFpEF and diastolic abnormalities are expected in the next years.

Methods. 18-month old female Fischer 344 rats were treated with oral administration of sacubitril/valsartan (60 mg/kg/die, 1:1 ratio) for 12 weeks. Age-matched and 3-month old young animals were administered with vehicle, and served as controls. Tail-cuff method was used to monitor blood pressure weekly. Echocardiography and left ventricle catheterization were employed to assess systolic and diastolic function, at baseline, during the treatment and before sacrifice.

Results. Mean blood pressure resulted increased in aging rats in comparison to young rats. At sacubitril/valsartan treatment completion, we observed a significantly reduction of blood pressure. As documented by pulsed wave Doppler, the decrease of E/A ratio along with increase of E deceleration time and isovolumetric relaxation time evidenced the impairment of diastolic function in aging rats. Sacubitril/valsartan exposure partially ameliorated diastolic performance in old rats. Similarly, hemodynamic analysis indicated alterations of diastolic part of cardiac cycle that were positively affected by sacubitril/valsartan. Both echocardiography and hemodynamics showed normal systolic parameters. To determine the effect of treatment on cardiac hypertrophy, heart weight-to-tibia length ratio was measured. Interestingly, this parameter was significantly reduced in sacubitril/valsartan-treated rats.

Conclusions. Our preliminary results evidenced a modulation by sacubitril/valsartan of active relaxation and passive diastolic compliance resulted altered in aging rats, although the specific molecular mechanisms are yet to be identified.

A489: DAPAGLIFLOZIN ATTENUATES DIASTOLIC DYSFUNCTION IN A MODEL OF HEART FAILURE

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Background. The results of trial with SGLT2 inhibitors raised possibility that this class of anti-hyperglycaemic drugs may provide cardiovascular benefits independently from their anti-diabetic effects. Although it has not been specified whether patients with significantly reduced risk for HF hospitalization had any particular form of HF, it is possible that heart failure with preserved ejection fraction (HFpEF) patients were appreciably represented. HFpEF is a challenging clinical syndrome and represents yet unresolved pathophysiological continuum with a consequent perception of lack of effective treatments. Moreover, HFpEF often share co-morbidities like hypertension and diabetes. Following noted dissociation between control of glycaemia and cardiac outcome, we have selected a hypertensive, non-diabetic model of HFpEF to examine the effects of SGLT2 inhibitor dapagliflozin on the progression of experimental heart disease independently from its effects on diabetes.

Methods. Seven-week-old Dahl salt-sensitive (Dahl/SS) rats were fed a high salt diet (8% NaCl) for 5 weeks to induce hypertension. Then, rats continued with a high salt diet and were orally administered with either dapagliflozin (0.1 mg/kg/day) or vehicle for the following 6 weeks. Diastolic and systolic function were monitored by echocardiography.

Results. Dapagliflozin ameliorated diastolic function as documented by echo-Doppler and heart catheterization, while blood pressure remained markedly elevated. Chronic in vivo treatment with dapagliflozin reduced diastolic Ca²⁺ and Na⁺ overload and increased Ca²⁺ transient amplitude in ventricular cardiomyocytes, although no direct action of dapagliflozin on isolated cardiomyocytes was observed. Dapagliflozin reversed endothelial activation and endothelial nitric oxide synthase deficit, with reduced cardiac inflammation and consequent attenuation of pro-fibrotic signaling. The potential involvement of coronary endothelium was supported by the endothelial upregulation of Na⁺/H⁺ exchanger 1 in vivo and direct effects on dapagliflozin on the activity of this exchanger in endothelial cells in vitro.

Conclusions. Several mechanisms may cumulatively play a significant role in the dapagliflozin-associated cardioprotection. Dapagliflozin ameliorates diastolic function and exerts a positive effect on the myocardium, possibly targeting coronary endothelium. The lower degree of endothelial dysfunction, inflammation and fibrosis translate into improved myocardial performance.

A490: VALUTAZIONE EPIDEMIOLOGICA DEI RICOVERI PER SCOMPENSO CARDIACO NELLA PROVINCIA DELL'AQUILA: FATTORI DI INSTABILIZZAZIONE DELLA MALATTIA E STRATEGIE DI PREVENZIONE

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Background. Lo scompenso cardiaco rappresenta una delle più frequenti cause di mortalità e morbilità nei paesi occidentali. La storia clinica dei pazienti con scompenso cardiaco è segnata da ospedalizzazioni ricorrenti che, oltre ad assorbire una quota assolutamente rilevante di risorse assistenziali, rappresentano una spia oggettiva di inadeguata gestione della sindrome e si associano inevitabilmente ad una scadente qualità di vita e una ridotta sopravvivenza.

Scopo. La presente indagine ha voluto identificare la presenza di fattori scatenanti o facilitanti la riaccutizzazione che conduce al ricovero ospedaliero, al fine di determinare come alcuni dei fattori precipitanti possano essere previsti e potenzialmente prevenuti.

Materiali e metodi. Nel periodo aprile/ottobre 2019 sono stati valutati al momento del ricovero 292 pazienti ospedalizzati per scompenso cardiaco nella provincia dell'Aquila, mediante la compilazione da parte di medici dei Reparti di accettazione di una apposita scheda. Sono stati raccolti dati relativi alla presenza di comorbidità, alla terapia domiciliare in atto, alla compliance terapeutica, alla rete familiare/sociale di supporto, alla frequenza dei controlli clinici e degli accessi ospedalieri nell'anno precedente all'attuale ricovero. È stato inoltre chiesto al medico compilatore di indicare una o più possibili cause ritenute responsabili dell'instabilizzazione.

Risultati. Lo studio ha interessato una popolazione di pazienti con età media di 80,5 anni, il 54% aveva sesso maschile e la maggior parte viveva in famiglia con somministrazione dei farmaci autonoma o affidata ad un familiare. Le comorbidità sono risultate: ipertensione arteriosa (58%), anemia (52%), insufficienza renale (50%), BPCO (41%), diabete mellito (26%) e pregresso ictus (9%). Al momento del ricovero, il 72% dei pazienti stava assumendo betabloccanti, il 42% ACE-i/ARBs, l'83% diuretici e il 49% antialdosteronici. Uno o più fattori precipitanti sono stati identificati nella maggior parte del campione: la causa di instabilizzazione più frequentemente identificata è stata l'infezione (31%), seguita da riaccutizzazione di BPCO (20%) e riduzione della terapia (17%). Nel gruppo di pazienti che ha effettuato un maggior numero di ricoveri nell'anno precedente, la causa principale è stata la riduzione della terapia (31%).

Conclusioni. L'indagine condotta ha evidenziato un utilizzo dei trattamenti raccomandati per lo scompenso cardiaco ben lontano dall'ottimale, sia in termini di percentuali di utilizzo che di dosaggi, una sottostima del ruolo dell'anemia come fattore di instabilizzazione e una scarsa aderenza alla terapia come fattore responsabile di un maggior numero di re-ricoveri. È dunque fondamentale, per ottimizzare la gestione dello scompenso cardiaco, prestare maggiore attenzione ai fattori che possono essere responsabili di esacerbazione del quadro clinico, la maggior parte dei quali risulta essere prevenibile. Le strategie terapeutiche devono mirare ad uno stretto controllo delle comorbidità, alla diffusione di programmi educativi centrati sul paziente e all'utilizzo di strategie di supporto multidisciplinari.

A491: NON INVASIVE HEMODYNAMIC PROFILES AND OUTCOME IN OUTPATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION TREATED WITH SACUBITRIL/VALSARTAN: AN ECHOCARDIOGRAPHIC STUDY

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Background. In patients with heart failure (HF) with reduced left ventricular (LV) ejection fraction (EF, HFREF), sacubitril/valsartan (S/V

improves outcome and LV remodeling. We investigated whether its favourable effect is maintained across the range of echocardiographically-derived hemodynamic profiles in HFREF patients.

Methods. In our multicenter, open-label study, HFREF patients underwent echocardiography at baseline before initiating S/V, and were classified according to the ratio of early transmitral Doppler velocity/early diastolic annular velocity (E/e') and cardiac index (CI, l/min/m²), as: profile-A) E/e' <13 and CI ≥2.0 mL/min; profile-B) E/e' <13 and CI <2.0 mL/min; profile-C) E/e' ≥13 and CI ≥2.0, profile-D) E/e' ≥13 and CI <2.0 mL/min. The composite rates of mortality/HF-hospitalizations were assessed across the 4 profiles by multivariable Cox proportional-hazards models during a 3-year follow-up.

Results. Among 727 patients, (mean age: 60.1 years; 15% women; mean LVEF: 29.8%), 630 (87%) completed the study. At baseline, 207 patients (29%) had a profile-A, 111 (15%) a profile-B, 233 (32%) a profile-C, and 176 (24%) a profile-D. Patients in profile-D had more comorbidities and worse renal and LV systolic function. Incidence-rate of the composite end-point (per 100 pts/year) progressively increased from profile-A to profile-D [12.5%, 15.7%, 21.0%, and 32.7%, respectively, P<0.0001]. After covariate-adjusted multivariable analysis hemodynamic profiles characterized by low cardiac output (B and D) remained independently associated with outcome (P<0.001).

Conclusion. In HFREF patients treated with S/V, low cardiac index but not increased filling pressures, is independently associated with poor outcome.

A492: TREATMENT WITH SACUBITRIL/VALSARTAN IS ASSOCIATED WITH HEMODYNAMIC IMPROVEMENT IN OUTPATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION: AN ECHOCARDIOGRAPHIC STUDY

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Background. In patients with heart failure (HF) with reduced ejection fraction (EF, HFREF), sacubitril/valsartan (S/V) improves outcome and cardiac remodeling. Little is known about possible mechanisms underlying its favourable effect.

Purpose. To assess the effects of S/V on echocardiographically-derived hemodynamic profiles in HFREF patients.

Methods. In our multicenter, open-label, HFREF patients treated with S/V underwent echocardiography at baseline and after 12 months and were classified into 4 groups according to the ratio of early transmitral Doppler velocity/early diastolic annular velocity (E/e') and cardiac index (CI, l/min/m²): profile-A: E/e' <13 and CI ≥2.0; profile-B: E/e' <13 and CI <2.0; profile-C: E/e' ≥13 and CI ≥2.0, profile-D: E/e' ≥13 and CI <2.0. Subsequent rates of the composite of death/HF-hospitalization were assessed across changes in the 4 profiles by multivariable Cox proportional-hazards models during 3-year follow-up.

Results. Among 727 patients, (mean age: 60.1 years; 15% women; mean left ventricular (LV) ejection fraction EF: 29.8%), 630 (87%) completed the study. Patients in profile-D had more comorbidities and worse renal and LV function. At follow-up, prevalence of profile-A increased from 29% to 45%, profile-B remained unchanged (15% to 15%); profile-C and D decreased from 32% to 23% and from 24% to 17%, respectively (P<0.0001 for all). Incidence-rate of the composite end-point (per 100 pts/year) progressively increased from profile-A to profile-D at follow-up [11.1%, 16.8%, 24.0%, and 46.5%, respectively, P<0.0001]. In covariate-adjusted Cox model only profile-D at follow-up remained independently associated with outcome compared to profile-A (P<0.001 for both).

Conclusion. In HFREF patients, the beneficial effect of S/V are accompanied by improvement of hemodynamic conditions. Patients with increased filling pressures and low CI at follow-up remain at increased risk of events despite treatment.

A493: PREVALENCE, PREDICTORS AND PROGNOSTIC IMPACT OF REVERSE LEFT VENTRICULAR REMODELING IN OUTPATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION TREATED WITH SACUBITRIL/VALSARTAN. A REAL WORLD STUDY

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Background. In patients with heart failure (HF) with reduced left ventricular (LV) ejection fraction (EF, HFREF), sacubitril/valsartan (S/V) improves outcome and cardiac remodeling. Little is known about prevalence, predictors and prognostic relevance of LV reverse remodeling (RR) in a real-world setting.

Methods. In our multicenter, open-label study, HFREF patients treated with S/V underwent echocardiography at baseline and after 12 months. RR was defined by a ≥15% reduction in LV end-systolic volume compared to baseline. Subsequent rates of the composite of death/HF-hospitalization were assessed by multivariable Cox proportional-hazards models during a 3-year follow-up.

Results. Among 727 patients, (mean age: 60.1 years; 15% women; mean LVEF: 29.8%), 630 (87%) completed the study. At follow-up, RR occurred in 204 (28%) patients and it was prevalent in actively treated patients than in withdrawals (30% vs 16%, P=0.006). By univariable logistic analysis, RR was associated with no history of HF-hospitalizations, non-ischemic etiology, and lower estimated LV filling pressures at baseline. Furthermore, prevalence of RR progressively increased with increasing doses of S/V (low-dose: 23%, intermediate-dose: 28%, high-dose 38%, P<0.01). By multivariable logistic regression, history of HF-hospitalizations, and high dose S/V were independently associated with LV RR. Incidence rates of the composite end-point was lower in RR than in non-RR patients (9.9% vs 17.1%, P<0.05). By multivariable Cox model, after controlling for S/V doses and other covariates, RR was independently associated with better outcome (HR: 0.54, 95% CI: 0.31-0.95, P<0.05).

Conclusion. Among HFREF patients LV RR is more prevalent in patients treated with high doses of sacubitril/valsartan and is associated with better outcome.

A494: THE BENEFITS OF SACUBITRIL/VALSARTAN IN THE TREATMENT OF PATIENTS WITH HEART FAILURE: A REAL-WORLD, SINGLE CENTRE EXPERIENCE

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Background. Heart failure (HF) is a chronic disease that requires lifelong management. In the S. Camillo De Lellis hospital in Rieti, Italy, a daily clinic has been set up to provide an accurate and personalised monitoring of patients diagnosed with HF. Generally, after 1 month from hospital discharge patients receive an in ambulatory dedicated follow-up visit; then a personalised treatment and calendar of follow-up visits is arranged (after 1, 3, 6, 9, or 12 months). The aim of the clinic is to improve the patients' compliance to therapy and quality of life, and to reduce the number of re-hospitalizations for HF and the associated costs. Sacubitril/valsartan is used in patients with long-term HF who have symptoms of the disease replacing ACE I. We assessed the impact of sacubitril/valsartan treatment on the patients referred to the clinic.

Methods. Between March 2017 and September 2019, 107 patients were referred to the clinic for HF. Of these, 54 patients (mean age 79.56 ± 6.39; 35 male and 14 females) were eligible for treatment with sacubitril/valsartan (24 mg/26mg, 49 mg/51mg, tablets ingested twice daily). Forty-nine patients concluded the 1-year follow-up.

Results. Treatment with sacubitril/valsartan improved the NYHA classification of all patients: class IV cases were annulled, class III cases were reduced from 55.1% to 30.6%, and class II cases were increased from 42.8% to 59.2%; for class I cases were increased from 0% to 10.2%. The mean ejection fraction also improved (from 30.85 ± 4.63% to 38.13 ±

4.38%), while the use of diuretics was reduced: furosemide dosage was decreased from 126.24 ± 60.03 mg to 80.10 ± 38.15 mg, and the potassium-sparing diuretic dose was reduced from 35.34 ± 26.31 mg to 5.04 ± 11.21 mg. Importantly, the number of re-hospitalizations for HF also decreased.

Conclusion. Therapy with sacubitril/valsartan in patients with HF is well tolerated, it improves the clinical symptoms and quality of life of patients, and reduces the number of hospitalizations, thus reducing costs for the national health system.

A495: SWITCH TO GLIFLOZINS AND BIVENTRICULAR FUNCTION IMPROVEMENT IN PATIENTS WITH CHRONIC HEART FAILURE AND DIABETES MELLITUS

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Background. Diabetes is the most common comorbidity of HF patients. SGLT2 inhibitors has been shown to reduce hospitalization in patients with HF. Several clinical studies have been conducted to investigate the effect of SGLT2 inhibitors on LV structure and its function. However, although many hypotheses have been put forward, the biological mechanisms through which SGLT2 inhibitors reduce HF hospitalization remain uncertain. The aim of our study was to evaluate the effect of SGLT2 inhibitors on right and left ventricular longitudinal myocardial function in T2DM patients with HF.

Methods. Seventy-eight consecutive outpatients with CHF and T2DM were screened in the Daunia Heart Failure Registry. Thirty-eight of them were enrolled and followed up between May 2019 and February 2020. Enrollment criteria included HbA1c ≥ 6.5%, eGFR ≥ 60 mL/min/1.73 m², age >18 years old and LVEF ≤ 50% with CHF. Exclusion criteria included previous amputation surgery and recurrent urinary tract infections. Medical history, heart rate, systolic blood pressure, Body Mass Index, NYHA functional class and medications were recorded and monitored. All patients underwent blood analysis, ECG, conventional, TDI and strain echocardiography in an ambulatory setting, under resting conditions at the beginning and after 3 months of therapy with SGLT2 inhibitors.

Results. Thirty-eight consecutive outpatients with CHF and T2DM (mean age 67 ± 7,60 years, male: 87%) were enrolled in the study. Twenty-one of them started the treatment with SGLT2 inhibitors, while the remaining seventeen continued their original therapy. The tissue Doppler-derived left ventricular systolic excursion velocity (S') significantly increased from 6,59±1,33 to 7,91±1,36 cm/s 3 months after the administration of SGLT2 inhibitors therapy versus the control group (p = 0,001). GLS showed a significant improvement from -10,15±2,33 to -12,79±3,66% in SGLT2 group versus control p=0,0001). LVEF statistically improved from 39,18±7,8% to 43,67±8,1% (p=0,001). Changes in left ventricular function were not significant in patients who did not started a therapy with SGLT2 inhibitors. Moreover, there was an improvement of right ventricular function, due to a statistically significant increment of TAPSE and of RV S' velocity (respectively from 19,68±2,90 to 21,05± 2,82 and from 11,01±2,15 to 12,89±2,85) and a statistically significant reduction of PAPs (from 29,38±7,19 to 23,65± 8,86 mmHg). The reduction of E/E' velocity ratio in SGLT-2 group (from 10,87±3,82 to 9,52±3,18) described an improvement of diastolic function statistically significant (p=0,03). Finally, a statistically significant reduction of mitral regurgitation was also described in SGLT-2 group.

Conclusions. In a real-world scenario, our results showed that the treatment with SGLT-2 inhibitors in patients with CHF and diabetes is associated with an echocardiographic biventricular function improvement. Large-scale trials are needed to clarify how antihyperglycemic drugs affect echocardiographic parameters.

A496: SWITCH TO SGLT2 INHIBITORS AND IMPROVED ENDOTHELIAL FUNCTION IN PATIENTS WITH CHRONIC HEART FAILURE AND DIABETES MELLITUS

Pietro Mazzeo (b), Adriana Mallardi (b), Lucia Tricarico (b), Michele Correale (b), Pasquale Maiellaro (b), Alessandra Leopizzi (b), Martino Fortunato (b), Salvatore Tucci (b), Michele Magnesa (b), Maria Delia Corbo (b), Massimo Iacoviello (b), Olga Lamacchia (b), Matteo Di Biase (b), Natale Daniele Brunetti (b)
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Background. The prevalence of patients with concomitant heart failure (HF) and diabetes mellitus (DM) continues to increase with the general aging of the population. T2DM frequently causes macrovascular and/or microvascular pathologic changes. Recently a new class of antidiabetic drugs, the SGLT2 inhibitors, have been demonstrated to reduce cardiovascular mortality and heart failure hospitalizations. The use of SGLT2 was associated in previous studies with an improved vascular function. We therefore sought to evaluate possible changes in endothelial

function assessed by flow-mediated dilation (FMD) in patients with CHF and diabetes shifting their therapy to SGLT2 inhibitors.

Methods. Seventy-eight consecutive outpatients with CHF and T2DM were screened in the Daunia Heart Failure Registry. Thirty-eight of them were enrolled and followed up between May 2019 and February 2020. Enrollment criteria included HbA1c ≥ 6.5%, eGFR ≥ 60 mL/min/1.73 m², age >18 years old and LVEF ≤ 50% with CHF. Exclusion criteria included previous amputation surgery and recurrent urinary tract infections. Medical history, heart rate, systolic blood pressure, Body Mass Index, NYHA functional class and medications were recorded and monitored. All patients underwent blood analysis, ECG and evaluation of endothelial function reserve assessed by FMD in an ambulatory setting, under resting conditions, at the beginning and after 3 months of therapy with SGLT2 inhibitors.

Results. Thirty-eight consecutive outpatients with CHF and T2DM (mean age 67 ± 7,60 years, male: 87%) were enrolled in the study. Twenty-one of them started the treatment with SGLT2 inhibitors, while the remaining seventeen continued their original therapy. After 3 month follow-up, the patients who started therapy with SGLT2i showed an improvement in endothelial function versus control group (18,60±6,478% vs 10,29± 3,4331 p<0,000552). Changes in FMD values were not significant in patients who did not changed T2DM therapy.

Conclusions. The beginning of therapy with SGLT2 inhibitors in patients with CHF and T2DM was associated in an observational non randomized study with an improved endothelial function.

A497: LEFT ATRIAL FUNCTION IN A REAL-LIFE POPULATION OF PATIENTS WITH CHRONIC HEART FAILURE AFTER THERAPY WITH SACUBITRIL/VALSARTAN

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Background. Left atrial (LA) enlargement has been demonstrated to be a predictor of adverse cardiovascular outcomes, such as atrial fibrillation (AF), heart failure (HF), and cardiovascular death. Previous studies showed LVEF improvement and reverse remodeling can be achieved after therapy with Sacubitril/Valsartan in real-world settings. We sought to investigate the association between left atrial (LA) structural and functional remodeling in patients with chronic heart failure after therapy with sacubitril/valsartan.

Methods. Patients with chronic HF, LV dysfunction (EF <35%), NYHA class II-III were followed up between September 2019 and March 2020. All patients underwent clinical and echocardiography follow-up at baseline and after 6 months of therapy with sacubitril/valsartan. Measures of LA structure [LA volume (LAV)] and function [left atrial ejection fraction (LAEF), peak atrial longitudinal strain (PALS) and peak atrial contraction strain (PACS)] were calculated.

Results. Fifty consecutive outpatients (mean age 67,06±8,48 years; 43 male) were enrolled in the study. At follow-up visit, LAEF (36,48±10,70 vs 44,86±12,55%, P <0.0000), Global PALS (14,19±7,24 vs 18,01±8,24%, p<0.0000), Global PACS (8,16±6,08 vs 9,90±6,76, p=0.045).

Conclusions. Treatment with sacubitril/valsartan in patients with systolic dysfunction is associated with an improvement in LA functional remodeling in a real-world scenario.

A498: SACUBITRIL/VALSARTAN IMPROVES RIGHT VENTRICLE FUNCTION IN A REAL-LIFE POPULATION OF PATIENTS WITH HF rEF

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Background. Observational studies have demonstrated that treatment with sacubitril/valsartan may improve left ventricular systolic and diastolic function in subjects with reduced left ventricular ejection fraction (LVEF) in real-world studies. Subjects with HF and reduced EF (HF rEF), however, are also characterized by an impaired right ventricular (RV) function. We therefore aimed to evaluate whether also RV function may improve after sacubitril/valsartan therapy.

Methods. Fifty consecutive patients (mean age 67,06±8,48 years; 43 male) with chronic heart failure and NYHA class II-III were followed up for 6 months after therapy with sacubitril/valsartan. Left and right ventricular function was assessed at baseline and after 6 months of therapy.

Results. At 6-month control, therapy with sacubitril/valsartan was associated with a significant improvement in a series of echo parameters: PAsP (35,46±9,77 vs 31,22±10,71 mmHg, p= 0.00088), TAPSE (17,78±2,89 vs 19,30±3,41 mm, p=0.000006); FAC (33,79±6,08 vs 38,21±6,87%, p=0.000000), RV TDI S' (10,5±1,74 vs 12,01±2,50 cm/sec, p=0.00001), RV GLS free wall (-17,86±5,35 vs -20,12±5,38%, p=0.000124), RV GLS 4 Ch (-13,60±4,79 vs -16,27± 4,71, p=0.000001).

Conclusions. In a real-world scenario, sacubitril/valsartan was associated with an improved RV function.

A499: THE IMPACT OF COVID-19 LOCKDOWN ON HEALTH STATUS AND LIFE QUALITY IN HEART FAILURE OUTPATIENTS

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Aims. Heart failure patients are frequently predisposed to recurrences and disease destabilization. They were hit by the COVID-19 outbreak and lockdown. The aim of our study is to evaluate the health status and life quality in heart failure (HF) outpatients by virtual visits, during the COVID-19 lockdown in Italy and to assess whether any changes are required to the management plan.

Methods. Previously hospitalized 160 HF outpatients were followed-up by telephone. Patients' experiences of their health status in terms of symptoms, blood pressure, body weight, and quality of life were recorded using the short version of Kansas City Cardiomyopathy Questionnaire (KCCQ-12).

Results. Patients were divided into two groups: 63 patients who presented at least one parameter of HF deterioration (Group 1) and 97 patients with no HF deterioration (Group 2). In comparison with group 2, group 1 reported significantly lower scores for KCCQ-12 summary (54.6 vs 50.8; $p=0.032$), and for items of physical function (4.5 vs 3.9; $p=0.013$), symptom frequency (5.4 vs 4.4; $p=0.018$), quality of life (4.1 vs 3.4; $p=0.002$) and social limitation (4.5 vs 3.7; $p=0.001$) domains.

Conclusions. The present study suggests the relationship between initial HF deterioration and worsening of the health status in HF outpatients, during the COVID-19 lockdown in Italy.

A500: REDUCTION IN HEART FAILURE HOSPITALIZATION RATE DURING COVID-19 PANDEMIC OUTBREAK

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Aim. To investigate the rate of hospital admissions for heart failure (HF) during the early days of the COVID-19 outbreak in Italy, compared with a corresponding period during the previous year and an earlier period during the same year.

Methods and Results. We performed a retrospective analysis on HF admissions number at 8 hospitals in Italy throughout the study period (February 21st to March 31st, 2020), compared with an inter-year period (February 21st to March 31st, 2019) and an intra-year period (January 1st to February 20th, 2020). The primary outcome was the overall rate of hospital admissions for HF. A total of 505 HF patients were included in this survey: 112 during the case period, 201 during intra-year period and 192 during inter-year period. The mean admission rate during the case period was 2.80 admissions per day, significantly lower compared with intra-year period (3.94 admissions per day; incidence rate ratio [IRR], 0.71; 95% confidence interval [CI], 0.56-0.89; $p=0.0037$), or with inter-year (4.92 admissions per day; IRR, 0.57; 95% CI, 0.45-0.72; $p<0.001$). Patients admitted during study period were less frequently admitted in II class compared with inter-year period ($p=0.019$). At covariance analysis NYHA class was significantly lower in patients admitted during inter-year control period, compared to patients admitted during case period ($p=0.014$).

Conclusion. Admissions for HF were significantly reduced during the lockdown due to the COVID-19 pandemic in Italy.

A501: AGING-ASSOCIATED CARDIAC DYSFUNCTION AND LEAKY GUT IN HETEROZYGOUS AKAP1 KNOCKOUT MICE

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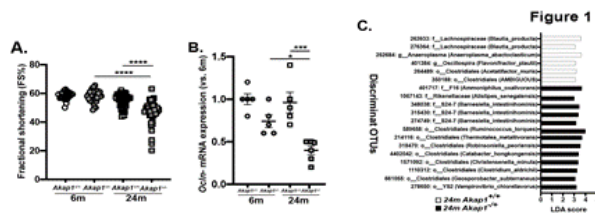
Background. Mitochondrial A-kinase anchoring proteins (mitoAKAPs) encoded by the Akap1 gene are crucially involved in multiple cellular processes, including cardiomyocyte survival and function. There is a correlation between ROS production, intestinal permeability and the composition of the intestinal microbiota, especially during aging. Whether Akap1 deletion affects microbiota composition, intestinal function during senescence is currently unknown.

Purpose. The purpose of the study was to shed light into the complex interplay between gut permeability and microbiota composition, cardiac function and aging in adult (6-month-old, 6m) and old (24-month-old, 24m) Akap1 wild type (Akap1^{+/+}) or Akap1 heterozygous knockout mice (Akap1^{+/-}).

Methods. Cardiac function was non-invasively analyzed by echocardiography in adult and old, Akap1^{+/+} and Akap1^{+/-} mice. Colon, serum and feces samples were collected after sacrifice in 6m and 24m mice of either genotype. Intestinal barrier permeability was evaluated in colon samples by Occludin (Ocln) and Tight junction protein ZO-1 (Tjp1) mRNA expression analysis. Systemic inflammation was measured by Tumor Necrosis Factor-alpha (TNF-alpha), Lipopolysaccharide (LPS), Interleukin-10 (IL-10) and Interleukin-1 (IL-1) circulating levels. Microbial DNA was extracted from feces samples and gut microbiota composition was evaluated by Illumina Mi-Seq analysis. Bioinformatic analyses were carried out to identify intestinal populations.

Results. Akap1 partial deletion accelerated the progression of cardiac dysfunction in 24m mice as demonstrated by a significant reduction of fractional shortening in Akap1^{+/-} 24m mice compared to Akap1^{+/+} 24m (Figure 1A). Colon permeability was impaired in Akap1^{+/-} 24m as shown by reduced Ocln expression (Figure 1B), while circulating TNF-a was increased in Akap1^{+/-} 24m. Next, we analyzed the differences in abundance of all 2042 Operational Taxonomic Units (OTUs) between age-matched Akap1^{+/+} and Akap1^{+/-}. We identified 10 OTUs differently represented in Akap1^{+/+} and Akap1^{+/-} 6m mice, while a bigger set of bacterial OTUs (19) were different between Akap1^{+/+} and Akap1^{+/-} 24m mice. LDA scores of differentially microbiome abundant taxa in Akap1^{+/+} and Akap1^{+/-} 24m (Figure 1C) showed different assortment in Clostridiales family (*Ruminococcus torques* specie), Porphyromonadaceae family (*Barseniella intestinihominis* specie) and Lachnospiraceae genus (*Blautia producta* specie), bacterial species that have been previously identified in patients with heart failure and involved in anti-inflammatory mechanisms.

Conclusion. mitoAKAPs play a crucial role in the maintenance of cardiac function and intestinal barrier during aging, since Akap1 partial deletion promotes gut permeability, bacteria translocation and systemic inflammation associated with systolic cardiac dysfunction.



A502: FAILURE TO RECOVER THE ATRIAL MECHANICAL FUNCTION IN PATIENTS WITH PERSISTENT OR LONG-LASTING PERSISTENT ATRIAL FIBRILLATION CONVERTED TO SINUS RHYTHM ON THE ECG: A RETROSPECTIVE COHORT STUDY

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Background. In the present retrospective cohort study we have evaluated the missed or delayed atrial mechanical recovery in a population of patients with persistent or long-lasting persistent atrial

fibrillation(AF) who achieved restoration of sinus rhythm on the ECG by electrical cardioversion (ECV).

Methods. The endpoint of our study was the failure to recover the normal mechanics of the left atrium. Inclusion criterion was the persistent or long-lasting persistent AF successfully treated by means of ECV, provided that a pertinent documentation was made available, comprising ECG, conventional 2D echo-color-Doppler and speckle tracking echocardiography(STE) evaluation, with also a STE assessment of the atria at the days 1, 30 and 90 from the ECV freely available in the clinical record of the patient.

Results. Out of a total of 80 patients with persistent or long-standing persistent AF, retrospectively enrolled, as many as 22.5% of them did not achieve the normalization of their atrial STE profile, even though they had been converted to sinus rhythm on the ECG by means of ECV. The building of ROC curves allowed us to establish that early measurements of global atrial strain could serve to predict both the risk of failure to recover the atrial mechanical function and the one of AF relapses over a 6 month follow-up. The values of 18% and 17% were also calculated to serve as cut off values, respectively, for the risk of atrial mechanical dysfunction and for the risk of AF relapses over a 6 month follow-up.

Conclusions. Failure to recover the atrial reservoir function can accompany a restoration of sinus rhythm on the ECG in patients with long-standing persistent AF. In this case a serial STE evaluation could be useful to evaluate the atrial hypofunction over time.

A503: FATAL INTESTINAL NECROSIS INDUCED BY SODIUM POLYSTYRENE SULFONATE IN A PATIENT WITH CARDIORENAL SYNDROME TYPE 4: NEED TO CONSIDER THE USE OF NEW SAFER CATION EXCHANGE RESINS FOR TREATMENT OF HYPERKALEMIA

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A fatal case of recurrent ischemic colitis related to the use of sodium polystyrene sulfonate is described in this case report. The intake for only three months of this ion exchange resin used to counteract the hyperkalaemia of patients with chronic renal failure or cardio-renal syndrome type 4 seems to have caused progressive intestinal damage, with persistence of the sodium polystyrene sulfonate crystals in biopsy intestinal specimens 14 months after the suspension of the drug. Therefore its use should be characterized by the utmost caution and it could be useful to shift these patients towards the use of the new cation exchange resins - patiromer and sodium zirconium cyclosilicate - which have shown a better safety profile.

A504: A CASE OF THYROTOXIC CARDIOMYOPATHY COMPLICATED BY CARDIOGENIC SHOCK: CLINICAL PICTURE, THERAPEUTIC APPROACH AND REVIEW OF THE LITERATURE

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For thyrotoxic dilated cardiomyopathy, evidence-based pharmacologic measures valid for heart failure should always be supplemented by the administration of specific thyroid therapies such as thionamides (methimazole, carbimazole or propylthiouracil), whose relatively long latency of action should be supported by the administration of beta-blocker therapy. In cases of cardiogenic shock, the administration of beta-blocker should be carried out only after the restoration of satisfactory blood pressure levels- with the prudent use of synthetic catecholamines, if necessary.

The authors examine several reports of the literature concerning thyrotoxic dilated cardiomyopathy. Case reports are analyzed comparatively. A case deriving from the direct experience of the authors is also presented.

A505: SACUBITRIL/VALSARTAN AS A USEFUL TOOL FOR ANTAGONIZING ANTHRACYCLINE-RELATED MYOCARDIAL DAMAGE: DESCRIPTION OF TWO CASES

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Anthracyclines are the cornerstone of treatment for many solid and hematological cancers such as breast cancer or lymphoma for the past 50 years. Nevertheless, in a non-negligible proportion of patients, they elicit

dilated cardiomyopathy as a side effect, which causes in turn cardiac decompensation. Conversely, for some years sacubitril/ valsartan has been proposed as a new therapeutic paradigm for all varieties of heart failure with reduced left ventricular ejection fraction, due to its balanced enhancement of natriuretic peptides' properties coupled with a blocking effect on the AT1 angiotensin receptors. In the present article, two clinical cases are illustrated in which the therapeutic action of sacubitril/ valsartan against anthracycline cardiomyopathy would seem to be demonstrated by the improvement of symptoms and echocardiographic parameters. Thus, further studies would be warranted for better evaluating the potential role of sacubitril/ valsartan as a novel therapeutic tool against anthracycline cardiotoxicity.

A506: PROGNOSTIC IMPACT OF POSITIVE EJECTION FRACTION CATEGORY TRANSITION IN HEART FAILURE

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Background. Heart failure (HF) can be classified according to the left ventricle ejection fraction (LVEF) into preserved (HFpEF, LVEF $\geq 50\%$), mid-range (HFmEF, LVEF 40-49%), and reduced ejection fraction (HFrEF, LVEF $< 40\%$). We hypothesized that patients showing a positive transition of the HF category during follow-up could portend a better prognosis.

Methods. We retrospectively analyzed HFrEF and HFmEF outpatients who underwent two transthoracic echocardiograms within 12 \pm 2 months to assess the prognostic impact of a positive HF category transition (HF+ group) vs a negative transition or stable HF category (HF- group). After the second echocardiogram, patients were followed up for the composite endpoint of cardiovascular death and heart transplantation.

Results. A total of 927 patients were enrolled (age 68 \pm 12 yrs; median LVEF 35%, interquartile range: 30% to 43%; 27% women), of which 236 (25%) had HFmEF and 691 (74%) HFrEF. At follow-up echocardiography, 250 patients (27%) displayed a positive transition in HF category (HF+ group). HF+ group showed a lower prevalence of ischemic aetiology ($p < 0.001$), similar baseline NT-proBNP levels ($p = 0.07X$), a better NYHA functional class (overall $p < 0.05$) and renal function ($p = 0.001$) compared to the HF- group. HF+ group also presented with better baseline echocardiographic parameters (including LV and atrial volumes, LV mass, and systolic pulmonary pressure; all $p < 0.05$). At the second assessment, a higher introduction rate of beta-blockers was reported for the HF+ group ($p = 0.001$), with a reduction of LV and atrial volumes, LV mass, and E/e' (all $p < 0.05$). Conversely, HF- group showed an increase in NT-proBNP levels ($p < 0.001$) and a reduction of eGFR ($p < 0.001$). After a median follow-up of 2.9 years, the composite endpoint was reported in 188 patients ($n = 26$ in HF+ group vs $n = 162$ in HF- group; $p < 0.001$). Kaplan-Meier analysis confirmed a worse outcome for the HF- group (log-rank test: $\chi^2 = 18.4$; $p < 0.001$). Stepwise Cox-regression analysis revealed that the protective value of a positive transition in HF category (HR: 0.29, 95% CI 0.11 – 0.76) was independent of clinical status (age, sex, NYHA class, history of coronary artery disease, and common cardiovascular risk factors), bio-humoral evaluation (including NT-proBNP and its change after 12 months) and therapy for neurohormonal antagonism. A positive association was found between Δ LVEF and Δ NT-proBNP (R^2 0.4; $p = 0.0002$). Incremental Chi-Square logistic regression analysis showed the added negative prognostic value of HF- pattern over clinical, demographic and biohumoral variables ($\chi^2 = 57$; $p = 0.003$). The assessment of a positive HF category transition to a model based on the presence of a significant reduction of Δ NT-proBNP ($> 30\%$ from baseline evaluation) improved patient reclassification, as demonstrated by continuous net reclassification improvement (12.1%, $p = 0.004$) and integrated discrimination improvement (4.1%, $p = 0.001$).

Conclusions. In patients with chronic systolic HF, a positive transition of HF category is significantly associated with a better prognosis, independently from the clinical and bio-humoral evaluation.

A507: INFLUENCE OF GENDER AND BODY MASS INDEX ON CIRCULATING LEVELS AND PROGNOSTIC VALUE OF NT-PROBNP IN CHRONIC HEART FAILURE

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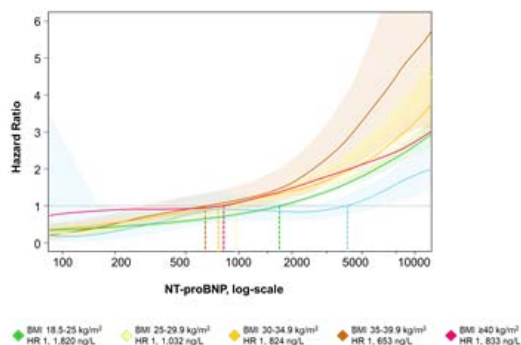
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Background. N-terminal fraction of pro-B-type natriuretic peptide (NT-proBNP) is a strong predictor of outcome in heart failure (HF). Circulating levels of NT-proBNP are higher in women than in men, and lower in obese vs. lean individuals. Still, the possible influence of either gender or body-mass index (BMI) on the prognostic value of NT-proBNP in HF is unclear. Therefore, we aimed to test the predictive power of NT-proBNP in female and male patients with HF across all the BMI categories.

Methods. We analyzed data from the international BIOS (Biomarkers In Heart Failure Outpatient Study) Consortium. Patients with stable chronic HF were classified as underweight (BMI <18.5 kg/m²), normal weight (BMI 18.5-25 kg/m²), overweight (BMI 25-29.9 kg/m²), mild obese (BMI 30-34.9 kg/m²), moderate obese (BMI 35-39.9 kg/m²), or severe obese (BMI ≥40 kg/m²). The prognostic role of NT-proBNP was tested for each BMI category for the endpoints of 5-year all-cause and cardiac death.

Results. The study population included 12,763 patients (age 66±12 years, 25% females, left ventricular ejection fraction -LVEF 33±13%). Most patients were overweight (n=5,176, 40%), followed by normal weight (n=4,299, 33%), mild obese (n=2,157, 17%), moderate obese (n=612, 5%), severe obese (n=314, 3%), and underweight (n=205, 2%). Circulating levels of NT-proBNP were higher in women than in men [1437 ng/L (IQR 561-3372) vs. 1194 (IQR 471-2785), p<0.001], and inversely correlated with BMI (β=-0.174, p<0.001), independently from other covariates (including age, gender, LVEF, HF etiology, NYHA class, atrial fibrillation, hypertension, diabetes, anemia, renal function, obstructive lung disease, and anti-neurohormonal therapies). The best NT-proBNP cut-offs for 5-year all-cause and cardiac death prediction were higher in women than in men, but lower as BMI increased, independently of gender (Figure). Finally, adding NT-proBNP to a clinical model (including age, gender, LVEF, HF etiology, NYHA class, atrial fibrillation, hypertension, diabetes, anemia, renal function, obstructive lung disease, and anti-neurohormonal therapies) improved risk prediction in all BMI categories, except in severe obesity.

Conclusions. The influence of gender and BMI on the prognostic significance and best cut-off for risk prediction of NT-proBNP is significant and should not be overlooked in the clinical management of patients with chronic HF.



A508: EFFICACIA DEL COLLOQUIO MOTIVAZIONALE SULL'USO DEI SERVIZI SANITARI E SULLA MORTALITÀ NEI PAZIENTI CON SCOMPENSO CARDIACO: UN'ANALISI SECONDARIA DELLO STUDIO RANDOMIZZATO CONTROLLATO MOTIVATE-HF
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Introduzione. I pazienti affetti da scompenso cardiaco (SC) sono accumulati da un frequente utilizzo dei servizi sanitari (servizi di emergenza-urgenza e ospedalizzazioni) e da un'elevata mortalità. Lo studio MOTIVATE-HF è un trial multicentrico randomizzato controllato che ha dimostrato l'efficacia del colloquio motivazionale (CM) nel migliorare i comportamenti di self-care (es. gestione quotidiana e risposta ai segni e sintomi della malattia) nei pazienti con SC (endpoint primario). Ciò nonostante, l'efficacia del CM nel ridurre l'uso dei servizi sanitari e la mortalità in questi pazienti è ancora poco conosciuta.

Scopo. In questa analisi secondaria dello studio MOTIVATE-HF, è stata valutata l'efficacia del CM nel ridurre l'uso dei servizi sanitari (servizi di

emergenza-urgenza e ospedalizzazioni) e la mortalità per tutte le cause nei pazienti con SC.

Disegno di studio. Studio multicentrico parallelo randomizzato controllato (1:1:1), con randomizzazione del campione in tre Bracci: (i) Braccio 1, CM solo per pazienti; (ii) Braccio 2, CM per pazienti e caregiver; (iii) Braccio 3, assistenza standard.

Metodi. Il campione è stato reclutato in tre centri italiani. Tutti i pazienti avevano una diagnosi di SC in classe NYHA II-IV. Sono stati esclusi i pazienti con sindrome coronarica acuta recente, residenti in lungodegenza e con declino cognitivo importante. I caregiver informali erano coloro che venivano identificati tali dai pazienti, ovvero che prestavano la maggior parte delle cure informali (es. coniugi e figli dei pazienti). L'intervento sperimentale consisteva in una sessione di CM face-to-face, seguito da 3 contatti telefonici entro 2 mesi dall'arruolamento. I dati sono stati raccolti al baseline e a 3, 6, 9 e 12 mesi dall'arruolamento. I confronti tra i tre Bracci sono stati effettuati mediante il test esatto di Fisher.

Risultati. È stato arruolato un campione di 510 pazienti (età mediana 74 anni; 58% maschi) randomizzati successivamente nei tre bracci (Braccio 1, n=155; Braccio 2, n=177; Braccio 3, n=178). Durante i 12 mesi dello studio, cumulativamente, 25 pazienti (16,1%) del Braccio 1, 30 pazienti (17%) del Braccio 2, e 20 pazienti (11,2%) del Braccio 3 hanno usato almeno una volta i servizi sanitari. Non sono state riscontrate differenze significative in nessun follow-up. Riguardo la mortalità per tutte le cause, a 3 mesi dall'arruolamento, sono deceduti 3 pazienti (1,9%) del Braccio 1, 1 paziente (0,6%) del Braccio 2 e 9 pazienti (5,1%) del Braccio 3. La differenza nei tre Bracci è risultata statisticamente significativa (p=0,02). A 6 mesi, sono deceduti 5 pazienti (3,2%) del Braccio 1, 3 pazienti (1,7%) del Braccio 2 e 12 pazienti (6,7%) del Braccio 3. La differenza nei tre Bracci è risultata al limite della significatività statistica (p=0,05). Non è stata rilevata alcuna differenza significativa a 9 e 12 mesi nei tre Bracci.

Conclusioni. Il CM non sembra essere efficace nel ridurre l'uso dei servizi sanitari nei pazienti affetti da SC, ma sembra esserlo nel ridurre la mortalità per tutte le cause, almeno nei primi mesi successivi all'intervento. Interventi ripetuti di CM condotti, per esempio, ogni 3 mesi, potrebbero rilevarsi efficaci nel migliorare quantomeno la mortalità.

A509: VALUTAZIONE MULTIPARAMETRICA DELLO STATO DI CONGESTIONE NEI PAZIENTI OSPEDALIZZATI PER SCOMPENSO CARDIACO ACUTO

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Introduzione. Lo stato di congestione è la principale causa di ricovero ospedaliero e recidiva nell'insufficienza cardiaca, tuttavia è difficile identificare i segni prodromici prima che si verifichi tale status. I peptidi natriuretici sono stati proposti come indicatori laboratoristici dello stato di congestione emodinamica. Più recentemente l'analisi dell'ecografia polmonare toracica ha dimostrato una buona accuratezza nel rilevamento della congestione polmonare.

Obiettivi. Valutazione della congestione con tre diversi metodi confrontando la congestione clinica con il BNP e lo studio della ecografia toracica. Analisi del diverso impatto prognostico nei valori di ammissione e dimissione del BNP e del conteggio delle linee B in una popolazione ammissa per insufficienza cardiaca acuta.

Metodi. Questo studio osservazionale monocentrico ha arruolato tutti pazienti ammessi per segni e sintomi clinici di insufficienza cardiaca acuta. In ogni soggetto abbiamo valutato i segni tradizionali di congestione clinica dando un punteggio da 0 a 5 tra cui distensione jugolare, rantoli polmonari, epatomegalia, edema periferico, terzo tono cardiaco; abbiamo anche misurato il valore del BNP e il numero di linee B mediante ecografia polmonare toracica usando un metodo semplificato che contava il numero di linee B su 4 spazi per ciascun sito toracico. Abbiamo valutate le tre diverse misurazioni subito dopo l'ammissione e prima della dimissione.

Risultati. Sono stati inclusi 215 pazienti, 133 avevano HFrEF e 83 avevano HFpEF. I pazienti con disfunzione sistolica hanno mostrato un aumento significativo del BNP al momento del ricovero (1150 vs 851 pg / ml p <0,002), mentre i segni di congestione e le linee B non differivano tra i gruppi. L'analisi univariata e multivariabile ha mostrato che un punteggio di congestione >3 punti e un numero di linee B >36 erano entrambi correlati con esito negativo. Al contrario, i valori di ammissione BNP non hanno raggiunto un significato prognostico. L'analisi pre dimissione ha mostrato che un punteggio di congestione >2, calo di BNP <33% e riduzione di B-lines <27% erano associati ad un aumento del tasso di eventi avversi. Con un AUC per il ΔBNP e per il Δ delle linee B e rispettivamente di 0,75 e 0,81.

Conclusioni. La valutazione comparata di congestione score BNP e B lines appare utile nel riconoscimento della congestione polmonare e sistemica. Il confronto tra i valori di ammissione e pre dimissione (DELTA congestion) appare il miglior metodo di stratificazione del rischio nei pazienti ammessi per insufficienza cardiaca acuta.

A510: EFFETTI DEL TRATTAMENTO CON METOLAZONE IN AGGIUNTA ALLA SOMMINISTRAZIONE DEL DIURETICO DELL'ANSA IN PAZIENTI OSPEDALIZZATI PER SCOMPENSO CARDIACO AVANZATO

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Introduzione. L'insufficienza cardiaca avanzata (HF) è una condizione che spesso richiede dosi elevate di diuretici dell'ansa. Le caratteristiche cliniche e farmacologiche hanno un impatto negativo sulla prognosi e sulla riospedalizzazione. Pertanto, questi pazienti hanno un alto rischio di insorgenza di resistenza al diuretico e, a causa della loro scarsa sopravvivenza, sono tradizionalmente esclusi dai più grandi studi randomizzati.

Obiettivi. Questo studio retrospettivo multicentrico valuta l'effetto dell'aggiunta del metolazone orale sulla risposta diuretica (misurata come produzione di urina ogni 40 mg di furosemide / die endovenoso), NTproBNP (definito come valori all'ammissione meno valore alla dimissione), variazione della funzione renale, variazione della dose del diuretico dell'ansa e sull'equilibrio elettrolitico in pazienti con scompenso cardiaco avanzato. Abbiamo anche confrontato gli effetti del metolazone sull'outcome per un periodo di follow-up medio di 6 mesi.

Metodi. Sono stati arruolati 92 pazienti con insufficienza cardiaca avanzata (ADHF) in classe NYHA IV con ridotta frazione di eiezione (EF <35%) prendendo una quantità media di 250 mg / die di furosemide endovenosa durante il periodo di ricovero. 46 pazienti hanno ricevuto un trattamento diuretico a ciclo tradizionale, più metolazone (gruppo M); la dose media varia da 5 a 15 mg / settimana in base alla valutazione clinica PA e diuresi giornaliera. 46 pazienti hanno continuato l'infusione diuretica a ciclo continuo con eventuale aggiustamento in relazione alla valutazione giornaliera (gruppo F).

Risultati. I pazienti nel gruppo M e i pazienti nel gruppo F hanno mostrato una simile prevalenza di malattia renale cronica al basale (CKD) [61% vs 70%; p=0,38]. I pazienti nel gruppo F hanno manifestato una risposta diuretica peggiore rispetto ai pazienti del gruppo M (440 ± 149 ml / 40 mg furosemide/die vs 741 ± 414 ml / 40 mg FUROSEMIDE / die; p <0,001). Inoltre, i pazienti del gruppo M hanno mostrato un aumento della riduzione dei livelli di NTproBNP alla dimissione rispetto ai pazienti del gruppo F (-4019 ± 5017 pg / ml rispetto a -1939 ± 3616 pg / ml; p=0,03). Non sono state riscontrate differenze, tra i due gruppi, in termini di sviluppo del WRF (gruppo M: 28% vs gruppo F: 24%; p=0,63) e squilibrio degli elettroliti alla dimissione; tuttavia, i pazienti del gruppo M hanno dimostrato un tasso più elevato di somministrazione di soluzione endovenosa di NaCl / KCL rispetto al gruppo F (48% vs 24%; p=0,02). Durante il periodo di follow-up, 16 pazienti nel gruppo M (35%) e 26 nel gruppo F (56%) hanno raggiunto l'endpoint composto di morte e riospedalizzazione (p=0,04).

Conclusioni. La somministrazione di metolazone potrebbe essere utile nei pazienti con resistenza al diuretico e scompenso refrattario. L'uso concomitante della terapia con tiazidici è associato a una migliore decongestione e a un tasso ridotto di resistenza diuretica nonostante un aumento della necessità di correzione dello squilibrio elettrolitico. Gli attuali risultati preliminari potrebbero offrire una alternativa terapeutica in pazienti affetti da scompenso cardiaco avanzato sottoposti a terapia con elevate dosi di diuretici dell'ansa

A511: TRAIETTORIE DELLA FUNZIONE RENALE E VALUTAZIONE DELLA CONGESTIONE IN PAZIENTI CON INSUFFICIENZA CARDIACA ACUTA

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Introduzione. Molti pazienti ricoverati con insufficienza cardiaca acuta (AHF) sviluppano un peggioramento della funzione renale (WRF) in termini di aumento della creatinina sierica e stima della velocità di filtrazione glomerulare (GFR) che possono riflettere diversi fenotipi. Non è chiaro se diverse traiettorie del deterioramento renale siano correlate a diversi esiti clinici e risoluzione della congestione durante il trattamento infusione.

Obiettivi. Il nostro obiettivo era quello di studiare il significato prognostico delle differenti traiettorie della funzione renale (RF). Abbiamo inoltre confrontato come i diversi sottotipi di RF correlavano con prognosi avversa e stato di congestione alla dimissione.

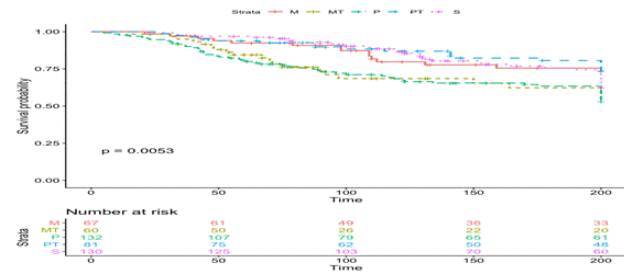
Metodi. Analisi retrospettiva di uno studio multicentrico randomizzato su diuretici dell'ansa infusione (Diur AHF). In ogni soggetto la RF è stata classificata in base all'andamento temporale durante il ricovero. Abbiamo riconosciuto 5 principali sottotipi: RF stabile creatinina e GFR cambiano meno del 20%; RF deteriorata aumento della creatinina e riduzione del

GFR superiore al 20%; Miglioramento della RF riduzione della creatinina e aumento del GFR di oltre il 20%; deterioramento transitorio della RF compromissione iniziale di creatinina e GFR seguita da un miglioramento prima della dimissione; e miglioramento transitorio di RF iniziale riduzione di creatinina e aumento di GFR seguita da nuovo peggioramento. Il Congestion Score è stato valutato dando 1 punto per ciascun segno clinico.

Risultati. Dei 291 pazienti arruolati, 77 non hanno avuto sostanziali modificazioni della RF, 75 hanno dimostrato una compromissione della RF, 44 avevano un miglioramento della RF, 73 avevano una riduzione della RF transitoria e 22 avevano un miglioramento della RF transitoria. I pazienti con RF invariato e deterioramento transitorio della RF hanno mostrato la migliore riduzione della congestione. Al contrario, i pazienti con miglioramento transitorio della RF e peggioramento persistente della RF avevano una riduzione della congestione più bassa. L'analisi di Kaplan-Meier ha rivelato che i pazienti con RF stabile e quelli con compromissione della RF transitoria avevano eventi avversi ridotti, mentre i soggetti con deterioramento RF persistente e miglioramento transitorio della RF. Nel modello multivariabile di rischio proporzionale di Cox solo congestione residua (HR 1.85 IC 1.5-3.7), deterioramento RF persistente (HR 2.3 IC 1.6-4.8) e miglioramento persistente (HR 1.4 IC 0.9-2.5) sono stati associati ad un aumento degli eventi avversi.

Tra le variabili valutate tramite analisi Cox regression, soltanto il congestion Score d'uscita (HR 2.41, IC: 2.11, 2.75), storia di scompenso cardiaco (HR 1.78 CI 1.29- 2.46) e miglioramento transitorio della RF (HR:2.52, CI 1.57- 4.05) erano associati ad un aumento degli eventi avversi (p <0.001)

Conclusioni. Il miglioramento transitorio la compromissione persistente di RF si associano ad una prognosi avversa. Le valutazioni simultanee di congestione e funzionalità renale potrebbero fornire informazioni utili per identificare il profilo di rischio nei pazienti ricoverati per AHF.



A512: INSUFFICIENZA CARDIACA ACUTA E CLASSIFICAZIONE DI STEVENSON: RUOLO DELL'ECOCARDIOGRAFIA NELL'IDENTIFICAZIONE DEI DIVERSI FENOTIPI

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Introduzione. La presentazione dell'insufficienza cardiaca acuta (AHF) è universalmente classificata in relazione alla presenza o assenza di congestione e alla condizione di perfusione periferica secondo il quadro di Stevenson. Questa presentazione considera la gittata sistolica cardiaca e la valutazione della ritenzione idro-salina mediante esame clinico, tuttavia fino ad ora non sono stati riportati dati in letteratura che confrontino la valutazione clinica ed ecocardiografica.

Obiettivi. Abbiamo valutato tutti i pazienti ammessi con diagnosi di AHF suddividendoli in base alla classificazione di Stevenson, ipotizzando che alcune misurazioni ecocardiografiche fossero correlate allo stato di congestione e di perfusione. Abbiamo quindi confrontato i 4 quadri clinici con i più comuni parametri eco.

Metodi. Studio multicentrico retrospettivo che ha comparato la valutazione clinica all'ingresso con i più comuni parametri ecocardiografici le prime 6 ore dall'ammissione in ospedale per un episodio di AHF. In tutti i pazienti, è stata eseguita una valutazione clinica specifica che valuta i segni di congestione e perfusione e i pazienti sono stati classificati in 4 gruppi secondo la classificazione di Stevenson. Gruppo A (caldo e secco), Gruppo B (freddo e secco) Gruppo C (caldo e umido) Gruppo D (freddo e umido). In ciascun paziente sono stati misurati i seguenti parametri: volumi ventricolari sinistri (LV), frazione di eiezione del ventricolo sinistro (LVEF); pattern doppler tramite rapporto E/e1, pressione sistolica dell'arteria polmonare (PAPS), escursione sistolica di picco anulare tricuspidalico (TAPSE) e diametro inspiratorio della vena cava (VCI).

Risultati. Abbiamo studiato 208 pazienti, 9 nel gruppo A, 10 nel gruppo B, 152 nel gruppo C e 37 nel gruppo D. I livelli di PA sistolica erano (124

[120-130] nel gruppo A, 102 [90-110] nel gruppo B, 130 [120-149] nel gruppo C e 99 [90-100] mmHg gruppo D; $p < 0,001$). L'esame ecocardiografico ha rivelato che i pazienti del gruppo D hanno manifestato un peggior LVEF e TAPSE (rispettivamente 28 [24-43] e 14 [11-17] mm) rispetto al gruppo A (38 [32-52] e 17 [16-20] mm rispettivamente), gruppo B (rispettivamente 35 [25-50] e 17 [16-21] mm) e gruppo C (40 [30-51] e 18 [14-20] mm rispettivamente); [PLVEF = 0,01 e PTAPSE = 0,001 rispettivamente]. Il rapporto E / e' e i valori PAP erano più alti nel gruppo C (18 [15-21] e 45 [35-50] mmHg) e D (19 [13-24] e 45 [40-55] mmHg) rispetto al gruppo A (15 [10-19] e 35 [28-48] mmHg), gruppo B (16 [13-17] e 40 [29-55] mmHg) [Pe / e' = 0,04 e PPAPs = 0,06 rispettivamente]. La VCI era più dilatata nei gruppi C (20 [16-24] mm) e D (23 [18-26] mm) rispetto agli altri gruppi (Gruppo A: 16 [15-22] mm; Gruppo B: 18 [17-20] mm; PVI = 0,03.).

Conclusioni. Un esame ecocardiografico eseguito all'ammissione in ospedale potrebbe essere utile per differenziare i quadri di Stevenson. Sebbene la maggior parte dei pazienti appartenga ai gruppi C e D e i gruppi "Dry" siano scarsamente rappresentati nel nostro campione, i nostri dati indicano che una valutazione ecocardiografica precoce è auspicabile in ciascun paziente con AHF al fine di stimare in modo non invasivo il quadro emodinamico.

A513: PREVALENCE, COMEDICATIONS, COMORBIDITIES, USE OF RESOURCES AND PROGNOSTIC ROLE OF HYPERKALEMIA IN A COMMUNITY OF 12,533,230 INHABITANTS AND IN 9,315 HEART FAILURE PATIENTS

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Background. Hyperkalemia is a life-threatening electrolyte abnormality. Although renin-angiotensin-aldosterone system inhibitors (RAASi) are potentially lifesaving, they may contribute to hyperkalemia. The availability of potassium-binding drugs might allow wider RAASi use or prevent RAASi discontinuation.

Methods. The prevalence, comedications, comorbidities and 1-year outcomes of hyperkalemia were investigated in a large healthcare administrative database including 12,533,230 inhabitants, and in the Italian Network on Heart Failure (IN-HF), a cardiology registry of 1,726 acute and 7,589 chronic HF patients. Healthcare costs related to hyperkalemia in general practice were also assessed.

Results. In the community-based analysis, the prevalence of hyperkalemia was 0.035%. After excluding patients on hemodialysis, hyperkalemia (n=2,314) was significantly and directly associated with diabetes, chronic kidney disease, HF, RAASi prescriptions, 1-year hospitalizations, and a 3-fold increase of annual healthcare costs, compared to age and sex matched normokalemic subjects (n=2,314). In the IN-HF registry, hyperkalemia affected 3.6% and 4.3% of chronic or acute HF patients, respectively, and was significantly associated with diabetes, kidney disease, and lesser use of RAASi, compared to normokalemic patients. Those with acute HF and hyperkalemia at hospital entry had significantly higher 1-year all-cause mortality compared to normokalemic patients, even after adjustment for available confounders.

Conclusions. In this contemporary analysis, hyperkalemia, although uncommon in the general population, was associated with increased hospitalization rates and a tripling of healthcare costs. Among HF patients, hyperkalemia was frequent and associated with underuse of RAASi; in decompensated patients, it remained independently associated with 1-year all-cause mortality.

A514: REDUCED LEFT ATRIAL CONTRACTILE FUNCTION ASSESSED BY SPECKLE TRACKING ECHOCARDIOGRAPHY PREDICTS WORSE OUTCOME IN HFREF

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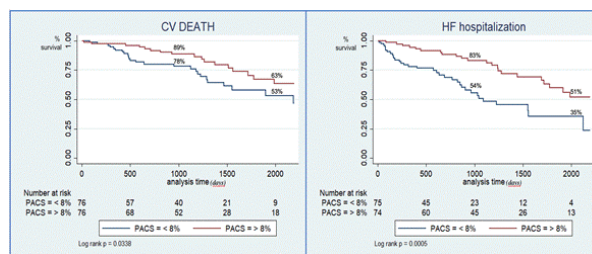
Background. In chronic heart failure (HF), the chronic raise of intracardiac pressures leads to a progressive remodeling of small pulmonary arteries up to pulmonary hypertension development. At the end of left atrial (LA) conduit phase, left heart and pulmonary end-systolic pressures equalize. This might have a negative impact on LA systole. The present study assessed whether peak atrial contraction strain (PACS), measured by speckle tracking echocardiography (STE), could be independently associated with prognosis in HF with reduced ejection fraction (HFREF).

Methods. 172 outpatients with HFREF were enrolled and prospectively followed for primary and secondary endpoint of cardiovascular (CV) death

and HF hospitalization respectively. Patients with non-sinus rhythm and previous cardiac surgery were excluded. After clinical and echocardiographic evaluation, off-line STE analysis was performed. Spline knotted survival model identified the optimal cut-off value for PACS.

Results. The 154 eligible patients were stratified based on PACS<8%(n=76) or PACS≥8%(n=76). No differences in sex or age were present between the 2 groups while those patients with reduced PACS had higher NYHA class, NT-proBNP, E/e' ratio and pulmonary systolic pressure and lower global longitudinal strain and reservoir atrial strain. Mean follow-up was 3.41±1.9 years, during which 117 events (51 CV death, 66 HF hospitalizations) were registered. Global PACS was a strong and independent predictor of CV death and HF hospitalization in univariate and multivariate analysis, even after adjusting for age, sex, LV strain, E/e', LA volume index (HR 0.6 per 5 unit decrease in PACS). Kaplan Meier curves showed a sustained divergence in event-free survival rates for the two groups (Fig. 1) for the prediction of primary and secondary endpoint.

Conclusions. Worsening PACS by STE had a significant and independent influence on CV outcome in HFREF. Therefore, although its evaluation is limited to patients with sinus rhythm, it could provide additive prognostic information for HFREF patients.



A515: RIGHT VENTRICULAR STIFFNESS AND LEFT ATRIAL DYSFUNCTION IN RISK STRATIFICATION OF CHRONIC HEART FAILURE

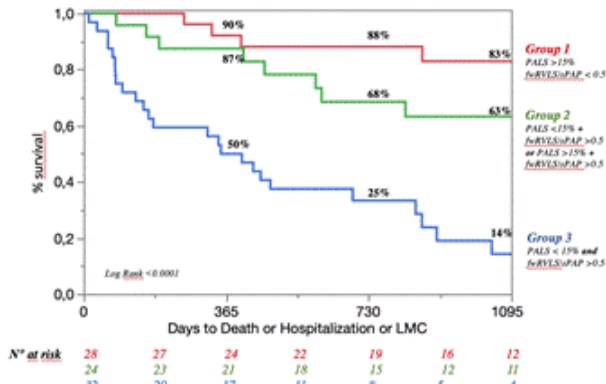
Giulia Elena Mandoli (a), Maria Concetta Pastore (a), Giovanni Benfari (b), Martina Setti (b), Dan Nistor (c), Flavio D'Ascenzi (a), Marta Focardi (a), Bernardo Baccani (a), Serafina Valente (a), Sergio Mondillo (a), Matteo Cameli (a) (a) DEPARTMENT OF MEDICAL BIOTECHNOLOGIES, DIVISION OF CARDIOLOGY, UNIVERSITY OF SIENA, SIENA, ITALY; (b) DIVISION OF CARDIOLOGY, DEPARTMENT OF MEDICINE, UNIVERSITY OF VERONA, VERONA, ITALY; (c) DEPARTMENT M3, UNIVERSITY OF MEDICINE AND PHARMACY TARGU MURES, ROMANIA

Background. In the last years, the phenotype of heart failure with reduced ejection fraction (HFREF) is changing from isolate left ventricular (LV) dysfunction to a more frequent development of right ventricular (RV) failure, due to the chronic increase of filling pressures which progressively involves left atrium (LA), pulmonary circulation (PC) and RV, leading to worse outcome. The present study investigated the prognostic value of different grades of LA and RV involvement in HFREF, using basic and advanced echocardiography.

Methods. 104 outpatients with HFREF were enrolled. Exclusion criteria were primary lung disease, non-sinus rhythm, previous cardiac surgery, poor acoustic window. Clinical examination and basic echocardiography were performed. Later, speckle tracking analysis was applied offline to measure peak atrial longitudinal strain (PALS) and a new marker of interaction between RV and PC: absolute free wall RV longitudinal strain(fwRVLS)/systolic pulmonary artery pressure(sPAP) ratio. The evaluated endpoints were all-cause or cardiovascular death and heart failure (HF) hospitalization.

Results. 84 patients [mean age: 60.1±11.5; 82% male, mean left ventricular ejection fraction (LV EF) 28±5%] were eligible, of whom 48 reached the combined endpoint. Population was divided into three groups: Group 1 [PALS ≥15 and fwRVLS/Spap ≤0.5]; Group 2 [PALS≤15 and fwRVLS/sPAP≤0.5]; Group 3 [PALS ≤15 and fwsRV/sPAP ≥0.5]. Mean follow-up was 3.5±0.3 years. The increasing severity groups were associated with higher LA volume index (LAVI), New York Heart Association (NYHA) class, mitral regurgitation (MR) and tricuspid regurgitation (TR) grades, lower LV EF, LV global longitudinal strain (GLS), PALS, tricuspid annular plane systolic excursion (TAPSE), sPAP, fwRVLS and global RVLS (p<0.0001). With univariate and adjusted multivariate analysis reduced PALS and fwRVLS/sPAP emerged as independent predictors of NYHA >2, and of any events with adjusted Cox models. Kaplan-Meier curves showed a clear divergence between the groups for the prediction of the combined endpoint (Fig. 1), cardiovascular death and HF hospitalization.

Conclusions. The coexistence of LA and RV damage could represent the hallmark of the progression to end-stage HF, with a considerable impact on prognosis. The measure of PALS and RV stiffness could help in the risk stratification of these patients in order to select the appropriate treatment.



A516: CARDIAC CONTRACTILITY MODULATION: SINGOLA ESPERIENZA IN UN CENTRO PER LA DIAGNOSI ED IL TRATTAMENTO DELLO SCOMPENSO CARDIACO

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Background. La Cardiac Contractility Modulation (CCM) rappresenta presidio terapeutico indicato per il trattamento dello scompenso cardiaco avanzato nei pazienti a terapia medica già ottimizzata, con ridotta Frazione di Eiezione (FE) e QRS non largo (<130 ms), quindi non candidati all'impianto di CRT, come evidenziato dall'ultimo consensus document del gruppo HF del ESC pubblicato nel maggio 2019. La terapia CCM produce un segnale bipolare bifasico ad alta energia non eccitatorio nel periodo refrattario assoluto ventricolare, mediante due elettrocateri a fissazione attiva, posizionati sul setto interventricolare destro (SIV), distanziati almeno di 1 cm l'uno dall'altro. L'uso a breve e lungo termine di questa terapia migliora sia la forza della contrazione ventricolare che la capacità di pompaggio del cuore modulando la contrattazione del miocardio che si traduce in un significativo miglioramento nella sintomatologia riferita.

Metodi. Descriviamo il caso clinico di un uomo di 82 anni affetto da SCC secondario a CMD a coronarie inendenni, in classe NYHA IVa, QRS di 115 ms, ipotensione, IRC, già portatore di ICD bicamerale (Incepta DR, Boston Scientific) e refrattario alla terapia medica domiciliare ottimizzata. All'esame ecocardiografico si riscontra una FE del 25%, presenza di ascite ed importante versamento pleurico. Inoltre, tra gli inizi di giugno e fine luglio 2020, il paziente ha effettuato 3 accessi al PS con altrettanti ricoveri per ospedalizzazioni per SC.

Risultati. Previa firma del consenso informato, il 25/8/2020 il paziente è stato sottoposto ad impianto di Optimizer Smart® (Impulse Dynamics) per la terapia CCM, in sede controlaterale al ICD già preesistente, tramite inserzione di due elettrocateri Capsure Sense 5076-58 (Medtronic) posizionati sul SIV. La terapia CCM è stata programmata per 10 h al giorno, con ampiezza delle uscite a 7,5V @ 20,56 ms. Il paziente già dopo primi giorni dalla procedura riferisce un miglioramento della sintomatologia. Al controllo strumentale ad un mese dall'impianto, l'erogazione totale della terapia CCM è del 82%, che ci garantisce almeno 8 h di terapia giorno per compensare ad una quota di pacing V di terapia anti-bradicardia del ICD (pari al 7%), alle VES ed altre frequenze ventricolari sopra i 110 bpm (in tutti i casi la terapia CCM viene inibita). Al controllo ecocardiografico, si nota una riduzione del versamento pleurico e assenza di ascite. Come dimostrato da dati di letteratura, entro il FU a 3 mesi si rendono evidenti gli effetti della CCM sul rimodellamento inverso del ventricolo sinistro.

Conclusioni. La CCM rappresenta una tecnologia efficace e sicura per il trattamento dello scompenso cardiaco a ridotta frazione di eiezione. Questa iniziale esperienza apre la possibilità al trattamento dei pazienti refrattari a terapia medica non.



A517: PREVALENCE OF CONCEALED CARDIAC AMYLOIDOSIS AMONG ELDERLY PATIENTS UNDERGOING POST-MORTEM EXAMINATION: A HISTOLOGICAL STUDY

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Background. Cardiac amyloidosis (CA) is traditionally considered a rare disease, but its prevalence has been recently reported to progressively increase, being found in up to 32% of patients with heart failure (HF) and normal left ventricular (LV) function at post mortem examination.

Aim. The real prevalence of CA in unselected population is at present largely unknown, especially in transthyretin CA (TTR-CA). Therefore, the aim of the present study was to determine the frequency, extent, and type of cardiac amyloid deposition in the heart of unselected patients aged ≥75 years with and without established HF, undergoing post-mortem evaluation.

Methods. We sought to investigate the presence of CA in a consecutive cohort of 83 unselected patients ≥75 years undergoing autopsy between April and June 2019. Patients deceased because of severe septic conditions and corpses not properly stored were excluded from the study. Cardiac specimens were collected from 5 cardiac sites (i.e. LV, right ventricle (RV), interventricular septum, left and right atria) and stained with haematoxylin-eosin, Congo-Red and Sirius Red. Immunohistochemistry with an extensive panel of antibodies was performed. The predominant patterns of amyloid distribution and localization were analysed.

Results. Among the study cohort of 55 patients, CA was found in 23 cases (42%), similarly distributed between light chains (AL) and TTR aetiologies (52% and 48% respectively). Their median age was 86 years (IQR 84 –91). The atria were systematically involved (100% of CA) and diffuse infiltration was found in almost half of samples, including subjects without HF. In the subgroup of 15 CA patients with cardiologic records and echocardiography, no difference emerged between amyloid distribution and LV dysfunction ((p=0.782), RV dysfunction (p= 0.919) or ischemic heart disease (p=0.256). Compared to TTR-CA, AL-CA patients had lower values of diastolic blood pressure (64±10 mmHg and 73±8 mmHg, p=0.030), lower frequency of left bundle branch block (9% vs 50%, p=0.046) and thicker LV posterior wall (14±3 mm and 10±2 mm, p=0.023). CA was similarly found in both genders, but women showed greater rates of RV involvement (p=0.033).

Conclusion. CA can be found in up to 42% of autopsied hearts from the general population ≥75 years, evenly distributed among TTR and AL etiologies, as far as samples are collected from multiple cardiac sites. Diffuse amyloid infiltration is observed in half of cases and the atria are invariably involved.

A518: IMPACT ON CLINICAL OUTCOMES OF RIGHT VENTRICULAR RESPONSE TO PERCUTANEOUS CORRECTION OF SECONDARY MITRAL REGURGITATION

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Background. Right ventricular function (RVF) is a strong determinant of prognosis in patients with reduced ejection fraction heart failure (HFrEF) and secondary mitral regurgitation (SMR). Percutaneous mitral valve repair (pMVR) can promote the recovery of RVF.

Aim. We sought to characterize the RV response to pMVR in HFrEF with SMR and to assess the influence of improved RVF after pMVR in this specific setting of patients.

Methods and Results. We included all the patients with HFrEF and SMR≥3+ successfully treated with pMVR between April 2012 and January 2020 in two tertiary care centers for HF. Improved RVF was defined as DRV FAC ≥5% at early follow-up (median time 4 months). The primary endpoint was a composite of death/heart transplant (D/HT). In total, 110

patients were included. Mean age was 67±12 years, mean LVEF was 31±8% and mean RVFAC was 31±10%. DRVAC ≥5% occurred in 54 (49%) patients and was independent from the measures of left ventricle recovery. During a median follow-up of 36 months (IQR 19-52), 40 patients (36%) died or were transplanted. After adjustment for other significant covariates, DRVAC ≥5% was significantly associated with lower risk of D/HT (HR 0.49, 95% CI 0.24-0.98 p <0.042) along with MR≤2+ at follow-up (HR 0.36; 95% CI 0.17-0.74 p=0.005).

Conclusions. In patients with HFREF and SMR, the improvement of RVF is frequent after pMVR and is associated with better long-term survival free from HT.

A519: HARD DECISIONS IN LIGHT-CHAIN CARDIAC AMYLOIDOSIS: A CHALLENGING CASE

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Background. Light-chain (AL) amyloidosis is the most common form of systemic amyloidosis, characterized by extracellular deposition of monoclonal light-chain immunoglobulins leading to progressive organ failure. The severity of cardiac involvement is the main predictor of survival. Patients with advanced cardiac amyloidosis (CA) usually do not benefit from traditional heart failure (HF) treatments and, further, may not undergo chemotherapy regimens with proven impact on disease progression. Therefore, accurate patient selection and risk stratification is needed.

Clinical vignette. We report the unusual case of a 50-year-old woman evaluated because of new-onset congestive HF with normal ejection fraction (EF) and AL-CA due to micro-molecular λ-type myeloma. Transthoracic echocardiography at presentation revealed biventricular hypertrophy, reduced left ventricle (LV) global longitudinal strain (GLS) (-14%) with an apical sparing pattern, restrictive filling pattern and right ventricle (RV) systolic dysfunction. Serum λ free light chains (FLCs) were pathologically increased (108 mg/dL, delta FLCs 93 mg/dL), brain natriuretic peptide (BNP) was 618 pg/L and persistent troponin T release were documented. Diuretic optimization was required to achieve hemodynamic stability and cytoreductive therapy with cyclophosphamide, bortezomib and dexamethasone (CyBorD) was started, yet halving bortezomib standard doses and providing strict monitoring due to severe cardiac involvement. Despite therapy up-titration, the patient persisted in NYHA III functional class and experienced recurring hospital admissions due to decompensated HF with hemodynamic deterioration (cardiac index 2.53 L/min/m², VO₂ peak 15.4 ml/kg/min equal to 50% of the predicted value). After collegial discussion, the patient was judged a good candidate for heart transplantation (HTx) followed by high-dose chemotherapy with autologous stem cell transplantation (ASCT). Nevertheless, after one year of CyBorD therapy, complete haematological response occurred (normalization of FLCs and no residual disease at bone marrow biopsy) with improved clinical condition: NYHA I-II functional class, BNP 70 pg/L, low daily diuretic dosages, LV-GLS of 20%, higher cardiac index (2.8 L/min/m²) and exercise capacity (VO₂ peak 20.8 ml/kg/min, 71% of the predicted value). Thus, the patient was withdrawn from HTx list and remained stable in NYHA I-II functional class after almost 3 years from clinical onset.

Clinical perspective. Prognostic stratification of patients with AL-CA is pivotal and relies on dedicated scores integrating NT-proBNP, troponin and FLCs values. These parameters reflect the severity of cardiac involvement, the hemodynamic status, the disease burden and the response to treatment. Therapeutic strategy should always be discussed in multidisciplinary teams and tailored on patients' needs. Currently, chemotherapy is the first line treatment for AL amyloidosis, with CyBorD regimen known to provide partial haematological response in 60% and cardiac response in 25% of cases. In rare cases, CyBorD therapy can be effective enough to obtain a complete haematological response and disease regression, providing long-term good clinical status, as experienced by our patient at 3-year follow-up. However, severe cardiac involvement can often limit the access to valuable curative therapies, including high dose chemotherapy and ASCT; in these settings, HTx followed by ASCT might represent a suitable approach. A tight follow-up strategy for clinical assessment and therapy adjustments is essential, as suggested by this case.

A520: UNEXPLAINED LEFT VENTRICULAR HYPERTROPHY IN PATIENTS UNDERGOING CARPAL TUNNEL SYNDROME SURGERY: PREVALENCE, CLINICAL AND PROGNOSTIC IMPLICATIONS

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Introduction. Carpal tunnel (CT) syndrome is a common finding in patients with cardiac amyloidosis (CA), resulting from progressive infiltration of transthyretin (TTR) and light chains proteins in the transverse carpal ligament. Amyloid can be histologically found in 10% of tenosynovial tissue biopsies performed in patients undergoing surgery for idiopathic CT syndrome. Interestingly, CT syndrome has been associated with development of heart failure (HF), atrial fibrillation (AF), atrio-ventricular (AV) block and pacemaker (PM) implantation.

Aim. To characterize the cardiovascular (CV) profile of patients with CT syndrome at the time of surgery and to investigate if specific phenotypes are associated with higher risk of CV events.

Methods. Records from 643 patients who underwent CT surgery between January 1, 2007 and March 31, 2019 at University Hospital of Trieste were retrospectively reviewed. Subjects with post-traumatic CT syndromes and known amyloidosis at the time of surgery were excluded. Data from cardiological examination, blood tests, ECG and echocardiograms were collected when available. Echocardiography at the time of CT surgery was reviewable in a subgroup of patients (echo-defined population). The primary endpoint was all-cause mortality. Secondary endpoints were: 1) a composite of hard CV events, including CV mortality, 2) PM implantation, and 3) new onset HF or HF hospitalization (HHF). Median follow-up was 70 months (IQR 33-105).

Results. The study population consisted of 181 patients. Median age at CT surgery was 72 years (IQR 63-79), 95% CT procedures were unilateral and 28% of patients underwent at least 2 CT procedures by the end of the study. Bilateral CT surgery at baseline was associated with an increased risk of all-cause death (p=0,048) and HHF (p=0,023). Patients undergoing bilateral CT surgery, either at baseline or during the follow-up, were more likely to receive a PM (p=0,001). In the echo-defined population, half patients had normal left ventricle (LV) wall thickness (non-LVH group, n=66, 51%), 35% (n=45) had explained LV hypertrophy (ExLVH group) and the reminder (n=21, 16%) had unexplained or unproportioned LV hypertrophy (UnLVH group). Compared to ExLVH and non-LVH patients, UnLVH patients had lower systolic values (p=0,015), thicker LV walls (p<0,001), larger LV volumes (p=0,050) and greater rates of ECG-echo discrepancy (p<0,001). Suggestive findings for CA were more frequent in UnLVH than ExLVH (24% vs 7%, p<0,001). LV hypertrophy (LVH) was associated with a greater risk of CV events (p=0,040), while only UnLVH was associated with higher risk of overall mortality (p=0,010) and new onset HF/HHF (p=0,026), with separation of the curves after 4 years from first CT surgery. Moreover, patients with LVH and suggestive echocardiographic findings of CA had higher rates of CV events (p<0,001), new onset HF/HHF (p<0,001) and PM implantation (p=0,003). Three patients, all with LVH at baseline, were diagnosed with CA after a median time of 46 months (IQR 31-66) from CT surgery.

Conclusion. CT syndrome, especially when bilateral, is associated to major CV events and all-cause mortality. LVH at the time of CT surgery is associated with higher CV risk, particularly in presence of UnLVH and suggestive findings for CA. Therefore, Plastic and Orthopaedic Hand Surgeons should become aware of the clinical and prognostic implications of CT syndrome and consider referring patients for cardiological evaluation at the time of surgery.

A521: THE PREVALENCE OF ECHOCARDIOGRAPHIC SUSPICION OF CARDIAC AMYLOIDOSIS IN THE REAL WORLD: RESULTS OF THE FIRST PHASE OF "TRANSTHYRETIN CARDIAC AMYLOIDOSIS: UNMASKING THE REAL PREVALENCE" - AN ITALIAN NATIONWIDE STUDY

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Introduction. Cardiac amyloidosis (CA) is under-diagnosed. Suspicion of CA often arises from echocardiographic findings. However, their real prevalence is still largely unknown.

Aim. To investigate the real prevalence of echocardiographic suspicion of CA in Italy.

Methods. This prospective multicentric study consists of two phases: 1) echocardiographic phase, and 2) clinical and instrumental phase. The results of phase 1 are presented here. Images of consecutive patients ≥ 55 years undergoing echocardiography in 12 Italian Centers were retrospectively analysed to look for the presence of all the following inclusion criteria: left ventricular (LV) ejection fraction (EF) $\geq 50\%$, LV thickness ≥ 12 mm for women and ≥ 13 mm for men and LV end-diastolic volume ≤ 85 mL/m². Patients had an echocardiographic suspicion of CA in presence of at least one additional criterion among: restrictive LV filling pattern, granular sparkling appearance, pericardial effusion, thickened interatrial septum (IAS) > 5 mm, thickened atrio-ventricular (AV) valves > 5 mm and apical sparing pattern. Subjects with a previous diagnosis of hypertrophic cardiomyopathy, CA or referred because of suspected CA were excluded.

Results. We reviewed 5358 consecutive echocardiograms and 1165 satisfied the inclusion criteria. Of them, 380 (7.1% of screened population; 32.6% of hypertrophic hearts; 44% inpatients and 56% outpatients) had a suspected echocardiogram for CA (study population). The median age was 77 (70-83 IQR) and males were 50.5%. Echocardiography was more frequently requested because of heart failure (20.2%), ischemic heart disease (15.1%) and presence of prosthetic valve (12.3%). Thickened IAS was the most frequent suggestive feature (44.5%) followed by pericardial effusion and restrictive LV filling pattern (30.5%, both), granular sparkling appearance of the myocardium (24.0%), thickened AV valves (19.5%) and apical sparing pattern at speckle-tracking analysis (16.8%). Patients with ≥ 3 suggestive echocardiographic features were 58/380 (15.2%). Compared to the others, they were more frequently males (62.1% vs 48.3%, $p=0.036$), had higher LV wall thickness (14.5 mm vs 13 mm; $p<0.001$), larger left atrial volume (71 ml vs 96 ml; $p=0.004$), lower LVEF (55% vs 60%; $p<0.001$), thicker right ventricle walls (7 mm vs 6 mm; $p<0.001$) and more dilated inferior vena cava (18 mm vs 15 mm; $p<0.0001$). Moderate-to-severe mitral regurgitation was more frequently found in presence of ≥ 3 suggestive echocardiographic features (71% vs 45%; $p=0.02$). Other valve diseases were equally distributed among subgroups.

Conclusion. More than 7% of the general population ≥ 55 years and $> 32\%$ of subjects with LV hypertrophy and normal EF have echocardiographic findings suggestive of CA. Thickened IAS is the most frequent suggestive finding. These observations indicate the need to increase the awareness of disease among Cardiologists as many patients with suggestive echocardiographic findings might be missed in everyday practice. In particular, those with ≥ 3 suggestive features are reasonably at higher risk of unrecognized CA, but phase 2 of this study is going to investigate this hypothesis.

A522: THE NATURAL HISTORY OF TACHYCARDIA-INDUCED CARDIOMYOPATHY: A LONG-TERM OBSERVATIONAL REGISTRY

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Background. Studies analyzing prevalence and natural history of "pure" tachycardia-induced cardiomyopathies (TICMP), through arrhythmic and left ventricular (LV) systolic dysfunction recurrences are scant.

Objective. The aims of this study were to assess the prevalence, characterization and long-term evolution of "pure" TICMP.

Methods. Patients admitted with persistent supraventricular arrhythmias (SVA) with heart rate > 100 bpm as the only known cause of LV systolic dysfunction were retrospectively analyzed. Study end-points were: 1) to assess the prevalence of "pure" TICMP (i.e. persistent recovery of LV ejection fraction (EF) $> 50\%$ from 6-month evaluation throughout the long-term follow-up); 2) a composite of death, heart transplant (HT) or major ventricular arrhythmias.

Results. 83 patients were enrolled and followed up for 54 months. A total of 56 (67%) patients showed to be "pure" TICMP, the remaining 33% of patients emerged as affected by dilated cardiomyopathy (DCM).

Noteworthy, 17 out of 56 "pure" TICMP (30%) had a temporary new drop in LVEF during follow-up associated to high-rate SVA relapse. At the logistic multivariable regression analysis, younger age (HR 0.61, IQR 0.45-0.81, $p=0.001$) and higher LVEF (HR 1.79 IQR 1.08-2.94 $p=0.023$) at baseline emerged as the only variables independently associated with the diagnosis of "pure" TICMP. TICMP patients showed less rate of major events than DCM patients (4% vs 26% in TICMP and patients respectively, $p=0.007$).

Conclusion. More than half of patients with high-rate SVA as the only possible cause of a newly diagnosed LV systolic dysfunction proved to be "pure" TICMP, with a subsequent benign outcome. Long term individual surveillance is required in TICMP patients, as arrhythmic recurrences, with possible new drop in LVEF, are very frequent in the long-term.

A523: GESTIONE DELLO SCOMPENSO CARDIACO AVANZATO CON INFUSIONI RIPETUTE DI LEVOSIMENDAN

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Background. A partire dagli anni 2000, nel trattamento degli stadi più severi di scompenso cardiaco (scompenso cardiaco cronico avanzato, SCCA e scompenso cardiaco End-Stage, SCES) si è progressivamente diffuso l'utilizzo del levosimendan (L), inotropo caratterizzato da peculiare meccanismo d'azione, che si discosta da quello degli altri della stessa categoria per minori effetti collaterali e minori interazioni farmacologiche.

Obiettivo. Valutare in pazienti affetti da SCCA ed SCES la presenza dei seguenti end-points: primario: correlazione tra somministrazioni ripetute di L e miglioramento dei parametri pre e post infusione relativi a classe NYHA, frazione di eiezione ventricolare sinistra (FEVS), NT-pro BNP, pressione arteriosa (PA), frequenza cardiaca (FC), distanza percorsa durante test del cammino in sei minuti (6mwt). Secondario: correlazione tra somministrazioni ripetute di L, riduzione del numero di ospedalizzazioni per SC e mortalità.

Materiali e metodi. A partire da Gennaio 2019 sono stati arruolati 19 pazienti che presentavano i criteri di inclusione: I) gravi sintomi, classe NYHA III o IV; II) FE $\leq 30\%$ e/o severa disfunzione diastolica; III) severa riduzione della capacità funzionale; IV) anamnesi di ≥ 1 ospedalizzazioni o visite ambulatoriali urgenti per riacutizzazione di scompenso cardiaco; ciascuno di questi criteri in presenza di terapia medica ottimale. I pazienti arruolati sono stati sottoposti ad infusioni di L secondo protocollo desunto dallo studio "Lion-Heart" che prevede: 0,2 mcg/kg/min per 6 h se eGFR ≥ 30 ml/h o 0,1 mcg/kg per 6 h se eGFR ≤ 30 ml/h ma ≥ 15 ml/min, ogni 14 ± 2 giorni.

Risultati. L'eziologia dello SCCA all'interno della popolazione in studio è stata nel 37% dei casi cardiomiopatia dilatativa (CMD) post ischemica, nel 21% cardiomiopatia da chemioterapici (CT), nel 26% miocardite, nel 16% CMD primitiva. L'endpoint primario si è verificato nel 100% dei pazienti. Non sono state evidenziate differenze significative tra i risultati osservati sui pazienti di sesso maschile rispetto a quelli di sesso femminile. La riduzione dei valori di NT-proBNP è stata più marcata nei pazienti con patologia di base non ischemica e maggiore nei pazienti con iniziale disfunzione ventricolare sinistra da cardiotoxicità rispetto a quelli affetti da miocardite. In merito all'endpoint secondario, nessun paziente è andato incontro a riospedalizzazioni per riacutizzazione di SC nel periodo di osservazione. È stata registrata una mortalità dell'11% a diciotto mesi, nella totalità dei casi dovuta a cause diverse dallo SC e non correlate alla terapia con L. Risultati interessanti che esulano dagli endpoint di studio sono stati: la possibilità di proseguire la terapia chemioterapica nel 100% dei pazienti oncologici e il decadere dell'indicazione ad impianto di ICD nel 31,5% che pazienti trattati con infusioni ripetute di L, grazie al significativo miglioramento dell'LVEF.

Limiti dello studio. In futuro il campione potrà essere ampliato per accrescere la sensibilità e specificità dei primi risultati ottenuti.

Conclusioni. Il L si conferma inotropo ideale per il trattamento di pazienti affetti da SCCA. La CMD post ischemica, risponde meno al trattamento con inodilatatori, probabilmente per la presenza di maggiore sostituzione fibrotica del tessuto miocardico, mentre ottime potenzialità di applicazione si prospettano per le cardiomiopatie dovute a CT e a miocardite.

A524: CARDIOGENIC SHOCK IN TAKOTSUBO SYNDROME: SHORT AND LONG-TERM OUTCOME

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Background. Tako-tsubo syndrome (TS) is characterized by acute left ventricular regional systolic dysfunction, generally transient and reversible, often triggered by a significant physical or emotional stressor. The clinical presentation resembles acute coronary syndrome in the absence of atherosclerotic obstruction of epicardial coronary arteries on angiography. Pathogenesis isn't completely understood and may involve brain-heart axis and neuro-hormonal stunning of the myocardium.

Materials and method. From January 2007 to January 2020, 80 patients with TS were admitted to our CCU. All the patients enrolled in this study met International Expert Consensus on Takotsubo Syndrome for the diagnosis of TS. We analyzed the clinical features, risk factors, both electrocardiographic (ECG) and echocardiographic tests on admission, discharge and follow-up focused on in-hospital complications (IH-Cs), especially cardiogenic shock.

Results. Fourteen (17.5%) experienced relevant IH-Cs (10% pulmonary oedema, 5% cardiogenic shock, 1.25% ventricular fibrillation, 1.25% ictus). Among patients with and without CS we found no gender difference (100% vs 87.5%, $p=0.44$). The average age CS was lower than 60 years ($p=0.01$). We did not observe any significant differences in risk factors in cohort with and without CS, except for diabetes which tends to be more frequent in CS patients (diabetes 50% vs 15%, $p=0.058$). Emotional and physical stress - are not involved in the onset of CS (50% vs 66.2, $p=0.6$). The incidence of arrhythmias did not demonstrate any differences among CS and not CS (0% vs 6.9% $p=0.58$). Ejection fraction (EF) at admission was significantly lower in CS group compared to the control group (35.7 ± 6.7 vs 46.5 ± 10.7 , $p=0.04$). Moreover, 75% of patients with CS had severe systolic dysfunction with a EF <35% (75% vs 25%, $p=0.002$). The WMSI was higher at admission (2.2 ± 0.11 vs 1.89 ± 0.3 , $p=0.004$) than at discharge (1.57 ± 0.19 vs 1.24 ± 0.27 , $p=0.038$). Patients with CS had a median Pro-BNP significantly higher than group without CS (CI 12000 – 22000 vs CI 1227 – 4518 $p=0.046$). The value of >12500, identified as optimal by ROC analysis, was 88% specific and 100% sensitive, in identifying patients with CS. Two patients with CS needed mechanical ventilation (50% vs 3.9% $p=0.0018$). 75% CS presented with mitral regurgitation and one of these had systolic anterior motion of the mitral valve and severe dynamic left ventricular outflow tract obstruction (LVOTO). 50 patients (62.5%) were followed up over a median period of 5.5 years: we observed 5 cases of recurrence (6.25%) and 8 deaths (10%), with no significant difference in the two groups. All the patients presented at FU had normal EF (62.1 ± 19.2) with an improvement of global and regional systolic function compared to values at discharge ($p=0.001$).

Conclusions. TS is often associated with IH-Cs and cardiogenic shock represent a marker of severity. We observed a larger incidence of CS in the young population. It's remarkable that diabetes would be configured as an independent risk factor that increases probability to develop cardiogenic shock, but this trend will need to be confirmed in further studies. We can conclude CS influence short term prognosis. The patient who exceeds a critical period in intensive care, despite of serious complications, seems to have a life expectancy no different from that of a healthy patient.

A525: ACUTE UNLOADING EFFECTS OF SILDENAFIL ENHANCE RIGHT VENTRICULAR-PULMONARY ARTERY COUPLING IN HEART FAILURE

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Background. Phosphodiesterase-5A inhibitors (PDE5i) are sometimes used in patients with advanced HFREF prior to heart transplant or LVAD to reduce RV afterload and mitigate the risk of right HF. Conflicting evidences exist regarding the impact of these drugs on right ventricular (RV) contractility. The aim of the study was to explore the acute effects of PDE5i on ventricular-vascular coupling and load-independent RV contractility.

Methods. 22 patients underwent right heart catheterization (RHC) and gated equilibrium blood pool SPECT, before and after 20-mg intravenous sildenafil. SPECT and RHC-derived data were used to calculate RV loading and contractility.

Results. PDE5i induced a reduction in RA pressure (-43%), pulmonary artery (PA) mean pressure (-26%) and wedge pressure (PAWP; -23%), with favorable reductions in PVR (-41%) and PA elastance (Ea; -40%), and increased cardiac output (+13%) (all $p<0.01$). RV ejection fraction increased with sildenafil (RVEF; +20%), with no change of RV contractility (RV $E_{es,sub}$, $p=0.74$), indicating that the improvement in RVEF was related to enhanced RV-PA coupling ($r=0.59$, $p=0.004$) by reduction of ventricular load. RV diastolic compliance (dV/dP) increased with sildenafil. The reduction in PAWP correlated with RV EDV reduction, while no relationship was observed with the change in LV transmural pressure, suggesting decreased pericardial constraint.

Conclusions. Acute PDE5i administration has profound RV afterload-reducing effects, improves RV EF, reduces RV volumes and lowers PAWP predominantly through relief of pericardial constraint, without effects on RV chamber contractility. These findings support further study of PDE5i in protection of RV function in advanced HFREF who are at risk of RV failure.

A526: LO SCOMPENSO CARDIACO COME IL CANCRO PER IL CUORE: UTILIZZO DELLA NUOVA CLASSIFICAZIONE TNM-LIKE IN TERMINI DI STRATIFICAZIONE PROGNOSTICA

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Introduzione. L'insufficienza cardiaca (IC) è una complessa sindrome clinica caratterizzata dall'incapacità da parte del cuore di espletare la propria funzione di pompa e quindi di garantire il corretto apporto di sangue a tutti gli organi. Nonostante i progressi in termini di prevenzione, diagnosi e terapia, l'IC rimane ancora associata ad un'elevatissima mortalità ed alla frequente necessità di ricorrere a ricoveri ospedalieri, al punto tale da essere considerata l'epidemia del terzo millennio. Attualmente, per la stratificazione del rischio dei pazienti affetti da IC, si utilizzano le classificazioni ACC/AHA, NYHA e MAGGIC score, le quali presentano però diversi limiti, primo fra tutti la cardiocentricità. Proprio con lo scopo di colmare i limiti evidenziati dalle altre nosologie, il nostro gruppo di ricerca ha proposto una nuova classificazione denominata HLM, ispirata alla ben consolidata stadiazione oncologica TNM, in cui H (H come T) rappresenta il danno cardiaco, L (L come N) il coinvolgimento polmonare e M (M come M) la disfunzione di alcuni organi periferici quali rene, fegato, SNC e sistema ematopoietico.

Obiettivo. Obiettivo dello studio è valutare l'efficacia della classificazione HLM, in termini di stratificazione del rischio di riospedalizzazione per eventi maggiori cardio-cerebrovascolari (MACCE) e di mortalità cardiovascolare nei pazienti con IC, confrontandola con NYHA, ACC/AHA e MAGGIC score.

Materiali e metodi. Il presente studio prospettico osservazionale multicentrico ha arruolato pazienti consecutivi affetti da, o a rischio di, IC. Ogni paziente è stato classificato in ingresso e in dimissione secondo HLM, NYHA, ACC/AHA e MAGGIC score. Tutti i pazienti arruolati sono stati sottoposti ad un follow-up a 12 mesi per valutare il tasso di riospedalizzazione per MACCE e mortalità cardiovascolare, così da poter confrontare le diverse nosologie in termini di stratificazione del rischio di mortalità e riospedalizzazione.

Risultati. Sono stati arruolati 1759 pazienti (70.5% maschi, età media di 70 ± 7.48 anni). I pazienti sono così distribuiti per il danno cardiaco: H1=8.12%, H2=46.58%, H3=19.88%, H4=11.9%. Il 70.3% presenta coinvolgimento polmonare: L0=29.89%, L1=20.97%, L2=32.51%, L3=16.18%. Il 51.2% presenta danno renale, il 26% disfunzione epatica, il 37% anemia e il 21.7% danno cerebrale: M0=25.10%, M1=32.43%, M2=28.88%, M3=13.64%. Tutte le classificazioni presentano delle curve di sopravvivenza significative per MACCE e mortalità cardiovascolare a 12 mesi ($p<0.001$). In particolare, l'area sotto la curva ROC (AUC) è maggiore per HLM rispetto a NYHA, ACC/AHA e MAGGIC score in termini di riospedalizzazione per MACCE (HLM = 0.687; NYHA = 0.642; ACC / AHA = 0.604; MAGGIC = 0.657) e morte cardiaca (HLM = 0.783; NYHA = 0.712; ACC / AHA = 0.623; MAGGIC = 0.737).

Conclusioni. Dai risultati emerge che la classificazione HLM presenta un potere prognostico predittivo superiore rispetto alle altre nosologie, sia in termini di riospedalizzazione per MACCE che di mortalità cardiovascolare, grazie ad una valutazione che si spinge oltre la visione cardiocentrica, fattore limitante delle altre classificazioni, analizzando in maniera olistica l'eventuale disfunzione di tutti quegli organi a stretto contatto con il cuore. L'HLM, dunque, sembra permettere, grazie alla determinazione di un quadro conoscitivo più approfondito e accurato, una maggiore appropriatezza terapeutica sia da un punto di vista etico che economico ed un utilizzo più efficace delle tecnologie per rallentare l'evoluzione dell'IC.

A527: HOSPITAL AT HOME FOR HEART FAILURE PATIENTS: OUR STRATEGIES TO IMPROVE HEALTH OUTCOMES

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Introduction. Heart failure (HF) is a common cause for hospitalization in elderly patient, it is increasing in term of prevalence and causes an elevated health care cost. Hospital at Home (H&H) is a valid alternative to hospitalization for patients affected by chronic diseases, if we perform a high-quality home health care, we can decrease the hospital readmission rate, due to the increase of all medical conditions. H&H is beneficial for patients and advantageous for health care system, but still there is a wide debate about the efficacy choice of the care model. We give here our contribution presenting our proposal of H&H, keeping in mind that the success, of H&H strategy, is achieved when the care, given in the patient's home, has the same efficacy and safety of the hospital care, with patient and care giver satisfaction, improved quality of life and reduction of the costs.

Our proposal of H&H. All patients had continuous monitoring of H&H care, it includes general physician visits, standard blood tests, pulse oximetry, spirometry, electrocardiography, arterial blood pressure

monitoring, weight monitoring and oral medication administration. Monitoring happens through machine-based algorithms, with a dedicated hardware by patients home and a dashboard remotely followed by a clinical staff, ready to any alarms produced by these algorithms. Furthermore participants communicate with their H&H team by telephone or email message service. The physician is available every day, at a set time, or on appointment for urgent issues and visits, for emergency events the patients is sent to hospital. Our proposal addresses to patients with a preexisting diagnosis of CHF, at stage C according to the American Heart Association criteria and a persistent functional impairment indicative of New York Heart Association (NYHA) class III or IV. They are considered eligible for H&H treatment to prevent acute decompensation of HF, the cardiac dysfunction includes systolic or diastolic dysfunction, abnormalities in cardiac rhythm, or preload and afterload mismatch. We use Mini-Mental State Examination for cognitive status, the SF 36 Survey for Quality of Life, the Minnesota Living with Heart Failure Questionnaire, the Mini Nutritional Assessment for nutritional status, the Cumulative Illness Rating Scale for comorbidity, and the Relative Stress Scale for the level of stress of the caregiver. We collect also traditional variables such as history of cigarette smoking, hypertension, type 1 and type 2 diabetes mellitus, obesity, alcohol consumption, lipid disorders, and familiarity for cardiac diseases. The admission to H&H is activated by a direct request of the general practitioner of the patient as an alternative to traditional hospital care or by a request from hospital ward physicians to allow early and protected discharge from the hospital. We perform an adequate education for patients, and family members, explaining the disease process and the importance of daily monitoring of: bodyweight, smoking cessation, physical activity and diet, compliance with drugs, and early recognition of symptoms indicative of worsening HF. Consultation with cardiologists is always possible by remote cardiologist control.

Conclusion. H&H appears to increase time to readmission, improve QoL, and reduce costs of index hospitalization compared to routine hospitalization in select patients with uncompensated HF. H&H does not significantly reduce readmissions or mortality, but all studies assessing this are underpowered to detect a statistically significant difference in these outcomes. The success of H&H is due also to advancement in telehealth technologies and increased demand for treatment at home. Larger clinical trials H&H for HF. Further development of HaH care will require additional research with new large studies.

A528: BI-VENTRICULAR MYOCARDIAL PERFORMANCE IN CONGESTIVE HEART FAILURE: EVALUATION OF VENTRICULAR DYSSYNCHRONY

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Background. Patients with heart failure (HF) exhibit ventricular dyssynchrony with negative effects on ventricular systolic and diastolic performance and poor prognosis. There isn't consensus about the best approach for estimate the dyssynchrony and for selecting candidates to resynchronization therapy (CRT). We sought to evaluate whether Myocardial Performance Index (MPI), calculated as differences between left and right ventricle (LV, RV), Δ MPI, represent a marker of interventricular dyssynchrony.

Methods. The study included 40 patients (22 males, 18 females, mean age 71 ± 13) with NYHA functional class II-III, chronic heart failure (77% ischaemic), in optimal drug therapy for at least three months. All patients underwent to a complete two-dimensional and Tissue Doppler Echocardiography (TDE), including assessment of MPI in both ventricles.

Results. Significant correlations were found between Δ MPI and QRS ($r = 0.41$, $p < 0.001$), with NYHA ($r = 0.66$, $p < 0.001$), with SPWMD ($r = 0.32$, $p < 0.05$), with LV ejection fraction ($r = -0.32$, $p < 0.05$), with S_{pw} wave at the septal site of LV ($r = -0.32$, $p < 0.05$), and with IVMD ($r = 0.44$, $p < 0.001$). Ten patients have been re-evaluated six months after CRT implantation, and Δ MPI significantly correlated with the difference between basal LVEF and six months after CRT implantation ($r = 0.43$, $p < 0.04$).

Conclusions. Δ MPI could represent an integrative and marker of interventricular dyssynchrony and could be considered as a new parameter in the patient selection process to be underwent to CRT.

A529: CARDIAC FIBROSIS: EMERGING AGENTS IN PRECLINICAL AND CLINICAL DEVELOPMENT

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Introduction. Myocardial fibrosis is a remarkably dynamic process mediated by different molecular pathways that represent potential targets of novel therapeutic interventions. TGF- β , connective tissue growth factor (CTGF) and galectin-3 (Gal-3) represent the most promising targets on which research has been currently focusing.

Area covered. Here, we discuss about the drugs already used in clinical practice for their known anti-fibrotic properties and, then, focus on

emerging pathway-specific agents, with strong evidences in preclinical studies, yet evaluated by only a few Phase I and Phase II concluded or ongoing trials.

Conclusion. A variety of preclinical evidences suggest that new drugs and molecules are potentially useful to target cardiac fibrosis and improve left ventricular function, reduce infarct size and scars, delay incident heart failure and cardiac dysfunction in animal models. However, there are very few clinical trials investigating the effect of such drugs in this setting, as well as a scarceness of new engineered molecules for specific targets.

A530: EFFETTO DEGLI INIBITORI DI SGLT2 NEI PAZIENTI CON SCOMPENSO CARDIACO: STUDIO PILOTA CON VALUTAZIONE DI PARAMETRI CLINICO-LABORATORISTICI E PROGNOSTICI

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Introduzione. L'insufficienza cardiaca (IC) e il diabete mellito (DM) spesso coesistono come pluripatologie, con notevole impatto sulla qualità di vita e sulla mortalità dei pazienti. Recentemente, supportati dagli ottimi risultati di numerosi trial, gli inibitori del cotrasportatore renale di sodio-glucosio 2 (SGLT2i) sono entrati nell'armamentario terapeutico del DM, mostrando tuttavia riduzione degli eventi cardiovascolari maggiori anche nei pazienti senza DM. L'obiettivo di questo studio pilota è valutare l'effetto di tali farmaci nel miglioramento della fitness cardiaca, attraverso la misurazione di parametri clinico-laboratoristici, integrati con esami radiologici avanzati e con la classificazione prognostica HLM (<https://doi.org/10.1016/j.jacc.2014.02.552>).

Materiali e metodi. tutti i pazienti arruolati sono stati divisi in due gruppi: Gruppo 1: pazienti con IC e DM in terapia con l'SGLT2i empagliflozin. Gruppo 2: pazienti con IC e DM non in terapia con SGLT2i. Tutti i pazienti hanno eseguito, al tempo 0, un esame clinico anamnestico, un elettrocardiogramma a 12 derivazioni, un ecocardiogramma color-Doppler, una scintigrafia miocardica con tracciante MIBG; è stata valutata la classe funzionale NYHA e lo stadio HLM, che valuta la funzionalità cardiaca, polmonare e il malfunzionamento di altri organi, in analogia alla TNM usata in oncologia. A 6 mesi tutti i pazienti sono stati sottoposti a un follow-up per le re-ospedalizzazioni per insufficienza cardiaca e per morte cardiovascolare, insieme ad una valutazione clinico-laboratoristica. A 12 mesi ripeteranno la scintigrafia con MIBG.

Risultati. Sono stati arruolati 66 pazienti (Gruppo 1: 20; Gruppo 2: 46;). L'83% è di genere maschile. Non sono state osservate differenze significative tra i due gruppi sull'eziologia ($p=0.343$) e la terapia ($p=0.99$) dell'IC. Nel gruppo 1, a 6 mesi di follow-up, si è mostrato un miglioramento della classe NYHA ($p=0.01$), dello stadio HLM ($p=0.01$), della frazione d'eiezione ($p=0.03$), dell'emoglobina glicata ($p=0.001$) e della clearance della creatinina ($p=0.04$) rispetto al tempo 0. Tale significatività non si è dimostrata nei pazienti del gruppo 2. Non vi sono differenze statisticamente significative per gli eventi di re-ospedalizzazione e morte cardiovascolare a 6 mesi tra i due gruppi ($p>0.05$). Non sono disponibili i dati di follow-up a 12 mesi.

Conclusioni. I nostri risultati preliminari mostrano che gli SGLT2i migliorano la fitness dei pazienti con scompenso cardiaco e diabete mellito, con un effetto positivo su specifici parametri, quali la frazione di eiezione, l'emoglobina glicata e la clearance della creatinina. Per quanto riguarda la prognosi di questi pazienti, il limite del follow-up a 6 mesi non ha mostrato differenze statisticamente significative tra i due gruppi in termini di re-ospedalizzazione e morte cardiovascolare. Un campione maggiore e un follow-up più esteso permetteranno di fare luce su tali risultati. La scintigrafia con MIBG a 12 mesi permetterà di aggiungere evidenze circa l'impatto di tali farmaci sul rischio ritmico di questi pazienti.

A531: HEART FAILURE WITH PRESERVED EJECTION FRACTION: A WEIGHTED PROGNOSTIC RISK SCORE BY USING NON-INVASIVE METHODS

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Objectives. We tested the prognostic role of a risk score including biohumoral evaluation, cardiopulmonary-echocardiographic stress (CPET-ESE) and lung ultrasound, in patients with heart failure (HF) with preserved ejection fraction (HFpEF), and subjects at risk of developing HF (American College of Cardiology/American Heart Association Stages A and B).

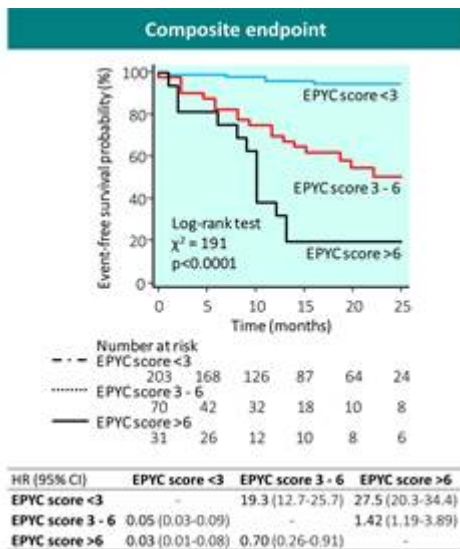
Background. Risk stratification of HFpEF patients can promote a more personalized treatment, prolong survival and optimize the quality of life.

Methods. We performed a resting clinical/biohumoral evaluation followed by a symptom-limited graded ramp bicycle CPET-ESE in 274 patients (45 Stage A, 68 Stage B and 161 Stage C-HFpEF) and 30 age and sex-matched healthy controls.

Results. During a median follow-up of 18.5 months, we reported 71 HF hospitalizations and 10 cardiovascular deaths. Cox proportional-hazards

regression for predicting adverse events identified five independent predictors and each was assigned a number of points proportional to its regression coefficient: Δ stress-rest B-lines >10 (3 points), peak oxygen consumption <16 mL/kg/min (2 points), minute ventilation/carbon dioxide production slope ≥ 36 (2 points), peak systolic pulmonary artery pressure ≥ 50 mmHg (1 point) and resting N-terminal pro-brain natriuretic peptide (NT-proBNP) >900 pg/mL (1 point). We defined three risk categories: low-risk (<3 points), intermediate-risk (3-6 points), and high-risk (>6 points). The event-free survival probability for these three groups were 93%, 52% and 20%, respectively. Hazard Ratio was 4.55 for each risk category upgrade (95% confidence interval [CI], 3.44-5.93). The area-under-curve (AUC) for the scoring system to predict events was 0.92 (95% CI 0.88-0.96), with an accuracy significantly higher than the individual components of the score (C-statistics: all $p < 0.01$ vs individual AUCs).

Conclusion. A weighted risk score including NT-proBNP, markers of cardiopulmonary dysfunction and indices of exercise-induced pulmonary congestion identifies HFpEF patients at increased risk for adverse events and Stage A-B subjects more likely to progress towards more advanced HF stages.



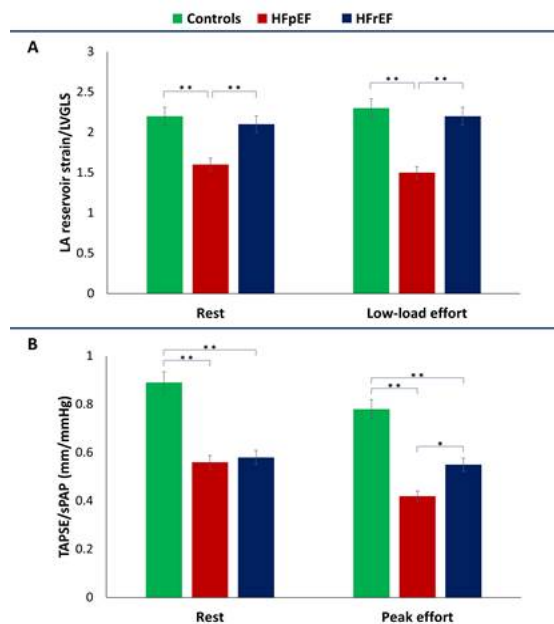
A532: HEART FAILURE WITH REDUCED AND PRESERVED EJECTION FRACTION: DIFFERENT PATHOPHYSIOLOGIC MECHANISMS BEHIND SIMILAR DISEASE SEVERITY

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Aims. We matched heart failure (HF) patients with reduced (HFREF) and preserved (HFpEF) ejection for baseline characteristics and disease severity. We used combined cardiopulmonary-exercise stress echocardiography (CPET-ESE) to analyse the pathophysiological mechanisms behind the different HF cohorts.

Methods and Results. We randomly matched 1:1 subjects with HFREF (n=42) and HFpEF (n=42) for age, sex, body mass index (BMI), peak oxygen consumption, and minute ventilation/carbon dioxide production slope. All the patients performed a symptom-limited graded ramp bicycle CPET-ESE together with 20 age, sex and BMI-matched healthy controls. During a median follow-up of 23 months, we observed six overall deaths and 40 HF hospitalisations. The distribution of events was not different between HFpEF and HFREF. When compared to HFREF, HFpEF showed a higher prevalence of metabolic syndrome (all $p < 0.05$) and higher values of high-sensitivity C-reactive protein (3.18, interquartile range [IQR] 1.72 – 5.66 vs 2.19, IQR 1.37 – 4.97 mg/L; $p < 0.0001$). Multipoint mean pulmonary artery pressure/cardiac output slope showed equally increased values in HFREF and HFpEF (4.1 ± 1.5 and 3.9 ± 1.8 mmHg/L/min) when compared to controls (1.8 ± 1.1 mmHg/L/min; $p < 0.0001$). HFpEF showed the uncoupling of both left atrium-left ventricle (LA-LV: LA reservoir strain/LV global longitudinal strain at low-load effort 1.5 ± 0.8 vs 2.2 ± 1.1 in HFREF; $p < 0.01$; Figure A) and right ventricle-pulmonary artery (RV-PA: peak tricuspid annular plane systolic excursion/systolic pulmonary artery pressure 0.42 ± 0.2 vs 0.55 ± 0.2 mm/mmHg in HFREF; $p < 0.01$; Figure B).

Conclusion. Despite a similar disease severity, HFpEF and HFREF reflect different pathophysiological mechanisms. HFpEF seems to be more specifically related to “double” LA-LV and RV-PA uncoupling, low-grade systemic inflammation and metabolic syndrome.

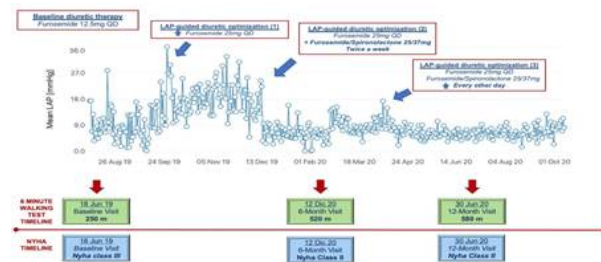


A533: THE LONGEST FOLLOW-UP AVAILABLE WITH VLAP DEVICE: A 1-YEAR GLANCE AT THE FUTURE

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A 75-year-old male patient suffering from non-ischemic-chronic heart failure with severely reduced ejection fraction (LVEF 25%) had frequent hospitalizations for HF-decompensation despite OMT (Beta Blockers, ACEib, loop diuretics, ARNI, CRT/ICD). CV risk factors: hypertension, previous smoker. Relevant comorbidities: CKD stage IIIa. His cardiac medical history begins in 2015 with diagnosis of non-ischemic cardiomyopathy with reduced ejection fraction, severe mitral regurgitation and moderate tricuspid regurgitation. He underwent mitral valve replacement and tricuspid valve repair. In the following years, the patient faced several HF-worsening episodes with NT-proBNP elevation, dyspnea, palpitation and dizziness. In June 2019, as symptoms persisted (NYHA functional class III) and no guidelines indicated-therapy was available, the patient was enrolled in VECTOR-HF clinical study, a first-in-human trial consisting in V-LAP™ (Vectorious Medical Technologies) device implantation. V-LAP™ is a battery-free left atrium monitoring system allowing remote monitoring of left atrial pressure (LAP). Once inserted through interatrial septum with percutaneous intervention, the measurements are daily collected by means of an external belt, sending data to physician via a cloud-based system. After 3 months, the right heart catheterization confirmed the accuracy of measurements (through comparison to PCWP). Once the reliability was confirmed, LAP trends have been monitored and guided the optimization of medical therapy, mainly diuretics. Of note, at 12 months from implantation, diuretics fine-tuning managed to lower LAP over time and no hospital readmission occurred. The patient experienced symptomatic relief, maintaining class NYHA II to date, and the functional capacity showed an amelioration as covered distance increased in consecutive 6-Minute walking tests: 250m before implantation, 520m at 6 months, 580m at 12 months (see Figure below). Moreover, in order to improve ventricular resynchronization, we used VLAP feedback to choose between different CRT configurations. This is, to the best of our knowledge, the longest follow-up available for a VLAP implanted-patient and the high degree of patient adherence to daily LAP measurements (nearly 100%) seems to confirm the ease of use of the device and helped us to earlier detect and treat any underlying disease progression which could lead to HF decompensation.



A534: IMPLANTABLE CARDOVERTER DEFIBRILLATOR IN ADVANCED HEART FAILURE PATIENTS: PROGNOSTIC IMPLICATIONS

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Background. The prevalence of patients with advanced heart failure (HF) ranges from 1% to 10% of HF population. These patients showed frequently a left ventricular ejection fraction (LVEF) lower than 30% and for this reason, according recent guidelines should install implantable cardioverter defibrillator (ICD). In this study we would like to evaluate the prognostic impact of ICD in advanced HF patients.

Methods. This is an observational retrospective study enrolling patients with diagnosis of acute heart failure (AHF) de novo or not, admitted to our department from January 2015 to January 2018 within 12 hours from emergency department admission. Patients underwent to clinical examination, laboratory analysis (NTproBNP, renal function haemoglobin) and echocardiography. Advanced heart failure patients were defined on the basis of ESC recent criteria. Patients were followed for one year after hospital discharge for the composite outcome of HF re-hospitalization and cardiovascular death through one year.

Results. A total of 122 acute advanced HF (AAHF) patients were included in this analysis. 94 patients were male, median age was 77[67-84] years, median of left ventricular ejection fraction (LVEF) was 25 [20-30]% and the median of serum levels of NTproBNP was 12375 [5346-26375] pg/ml. HF etiology in our population was distributed as follows: 9 patients had dilated hypertensive cardiomyopathy, 26 patients had valvular cardiomyopathy, 35 patients had primitive (dilated, restrictive or hypertrophic) cardiomyopathy and 52 patients had ischemic cardiomyopathy. 80 patients showed a known diagnosis of HF and 31 patients had ICD. Multivariable Cox regression analysis did not show any relationship with in-hospital mortality and one month adverse events occurrence about the presence of ICD, HF etiology, previous AHF hospitalization, LVEF and renal function. At six months of follow-up, multivariable analysis showed that presence of ICD (HR 0.03[0.004-0.272]; p=0.001), increasing in LVEF (0.83[0.70-0.98]; p=0.03) and increasing in eGFR (0.95[0.91-0.99]; p=0.02) were all protective factors for HF hospitalization and cardiovascular death; conversely previous diagnosis of HF was related to poor prognosis (5.78[1.10-30.21]; p=0.04). Similarly, at one year were confirmed the same findings for ICD(p=0.002), LVEF(p=0.03), eGFR (p=0.02) and previous diagnosis of HF(p=0.02).

Conclusions. In AAHF patients the presence of ICD results in a protective effect on long term incidence of HF hospitalization and cardiovascular death. Other determinants which recognize a prognostic impact together with ICD are LVEF, eGFR and previous HF diagnosis. These data suggest that arrhythmic substrate should be frequently related to long term prognosis in advanced HF patients.

A535: CLUSTERING ACUTE HEART FAILURE PATIENTS ACCORDING DIASTOLIC DYSFUNCTION DEGREE: A SINGLE CENTRE EXPERIENCE

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Background. Different studies in heart failure (HF) setting evaluated diastolic dysfunction degree through echocardiography. The interest by researchers in this topic leads to better recognize diastolic dysfunction favouring the standardization of its definition through a consensus document.¹ In this study we would like to identify the phenotype of acute heart failure (AHF) patients according diastolic dysfunction degree.

Methods. This is an observational retrospective study enrolling patients with diagnosis of acute heart failure (AHF) de novo or not, in sinus rhythm admitted to our department from June 2015 to October 2018 within 12 hours from emergency department admission. Patients underwent to echocardiography to assess diastolic dysfunction degree: normal diastolic function, diastolic dysfunction grade I, grade II e and grade III according the recent consensus document.¹ Patients were followed for one year after hospital discharge for the composite outcome of HF re-hospitalization and cardiovascular death through one year.

Results. A total of 277 AHF patients in sinus rhythm were included in this analysis. Median age was 79[71-84] years, median of left ventricular ejection fraction (LVEF) was 40 [30-50]% and the median of serum levels of NTproBNP was 7871 [3180-17025] pg/ml. 68% of patients had normal diastolic function, 12% had diastolic dysfunction grade I, 10% grade II and 10% grade III. Among groups of diastolic function, no differences statistically significant were found in terms of age, gender, comorbidities, length of hospital stay, renal function and PASP. Patients with severe diastolic dysfunction (grade III) demonstrated higher admission NTproBNP levels (grade III 15538[8052-33724]; vs grade II 5428 [3107-11654]; vs grade I 8193[1740-17756]; vs normal: 7611 [3223-15245] pg/ml; p=0.008) with respect to other groups. Moreover, patients with diastolic dysfunction grade III showed lower median values of LVEF

(grade III 27 [21-35]; vs grade II 40 [30-47]; vs grade I 37[25-50]; vs normal: 40 [30-55]%; p<0.001) and TAPSE (grade III 16[12-18]; vs grade II 20[18-21]; vs grade I 18[15-21]; vs normal: 17 [15-20]mm; p=0.01) compared to other groups. Moreover, patients with severe diastolic dysfunction were more frequently classified as advanced HF patients (grade III 58%; vs grade II 23%; vs grade I 47%; vs normal: 23%; p<0.001) with respect to other groups. In terms of one year adverse events and in-hospital mortality no differences were found among groups.

Conclusions. Dividing our AHF population according diastolic function did not show any differences among groups in terms of age, gender and comorbidities. Patients with more severe diastolic dysfunction showed a more severe left and right ventricular dysfunction. However, differently from the classification of LVEF, we did not find any differences among diastolic function groups in terms of adverse events occurrence.

A536: PREVALENCE AND PROGNOSIS OF CARDIAC CACHEXIA IN ACUTE HEART FAILURE PATIENTS

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Background. Cachexia is characterized by a pathological shift of metabolism towards a catabolic state. The prevalence of cardiac cachexia in heart failure (HF) patients is around 10% and it recognizes a negative prognostic impact. In this study we would like to evaluate prevalence and prognosis of cardiac cachexia in acute heart failure (AHF) patients.

Methods. This is an observational retrospective study enrolling patients with diagnosis of acute heart failure (AHF) de novo or not, admitted to our department from January 2015 to September 2018 within 12 hours from emergency department admission. Patients underwent to clinical examination, laboratory analysis and echocardiography. Cardiac cachexia was defined as unintentional weight loss, with or without skeletal muscle wasting, of at least 5% of baseline weight during the previous year. For the diagnosis, three of the following factors are also required: anorexia, fatigue, reduced muscle strength, reduced fat-free mass index, and abnormalities in blood biomarkers (haemoglobin \leq 12 g/dL, serum albumin $<$ 3.2 g/dL, elevated IL-6, or increased C-reactive protein).¹ Patients were followed for one year after hospital discharge for the composite outcome of HF re-hospitalization and cardiovascular death through one year.

Results. A total of 415 AHF patients were included in this analysis. 111 patients met the criteria for the diagnosis of cardiac cachexia. Median age was 78[70-83] years. Patients with cardiac cachexia showed higher age (79[73-84] vs 77[68-82] years; p=0.005), length of hospital stay (12[8-15] vs 9[6-13] days; p=0.004) and RDW (14.9[13.9-16.3] vs 15.3[14.3-16.9]; p=0.02) with respect to patients without cachexia. Moreover, patients with cachexia demonstrated reduced eGFR (53[38-68] vs 48[31-60] ml/min/m²; p=0.03) and TAPSE (18[15-20] vs 15[14-19] mm; p=0.002) compared to patients without cachexia. No differences were found among groups in terms of NT-proBNP. In-hospital mortality was higher in patients with cachexia compared to other patients (6.3% vs 1.3%; p=0.005). Univariate Cox regression analysis confirmed the poor prognosis of patients with cachexia at one month (HR 2.53 [1.24-5.19]; p=0.01), six months (HR 2.47 [1.61-3.77]; p<0.001) and one year (HR 2.04 [1.40-2.98]; p<0.001).

Conclusions. Patients with cardiac cachexia were characterized by renal dysfunction and right ventricle dysfunction. These alterations should act as worsening factors in terms of abdominal venous congestion and subsequent malabsorption. Finally, in our population, cardiac cachexia was related to poor short term and long term outcome as confirmed by recent studies.

A537: DISCOVERING ADVANCED HEART FAILURE PATIENTS; CLINICAL CHARACTERISTICS AND PROGNOSTIC BURDEN

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Background. The prevalence of patients with advanced heart failure (HF) ranges from 1% to 10% of HF population. A recent position statement of Heart Failure Association (HFA) of European Society of Cardiology (ESC), defined advanced HF according four criteria including LV dysfunction, symptoms severity and HF hospital admission. In this study we would like to evaluate clinical and prognostic characteristics of HF patients in advanced stage.

Methods. This is an observational retrospective study enrolling patients with diagnosis of acute heart failure (AHF) de novo or not, admitted to our department from January 2015 to January 2019 within 12 hours from emergency department admission. Patients underwent to clinical examination, laboratory analysis (NTproBNP, renal function haemoglobin) and echocardiography. Advanced heart failure patients were defined on the basis of ESC recent criteria. Patients were followed for one year after hospital discharge for the composite outcome of HF re-hospitalization and cardiovascular death through one year.

Results. A total of 601 AHF patients were included in this analysis.

Median age was 78[70-83] years, median of left ventricular ejection fraction (LVEF) was 45 [33-55]% and the median of serum levels of NTproBNP was 7851 [3222-17543] pg/ml. In our sample we found 122 patients who met the criteria of advanced HF. Comparing patients with advanced HF and without we found that advanced HF patients were more frequent affected by not ischemic cardiomyopathy with respect to patients not advanced (85% vs 49%; $p < 0.001$). Moreover, patients not advanced were more frequent de novo HF with respect to advanced ones (54% vs 34%; $p < 0.001$). Advanced heart failure patients showed higher values of NTproBNP (12375[5346-26375] vs 6652[2552-13782] pg/ml; $p < 0.001$) and creatinine (1.20[0.88-1.99] vs 1.07[0.82-1.50] mg/dL; $p = 0.002$) and lower values of TAPSE (18 [15-20] vs 16 [13-19] mm; $p < 0.001$), eGFR (48 [30-66] vs 52 [38-38] ml/min/m²; $p = 0.05$) and serum sodium (140 [138-143] vs 139 [136-141] mEq/L; $p = 0.001$) with respect to not advanced HF patients. Univariate analysis showed that advanced HF was related to poor prognosis in terms of one year cardiovascular death or HF re-hospitalization (HR 1.83 [1.32-2.54]; $p < 0.001$) and in terms of in-hospital mortality (HR 2.53 [1.01-6.53]; $p = 0.05$).

Conclusions. Advanced HF patients showed a worse neuro-hormonal and renal pattern compared to not advanced ones. Similarly, these patients experienced a worse right ventricular function and were more prone to adverse events development at one year. Further study are mandatory to better manage these patients improving their outcome.

A538: KETONE BODIES ATTENUATE HEART FAILURE PROGRESSION THROUGH AN AMELIORATION OF MITOCHONDRIAL FUNCTION

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Background. Beta hydroxybutyrate (BHB) is the main ketone body produced during fasting or carbohydrate deprivation as an alternative fuel. Beyond this role, emerging evidence suggests that BHB produces a direct protective effect, especially in neurodegenerative processes, probably acting on histone acetylation and gene expression program. After myocardial infarction (MI), mitochondrial dysfunction and metabolic impairment are mirrored by increased levels and utilization of BHB. However, whether such increase in BHB is adaptive or maladaptive in the injured myocardium has never been evaluated.

Aim. Here we aim to investigate the functional role of BHB on cardiac function after ischemia, exploring its effects *in vivo*, *ex vivo*, and *in vitro*.

Results. In cultured cardiomyoblasts (H9C2), the administration of BHB (3 mM) reduces the activation of caspase-3 in response to ischemia, as well as the number of Tunel positive nuclei. Specifically, the mitochondrial apoptotic pathway is affected, as BHB reduces cytochrome-C release induced by ischemia. Mitochondrial structure and interconnections, soundly affected by ischemia, are retained in presence of BHB, as well as mitochondrial membrane potential (TMRE). The preserved mitochondrial health is further supported by higher levels of PGC1 α detected in cells exposed to ischemia plus BHB compared to ischemia alone. To explore the *in vivo* effects of BHB on ischemia-damaged myocardium, we administered carbohydrate-null diet (Ketogenic Diet-KD), or standard diet-supplemented with BHB, to post-MI mice. Both mice treated with KD and BHB supplemented diet exhibited preserved ejection fraction and left ventricular internal diameter respect infarcted mice fed regular chow. The protective effect of BHB on myocardial function coincided with increased levels of PGC1 α in the myocardium of treated mice, both as protein and transcription levels. Interestingly, in the hearts of diet-treated MI mice we also observed a significant difference in the histone acetylation pattern.

Conclusions. BHB protects cardiac cells from apoptotic and mitochondrial damage induced by ischemia. Through means of its ability to regulate epigenetic modifications, BHB could activate a gene expression program able to support mitochondrial function, thereby representing a powerful novel therapeutic strategy in heart failure.

A539: GLYCATION OF RYANODINE RECEPTORS IN PERIPHERAL LYMPHOCYTES PREDICTS THE RESPONSE TO CARDIAC RESYNCHRONIZATION THERAPY

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Introduction. Cardiac resynchronization therapy (CRT) is an effective treatment for patients with advanced heart failure (HF). The management of these patients depends on biomarkers for monitoring disease progression and therapeutic response. HF patients exhibit a pathologic remodeling of Ryanodine Receptors (RyRs) in heart, muscle, as well as circulating lymphocytes, leading to intracellular calcium leak, which has been shown to correlate with the clinical outcome.

Hypotheses: 1) post-translational modifications of RyR in circulating

lymphocytes in HF patients can predict CRT response; 2) CRT can improve the remodeling of RyRs and intracellular calcium leak.

Methods. To test this hypothesis, we enrolled 34 patients who underwent CRT and examined RyR remodeling in peripheral lymphocytes before and 1 year after CRT using established biochemical and flow-cytometry assays. Non-responders to CRT were defined after 1 year of follow-up as patients with at least one of the following characteristics: deteriorating function (HF-related death, need for heart transplantation), increase in LVEF \leq 4%, worsening in peak O₂ consumption, in Quality-of-Life score, or in the distance walked in 6 min.

Results. We found that post-translational remodeling of RyR (i.e. oxidation, phosphorylation, glycation) was significantly ($P < 0.01$) reduced in circulating lymphocytes isolated from CRT responders compared to pre-CRT levels and to non-responders. Similarly, the binding to RyR of its stabilizing subunit (calstabin) was markedly increased by CRT, whereas intracellular Ca²⁺ leak was attenuated ($P < 0.01$). Importantly, these phenomena were not observed in CRT non-responders. Moreover, in a multivariate regression analysis, we observed that RyR glycation in peripheral lymphocytes at baseline was independently associated with CRT response at 1-year follow-up ($P < 0.05$).

Conclusions. This is the first study showing that CRT response can be predicted by the level of RyR glycation in peripheral blood lymphocytes. Moreover, we demonstrate that CRT responders exhibit a significantly reduced intracellular Ca²⁺ leak through RyR in lymphocytes, mirrored by diminished post-translational modifications compared to baseline and to CRT non-responders.

A540: LA TRANSIZIONE DALLA FASE 2 DELLA GESTIONE DEL COVID-19 ALLA RILEVAZIONE DI BIG DATA NEI PAZIENTI CON SCOMPENSO CARDIACO CRONICO: FATTORI OSTATIVI E AGEVOLANTI DEL MONITORAGGIO DA REMOTO

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Introduzione. Prestazioni di Televisita, Telesalute e Teleconsulto multidisciplinare costituiscono attività chiave della Telemedicina (TLM), intesa a migliorare gli standard di salute per il cittadino nell'ambito delle malattie croniche e, in particolare, nello scompenso cardiaco, contribuendo all'efficientamento delle risorse.

Metodi. Un'analisi mista, quali-quantitativa, è stata posta in essere presso l'Azienda Ospedaliera Universitaria (AOU) San Giovanni di Dio e Ruggi di Aragona di Salerno allo scopo di analizzare le modalità e le finalità della rilevazione di big data nei pazienti con scompenso cardiaco cronico. In presenza di Covid-19, è stato necessario utilizzare la telemedicina come modalità alternativa per i pazienti con scompenso cardiaco cronico allo scopo di garantire la ripresa delle prestazioni ambulatoriali ospedaliere nel rispetto delle norme definite per la gestione della fase 2. In tal senso, è stato possibile sfruttare la fase due come trampolino di lancio per la transizione verso un nuovo modello di gestione dello scompenso cardiaco basato sulla telemedicina. I pazienti coinvolti nell'analisi sono stati selezionati in base a vari criteri: tipo di connettività, presenza di caregiver, classe NYHA I- II-III, non indicazione a procedure interventistiche e intervallo di circa 4-6 mesi tra le visite nei precedenti controlli. Partendo da questi criteri, essi sono stati assegnati a una classe di priorità B e candidati al teleconsulto. I pazienti con classe di priorità di tipo A, in considerazione della criticità delle proprie condizioni di salute, sono stati convocati a visita tradizionale. Infine, i pazienti di classe C sono stati indirizzati ad un appuntamento di controllo a lungo termine. I pazienti di classe B, che hanno fornito il consenso al controllo da remoto, sono stati contattati telefonicamente o con videochiamata per il controllo di parametri clinici e di eventuali sintomi. Attraverso una mail creata ad hoc, i pazienti o i caregiver hanno avuto la possibilità di inviare esami ematochimici e strumentali richiesti dallo specialista; laddove necessario, sono state effettuate variazioni di terapia. Durante il processo di teleassistenza, è stato possibile raccogliere dati qualitativi e quantitativi intesi a fornire evidenze sui fattori di successo e sui fattori ostativi all'implementazione di un modello di telemedicina nella gestione dello scompenso cardiaco cronico.

Discussione. L'utilizzo di infrastrutture di telecomunicazione tipo tele/videoconferenza, posta elettronica, chat e devices ha consentito la relazione a distanza tra utenti /caregiver e medici, ha permesso il monitoraggio del peso e dei fluidi con possibilità di regolare prontamente la terapia diuretica; ha facilitato il controllo della frequenza cardiaca, della pressione arteriosa e delle aritmie; ha permesso di titolare i farmaci e di migliorare gli interventi educativi stimolando empowerment ed auto-controllo della malattia; ha contribuito al riconoscimento precoce e ha migliorato il controllo dei fattori precipitanti.

Conclusioni. Il successo del TLM dipende dal sinergismo di vari fattori: la scelta dei parametri vitali integrata con algoritmi di controllo individualizzati, la promozione di programmi educazionali per una buona aderenza del paziente al programma di monitoraggio, formazione specifica del personale coinvolto (Infermieri, Medici, Data manager), integrazione ospedale-territorio.

A541: CLINICAL BENEFIT OF SACUBITRIL-VALSARTAN IN PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION

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Background. Sacubitril-valsartan is effective in reducing cardiovascular death and hospitalization in patients with heart failure and reduced ejection fraction (HFrEF). Aim of this prospective study was to investigate the potential benefit of sacubitril-valsartan therapy on clinical outcomes (hospitalization for HF and dyspnea) and on various echocardiography parameters.

Methods. From September 2017 sacubitril-valsartan was initiated and titrated in 41 consecutive patients with symptomatic HFrEF (NYHA functional class ≥II) despite optimal medical therapy, LVEF ≤35%, preserved renal function (eGFR ≥30 mL/min/1.73 m²) and systolic blood pressure ≥100 mmHg. Every 6 months a clinical follow-up and a transthoracic echocardiography was obtained in all patients. We evaluated hospitalization for HF rate, symptoms improvement, left ventricular ejection fraction improvement (LVEF), end-diastolic (LVEDV) and end-systolic LV volume (LVESV) changes, right ventricular (RV) longitudinal function improvement, improvement of mitral valve (MV) regurgitation and systolic pulmonary artery pressure (sPAP) reduction.

Results. Median follow-up time was 412 days (IQR 221-556). A total of 6 patients prematurely discontinued the drug, 4 because of symptomatic hypotension and in 2 cases for allergy to the drug. 3 patients died during the follow-up. Patients who did not discontinue with sacubitril-valsartan therapy showed low rate of hospitalization for HF (8.35%). Dyspnea significantly improved during the follow-up period (NYHA 1.9 ± 0.9 vs 2.7 ± 0.5, p<0.001). LVEF was significantly increased in patients who did not discontinue sacubitril-valsartan (33.9 ± 8.8% vs 28.6 ± 7.6%, p=0.008) and LV volumes were decreased (LVEDV 151.1 ± 51.7 ml vs 174.0 ± 55.3 ml, p=0.08; LVESV 103.0 ± 42.7 ml vs 126.4 ± 49.0 ml, p=0.04). MV regurgitation entity was significantly improved in patients who continued sacubitril-valsartan (p=0.01). Improvement of RV longitudinal function (TAPSE 19 ± 3.5 mm vs 17.1 ± 4.3 mm, p=0.05) was found and sPAP were significantly decreased. (32.2 ± 9.1 mmHg vs 38.1 ± 11.0 mmHg, p=0.031).

Conclusions. In our HFrEF population, sacubitril-valsartan is associated with improvement of LVEF, LVEDV, LVESV, RV longitudinal function, MV regurgitation entity, sPAP, hospitalization for HF rate and dyspnea degree.

A542: ADHERENCE TO EVIDENCE-BASED TREATMENTS FOR REDUCED EJECTION FRACTION HEART FAILURE ACROSS AGE STRATA: A NATIONWIDE COHORT STUDY

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Aims. Despite the improvement in survival obtained with guideline-directed medical treatments (GDMT) in reduced ejection fraction heart failure (HFrEF), rates of undertreatments remain high. Older age does not contraindicate GDMT in HFrEF, but in clinical practice frequently limits the maximization of HFrEF treatments. In this study we assessed the current adherence to evidence-based therapies for HFrEF across age strata (<70 years, 70-79 years and ≥80 years) in a large cohort of unselected patients with HFrEF.

Methods. Patients with EF<40% from the Swedish HF Registry were included. Indications to GDMT were determined according to level I-IIa recommendations in the ESC guidelines published in 2016.

Results. Among 27,430 patients with HFrEF, 8515 (31%) were <70 years, 9392 (34%) between 70 and 70-79 years and 9523 (35%) ≥80 years old. Comorbidities, with the exception of diabetes, were more frequent and HF was more severe at increasing age. The rate of renin-angiotensin system inhibitors/angiotensin receptor neprilysin inhibitors and betablockers administration decreased with age (95 and 95%, respectively in patients <70 years old vs 80 and 88% in patients ≥80 years old, p<0.001). Similarly, mineralocorticoid receptor antagonists were less likely prescribed in elderly patients (54% in patients <70 years old vs 35% in patients ≥80 years old, p<0.001). The likelihood of target dose achievement of GDMT was consistently less likely in patients ≥80 years old compared to younger patients. Devices, including implantable cardioverter defibrillator and cardiac resynchronization therapy, were less likely implanted among patients ≥80 years old with potential indication according to current guidelines compared to younger patients. Age ≥80 years old emerged as independently associated with lower rates of all the GDMT for HFrEF after correction for a large set of covariates.

Conclusions. In this large cohort of patients with HFrEF the use of GDMT remains suboptimal and the implementation of GDMT in the elderly although avoiding prescription of GDMT in elderly patients is not supported by the current evidences.

A543: FACTORS DICTATING THE DECISION TO PROCEED WITH RIGHT HEART CATHETERIZATION AFTER A VISIT FOR PULMONARY HYPERTENSION: THE IMPORTANCE OF PROPER REFERRAL

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Background. Haemodynamic assessment by right heart catheterization (RHC) is mandatory for diagnosis and classification of pulmonary hypertension (PH). Nevertheless, the decision to carry out RHC is contingent on the likelihood of underlying left heart disease or lung disease, as inferred by clinical evaluation. The purpose of this investigation was to assess which factors dictate the decision to withhold or perform RHC after the initial visit at a PH referral centre.

Methods. We retrospectively reviewed the records of the subjects referred to our PH outpatient unit between January 2017 and December 2019. Patients were divided into two groups according to whether they received or not indication to RHC within 3 months from the baseline visit. Categorical and continuous variables were compared by chi-square and t-test, respectively. The correlates of RHC indication were determined by means of a logistic regression model including the variables significantly different between the RHC and no-RHC groups.

Results. One hundred ninety-two patients were included in the analysis (69% females, mean age 68 ± 12 years). RHC was carried out within 3 months in 54 of them (28.1%) and confirmed the presence of pre-capillary PH in 35. Compared with the 138 subjects without RHC indication, those who underwent RHC had more often HIV infection (7% vs. 0.7%, P=0.01), more often carbon monoxide diffusing capacity (DLCO) <60% (37% vs. 21%, P=0.02) and less often moderate-severe obstructive or restrictive alterations (19% vs. 33%, P=0.04) at pulmonary function testing (PFT). At echocardiography, RHC patients had more commonly a peak tricuspid regurgitation velocity (TRV) >2.8 m/s, alone (91% vs. 57%, P <0.001) or with ≥1 abnormality among right ventricular (RV) dilation, right atrial enlargement, RV outflow tract acceleration time <105 ms, or D-shaped left ventricle (78% vs. 35%, P=0.003). Referral by cardiologists (rather than from other specialists) was also more frequent for the RHC group (56% vs. 23%, P <0.001). In multivariate analysis, RHC indication was significantly associated with a DLCO value <60% and the echocardiographic demonstration of TRV >2.8 m/s and ≥1 sign of PH (Table), as well as with referral by cardiologists.

Conclusions. These results suggest that the decision to proceed with RHC in this single-centre cohort was consistent with the recommendations of current guidelines. However, RHC was also 50% more likely when patients came to attention upon cardiologist advice, indicating that referral from non-cardiologists is less often appropriate. This finding highlights the need to improve the knowledge about PH in the medical community at large.

	Univariate		Multivariate	
	OR	95% IC	OR	95% IC
PFT moderate-severe alteration	0.46	0.21-0.98	0.18	0.05-0.46
DLCO <60%	2.19	1.10-4.36	6.21	2.03-18.95
HIV infection	10.80	1.18-98.97	23.22	0.82-655.97
Cardiologist referral	4.14	2.13-8.07	5.53	2.21-13.80
TRV >2.8 m/s and ≥1 additional echocardiographic sign of PH	3.88	1.55-9.71	5.39	1.79-16.25

A544: FIBRILLAZIONE ATRIALE DI NUOVA INSORGENZA IN PAZIENTI CON SCOMPENSO CARDIACO A PRESERVATA FRAZIONE DI EIEZIONE VENTRICOLARE SINISTRA

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Introduzione. La fibrillazione atriale (FA) è l'aritmia più comune nei pazienti con scompenso cardiaco, e può condurre a ridotta funzione cardiaca e peggioramento dei sintomi di scompenso cardiaco. La FA di nuova insorgenza in pazienti con scompenso è associata a peggioramento della prognosi, a causa di un ulteriore deterioramento della funzione cardiaca. Inoltre, questa associazione caratterizza i pazienti con scompenso più avanzato. Tuttavia, l'impatto prognostico di un episodio di FA su pazienti con insufficienza cardiaca con frazione di eiezione conservata (HFpEF) non è chiaro.

Metodi. 126 pazienti ospitati consecutivamente nella nostra Unità di Cardiologia da gennaio 2017 a dicembre 2019 sono stati valutati retrospettivamente. Di questi, 59 hanno presentato una AF di nuova insorgenza nel contesto di HFpEF precedentemente nota. I restanti 67 pazienti hanno presentato FA di nuova diagnosi senza insufficienza cardiaca. Per ogni paziente, sono state raccolte caratteristiche demografiche e cliniche, comorbidità, dati strumentali ed outcomes clinici (percentuale di aritmia cardiovertita, durata del ricovero). Per esaminare la relazione tra le caratteristiche dei pazienti ed outcomes clinici, sono stati impiegati il test di Student t test chi-quadro.

Risultati. I pazienti con FA e HFpEF erano significativamente più anziani (76,7 contro 72,9 anni) e presentavano più comorbidità (in media 4 contro 3 morbidità) rispetto a quelli con la sola FA. La durata del ricovero era significativamente più lunga (in media 5 giorni) per il gruppo FA + HFpEF rispetto al gruppo con FA da sola (in media 4). La percentuale di FA cardiovertita era significativamente maggiore nei pazienti con FA senza HFpEF (58/67 = 86%) rispetto ai pazienti con FA e HFpEF (39/59 = 66%). I principali mezzi impiegati per la cardioversione erano l'amiodarone, seguito dai farmaci antiaritmici A1c e dalla cardioversione elettrica. Ma le nostre scelte in percentuale non erano significativamente differenti nei due gruppi di pazienti.

Conclusioni. I nostri pazienti ospedalizzati con FA di nuova insorgenza e HFpEF nota hanno presentato outcomes clinici peggiori rispetto ai pazienti con FA senza HFpEF. Ciò è in parte dovuto alle differenze di età e comorbidità tra i due gruppi. Forse sono necessarie ulteriori evidenze per fornire alternative terapeutiche appropriate nei pazienti con FA di nuova diagnosi e HFpEF nota.

A545: L'IMPATTO PROGNOSTICO DI UNO SCOMPENSO CARDIACO CON FEVS PRESERVATA NEI PAZIENTI CON EMBOLIA POLMONARE ACUTA

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Introduzione. L'embolia polmonare acuta è una condizione ad elevata mortalità. La stratificazione prognostica di questi pazienti è il primo passaggio per l'adozione di un'idonea strategia di trattamento. In accordo con quanto suggeriscono le linee guida, la presenza di compromissione emodinamica (shock o ipotensione) individua pazienti "ad alto rischio". I pazienti non ad alto rischio andrebbero ulteriormente stratificati adottando uno score clinico-prognostico validato, PESI score o sua versione semplificata sPESI, per distinguere pazienti a rischio intermedio e basso. Questo sistema di score conferisce un punteggio più alto ai pazienti con scompenso cardiaco cronico. Tuttavia, non è chiaro quale peso prognostico possa avere lo scompenso cardiaco con FEVS preservata (HFpEF).

Metodi. Abbiamo eseguito una valutazione retrospettiva di due gruppi di pazienti, consecutivamente ricoverati presso la nostra U.O. di Cardiologia-Utic con diagnosi di EP tra l'Aprile 2016 ed il marzo 2020. Sono stati esclusi dello studio i pazienti con scompenso cardiaco a FEVS ridotta. Trenta pazienti avevano una normale funzione ventricolare sinistra. Trentotto pazienti presentavano uno scompenso cardiaco con FEVS conservata. Abbiamo descritto per ogni paziente le caratteristiche demografiche e cliniche, i fattori predisponenti, le comorbidità, gli scores predittivi diagnostici (score di Wells e Ginevra score), i valori del D-Dimero, i risultati degli esami strumentali (ECG, ecocardiogramma, CUS, TC-angio del torace), e i punteggi PESI-sPESI score. Sono stati considerati outcomes clinici un combinato delle complicanze (infarto polmonare, emorragie, ictus, necessità di ventilazione), la morte, la durata del ricovero. Per saggiare, nei due gruppi di pazienti la relazione tra caratteristiche dei pazienti e i relativi outcomes clinici sono stati calcolati i coefficienti di correlazione di Pearson-Spearman.

Risultati. I 68 pazienti studiati (29 M, 39 F), avevano età media 72 anni (min. 27, max 94). I pazienti con HFpEF avevano una età più avanzata, una prevalenza significativa del sesso femminile, ed avevano una maggiore comorbidità. Gli outcomes clinici combinati (durata del ricovero - complicanze - morte) non hanno mostrato una correlazione statisticamente significativa con l'HFpEF, mentre la sola durata del ricovero si è mostrato un outcome correlato significativamente con l'HFpEF.

Conclusioni. I pazienti con EP e concomitante HFpEF che abbiamo avuto ricoverati tra aprile 2016 e marzo 2020, non hanno avuto un'evoluzione clinica complessivamente peggiore rispetto a quelli senza scompenso cardiaco. Tuttavia hanno avuto ricoveri mediamente più lunghi, probabilmente per l'età media più avanzata e per il maggior numero di morbidità associate.

A546: PROGNOSTIC ROLE OF SUBCLINICAL CONGESTION IN HEART FAILURE OUTPATIENTS: FOCUS ON RIGHT VENTRICULAR DYSFUNCTION

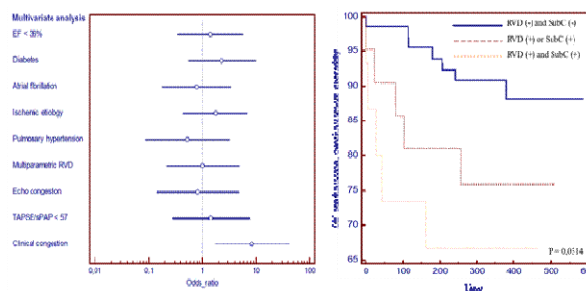
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Background. Subclinical pulmonary and peripheral congestion (SubC) is an emerging concept in heart failure (HF), correlating with worse prognosis in mortality and re-hospitalization rate. Numerous papers have been published on ultrasound assessment of residual pulmonary and abdominal congestion at discharge but very few monocentric studies have evaluated the prognostic impact in an outpatient setting and its strict relationship with right ventricular dysfunction (RVD).

Methods. In this observational, multicentric, non-randomized, retrospective study, 109 consecutive outpatients with symptomatic, stable HF were enrolled regardless of ejection fraction (EF) and etiology. Severe pulmonary disease, primary pulmonary hypertension, recent coronary syndromes, recent angioplasty or surgery were excluded. The degree of congestion focused on systemic congestion and signs of elevated filling pressures of the right ventricle (RV) were systematically evaluated by physical exam. Immediately after TTE was performed to define multiparametric right ventricle dysfunction (RVD), estimated right atrial pressure (eRAP) and pulmonary artery systolic pressure (sPAP). Outcome data were obtained by scheduled visits and phone calls.

Results. The study aims to evaluate how clinical and ultrasound signs of congestion could impact on prognosis, especially in RVD patients: the assessed outcomes were mortality from cardiovascular causes, re-hospitalization for HF, urgent evaluation regarding diuretic therapy titration. The average follow up was 376 ± 117 days. TAPSE/sPAP ratio and clinical congestion were powerful predictors of outcome at univariate analysis. The main results are summarized in the graphs below.

Conclusion. RV/pulmonary uncoupling is a strong predictor of outcome in HF outpatients, TAPSE/sPAP ratio is a simple and affordable surrogate measure. When SubC is identified in RVD outpatients dramatically impacts prognosis. Due to the strict relationship between RVD, pulmonary hypertension, RV/pulmonary coupling and congestion the multivariate analysis fails in identifying echocardiographic independent predictors of outcome. When clinical signs of overt HF are present the prognosis is poor, resulting in the main independent predictor of future events.



A547: THE FAVOURABLE ALLIANCE BETWEEN CARDIOMEMS AND LEVOSIMENDAN IN PATIENTS WITH ADVANCED HEART FAILURE

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Background. Heart failure (HF) exhibits phases of exacerbation punctuated by periods of clinical stability. In the past years, different devices have been investigated to help in identifying early decompensation events in patients with HF and reduced ejection fraction (EF), reducing hospital admissions. In particular, the CardioMEMS (Abbott Medical, Inc., Abbott Park, IL, USA) is an implantable device positioned in the pulmonary artery (PA) able to detect higher cardiac filling pressures, an objective measure of 'haemodynamic congestion', estimated to rise more than 2 weeks before the onset of symptomatic clinical congestion. In this report, we present the first patient experience with levosimendan infusion led by CardioMEMS.

Case summary. A 68-year-old man with HF and reduced EF was enrolled in our HF Clinic from October 2017. The patient's comorbidities included: chronic kidney disease stage 3B with secondary anaemia, hypothyroidism, dyslipidaemia, carotid atherosclerosis, chronic obstructive pulmonary disease, sizeable inguinal hernia, hypertension, paroxysmal atrial fibrillation and obesity. His cardiovascular history started in 2004 for the appearance of dyspnoea with left ventricle (LV) dilation and reduction of systolic function (EF 42%). Coronary angiography showed no evidence of critical coronary atherosclerotic disease. Despite the optimal medical therapy, from 2004 to 2015, he suffered more than 20 hospitalizations for exacerbation of chronic HF with a progressive reduction of EF. In 2015 for the evidence of EF <35%, he underwent biventricular ICD implantation. Furthermore, he was newly subjected to coronary angiography with the indication of stenting on a critical lesion at the mid-portion in the circumflex. In 2017, severe mitral regurgitation treated by positioning of MitraClip (Abbott Laboratories, Menlo Park, CA, USA); at discharge, the patient was enrolled in our departmental HF Clinic (October 2017). The echocardiogram showed a dilated left ventricle with severely reduced EF (29%) and increased pulmonary artery systolic pressure (40 mmHg). From October 2017 to May 2019, the patient went through numerous hospitalizations, despite optimal medical therapy; subsequently, was adopted a strategy of levosimendan infusions guided by CardioMEMS. The patient was monitored daily by CardioMEMS; if the cardiologist

detected a trend towards increasing diastolic PA (PAd) pressures, the patient was contacted, and his medications adjusted to lower PAd to the patient-specific goal. If three consecutive readings exceeded this threshold, it was decided for the therapy changes (e.g. increasing the dosage of a diuretic or making a change to any other HF therapies). The dosage of the drug was titrated up to the maximum tolerated dose, including the worsening of renal function. From June 2019 to December 2019, the patient had only two hospitalizations scheduled for levosimendan infusion and none for HF exacerbation.

Discussion. Our case supports the combination of CardioMEMS and levosimendan for the optimal management of patients with advanced HF. These results further strengthen the development of a randomized clinical trial to demonstrate the clinical usefulness of this device in combination with the levosimendan infusion programme in advanced HF patients.

A548: LA DIAGNOSI DI SCOMPENSO CARDIACO AL DEA: STUDIO RETROSPETTIVO MONOCENTRICO SULL'APPROPRIATEZZA DELLA DIAGNOSI AL RICOVERO E L'UTILITÀ DEL CARDIOLOGO IN PS

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Introduzione. Lo scompenso cardiaco è una delle patologie maggiormente diagnosticate. In molti casi la diagnosi di primo approccio si basa solo sui valori del BNP. Lo scompenso cardiaco può essere ospedalizzato nell'intera area medica. Dalla corretta diagnosi di dimissione dipende la verifica delle esatte dimensioni del problema epidemiologico, e la conseguente allocazione di risorse da destinare al disegno della rete assistenziale. Scopo del presente contributo è quello di verificare retrospettivamente i riflessi della esatta definizione diagnostica alla dimissione e i riflessi di questa sulla prognosi.

Materiali e metodi. Sono state analizzate retrospettivamente dal 1 gennaio al 31 dicembre 2017, 723 cartelle cliniche di pazienti dimessi con diagnosi principale di insufficienza cardiaca al primo accesso. Come criterio di esclusione coloro i quali avevano la diagnosi di scompenso cardiaco come secondaria. Secondo la Società Europea di Cardiologia le componenti essenziali per la formulazione della diagnosi nei pazienti naïves, deve comprendere, oltre al quadro clinico, evidenza obiettiva di disfunzione cardiaca, obiettivata attraverso un percorso di imaging cardiaco. È stata indicata come appropriata la diagnosi di scompenso cardiaco per i pazienti che avessero almeno 1 dei seguenti elementi diagnostici: Ecocardiogramma; Esame emodinamico/CVG/PTCA; Scintigrafia miocardica. Inoltre è stata valutata la mortalità complessiva ed in funzione del reparto di ricovero.

Risultati. I deceduti totali sono stati 152 con una mortalità totale a 30 giorni dall'accesso del 21%. La quota maggiore dei decessi (90/152 pari al 59% del totale) avveniva nel corso del ricovero indice. La mortalità a 30 giorni scorporata dagli eventi intraospedalieri è stata dell'8,6% (62 decessi). Il 75% delle dimissioni per scompenso cardiaco è avvenuto dall'area medica non cardiologica, il 25% dall'area cardiologica. La mortalità complessiva (in-hospital + 30 giorni) dei pz ricoverati nell'area Cardiologica è risultata pari al 24% a fronte della mortalità dell'area medica pari al 16%. Analizzando retrospettivamente la omogeneità di percorso diagnostico tra i pazienti ricoverati in area cardiologica ed area non cardiologica, emergeva un dato: dei 152 pz ricoverati nell'area cardiologica - 150 (98,6%) erano stati sottoposti ad imaging cardiovascolare a sostegno dell'ipotesi diagnostica; per contro, dei 571 pz ricoverati nell'area medica - 380 (66,5%) soddisfacevano i criteri diagnostici ESC. La mortalità ricalcolata alla luce dell'appropriatezza diagnostica risulta pertanto: area cardiologica: 36/150 ovvero 24%; area medica: 116/380 ovvero 30%.

Conclusioni. L'analisi dei dati mostra una eccessiva semplificazione nel porre diagnosi di scompenso cardiaco, spesso basandosi solo sul dato numerico del BNP. Una rilettura dei dati mostra in realtà una riduzione della mortalità dell'area cardiologica a fronte di quella medica; quindi per una ottimizzazione delle risorse e dei costi, ed il raggiungimento di un iter diagnostico terapeutico congruo ed appropriato, la figura del cardiologo di PS si rivela fondamentale, consentendo un più semplice accesso al cardiomaging.

TELECARDIOLOGIA ED e-HEALTH

A549: ROUTINE OUTPATIENT VISITS DURING SARS-CoV-2 GLOBAL PANDEMIC

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Background. The inability to carry office visits was collateral damage caused by the coronavirus disease 2019 (COVID-19) pandemic. Tele-

health is a relatively new, and yet fundamental amid the current crisis, resource to bridge the gap between physicians and patients.

Methods. We report our experience with telemedicine and describe the major events occurred in our patients. 121 consecutive adult patients with arterial hypertension (F/M: 56/65; mean age: 66.8 years) were enrolled. 33 patients (27%) had also diabetes, 94 (78%) were also affected from dyslipidemia and 11 (9%) had CAD. They all referred to our ambulatory of hypertension, in most of case for several years. Given the impossibility to continue routine outpatient visits during lockdown, they were all phone called by three residents in order to detect their state of health or any events they could have experienced over this period. They were all asked about their own blood pressure values, the occurrence of new symptoms and of new-onset both cardiovascular and non cardiovascular events. We also followed a self-made preset form.

Results. 31 of them (26%) experienced cardiovascular symptoms/events during this period: 11 had hypertensive peaks, in one case associated with nausea and vomiting while 2 of them had hypotensive episodes; 10 had typical angina and/or dyspnoea while 4 had atypical angina; 6 had palpitations; 1 of them developed new onset atrial fibrillation resolved with pharmacologic cardioversion during hospitalization; 1 had syncope; 1 patient reported new onset peripheral edema; 2 patients died during lockdown for non cardiovascular causes. 17 of them also developed non cardiovascular symptoms, 7 of whom were severe anxiety and/or panic attacks. Almost all patients had important lifestyle changes, in 15 cases (12,3%) associated with weight increase.

Conclusion. The impossibility to access to routine outpatient visits during lockdown due to global pandemic of SARS-CoV-2, has brought out the risk of underestimating consequences of chronic disease, in absence of appropriate follow-up. Nevertheless, the two deaths we report were not related to cardiovascular disease. The risk is that both the missing of cardiovascular control visit and the extension of the waiting list, could provoke serious complications in patients suffering from chronic cardiovascular disease.

A550: REMOTE MONITORING: HOW CAN IT IMPACT THE MANAGEMENT OF PAH PATIENTS

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Background. Telemonitoring is being increasingly used for chronic disease monitoring. While the primary aim of telemonitoring is to improve chronic disease management and decrease hospitalizations, the potential impact on patient's health-related quality of life may be an additional benefit. Pulmonary arterial hypertension (PAH) is a chronic disease that modifies the patient's quality of life. The aim of our study was to evaluate whether telemonitoring, on the basis of encouraging results in subjects with heart failure, could significantly affect the quality of life and perception of the disease in subjects with PAH.

Methods. Thirty consecutive outpatients with PAH were subjected to the SF-36 (v1) STANDARD Health Questionnaire to understand the quality of life, daily life activities that they were and were not able to do and their state of mind about others and about their pathology. Subsequently, patients were randomized into two groups; and one of these was subjected to a structured and continuous telephone follow-up of 15, 30, 60 and 120 days on the extent of dyspnea, edema, diuresis, weight body, blood pressure, and heart rate.

Results. Patients undergoing remote monitoring with respect to the control group showed statistically significant differences, however, with respect to the perception of the quality of life (0.27 ± 0.59 vs -0.40 ± 0.6325 , $p=0.005$) and in the limitation of 100 m (1.2 ± 0.41 vs 1.73 ± 0.70 , $p=0.017$).

Conclusion. The perception of the health status (both physical and emotional), of patients with PAH can be improved by telemedicine nursing telephone follow-up; remote monitoring could better improve outpatient management of the patient suffering from PAH.

A551: LA GESTIONE DELLE MODALITÀ DIAGNOSTICHE E DELLE IMMAGINI DIGITALI IN UN CATH LAB

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Obiettivi. Presentare gli aspetti tecnologici e gestionali di particolare rilievo connessi all'implementazione ed utilizzo, all'interno di un'unità operativa di cardiologia interventistica, dei sistemi informatici, di gestione delle immagini diagnostiche e dell'integrazione delle differenti modalità di imaging.

Metodi. Le modalità diagnostiche (angiografo, ecografo, poligrafo,

imaging intravascolare) hanno assunto un ruolo ormai consolidato e strategico nella diagnosi e cura delle principali patologie cardiache. Grazie ai notevoli progressi della diagnostica per immagini è stato possibile implementare nuove applicazioni cliniche migliorando il workflow sotto moltissimi aspetti. Il periodo di emergenza sanitaria, di questi mesi, dovuta al COVID-19 ha fatto comprendere, quanto ancor di più, l'integrazione e la condivisione digitale e informatica sia importante. La dotazione tecnologica del laboratorio di emodinamica, pur sviluppandosi in tempi e con modalità differenti, richiede oggi una gestione, sotto l'aspetto informatico e digitale, per essere disponibile e utile sia in fase intraprocedurale sia in tempi successivi (archivio immagini, rendicontazione, gestione magazzino, gestione documentale). L'utilizzo di questi sistemi è caratteristico per ciascuna professione sanitaria che contribuisce, con le proprie competenze, al lavoro di equipe all'interno del laboratorio di emodinamica. Tali sistemi e tecnologie necessitano di attività di gestione e amministrazione ed il tecnico sanitario di radiologia medica, per le proprie competenze acquisite sia nel corso di laurea abilitante la professione e sia con percorsi post-laurea specifici, rappresenta, sicuramente la figura più idonea.

Risultati. La completa connessione di tutte le modalità diagnostiche, la perfetta connettività, attività di manutenzione e gestionali, rappresentano uno dei aspetti essenziali per garantire, al cardiologo interventista, risposte in tempo reale al fine di incrementare la capacità interpretativa del cardiologo, migliorare l'assistenza.

Conclusioni. Le competenze professionali unitamente alla corretta gestione, utilizzo e condivisione delle modalità diagnostiche e tecnologiche rappresentano il valore aggiunto su cui il laboratorio di emodinamica deve puntare.

A552: VALIDATION OF REMOTE MEASUREMENT OF THE QTc INTERVALS USING AN APPLE WATCH

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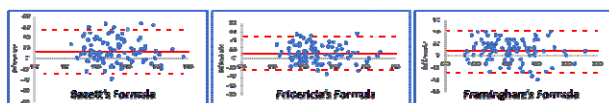
Introduction. In many circumstances, especially in the Covid-19 period, it could be necessary to measure the QT interval repeatedly and even daily.

Hypothesis. The aim of this study was to evaluate the feasibility of remote measuring LI-LII and V2 leads with using a commercially available Apple Watch Series 4 (Apple Inc., Cupertino, CA, USA).

Methods. The accuracy of the QTc calculation with the smartwatch compared to the standard ECG was tested using different formulae. Eighty-one patients admitted to our CCU and 19 subjects admitted to the outpatient clinic for routine cardiovascular evaluation were studied. LI-LII and V2 tracings were obtained immediately after the recording of the standard 12-lead ECG. The LI was recorded with the smartwatch on the left wrist and the right index finger on the crown; recording LII was obtained with the watch on the left lower abdomen and the right index finger on the crown; The chest lead V2 was recorded with a smartwatch in the fourth intercostal space left parasternal with the right index finger on the crown. All recorded 30" ECGs were digitally stored using the health application of an iPhone Series 10 in the pdf format (Apple Inc., Cupertino, CA, USA). The advantage of saving the ECG in pdf format is that it can be sent also via e-mail.

Results. There was an agreement between the QT-LI, QT-LII, QT-V2 and QT mean intervals of smartphone electrocardiography tracings and standard electrocardiography (Respectively, Spearman's correlation coefficient: 0.881; 0.885; 0.801; 0.911 [p<0.001]). The reliability of the QTc measurements was tested with Bland-Altman analysis using Bazett's, Friedericia's, and Framingham's formulas between standard ECG and smartwatch (Figure).

Conclusions. These data demonstrated the feasibility to measure the QTc in LI, LII, and V2 leads with a smartwatch with results comparable to that performed with the standard ECG. These data could have an important clinical impact both for the widespread diffusion of smartwatches and for the monitoring of drug-induced QT interval prolongation, especially in the Covid-19 era.



A553: LA TELEMEDICINA PER IL CUORE: UN NUOVO STRUMENTO PER I PAZIENTI CON SCOMPENSO CARDIACO?

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Lo scompenso cardiaco (SC) rappresenta oggi una e vera propria criticità, essendo caratterizzato da elevata morbilità, mortalità e comportando ingenti costi sociali ed economici. Lo SC interessa circa il 10% della

popolazione anziana ed è responsabile dell'1-2% della spesa sanitaria totale, con più del 75% della spesa riconducibile ai ricoveri ospedalieri. I dati concernenti le ospedalizzazioni dei pazienti con SC consentono di fare alcune considerazioni: i tassi di re-ospedalizzazione sono molto elevati (circa 40% a 12 mesi dalla dimissione), inoltre, molti ricoveri riguardano forme lievi di SC, e sarebbero dunque potenzialmente evitabili tramite un miglior follow-up.

Questi dati sono condizionati da vari fattori, alcuni riconducibili alla complessità intrinseca dello SC e dei pazienti che ne sono affetti, altri legati al frequente drop-out assistenziale tra ospedale e territorio e alla scarsa aderenza terapeutica dei pazienti. Vista l'entità epidemiologica ed economica dello SC, e l'effetto prognostico negativo legato alle ospedalizzazioni, si stanno attuando varie strategie per cercare di migliorare il percorso di cura dello SC, al fine di migliorarne la qualità di vita dei pazienti e garantire la sostenibilità del sistema sanitario. Tra queste, si sta sempre più evidenziando la necessità di potenziare l'assistenza territoriale mediante la creazione di percorsi dedicati, un maggior coinvolgimento del Medico Curante e il telemonitoraggio. La disponibilità di strumenti che consentono una comunicazione costante tra il paziente e la struttura assistenziale può consentire di aumentare il grado di coinvolgimento attivo del paziente, superare le barriere logistico-organizzative assicurando una maggior equità di trattamento, inoltre, può consentire una terapia non solo personalizzata ma anche ottimizzata in tempo reale, andando ad intercettare e correggere eventuali variazioni cliniche prima che portino ad instabilizzazioni conclamate con necessità di ricovero. I potenziali benefici del telemonitoraggio sono ancor più enfatizzati nel contesto della recente emergenza da COVID-19, che ha visto una riorganizzazione di tutti i settori della vita, ivi inclusa la sanità, con necessità di limitazione dei rapporti interpersonali.

Presso il nostro Centro abbiamo quindi deciso di avviare uno studio con lo scopo di fare una valutazione post marketing dell'utilizzo di un sistema di telemedicina nei pazienti affetti da SC, in termini di utilità del servizio, aderenza al suo uso e qualità di vita. Valuteremo, inoltre, il coinvolgimento del Medico di Medicina Generale. Lo studio prevede l'arruolamento nell'arco di 6 mesi di 24 pazienti fra quelli inviati dal Medico di Medicina Generale al nostro Centro per sospetto scompenso cardiaco (riacutizzazione o primo episodio). I pazienti arruolati, tramite il sistema di telemonitoraggio, trasferiranno al centro i seguenti parametri: peso, pressione arteriosa, frequenza cardiaca, ritmo, saturazione O₂, temperatura e scala di percezione dello stato di salute da 1 a 5. I pazienti saranno osservati almeno 3 volte in tempi differenti: al basale, alla dimissione del device (verosimilmente intorno al 30° giorno) e a 90 giorni.

Obiettivo del lavoro è di documentare i potenziali innumerevoli benefici di questo nuovo strumento, nell'ambito di una patologia già così drasticamente attuale e con rilevanza sanitaria, sociale ed economica in continuo aumento.

A554: IMPACT OF TELEMEDICINE NETWORK PROVIDED BY LOCAL PHARMACIES IN THE MANAGEMENT OF SYMPTOMATIC TACHYARRHYTHMIAS DURING THE COVID-19 OUTBREAK

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Background. During the lockdown period in Italy, from March 11th to May 4th 2020, a progressive increase in COVID-19 cases occurred in all Italian regions, in particular in the Lombardy Region. The current rise in COVID-19 cases has led to an increasing involvement of hospitals, in order to face the Coronavirus outbreak, shifting healthcare resources towards the management of COVID+ patients. This has led, on the other hand, to a progressive decrease in hospital admissions due to conditions not associated with SARS-CoV2 infection. In other European countries interested by a national lockdown, a decrease in registered new-onset atrial fibrillation (AF) cases was observed, as a consequence of a reduction in admissions to the Emergency Department (ED). Undiagnosed AF patients can develop complications that could potentially translate into poorer long-term outcomes.

Purpose. In this scenario, we aimed to verify the impact of telemedicine during lockdown, in comparison with the same period in 2019.

Materials and method. We analyzed 12-lead ECGs recorded by 5000 country pharmacies, evaluated and stored in one telemedicine platform provided by Health Telematic Network (HTN), in cooperation with our Cardiology Department, Federfarma (Pharmacists' National Association), and Italian National Health Institute.

Results. During the lockdown period in 2020, 6,104 ECGs were performed in territorial pharmacies, compared to 17,280 ECGs recorded in the same period in 2019. Among ECGs performed, we detected AF in 344 patients (5.64%) in lockdown period, compared to 393 cases (2.27%)

detected in the same period in 2019, with an increase of 40.25%. We detected also Atrial Flutter in 32 patients (0.52%) in lockdown period, compared to 25 cases (0.14%) detected in the same period in 2019. The difference was +26.92%. Moreover, we found Paroxysmal Supraventricular Tachycardia in 8 patients (0.13%) during lockdown, compared to 6 cases (0.03%) detected in the same period in 2019, with an increase of 23.07%. In lockdown period, a total of 384 patients (6.29%) were referred to ED because of symptomatic tachyarrhythmia, compared to 424 patients (3.47%) referred to ED in the same period in 2019, with an increase of 55.16%. In the Lombardy Region, during lockdown period, were reported 194 cases of tachyarrhythmia in territorial pharmacies (about 50.52% of all cases in Italy). Among these, 93 cases of tachyarrhythmia were in the Brescia area (about 47.94%), whereas 50 cases were in the Bergamo one (about 25.77%).

Conclusion. These data shown that, during the COVID outbreak period, a large number of patients with cardiovascular symptoms preferred to go to territorial pharmacies rather than the closer hospital. Telemedicine played a prominent role in managing patients with cardiovascular symptoms at home. Moreover, this service allowed to refer to the hospital only patients with clinically relevant tachyarrhythmia, avoiding the risks of treatment delay, especially in Italian region the most affected by the COVID-19 outbreak. This once again underlines how telemedicine network provided by pharmacies may become an important tool offered to citizens, especially during coronavirus pandemic emergency, within the Italian National Health System services.

A555: ROLE OF TELEMEDICINE NETWORK PROVIDED BY PHARMACIES TO DETECT ACUTE MYOCARDIAL INFARCTION IN PATIENTS WITH CHEST PAIN DURING THE CORONAVIRUS PANDEMIC

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(a) UNIVERSITY OF BRESCIA, ITALY; (b) ASST SPEDALI CIVILI AND UNIVERSITY OF BRESCIA, ITALY; (c) CARDIOLOGY UNIT, ASST SPEDALI CIVILI OF BRESCIA, ITALY; (d) HTN HEALTH TELEMATIC NETWORK, BRESCIA, ITALY; (e) NATIONAL INSTITUTE OF HEALTH, BRESCIA, ITALY; (f) ITALIAN SOCIETY OF TELEMEDICINE AND E-HEALTH, BRESCIA, ITALY

Background. During the lockdown period in Italy, from March 11th to May 4th 2020, a progressive increase in COVID-19 cases occurred in all Italian regions, in particular in the Lombardy Region. The current rise in COVID-19 cases has led to an increasing involvement of hospitals, in order to face the Coronavirus outbreak, shifting healthcare resources towards the management of COVID+ patients. This has led, on the other hand, to a progressive decrease in hospital admissions due to conditions not associated with SARS-CoV2 infection. During COVID-19 outbreak period, it has been observed a decrease in hospital admissions for acute myocardial infarction. This phenomenon put in serious difficulty the clinical management of COVID-free patients with cardiovascular disease, at the beginning of phase 2 (starting from May 4 2020).

Purpose. In this scenario, we aimed to verify the impact of telemedicine during lockdown, in comparison with the same period in 2019.

Materials and method. We analyzed 12-lead ECGs recorded by 5000 country pharmacies, evaluated and stored in one telemedicine platform provided by Health Telematic Network (HTN), in cooperation with our Cardiology Department, Federfarma (Pharmacists' National Association), and Italian National Health Institute.

Results. During the lockdown period, were recorded 6,104 ECGs in territorial pharmacies, compared to 17,280 ECGs done in the same period in 2019. Chest pain symptom represented the cause of recording ECG in 298 patients (4.88%) during the lockdown period, compared to 402 patients (2.33%) in the same period in 2019, with an increase of 109.86%. In the Lombardy Region, during lockdown period, were reported 118 accesses to territorial pharmacies for chest pain (about 39.50% of total cases in Italy). Among these, 36 accesses were in the province of Brescia (about 30.50%), whereas 28 of them were in the province of Bergamo (about 23.73%). Among ECGs performed, 8 showed typical abnormalities of acute myocardial infarction with ST elevation (STEMI, 2.68%) in the lockdown period, compared to 7 STEMI (1.74%) detected in the same period in 2019, with an increase of 54.17%. These patients were referred to Emergency Department (ED) suddenly, for the therapeutic intervention.

Conclusion. These data shown that a large number of patients with cardiovascular symptoms preferred to go to territorial pharmacies rather than hospitals during the COVID outbreak period. Telemedicine played a prominent role in managing patients with cardiovascular symptoms at home. Moreover, this service allowed patients with STEMI to access to the hospitals faster, avoiding the risks of a serious diagnostic delay. Furthermore, by analyzing the data of Lombardy Region, it was possible to show how a significant component of access to local pharmacies for chest pain occurred in the region most affected by the COVID-19 outbreak.

A556: PATIENT SATISFACTION WITH TELEHEALTH IN CARDIOLOGY: LESSONS AND CAUTION FROM THE RESPONSE TO COVID-19 RESTRICTIONS

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Introduction. The rise of COVID-19 and the issue of a mandatory stay at home order in March 2020 led to the utilization of a direct to consumer model for cardiology telehealth (tele). Kentucky serves as a unique study location. Besides practice specific restrictions, Kentucky contributes to the state's top 10 ranking in age adjusted total cardiovascular deaths per 100,000 persons. This is further compounded by the fact that Kentucky is in the bottom 10 states in the country for household income and about 1 in every 4 households do not have a broadband internet connection. The utilization of cardiology tele in this unique Kentucky population is not well represented in the literature.

Methods. We constructed an online survey through Qualtrics and invited all patients who had a visit scheduled during the COVID-19 tele only time frame to participate. Questions were mostly Likert or Likert-type, and included factors for declining tele appointments, advantages and disadvantages associated with tele, and patient satisfaction ratings of tele and in-person (IP) visits in the key areas of patient-centered communication, clinical competence, interpersonal skills and supportive environments. We had 193 responses to our survey (9.5% response rate).

Results. Advantages and Disadvantages of Telehealth: Reduced travel time, lower visit wait time and cost savings were seen as big advantages with tele. Fewer than 10% rated any of the potential issues as a big disadvantage; by contrast, individual survey items were rated as 'Not a Disadvantage' by 67-86% of respondents. Privacy concerns were the least problematic, with only 14.2% of respondents reporting this as at least somewhat of a disadvantage. Poor internet connectivity was of most concern rated as at least somewhat of a factor by 33.0% of respondents. **Comparison of In-Person and Telehealth:** Both IP and tele were viewed favorably, but IP rated somewhat higher across all 11 domains. Only the clinical competence domain generated a significantly lower mean score for tele (3.7 vs 4.2, p=0.007), and this was driven entirely by the low rating on the thoroughness of the clinical exam. No significant differences were seen for Patient-Centered Communication (Cronbach's alpha: Tele = 0.920; IP = 0.973), Supportive Environment, & Interpersonal Skills (Cronbach's alpha: Tele = 0.931; In-P = 0.927). There was also high reliability among items within each survey domain, as Cronbach's alpha values ranged from 0.879 to 0.973.

Conclusion. This study takes advantage of the natural experiment provided by the COVID-19 pandemic to provide a comparative assessment of patient satisfaction with tele and IP appointments. Tele offers both opportunities and challenges. Patterns of satisfaction are consistent across modalities. Tele is a viable alternative to IP cardiology appointments. Physicians seem to be able to adapt well. The clinical exam is an issue that needs to be addressed. **Limitations:** The dangers of COVID-19, especially for these patients, nearly ensures a positive bias toward tele. This may disappear entirely in a "normal" situation. As a result, we might have seen less difference between tele and in-person than we might have originally expected. It highlights the need for RCTs to truly evaluate differences between IP and tele experience.

A557: MULTICHANNEL ELECTROCARDIOGRAMS OBTAINED BY A SMARTWATCH FOR THE DIAGNOSIS OF ACUTE CORONARY SYNDROMES: THE SMART AMI TRIAL

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Antonio Curcio (a), Serena Migliarino (a), Annalisa Mongiardo (a),

Salvatore De Rosa (a), Ciro Indolfi (a)

(a) MAGNA GRAECIA UNIVERSITY, CATANZARO

Background. Smart watches are increasingly popular and used for digital health information. Apple watch series 4 (Apple Inc, Cupertino, CA, USA) introduced an integrated ECG tool which allows recording a single-lead ECG. The aim of the present study was to prospectively investigate the feasibility and the accuracy of the Apple Watch in patients admitted in our CCU with the diagnosis of acute coronary syndrome compared with a standard 12-lead ECG.

Methods. A commercially available Apple Watch series 4 (Apple Inc., Cupertino, CA, USA) was used positioning the sensor in different body positions to obtain nine bipolar ECGs (corresponding to Einthoven leads I, II and III and Precordial leads V1-V6) that were compared with a simultaneous standard 12-lead ECG. The DI was recorded with the Apple Watch on the left wrist and the right index finger on the crown, recording DII was performed with the watch on the left lower abdomen and the right index finger on the crown, and DIII with the watch on the left lower abdomen and the left index finger on the crown. The pseudo-unipolar Wilson-like chest leads were recorded corresponding to the location of V1-V6 (V1=fourth intercostal space right parasternal, V2=fourth intercostal space left parasternal, V3= between V2 and V4, V4= lead at the fifth intercostal space mid-clavicular line, V5=lead at the fifth intercostal space anterior axillary line, V6=lead at the fifth intercostal space mid-axillary line,

respectively). All recorded ECGs were digitally stored using the Health Application of an iPhone Series 11 Pro (Apple Inc., Cupertino, CA, USA). One-hundred subjects were included in the study. Fifty-five patients had a STEMI and were treated with primary angioplasty within 60 minutes of hospitalization. Twenty-seven patients had a NSTEMI and 18 age-matched subjects were included as control.

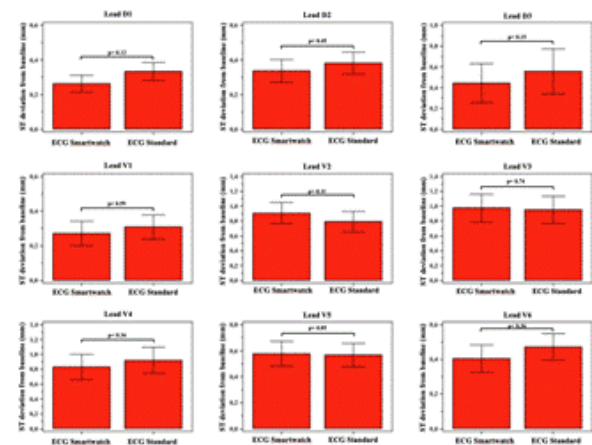
Results. A very good agreement was found between Smartwatch ECG and Standard ECG for the identification of normal ECG, ST segment elevation and NSTEMI alterations (Cohen's kappa 0.90 [95% CI 0.78 to 1], 0.88 [95% CI 0.78 to 0.97], 0.85 [95% CI 0.74 to 0.96]), respectively. The sensitivity and specificity of Smartwatch ECG for the diagnosis of normal ECG were 84% (95% CI 60 to 97) and 100% (95% CI 95 to 100), STE deviation were 93% (95% CI 82 to 99) and 95% (95% CI 85 to 99) (Figure 1), NSTEMI ECG alterations were 94% (95% CI 81 to 99) and 92% (95% CI 83 to 97), respectively.

Conclusions. Our study demonstrated a good correlation between the leads evaluated with the apple watch and the traditional electrocardiogram, both in the recognition of the elevation and the sub-elevation of the ST segment. Obviously, the diagnosis of heart attack is much more complex due to the need of the clinical context and laboratory tests, but this could be an initial and quick method to direct the diagnosis.

the presence of moderate-severe RV systolic dysfunction (tricuspid annular systolic excursion, TAPSE <17 mm). The primary endpoint of the study was all-cause mortality at 1-year. Secondary endpoints included cerebrovascular accident, myocardial infarction, permanent pacemaker implantation, endocarditis and re-hospitalization for all causes.

Results. At baseline, 23 (8.7%) patients were in Stage 0/1 (no cardiac damage/left ventricular damage), 106 (40.4%) in Stage 2 (left atrial or mitral valve damage), 59 (22.5%) in Stage 3 (pulmonary vasculature or tricuspid valve damage) and 74 (28.3%) in Stage 4 (right ventricular damage). At 30-day after TAVI, a lower prevalence of advanced stages of cardiac damage than baseline, mainly driven by a significant improvement in left ventricular diastolic parameters and right ventricular function, was reported. At 1-year, a stepwise increase in mortality rates was observed according to staging at baseline: 4.3% in Stage 0/1, 6.6% in Stage 2, 18.6% in Stage 3 and 21.6% in Stage 4 (p= 0.08). No differences were found in secondary endpoints.

Conclusion. TAVI has an early beneficial impact on the left ventricular diastolic and right ventricular function. However, the extent of cardiac damage at baseline significantly affects the risk of mortality at 1-year after the procedure.



VALVULOPATIE

A558: EXTENT OF CARDIAC DAMAGE AND MORTALITY IN PATIENTS UNDERGOING TRANSCATHETER AORTIC VALVE IMPLANTATION

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Aims. Degenerative aortic stenosis (AS) is the most common heart valve disease among people >65 years in developed countries, with an increasing prevalence due to population ageing. A recently proposed staging classification of AS is based on the assumption that there is a continuum in the pathophysiology of LV structural and functional changes induced by AS. Such system showed prognostic ability among patients from the PARTNER 2 trial as well as in asymptomatic subjects with moderate to severe AS, thus challenging the current management of the disease. The aim of our study was to assess the prognostic performance of this staging classification in a real-world cohort of patients undergoing transcatheter aortic valve implantation (TAVI) and to investigate the eventual impact of the procedure on the extent of extra-aortic valve cardiac damage.

Methods. A staging classification was applied to 262 patients from the EfficTAVI Registry. The following criteria for staging classification of cardiac damage were applied at baseline (within 1 month before TAVI) and after the procedure (within 30-day): Stage 0, no extra-aortic valve cardiac damage; Stage 1, LV damage as defined by the presence of LV hypertrophy (LV mass index >95 g/m² for women, >115 g/m² for men), severe LV diastolic dysfunction (E/e' >14) or LV systolic dysfunction (LV ejection fraction, LVEF <50%); Stage 2, left atrial (LA) and/or mitral valve damage as defined by the presence of LA enlargement (LA volume >34 ml/m²) and/or moderate-severe mitral regurgitation and/or atrial fibrillation; Stage 3, pulmonary vasculature and/or tricuspid valve damage as defined by the presence of systolic pulmonary hypertension (systolic pulmonary arterial pressure, PAPS>60 mmHg) and/or moderate/severe tricuspid valve regurgitation; Stage 4, right ventricular (RV) damage as defined by

A559: RIPARAZIONE PERCUTANEA DI INSUFFICIENZA TRICUSPIDALE MEDIANTE SISTEMA MITRACLIP – CASO CLINICO

Martina Belli (a), Massimo Marchei (a), Saverio Muscoli (a), Marco Di Luozzo (a), Daniela Benedetto (a), Enrica Mariano (a), Pasquale De Vico (a), Angela Sanseviero (a), Michela Bonanni (a), Francesco Romeo (a), Valeria Cammalleri (a)
(a) POLICLINICO TOR VERGATA

L'insufficienza tricuspidale è una valvulopatia determinata da anomalo passaggio di sangue dal ventricolo destro in atrio destro per inadeguata apposizione dei lembi valvolari. La terapia di scelta è quella cardiocirurgica e nei pazienti ad alto rischio, al momento, l'unica alternativa è quella medica. Negli ultimi anni, però, si sta affermando la possibilità di una terapia percutanea che consiste nell'apposizione di una clip metallica a livello dei lembi. Presentiamo il caso di una paziente con insufficienza tricuspidale severa ed elevato rischio chirurgico, sottoposta a trattamento percutaneo della valvulopatia mediante sistema MitraClip (Abbott Vascular, Menlo Park, CA).

Paziente di 78 anni, dislipidemia, ipertesa, affetta da fibrillazione atriale permanente, insufficienza renale cronica, anemia ed ipertensione polmonare. Pregressa sostituzione valvolare aortica (1997) e mitralica (2013) con protesi meccaniche. A Novembre 2019 per l'ennesimo episodio di scompenso cardiaco veniva ricoverata presso la nostra UOC di Cardiologia in condizioni emodinamiche labili e con sintomatologia dispnoica presente anche a riposo (classe NYHA III-IV). L'ecocardiogramma transtoracico (TTE) mostrava funzione sistolica globale del ventricolo sinistro nei limiti. Normale funzione della protesi in sede aortica e della protesi mitralica. Ventricolo destro ai limiti alti della norma con conservata funzione sistolica di pompa. Insufficienza tricuspidale di grado severo da retrazione sisto-diastolica dei lembi e dilatazione anulare (48 mm). Lo stesso giorno si eseguiva ecocardiogramma transesofageo (ETE) che confermava una valvola tricuspidale con retrazione fibrotica dei lembi e dilatazione anulare con insufficienza di grado severo. Durante il ricovero, la paziente veniva sottoposta a terapia diuretica infusionale ad alti dosaggi ed ottimizzazione della terapia per il controllo della frequenza cardiaca e successivamente veniva dimessa in relativo buon compenso emodinamico. A Maggio 2020 per il ripresentarsi della sintomatologia dispnoica, nonostante terapia diuretica massimale, veniva ricoverata nuovamente presso l'UOC di Cardiologia. In considerazione della sintomatologia riferita e delle comorbidità della paziente, in particolare il rischio di un terzo intervento cardiocirurgico, l'eventuale trattamento chirurgico della tricuspidale risultava gravato da un'elevata mortalità (EuroSCORE II 12,15%). Si poneva, pertanto, indicazione a trattamento percutaneo della valvulopatia tricuspidale. La paziente veniva sottoposta ad intervento in sala di emodinamica, in sedazione profonda sotto monitoraggio ETE. Da accesso venoso femorale destro, si inseriva lo SGC in atrio destro, allo sbocco della vena cava superiore, e veniva posizionata una clip tra il lembo settale e in lembo anteriore. Il device time, definito come il tempo intercorso tra il posizionamento del CDS in atrio destro e il rilascio della clip, è stato di 24 minuti. L'ecocardiogramma eseguito immediatamente dopo documentava riduzione del rigurgito tricuspidale da massivo a lieve-moderato, in assenza di stenosi (Grad medio 2 mmHg). Il decorso clinico successivo è stato privo di complicanze e la paziente veniva dimessa in compenso emodinamico. Al controllo dopo un mese, la paziente riferiva un netto miglioramento della sintomatologia e TTE confermava un rigurgito tricuspidale lieve-moderato in presenza di clip ben funzionante. La riparazione percutanea della valvola tricuspidale con device MitraClip è da considerarsi attualmente un trattamento di riduzione dell'insufficienza tricuspidale sperimentale, ma nonostante ciò i risultati sembrerebbero promettenti e potrebbe affermarsi come una valida alternativa all'intervento cardiocirurgico in pazienti inoperabili e con ridotta aspettativa di vita.

A560: CONCOMITANT FUNCTIONAL MITRAL REGURGITATION DURING THE NATURAL HISTORY OF AORTIC VALVE STENOSIS

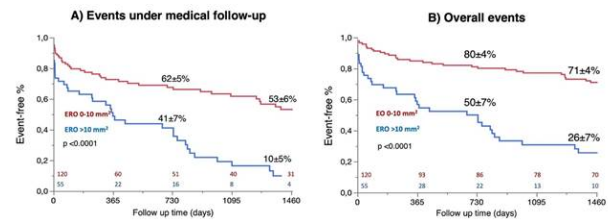
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Introduction. The importance of functional-mitral-regurgitation (FMR) in patients with aortic-valve-stenosis (AS) is unknown, due to the infrequent quantification and absence of studies. In addition, FMR prognostic relevance has only been studied before aortic valve replacement, and no data are available during the medical follow-up.

Methods. Consecutive echocardiograms between 2010-2014 were retrospectively reviewed. Inclusion criteria were transaortic-velocity >2.5 m/sec and mitral effective-regurgitant-orifice area (ERO) in the presence of mitral regurgitation. Organic mitral valve disease was an exclusion-criteria. Primary-endpoint was heart-failure or death under medical-management. Secondary endpoint was heart-failure or death.

Results. Eligible patients were 189, age 79±8 years, 61% NYHA/II, indexed-aortic-valve area (AVA) 0.55±0.17 cm²/m². Mitral ERO was 7.6±4.2 mm² (>10 mm² in 30% of patients). Longitudinal function (by S'-TDI) was associated with mitral ERO independently of ejection fraction and ventricular volumes (p=0.01). ERO >10 mm² (threshold identified by spline survival-modelling) was associated with severe symptoms (OR 3.1[1.6-6.0]; p=0.0006) and higher pulmonary-arterial-pressure (OR 3.0 [1.4-5.9]; p=0.002). Follow-up was completed for 175 patients. After 4.7 [1.4-7.2] years, 87 (50%) patients underwent AVR, 66 (38%) had heart-failure, 64 (37%) died. No procedure on FMR was required. Mitral ERO was independently associated with primary and secondary endpoints both as continuous variable (HR 1.15 [1.00-1.30]; p=0.04 and HR 1.23 [1.05-1.43]; p=0.01 per 5 mm² ERO increase) or as ERO > vs. ≤10 mm² (Figure). Adjustment for S'-TDI or subgroup-analysis did not affect results. The analysis by AVA revealed the incremental prognostic role of mitral ERO over AS severity.

Conclusion. AS patients with concomitant FMR >10 mm² holds higher risk during medical follow-up. FMR quantitation, even for volumetrically modest regurgitation, provides incremental prognostic information over AS severity.



A561: BICUSPID AORTIC VALVE DISEASE FROM INFANCY TO OLDER AGE: A 25-YEAR EXPERIENCE FROM AN ITALIAN REFERRAL CENTRE

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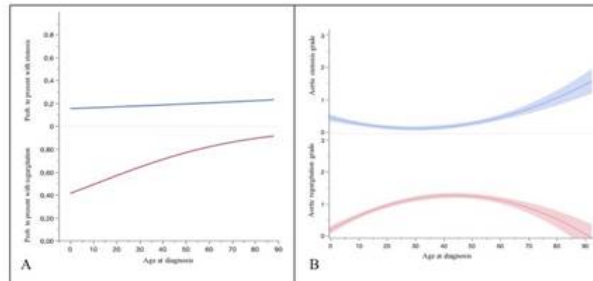
Background. Bicuspid aortic valve (BAV) is the most common congenital heart defect, with considerable risk of morbidity and mortality. The purpose of the study was to analyse clinical and echocardiographic presentation of BAV in a large volume tertiary Italian centre and to test their interaction with full-age span, sex and first diagnosis versus second referral.

Methods. Consecutive patients of all ages diagnosed with BAV in our centre from January 1988 to December 2012 were retrospectively included. Exclusion criteria were: associated complex congenital cardiac disease, systemic syndrome and previous cardiac surgery.

Results. Eligible patients were 790, divided by age quartiles (the mean age of the sub-groups was respectively 3.8±3.3 years, 18.1±4.7 years, 37.6±6.2 years and 59.2±8.3 years). Global mean age was 29.6±21.6 years with a male predominance of approximately 3:1. 72% of patients had any grade BAV dysfunction. Aortic valve stenosis was more frequent in the first (24%) and fourth (24%) quartile. This corresponds to a double-peak stenosis severity curve (B), being more severe at a very young age and in the elderly. Aortic valve regurgitation was more prevalent in each quartile than stenosis, with a prevalence of 72% in the second and 77% in the third quartile. This corresponds to a single-peak regurgitation severity curve (B), being more severe in the fourth and fifth decades of life. Patients with previously diagnosed BAV had more significant valve dysfunction in comparison to patients with first diagnosis of BAV, either stenosis (15% vs 21%, p=0.024) or regurgitation (58% vs 68%, p=0.006). The rate of new diagnosis and the prevalence of valve dysfunction showed minor and not significant fluctuation over time (respectively, p=0.22, p=0.38).

Conclusion. The main value of the present study is the extensive evaluation of prevalence and severity of bicuspid aortic valve in a large

population of consecutive patients. The dominant bicuspid aortic valve dysfunction in this large Italian community is regurgitation, with higher severity of disease in the fourth and fifth decades of life. Indeed, it is mandatory to search for significant regurgitation when a bicuspid aortic valve is diagnosed, especially in the third to fifth decades, with a careful follow-up, since it can be associated with significant medical and surgical morbidity over the life of affected individuals.



A562: RIGHT VENTRICULAR FREE WALL STRAIN IS AN INDEPENDENT PREDICTOR OF OUTCOME IN PATIENTS WITH FUNCTIONAL MITRAL REGURGITATION UNDERGOING MITRACLIP TREATMENT

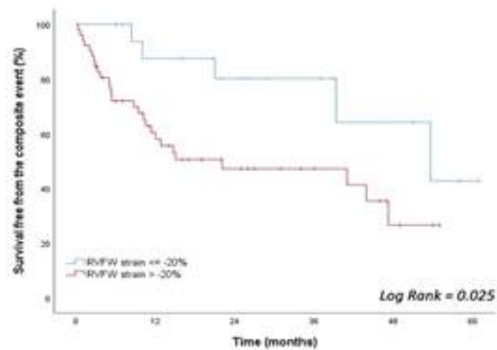
Michele Bellino (a), Giuseppe Iuliano (a), Cesare Baldi (a), Michele Roberto Di Muro (a), Vincenza Procaccini (a), Maria Vincenza Polito (a), Michele Ciccarelli (a), Gennaro Galasso (a), Carmine Vecchione (a), Rodolfo Citro (a) (a) A.O.U. SAN GIOVANNI DI DIO E RUGGI D'ARAGONA

Background. MitraClip implantation is an emerging technique for patients with heart failure and moderate-severe functional mitral regurgitation (FMR). Right ventricular dysfunction has been associated to the onset of adverse events during the follow-up in this clinical setting. Although right ventricular free wall (RVFW) strain ≤ -20% has been identified as a cut-off value to discriminate patients with adverse outcome, its role is still controversial.

Aims. The aim of this study is to evaluate right ventricular function by traditional and novel echocardiographic parameters in patients with moderate-severe FMR successfully treated with MitraClip.

Methods and Results. Overall population included 70 consecutive patients (mean age 70.8 ± 9.1yy; 72% male) with FMR, retrospectively enrolled from September 2014 to December 2019. Mean left ventricle ejection fraction (LVEF) was 34.3% ± 7.9. Patients were divided into two groups according to the value of RVFW strain: ≤ -20% (18 patients); > -20% (52 patients). During follow-up all cause death, cardiovascular death and rehospitalization for heart failure were considered. Mean time follow-up was 20 ± 17.2 months. At univariable analysis, EuroSCORE II (p=0.031), STS (p=0.017), LVEF (p=0.011), indexed left ventricular end-diastolic volume (p=0.008), TAPSE (p=0.020) and RVFW strain (p=0.005) were associated with higher rate of composite endpoint. On multivariable logistic regression analysis, STS (p=0.037), LVEDVi (p=0.010), RVFW strain (p=0.021) were the only independent correlates of composite endpoint. Kaplan-Meier survival curve analysis demonstrates that RVFW strain > -20% affect the outcome in terms of freedom from composite endpoint of death and rehospitalization for heart failure (p < 0.05; see Figure).

Conclusions. Our study demonstrates that RVFW strain in patients with moderate-severe FMR undergoing MitraClip implantation is an independent predictor for composite endpoint of death and rehospitalization for heart failure at mid-term follow-up. Further data on larger population will be required to confirm our observations.



Number at risk	0	12	24	36	48	60
RVFW strain ≤ -20%	18	14	10	7	4	1
RVFW strain > -20%	52	24	14	8	3	0

A563: VENTRICULAR ARRHYTHMIAS IN PATIENTS WITH SEVERE AORTIC VALVE STENOSIS BEFORE AND AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION

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Background and purpose. Transcatheter aortic valve implantation (TAVI) has become a first-line treatment for most patients with severe aortic stenosis (AS) at intermediate/high surgical risk. Previous studies have shown that the procedure is associated with a reduction in total mortality. However, there are scarce data regarding the effects of TAVI on ventricular arrhythmias (VAs). The aim of this study was to assess the effects of TAVI on ventricular arrhythmic burden and cardiac autonomic function in patients with severe AS.

Methods. We studied consecutive patients with severe aortic stenosis, admitted to our department of Cardiology to undergo TAVI. Patients with previous cardiac surgery or percutaneous revascularization, acute coronary syndrome, significant structural or valvular heart disease or other comorbidities were excluded. Before TAVI procedure all patients underwent transthoracic Doppler echocardiography (TTDE) with global longitudinal strain (GLS) examination and 24-hour ECG Holter monitoring to assess ventricular arrhythmic burden and heart rate variability (HRV). A clinical follow-up was performed 6 months after discharge. A subgroup of 24 patients (58.5%) underwent TTDE, whereas 22 patients (53.6%) underwent 24-hour ECG Holter monitoring at 6-month follow-up.

Results. Forty-one patients (27 female, mean age 81±6 years) were enrolled in the study. At 6-month follow-up, 2 patients (4.9%) died from non-cardiovascular causes, 2 patients (4.9%) were hospitalized because of acute heart failure and 6 patients (14.6%) required a permanent pacemaker implantation. At follow-up, compared to baseline, the mean aortic valve gradient (51.7±12 vs 7±3 mmHg, p<0.001), LV mass (250.7±78 vs 200.9±68 g, p=0.001) and intraventricular septum thickness (13.3±1.5 vs 12.3±1.9 mm, p=0.006) were significantly reduced, there were no other significant changes at echocardiographic examination. No significant differences were found in ventricular arrhythmic burden 6 months post-TAVI compared to baseline (PVCs 548.7±1000 vs. 892.9±3269, p=0.65). Mean heart rate was found to be higher at follow-up compared to baseline (80.6±7 vs. 72±7 bpm, p=0.037). No significant differences were detected in time-domain HRV parameters, whereas the amplitude of very low-frequency (VLF) showed lower values at follow-up compared to baseline (17.9±7.4 vs. 24.4±6.6 ms, p=0.045).

Conclusions. Our data show that in patients with severe AS undergoing TAVI does not seem to have significant effects on ventricular arrhythmic burden, despite echocardiographic and clinical improvement. Similarly, our data failed to show significant improvement of sympatho-vagal balance at follow-up compared to baseline.

A564: REGISTRO MONOCENTRICO SULL'ENDOCARDITE INFETTIVA: PREVALENZA DELLE COMPLICANZE E LORO TRATTAMENTO

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Background. L'endocardite infettiva (EI) è una patologia che continua ad avere una elevata mortalità, e nonostante sia una patologia rara la sua incidenza sta subendo un trend in aumento a causa di nuovi fattori di rischio quali l'impianto di protesi valvolari e device intracardiaci ed il progressivo invecchiamento della popolazione.

Metodi. Attraverso lo studio retrospettivo di 43 pazienti (23 maschi, 20 femmine, età media 65 ± 14 anni) con diagnosi di EI effettuato secondo i criteri di Duke, abbiamo analizzato la relazione tra caratteristiche generali del paziente ed ecocardiografiche dell'EI, e a) l'insorgenza di eventi embolici sistemici/stroke, b) il ricorso al trattamento chirurgico.

Risultati. I pazienti che hanno avuto eventi embolici/stroke erano più giovani (p=0.016) e prevalentemente maschi (chi-square= 0.025) e avevano una migliore FE (p=0.002); la sede dell'EI era con maggiore frequenza la valvola nativa (70%, chi-square=0.018) rispetto alle protesi e ai device; la valvola più spesso interessata era la mitrale (55,6% e con una minore prevalenza l'aorta 33,3%) e avevano una minore prevalenza di CAD (chi-square=0.012) e di FA (chi-square=0.03). Non è stata dimostrata associazione tra tali eventi e maggiore dimensione della vegetazione, grado di insufficienza valvolare, o presenza di complicanze perianulari quali ascesso, fistola e pseudoaneurisma. Attraverso l'analisi di regressione logistica si è evinto che FE e sede (valvola nativa) siano predittori di embolia/stroke mentre l'età è rimasta di poco non significativa. Per quanto riguarda il ricorso al trattamento chirurgico, non c'era differenza significativa per quanto concerne età, FE, e dimensioni della vegetazione. Rispetto ad i pazienti non operati, i pazienti andati ad

intervento avevano avuto più eventi embolici/stroke rispetto a quelli non operati (chi-square=0.024) e avevano più spesso un'EI su valvola nativa (75%) e meno frequentemente un'EI su protesi o device (chi-square=0.001); le valvole più frequentemente coinvolte erano la valvola aorta (50%) e la mitrale (43,8%) con un chi-square di 0.001, il grado di insufficienza era prevalentemente severo (60%, chi-square=0.006). Non c'era differenza nella prevalenza di accessi e fistole tra i due gruppi mentre gli pseudoaneurismi andavano più spesso incontro all'intervento (chi-square=0.004). All'analisi di regressione logistica, sono risultati predittori di ricorso al trattamento cardiocirurgico l'età (p=0.008), la FE (p=0.007), la dimensione della vegetazione (p=0.044), l'embolizzazione/stroke (p=0.030) ed il grado di insufficienza valvolare (p=0.044).

Conclusioni. La maggior parte dei nostri risultati riguardanti i predittori di intervento chirurgico nei pazienti affetti da endocardite sono in accordo con l'attuale letteratura, mentre sono nuovi e inattesi quelli riguardanti l'associazione tra intervento chirurgico e processo infettivo su valvola nativa o migliore FE. Anche l'associazione tra minore età dei pazienti ed embolismo e tra migliore FE ed eventi embolici è un risultato del tutto inatteso ma molto interessante per il management di questi pazienti.

A565: PULMONARY EMBOLISM AND RIGHT-SIDED INFECTIVE ENDOCARDITIS: A MULTICENTER STUDY

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The incidence of embolic events in tricuspid valve infective endocarditis (TVIE) have received less attention than left-sided infective endocarditis (LSIE) owing to lower mortality and morbidity of pulmonary embolism (PE) and to the relatively low prevalence of the right-sided infective endocarditis (RSIE). However, the identification of patient at high risk who will benefit from a more aggressive therapeutic strategy may improve the prognosis. Furthermore, the incidence of RSIE is steadily increasing and it has been reported to be associated with the highest risk of embolism.

From January 2015 to May 2020, 167 patients (Pts) in 6 centers were found to have definite infective endocarditis. Imaging for PE including computed tomography (CT) pulmonary angiography (26pts) and lung scintigraphy (1pts) was performed in 27 pts (16%) who represent our study group. 23 were male, 4 female, average age 50.74 ± 18.62 years. All patients underwent transthoracic echocardiography (E), 19 transesophageal (TE) E and 12 three dimensional (3D) TEE. 52 vegetations (V) were detected. In 18 pts two or more vegetations were found. Native tricuspid valve was the most frequently involved valve (37 V, 71%), followed by catheter (5 V, 9.6%), tricuspid valve prosthesis (4 V, 7.7%), chordae and papillary muscle (2 V, 3.8%) and one vegetation (1.9%) in each of the following: pulmonic valve, inferior vena cava, eustachian valve, and right atrium. Vegetations were found most frequently in the anterior leaflet in 18 V (34.6%) followed by the posterior leaflet in 11 V (21%). The most common vegetations morphology was raceme-like shaped (36.5%). All the patients with PE had a vegetation max length more than 1 cm. *Staphylococcus aureus* (*S. aureus*) was the most common causative pathogen (13 pts, 48%), also in patients who underwent surgery 5/9 patients were *S. aureus* positive. TEE 3D detected the largest vegetations maximal length.

The imaging for PE was utilized in 16% in RSIE which is lower when compared to LSIE. The incidence of PE in patients who underwent imaging for PE was very high (26/27 pts) and was present in all patients with vegetation size larger than 1 cm (17.5 ± 6.7 mm by TEE). Most of the patients with PE had *S. aureus* infection. Limitations of study leading to a selection bias were that it was a retrospective study, it is not an all-comer study and that only patients with echocardiographic detection of vegetations who underwent CT were included. Furthermore being the CT currently mainly performed only if a clinical suspicion exist, leads to a second selection bias.

However, even with these limitations, our results suggest that imaging for PE is underutilized in clinical practice. In addition, it should be advised in the presence of vegetations size larger than 1 cm and *S. aureus* infection and not only in the presence of strong clinical suspicion of PE. This behavior would identify patients at high risk who will benefit from a more aggressive therapeutic strategy and may improve the prognosis. Further prospective studies are required to better confirm our hypothesis.

A566: CORRELATION OF ATRIAL AND VENTRICULAR STRAIN IMPROVEMENT AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION

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Background. Aortic stenosis (AS) is the most common heart valve disease encountered in clinical practice. The afterload increase imposed by severe AS creates concentric left ventricular (LV) remodeling and diastolic dysfunction, as well as progressive left atrial (LA) enlargement and dysfunction. There is emerging data showing that LA function evaluated by peak atrial longitudinal strain (PALS) is more sensitive than LA volume to assess subtle LA reverse remodeling after transcatheter aortic valve implantation (TAVI). The aim of this study was to assess the impact of TAVI on changes in LA size and phasic function by using comprehensive quantification of LA volumes and 2-dimensional speckle tracking imaging, in patients with symptomatic severe AS undergoing TAVI. We also sought to examine the correlation between PALS and other traditional and advanced echo parameters as left ventricular function using multilayer global longitudinal strain (GLS) by 2D speckle-tracking echocardiography (STE).

Methods. We prospectively enrolled 70 patients (mean age 80.5 ± 5 years, male 40%) with severe symptomatic AS undergoing TAVI between 2018 and 2020. Exclusion criteria were prior valve surgery, severe mitral stenosis, permanent atrial fibrillation and poor ultrasound acoustic window. Echo-Doppler assessment, including GLS and PALS, was performed before and after 1-3 months to TAVI procedure. Changes (D) of the main echo parameters before and after intervention were computed. On the basis of changes in PALS, the study population was divided in two groups: no improvement in PALS (NPALS) and improvement in PALS (IPALS).

Results. In the early follow-up after the procedure, a significant reduction of relative wall thickness ($p=0.006$), LA volume ($p=0.036$) and E peak velocity ($p=0.030$) in the overall population was observed. Although LV volumes and ejection fraction didn't change, there was a significant improvement in PALS ($P<0.001$) and GLS ($p=0.03$) after TAVI. PALS improvement was observed in 50 patients (71%). The two groups (IPALS and NPALS) were comparable for sex, age, risk factors, and for baseline echocardiographic parameters. In the IPALS group, a significant improvement of GLS after procedure was detected (Δ GLS 18.8 ± 21 in IPALS vs -4.1 ± 22 in NPALS, $p=0.001$). By a multiple linear regression analysis performed in the pooled population, after adjusting for baseline confounders, the association between Δ PALS and Δ GLS remained significant ($\beta=0.41$, $p=0.001$).

Conclusion. Afterload reduction following TAVI induced relevant hemodynamic changes. In this study PALS was confirmed as an early echocardiographic marker of recovery of LA structure, and its improvement is correlated with GLS. Further study and a longer follow-up are needed to evaluate the impact of these findings on clinical outcomes.

A567: MIGLIORAMENTO CLINICO ED ECOCARDIOGRAFICO A SEGUITO DI INTERVENTO PERCUTANEO DI CORREZIONE DELL'INSUFFICIENZA TRICUSPIDALICA: UNA RICERCA SISTEMATICA E META-ANALISI

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Introduzione. Il trattamento percutaneo dell'insufficienza tricuspidalica (IT) severa è possibile mediante numerosi nuovi dispositivi, ma le evidenze riguardo la loro sicurezza ed efficacia sono scarse.

Metodi. Da una ricerca sistematica di database elettronici sono stati selezionati 12 studi che riportavano risultati clinici di pazienti con IT significativa trattata con dispositivi transcatteretere. In totale 412 pazienti sono stati trattati con MitraClip (Abbott; $n=292$; 70.9%), Pascal (Edwards; $n=28$; 6.8%), Cardioband (Edwards; $n=30$; 7.3%), Trialign (Mitalign; $n=15$; 3.6%) e Forma (Edwards; $n=47$; 11.4%). È stato considerato il più lungo follow-up disponibile e sono stati esclusi gli studi che non riportavano almeno un risultato clinico di interesse. Abbiamo svolto una meta-analisi con metodica *random-effect* in modo da correggere una elevata eterogeneità tra gli studi. A seguire, con k indichiamo il numero di studi combinati per singolo risultato clinico analizzato.

Risultati. L'incidenza di IT di grado 3-4/4 è risultata 89% (95% Intervallo di Confidenza [IC] 0.78-1; I2 18%; $k=9$) e il 90% dei pazienti era in classe funzionale NYHA 3-4 (95% IC 0.80-0.99; I2 0%; $k=11$). Il 6 Minutes Walking Test (6MWT) pre-trattamento era 220 m (95% IC 186-253 m; I2 77%; $k=5$). Ad un follow-up mediano di 30 giorni l'incidenza di morte per

tutte le cause è stata 0.08 (95% IC 0.03-0.1; I2 42%; $k=7$) e la proporzione di soggetti con IT 3-4/4 è stata 14% (95% IC 3.9-24%; I2 64%; $k=6$), ovvero significativamente più bassa che pre-trattamento (Odds Ratio [OR] 0.02; 95% IC 0.004-0.06; $p<0.0001$; I2 51%; $k=6$). Dopo il trattamento percutaneo, i pazienti erano meno frequentemente in classe funzionale NYHA 3-4 (OR 0.06; 95% CI 0.02-0.13; $p<0.0001$; I2 59%; $k=9$) e hanno presentato un significativo miglioramento del 6MWT (differenza media: +49 m; 95% CI 22-78 m; $p=0.0005$; I2 18%; $k=5$).

Conclusioni. In questa meta-analisi, la strategia di trattamento percutaneo dell'IT con i diversi dispositivi disponibili è risultata sicura ed associata ad un miglioramento dei parametri funzionali ed ecocardiografici al follow-up.

A568: PROCEDURAL AND CLINICAL OUTCOMES OF TYPE 0 VERSUS TYPE 1 BICUSPID AORTIC VALVE STENOSIS UNDERGOING TRANSCATHETER VALVE REPLACEMENT: INSIGHT FROM THE BEAT REGISTRY

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Background. Although bicuspid aortic valve (BAV) is not considered a "sweet spot" to trans-catheter aortic valve replacement (TAVR), a certain number of BAV underwent TAVR. Whether BAV phenotype affects outcomes following TAVR remains debated. We aimed at evaluating the impact of BAV phenotype on procedural and clinical outcomes after TAVR using new generation trans-catheter heart valves (THVs).

Methods. Patients included in the BEAT registry were classified according to the BAV phenotype revealed at multi-slice computed tomography (MSCT) in type 0 (no raphe) vs. type 1 (1 raphe). Primary end-point was Valve Academic Research Consortium-2 (VARC-2) device success. Secondary end-points included procedural complications, rate of permanent pacemaker implantation, clinical outcomes at 30-day and 1-year.

Results. Type 0 BAV was present in 25(7.1%) cases, type 1 in 218(61.8%). Baseline characteristics were well balanced between groups. Moderate-severe aortic valve calcifications at MSCT were less frequently present in type 0 vs. type 1 (52%vs.71.1%, $p=0.05$). No differences were reported for THV type, size, pre and post-dilatation between groups. VARC-2 success tended to be lower in type 0 vs. type 1 BAV (72%vs86.7%; $p=0.07$). Higher rate of mean transprosthetic gradient ≥ 20 mmHg was observed in type 0 vs. type 1 group (24%vs6%, $p=0.007$). No differences were reported in the rate of post-TAVR moderate-severe aortic regurgitation and clinical outcomes between groups.

Conclusions. Our study confirms TAVR feasibility in both BAV types, however a trend toward a lower VARC-2 device success and a higher rate of mean transprosthetic gradient ≥ 20 mmHg was observed in type 0 vs. type 1 BAV.

A569: SAFETY OF TRANSFEMORAL TAVI IN PATIENTS AFFECTED BY SEVERE COPD: A SINGLE CENTER EXPERIENCE

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Background. The association between severe chronic obstructive pulmonary disease (COPD) and in-hospital mortality (IHM) as well as incidence of post-procedural intubation and length of in-hospital stay (LOHS) in patients with severe aortic stenosis (AS) undergoing transfemoral (TF) transcatheter aortic valve implantation (TAVI) is still unclear.

Purpose. We evaluated the impact of severe COPD on IHM, post-procedural tracheal intubation and LOHS in patients with severe AS undergoing TF TAVI.

Methods. We retrospectively analyzed a total of 467 consecutive patients who underwent transfemoral TAVI in our center between 2011 and 2019. We divided the patients in Group 1 (affected by severe COPD) and Group 2 (without COPD). We further divided the patients affected by COPD into Subgroup A (on COPD medical treatment) and Subgroup B (without COPD medical treatment).

Results. A total of 467 patients who underwent TF TAVI were included in this analysis. 40% ($n=190$) had a diagnosis of COPD (Group 1) and 60% ($n=277$) were not affected by COPD (Group 2). In Group 1, 25% ($n=49$) of patients were receiving medical treatment for COPD (Subgroup A), while 75% ($n=141$) were not on COPD medications (Subgroup B). The mean age was 81.83 ± 6.67 in Group 1 vs 81.33 ± 7.21 in Group 2 ($p=0.45$), and 82.12 ± 7.6 in Subgroup A vs 82.14 ± 6.82 in Subgroup B ($p=0.98$). The gender distribution showed 127 (45%) men in Group 1 vs 96 (50%) men in Group 2 ($p=0.33$), and 21 (42%) men in Subgroup 1 vs 75 (53%) men in Subgroup B ($p=0.28$). The mean EuroSCORE II was 8.56 ± 7.03 in Group 1 vs 7.47 ± 7.57 in Group 2, $p=0.11$, and 8.01 ± 5.49 in Subgroup A vs 8.75 ± 7.5 in Subgroup B, $p=0.52$. There was no difference observed for in-hospital mortality between Group 1 and Group 2 (0.04% vs 0.05%;

$p=0,6$) and between Subgroup A and Subgroup B (0,04% vs 0,04%; $p=0,7$). Similarly, the incidence of post-procedural intubation was comparable between Group 1 and Group 2 (0,06% vs 0,03%; $p=0,18$), and between Subgroup A and Subgroup B (0,08% vs 0,05%; $p=0,78$). Finally, also the mean length of in-hospital stay was similar between Group 1 and Group 2 ($10\pm 4,46$ days vs $9,68\pm 5,02$ days; $p=0,47$), and between Subgroup A and Subgroup B ($10,36\pm 4,24$ days vs $9,87\pm 4,54$ days; $p=0,5$).

Conclusions. In patients with severe aortic stenosis treated with transfemoral TAVI, the presence of severe COPD does not affect in-hospital mortality, incidence of post-procedural intubation and length of in-hospital stay. COPD medications do not impact any of the outcomes evaluated. Therefore, TF TAVI is a safe procedure also for patients affected by severe chronic obstructive pulmonary disease that are not on COPD medications.

A570: STRESS ECHOCARDIOGRAPHY AND STRAIN IN AORTIC REGURGITATION (SESAF PROTOCOL): LEFT VENTRICULAR CONTRACTILE RESERVE AND MYOCARDIAL WORK IN ASYMPTOMATIC PATIENTS WITH SEVERE AORTIC REGURGITATION

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Objectives. To analyze left ventricular (LV) myocardial deformation in asymptomatic patients with severe aortic regurgitation (AR), and its correlation with functional capacity and contractile reserve (CR).

Background. Chronic AR natural history is characterized by a prolonged silent phase before the onset of symptoms and overt LV systolic dysfunction. In patients with severe asymptomatic AR, the assessment of LV longitudinal deformation could have an important role in decision-making and surgery timing, above all if a correlation with prognostic indicator, such as functional capacity and CR is found.

Methods. Standard echocardiography, lung ultrasound, and LV 2D speckle tracking analysis were performed at rest and during exercise in asymptomatic patients with severe AR and in age- and sex-comparable healthy controls. CR was defined as increase in LV ejection fraction (EF) $>5\%$ during exercise.

Results. 115 patients with AR (58,2% males; $52,3\pm 18,3$ years) and 55 controls were enrolled. Baseline LVEF was comparable between the groups. Resting LV global longitudinal strain (GLS) and myocardial work efficiency (MWE) were significantly reduced in AR than controls (GLS %: $-15,8\pm 2,8$ vs $-21,4\pm 4,4$, $p<0,001$; MWE %: $87,1\pm 3,3$ vs $94,4\pm 4,1$, $p<0,001$). Among AR patients, those without CR (CR-) showed reduced resting LV GLS ($-12,6$ vs $-16,8$, $p<0,001$), reduced MWE (85,3 vs 90,2, $p<0,001$), and increased B-lines than those with CR (CR+). At multivariate analysis, resting MWE was closely related to peak effort Watts, VO_2 , E/e' and number of B-lines. Both GLS and MWE were found to be strong independent predictors of CR. A resting LV GLS cutoff of -12% differentiated CR+ and CR-, with 78% of sensitivity and 84% of specificity).

Conclusions. Lower resting values of LV GLS and MWE in patients with severe, asymptomatic AR suggest an early subclinical myocardial damage, which is closely associated with lower exercise capacity, greater pulmonary congestion, and blunted LV CR during stress.

A571: IL RUOLO FISIOPATOLOGICO DELL'ATRIO DESTRO NEI PAZIENTI CON FIBRILLAZIONE ATRIALE E INSUFFICIENZA TRICUSPIDALE

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Introduzione. L'insufficienza tricuspidale funzionale (FTR) si manifesta in assenza di lesioni strutturali dei componenti dell'apparato valvolare che risultano deformati dal rimodellamento del ventricolo e/o dell'atrio destro. Tra i vari fenotipi clinici, la forma idiopatica è frequentemente associata a fibrillazione atriale (FA). Evidenze scientifiche identificano la dilatazione dell'anulus tricuspidale (AT) come il principale determinante del rigurgito tricuspidale in questo gruppo di pazienti. Restano da chiarire i fattori fisiopatologici di questo fenomeno.

Metodi. 83 pazienti consecutivi affetti da FA permanente e FTR ($61\pm 9,9$ anni, 67% donne), sono stati arruolati in maniera prospettica e confrontati con 83 volontari sani comparabili per sesso e superficie corporea. La geometria e la funzione delle camere cardiache del cuore destro e dell'AT è stata valutata con ecocardiografia tridimensionale.

Risultati. Circa i 2/3 dei pazienti con FA permanente presentavano FTR di grado moderato o severo. Il 93% dei pazienti presentava dilatazione dell'atrio destro (AD), mentre era estremamente ridotta la quota di pazienti con dilatazione (27%) o disfunzione sistolica (12%) del ventricolo destro (VD). L'area telediastolica dell'AT (ATTD) presentava la maggiore correlazione con il volume minimo dell'AD (ADV_{min} $r=0,6981$, $p<0,0001$), ma solo una moderata correlazione con il volume telediastolico del VD (VDTD) ($r=0,3405$, $p=0,0019$). All'analisi multivariata, sia ADV_{min} che VDTD erano indipendentemente associati con l'area ATTD nei soggetti sani ($R^2=0,6002$, $p<0,0001$), ma solo ADV_{min} era indipendentemente associato con l'area ATTD nei pazienti con FA permanente ($R^2=0,4984$, $p<0,0001$). Il volume dell'AD e ATTD erano gli unici predittori del grado di severità della FTR.

Conclusioni. Nei pazienti con FA permanente, la dilatazione dell'AD è il fattore fisiopatologico più importante per lo sviluppo di FTR, inoltre, la severità del rigurgito è strettamente correlata a ADV_{min} e ATTD. Il nostro studio corrobora l'ipotesi della genesi atriale dell'insufficienza ("atriogenic FTR") e supporta la necessità delle terapie di controllo del ritmo nei pazienti affetti da FA.

