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Effects of consistent atrial pacing and atrial rate stabilization – two pacing algorithms to suppress recurrent paroxysmal atrial fibrillation in brady-tachy syndrome

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Background and method Recently, various dedicated atrial pacing algorithms have been proposed to prevent atrial fibrillation (AF). Consistent atrial pacing (CAP; an algorithm for automatic atrial overdrive) and atrial rate stabilization (ARS; an algorithm for preventing the 'short-long' sequences) were tested in 16 patients with brady-tachy syndrome and recurrent paroxysmal AF (≥3 episodes per month).

Results In the population as a whole, pacing with CAP was associated with a significant reduction in AF burden in comparison with DDDR pacing. With regard to the effects on AF burden, 11 patients (69%) were found to benefit significantly from CAP or ARS pacing algorithms (reduction >50% in AF burden). In detail, seven patients were responders to both algorithms, two to CAP only and two to ARS only. Two patients exhibited a significant increase in AF burden with the ARS algorithm. With regard to the effects on number of mode switches per day, seven patients (44%) were found to benefit significantly from CAP or ARS pacing algorithms (reduction in mode switches per day >50%). In detail, five patients were responders to both algorithms and two to ARS only. Two patients had a significant increase in the number of mode switches per day with both CAP and ARS algorithms.

Conclusion The response to ARS and CAP algorithms is heterogeneous. In 31–69% of patients with brady-tachy syndrome a significant reduction in AF burden and/or mode switch episodes can be obtained with ARS and/or CAP algorithms; however, in a few patients an increase in AF episodes and/or AF burden may occur
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Key Words: Atrial fibrillation, brady-tachy syndrome, dual-chamber pacing, pacing algorithms, overdrive atrial pacing, rate responsive.

Introduction

The optimal treatment for paroxysmal atrial fibrillation (AF) in the setting of bradycardia is still a matter of debate. Previous studies, both prospective and retrospective, showed that patients with sinus node disease, chronotropic incompetence and recurrent paroxysmal AF may benefit from atrial pacing (AP) in terms of paroxysmal AF prevention[1–13].

Recently, various pacing algorithms have been designed to suppress AF by overdrive pacing[14–20]; the rational basis for the use of these algorithms is to reduce the dispersion of conduction and refractoriness, to reduce the frequency of premature atrial complexes (PACs), to prevent short–long cycles and to maintain a high degree of exit blocks for ectopic atrial rhythms. Among these algorithms, some are designed for continuous automatic atrial overdrive, such as the consistent atrial pacing (CAP) algorithm; other algorithms, such as atrial rate stabilization (ARS), are designed for preventing the 'short–long' sequences of atrial cycle lengths that may follow a PAC and may trigger an episode of AF[18,20].

The aim of the present study was to evaluate the effectiveness of CAP and ARS in suppressing paroxysmal AF recurrences and AF burden in comparison with standard DDDR pacing in patients with sick sinus syndrome and frequent AF episodes.

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Method

Patients

Sixteen patients (six male, 10 female; mean age 74 ± 12 years) affected by brady-tachy syndrome were implanted with a Medtronic Thera DR 7940/7960 (Medtronic Inc., Minneapolis, MI, U.S.A.) dual-chamber pacemaker. This device has a programmable rate-responsiveness function that uses a piezoelectric sensor and an automatic mode switch mechanism that changes from an atrial tracking to a non-atrial tracking mode (DDIR mode), based on atrial tachycardia detection criteria[21]. The Thera DR algorithm monitors the atrial channel continuously in patients programmed to the DDD and the DDDR modes. At each beat the mean atrial rate is calculated and compared with a programmable value. If it exceeds this value for a programmable period of time, then the algorithm identifies an atrial tachycardia and causes the pacemaker to switch to DDIR pacing mode (i.e. the ventricular pacing rate decreases slowly until it reaches the sensor-indicated rate). When the tachycardia has stopped, the programmed atrial tracking mode (DDD or DDDR) is restored. The reliability of the automatic mode switch mechanism in detecting paroxysmal AF has been estimated and reported previously[21,22].

The programming parameters for paroxysmal AF detection were selected in order to reduce the likelihood that non-sustained paroxysmal AF would fulfill diagnostic criteria for sustained AF, and to ensure that intermittent failure to sense atrial events would not be inappropriately classified as paroxysmal AF[21–23]. An atrial passive lead was implanted in the right auricle in 10 patients, and in six patients an atrial screw-in lead was implanted in the low inter-atrial septum, as previously described[24].

Inclusion criteria included the following: documented sinus bradycardia below 50 beats . min^{-1} and/or sinus arrest in excess of 3 s on two occasions; and at least three episodes per month of symptomatic AF during the 3 months before implant. Patients with heart failure, severe angina pectoris, or left atrium enlargement (left atrial dimension >45 mm at M-mode echocardiography) were excluded. Patients with angina were excluded in order to prevent induction of ischaemia by high AP rates. Heart failure patients were excluded because of their usually unstable arrhythmia profile.

Pacing algorithms

The software for both CAP and ARS pacing algorithms can be loaded into the RAM memory of the pacemaker via telemetry, using a custom research telemetry device that is linked to a standard IBM-class personal computer. The software allows diagnostic data to be recorded that can then be interpreted using a special Microsoft Excel spreadsheet, including AP percentage, number of algorithm pacing pulses, number of premature atrial and ventricular complexes, and number and duration of automatic mode switching episodes. These data are more detailed than those usually obtainable from Thera pacemaker diagnostics. The software also allows these data to be recorded when the algorithms are switched off, making it possible to compare results with standard DDDR pacing.

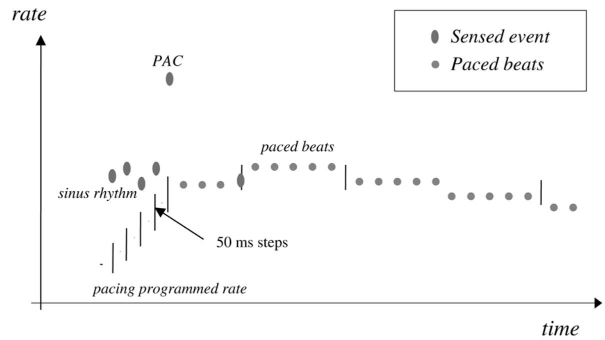

Figure 1 **Consistent atrial pacing (CAP) algorithm operation. PAC=premature atrial complex.**

The CAP algorithm (Fig. 1) monitors beat-by-beat spontaneous atrial activity and, in order to overdrive suppress this activity, updates the atrial escape interval (AEI) according to a programmable sequence. The CAP feature is available in DDD, DDDR, AAI and AAIR modes.

After every sensed atrial event outside the post-ventricular atrial refractory period, the AEI is shortened by a programmable value, usually 50 ms. After a programmable number of paced atrial events, usually 10, the AEI is lengthened by a programmable value, usually chosen to be as long as 20 ms. AEI shortening is limited by the programmed upper rate value, whereas AEI lengthening is limited by the programmable lower rate value.

If the spontaneous sinus rhythm is faster than the sensor-induced pacing rate, then the CAP algorithm attempts to pace the atrium at a cycle shorter than sinus rhythm cycle until the upper rate limit is reached.

The ARS algorithm (Fig. 2) is a feature that is designed to inhibit the onset of atrial tachyarrhythmias by eliminating the long pause that typically follows a premature atrial contraction. The ARS feature is available in DDDR, DDD, AAIR and AAI modes.

When ARS is enabled, each non-refractory atrial event begins an escape interval equal to the last P–P interval, plus a programmed increment value. If this escape interval elapses, then the pacemaker delivers an atrial pace and recalculates its ARS interval using the current atrial interval. If the atrial rate is stable, then the ARS escape interval does not elapse. After a PAC, the ARS escape interval stabilizes the atrial rate and gradually returns it to the intrinsic or programmed rate. When rate responsiveness is activated by physical activity, the pacemaker applies the shortest AEI between that determined by the sensor and that calculated by the algorithm.

Runs of ventricular tachycardia continuously reset the AEI, leading to AP suppression. Occurrences of ventricular arrhythmia are monitored by the algorithm and stored in the

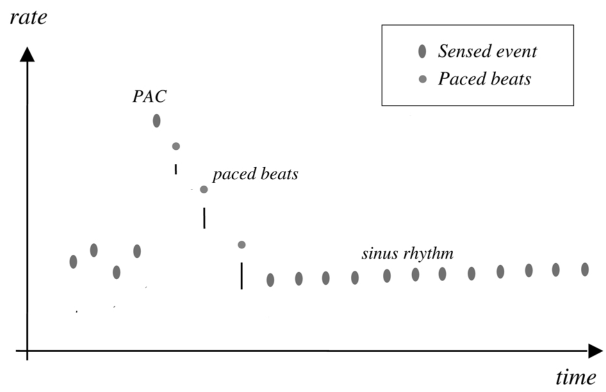

Figure 2 **Atrial rate stabilization (ARS) algorithm operation. PAC=premature atrial complex.**

memory of the device. When paroxysmal AF occurs and automatic mode switching is activated, the algorithm is switched off. The algorithm starts working again once automatic mode switches back at the termination of atrial tachyarrhythmia.

Study protocol

The patients underwent implantation of a Thera DDDR pacemaker according to usual methods. Whether the atrial lead was implanted into the right atrial appendage or into the inter-atrial septum was based on the physician's judgement[24].

At baseline, a clinical evaluation, 12-lead ECG, echocardiography and 24-h Holter monitoring were performed. After a stabilization period of 4–6 weeks, all patients were randomly assigned to programming in DDDR, in CAP or in ARS mode, with subsequent crossover after 3 months in order to test all three pacing modalities for periods of 3 months in each patient. A follow-up visit was scheduled at the end of each 3-month treatment period, and included clinical evaluation, a check of pacemaker functions and diagnostic data retrieval. At the end of the follow-up visit, patients were crossed to another pacing modality according to the study protocol.

Diagnostic data were retrieved using the Thera D(R) high-rate atrial tachycardia detection feature, which has been reported to have high sensitivity and specificity for detection of atrial tachyarrhythmias[21–23]. Diagnostic data include the total duration of atrial arrhythmias (expressed in seconds), the number of the arrhythmic episodes (a counter that is saturated at 255 episodes) and, for the first 14 episodes, indicate the tachycardia rate and the duration and time of day of mode switches. AF burden was calculated as the total duration of atrial arrhythmias during the period of evaluation and is expressed as minutes per day.

The same high-rate tachycardia detection feature allowed measurement of PACs during the period of evaluation (a parameter that was normalized as a function of time and expressed as number of PACs per day) and percentage of AP (a parameter that is derived from the number of the paced and sensed sequences: AS-VS, AS-VP, AP-VS and AP-VP). During atrial arrhythmias the AP percentage counter is frozen, because atrial refractory events fall within the interval between atrial and ventricular sensed events.

The number of mode switch episodes and AF burden were measured at each follow-up visit in order to quantify recurrence of paroxysmal AF. Moreover, the percentage of atrial paced beats and the number of PACs were recorded from the pacemaker diagnostics in order to correlate them with atrial episodes.

Drug treatment instituted before implant, if tolerated but ineffective for paroxysmal AF suppression, was maintained after pacemaker implantation and during the follow-up periods. Neither types nor doses of drugs were changed, and the drugs included antiarrhythmic drugs, beta-blockers, calcium channel blockers and digoxin.

Constant pacemaker programming and lead position was ensured throughout the follow-up period. No patients received cardioversion, either electrical or pharmacological, during the study.

Statistical analysis

Summary data are expressed as means ± standard deviation, or as numbers and percentages of patients. When comparing clinical quantities, such as PACs per day, AF burden and the others reported in Table 1, we studied the distributions of values in order to evaluate whether gaussian behaviour was present or absent. Consequently, differences between distributions during different periods (i.e. DDDR, CAP and ARS periods) were compared using Friedman repeated measures analysis of variance on ranks, along with the Student–Neuman–Keuls method for multiple comparisons. $P < 0{\cdot}05$ for two-sided comparisons was considered statistically significant.

Correlation between parameters was calculated using non-parametric Spearman's rho (r), a rank-order correlation coefficient that measures associations at the ordinal level. The values of the correlation coefficient r range from –1 to 1. The sign of the correlation coefficient r indicates the direction of the relationship (positive or negative) and its absolute value indicates the strength, with larger absolute values indicating stronger relationships. If the P value is very small ($P < 0{\cdot}05$), then the correlation is significant and the two variables are linearly related.

Multiple linear regression was used to predict typical values of one dependent variable as a function of previously chosen independent variables. In the process of performing multiple linear regression estimations, an analysis of variance was also conducted. Results from this analysis are contained in analysis of variance tables in the form of F statistics and related P values. If the significance value of the F statistic is small ($P < 0{\cdot}05$), then the independent variables explain well the variation in the dependent variable. For statistical analysis, SPSS software (SAS Institute Inc., Cary, NC, U.S.A.) was used.

Table 1 Data retrieved from the pacemakers

	MS (number . day – 1)			AF burden (h . day – 1)			PACs (number . day – 1)			AP% (h . day – 1)		
Patients ID	CAP	DDDR	ARS	CAP	DDDR	ARS	CAP	DDDR	ARS	CAP	DDDR	ARS
1	0·50	0·39	0·32	0·91	0·03	0·01	145·05	109·46	77·15	99·0	95·6	99·0
2	2·83	2·83	2·83	0·09	0·34	0·62	241·42	1260·52	2808·04	98·3	88·0	91·4
3	2·83	2·83	0·00	0·03	0·23	0·00	1283·55	6024·23	86·71	98·2	94·2	90·0
4	2·83	2·83	2·83	3·95	4·71	3·79	3050·99	3856·77	3030·98	97·6	81·3	65·8
5	0·10	0·01	0·05	1·27	1·20	0·94	20·65	21·56	19·58	98·6	86·5	87·8
6	1·31	0·29	0·54	0·02	0·04	0·01	1614·50	432·90	2422·30	96·0	73·0	90·0
7	4·55	4·55	3·58	0·52	0·81	0·82	63·60	77·30	99·30	99·0	71·0	78·0
8	0·00	0·00	0·00	0·00	0·00	0·00	2·70	14·50	26·60	99·0	97·0	85·0
9	0·07	0·90	0·00	0·00	0·03	0·00	74·49	227·89	32·54	96·7	45·7	34·8
10	2·83	2·83	2·83	1·81	2·62	9·65	4008·73	4334·30	4567·75	96·2	88·0	73·0
11	2·83	2·83	2·83	2·82	11·78	8·49	947·59	15280·66	2765·14	93·7	95·0	80·0
12	0·03	0·08	0·03	0·02	0·05	0·00	73·21	300·98	305·64	99·0	96·4	94·0
13	0·09	0·21	0·06	0·00	0·00	0·00	22·94	76·86	114·72	98·6	62·0	31·0
14	2·83	2·83	0·53	10·47	12·08	0·07	556·59	4139·28	42·08	97·9	90·3	85·6
15	0·01	0·11	0·00	0·00	0·00	0·00	235·31	1221·15	371·25	94·5	85·0	75·5
16	0·01	1·26	0·06	0·00	0·11	0·00	342·52	2854·17	250·47	94·5	88·0	91·0
Mean	1·48	1·55	1·03	1·37	2·13	1·52	792·74	2514·53	1063·77	97·30	83·56	78·24
SD	1·55	1·49	1·38	2·70	4·03	3·10	1184·71	3924·28	1498·41	1·81	14·19	19·65
Median	0·91	1·08	0·19	0·06	0·17	0·01	238·37	827·03	182·60	98·05	88·00	85·30

The data recorded are as follows: the number of mode switches (MS) per day; the atrial fibrillation (AF) burden, measured as time spent in AF; the number of premature atrial complexes (PACs) per day; and the percentage of atrial pacing (AP%). ARS=atrial rate stabilization; CAP=consistent atrial pacing; SD=standard deviation.

Results

General findings

In all of the 16 patients enrolled the data retrieved from pacemaker diagnostics allowed us to estimate the number of mode switches per day, the percentage of AP, the number of PACs per day and the AF burden, measured as percentage of time in AF or as time (hours per day) spent in AF. These data are summarized in Table 1.

The frequency data and mode switch number in general were normalized to the actual follow-up duration (no statistically significant differences were found among follow-up durations in the three pacing modalities). Seven of the 16 patients filled the mode switch counter in at least two of the three follow-up periods, and in these cases the normalized data were calculated by dividing the mode switch number by the mean follow-up period (90 days).

Comparison among DDDR, CAP and ARS

Comparison of the three 3-month pacing periods (DDDR, CAP and ARS) is shown in Fig. 3 for the whole population of 16 patients. Both for CAP and ARS a significant reduction in AF burden was found in comparison with DDDR pacing. Moreover CAP significantly reduced the number of PACs per day in comparison with DDDR pacing and significantly increased the percentage of AP in comparison with the other pacing modalities.

The effectiveness of the two pacing algorithms in comparison with DDDR pacing was also evaluated by counting the number of patients in whom the reduction in percentage of time in AF or in mode switches per day was significant (>50%) in comparison with the DDDR-only period.

With regard to the reduction in percentage of time in AF, 11 patients (69% of the tested population) were found to benefit significantly from CAP or ARS pacing algorithms; they exhibited a reduction in percentage of time in AF greater than 50% in comparison with the DDDR pacing mode. In detail, seven patients (44%) were responders to both algorithms, two patients to CAP only and two patients to ARS only. It is noteworthy that two patients experienced a significant increase in AF burden with the ARS algorithm.

Regarding the reduction in number of mode switches per day, seven patients (44% of the tested population) were found to benefit significantly from CAP or ARS pacing algorithms; they exhibited a reduction in mode switches per day of greater than 50% in comparison with the DDDR pacing mode. In detail, five patients (31%) were responders to both algorithms and two responded only to ARS. It is noteworthy that two patients had a significant increase in the number of mode switches per with both CAP and ARS algorithms.

No significant differences in baseline profile during DDDR pacing (percentage of AP, number of PACs, mode switches per day and AF burden) were found on comparing responders with non-responders to each or both of the pacing algorithms (a positive response was defined as a reduction of >50% in mode switching or in AF burden). In no patient was transition from paroxysmal AF to chronic stable AF observed.

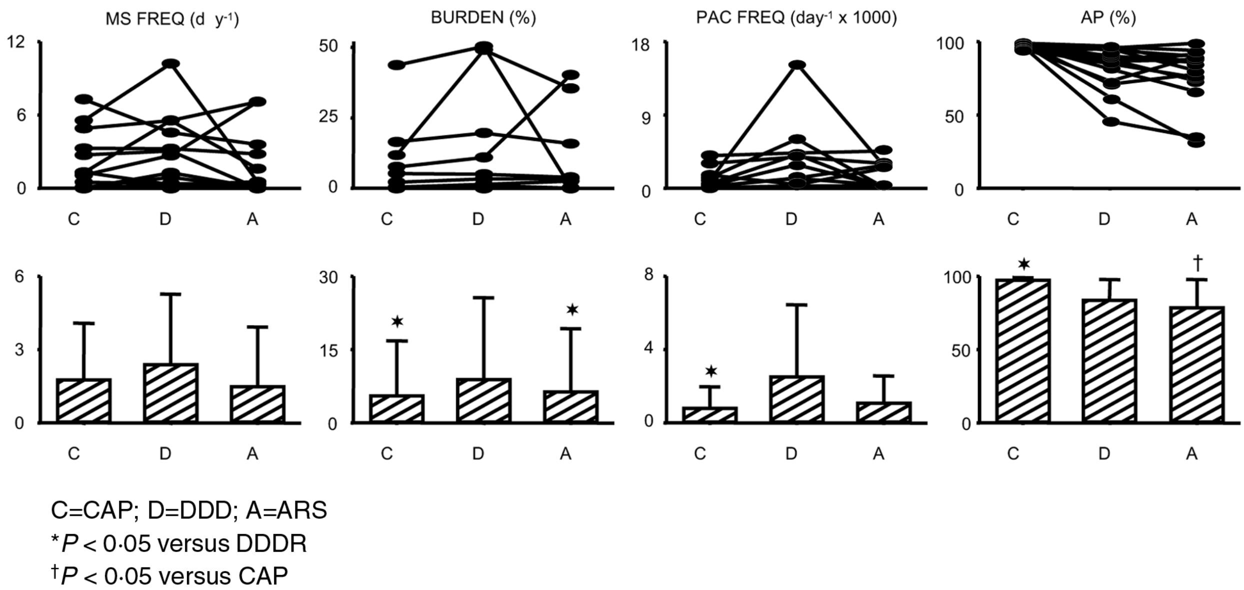

Figure 3 **Results of Friedman repeated measures analysis of variance on ranks, along with Student–Neuman–Keuls method for multiple comparisons. AP(%)=percentage of atrial pacing; ARS=atrial rate stabilization; BURDEN=atrial fibrillation burden; CAP=consistent atrial pacing; MS=mode switches; PAC=premature atrial complex.**

Correlations among the changes observed in mode switches, AF burden, percentage of AP and PACs per day in the tested pacing modalities were examined. In the population as a whole, a significant correlation was found between the changes in AF burden and in mode switches that occurred during ARS and CAP in comparison with DDDR pacing (Fig. 4). In both scatterplots a degree of inter-individual variability in the response to the two algorithms can be detected. Moreover, the type of distribution in percentage changes versus DDDR, both for AF burden and mode switching, does not exhibit a significant correlation between the extent of the response and the site of implant (in the right atrial appendage or in the inter-atrial septum).

Multiple regression analysis

At multiple regression analysis, AF burden during DDDR pacing was significantly predicted by PACs and AP percentage according to the following equation (at analysis of variance F = 8·0 and $P = 0{\cdot}005$):

$$\text{AF burden}_{DDDR} = 0{\cdot}745\ \text{PACs}_{DDDR} - 0{\cdot}006\ \text{AP}_{DDDR}$$

The correlation between PACs and AF burden was statistically significant ($P = 0{\cdot}002$).

Moreover, AF burden during ARS was significantly predicted by PACs and AP percentage according to the following equation (at analysis of variance F = 11·0 and $P = 0{\cdot}002$):

$$\text{AF burden}_{ARS} = 0{\cdot}791\ \text{PACs}_{ARS} - 0{\cdot}093\ \text{AP}_{ARS}$$

The correlation between PACs and AF burden was statistically significant ($P < 0{\cdot}001$).

AF burden during CAP was not significantly predicted by equations including PACs and AP percentage.

At multiple regression analysis AF burden during DDDR pacing and during ARS was also significantly predicted by equations including PACs, AP percentage and mode switches (MS). For DDDR pacing the relationship was as follows (at analysis of variance F = 5·2 and $P = 0{\cdot}015$):

$$\text{AF burden}_{DDDR} = 0{\cdot}672\ \text{PACs}_{DDDR} - 0{\cdot}013\ \text{AP}_{DDDR} + 0{\cdot}142\ \text{MS}_{DDDR}$$

The correlation between PACs and AF burden was statistically significant ($P = 0{\cdot}013$).

For ARS mode the relationship was as follows (at analysis of variance F = 7·451 and $P = 0{\cdot}004$):

$$\text{AF burden}_{ARS} = 0{\cdot}653\ \text{PACs}_{ARS} - 0{\cdot}093\ \text{AP}_{ARS} + 0{\cdot}199\ \text{MS}_{ARS}$$

The correlation between PACs and AF burden was statistically significant ($P = 0{\cdot}017$).

At multiple regression analysis AF burden during CAP was not significantly predictable by these variables.

In the population as a whole AF burden was significantly correlated to number of mode switches per day in all of the pacing modalities (Fig. 5): during DDDR, $r = 0{\cdot}655$ ($P = 0{\cdot}006$); during ARS, $r = 0{\cdot}847$ ($P < 0{\cdot}001$); and during CAP, $r = 0{\cdot}838$ ($P < 0{\cdot}001$).

As shown in Fig. 6 the changes in AP percentage and in PACs observed during ARS and CAP, in comparison with DDDR, were not significantly related to each other, thus indicating independent effects of these two variables.

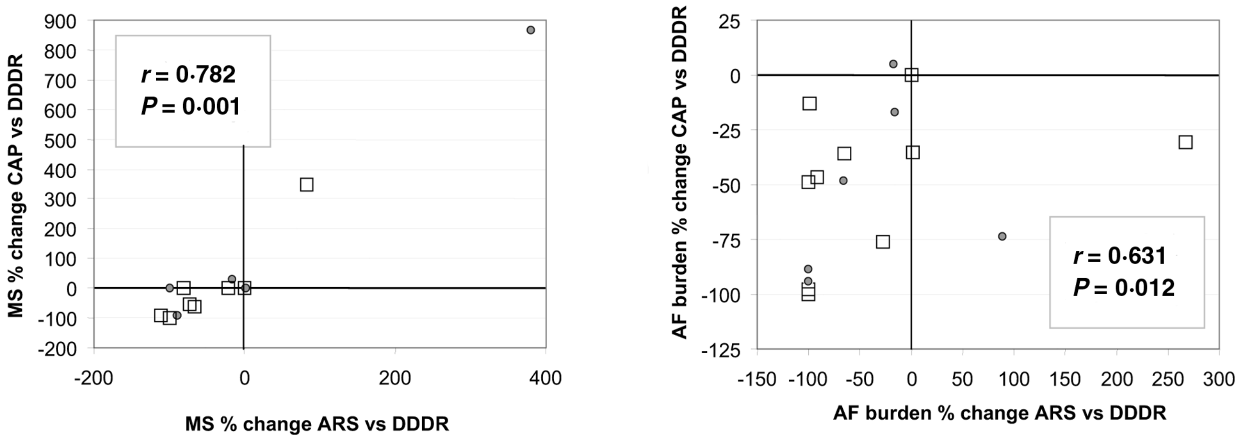

Figure 4 **Correlation between the changes in atrial fibrillation (AF) burden (right) and mode switches (MS) per day (left) occurring during consistent atrial pacing (CAP) and atrial rate stabilization (ARS) in comparison with DDDR pacing. Patient with standard atrial lead site (☐) or inter-atrial septum implant (●).**

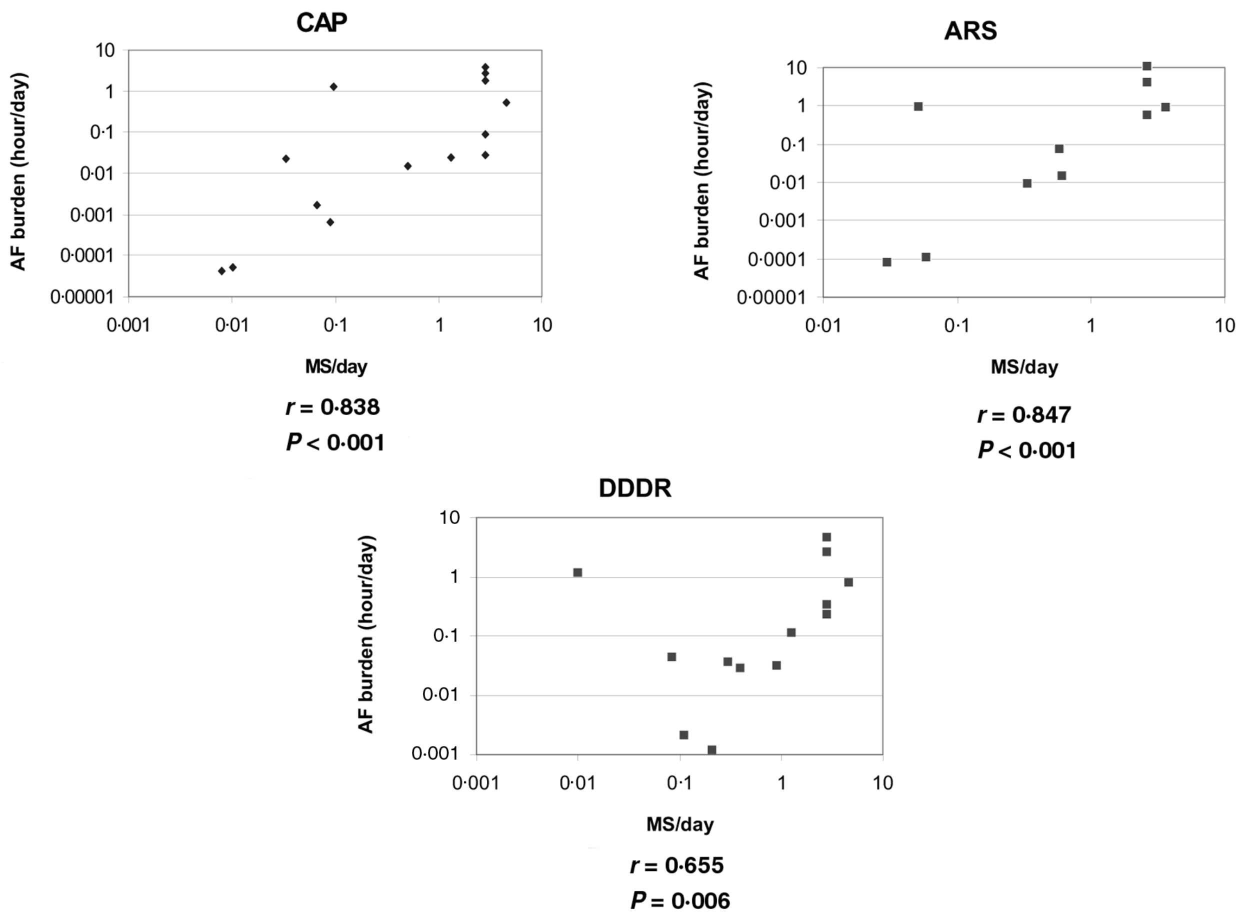

Figure 5 **Correlation between atrial fibrillation (AF) burden and the number of mode switches per day, shown in a logarithmic scale, for consistent atrial pacing (CAP; top left), atrial rate stabilization (ARS; top right) and DDDR (bottom).**

Discussion

In patients with recurrent AF in the setting of bradycardia, implantation of a DDDR pacemaker is usually associated with reduction in AF episodes[13,21], but a substantial proportion of patients continue to exhibit recurrent AF after pacemaker implantation. In order to improve the efficacy of dual-chamber pacing in reducing symptomatic and

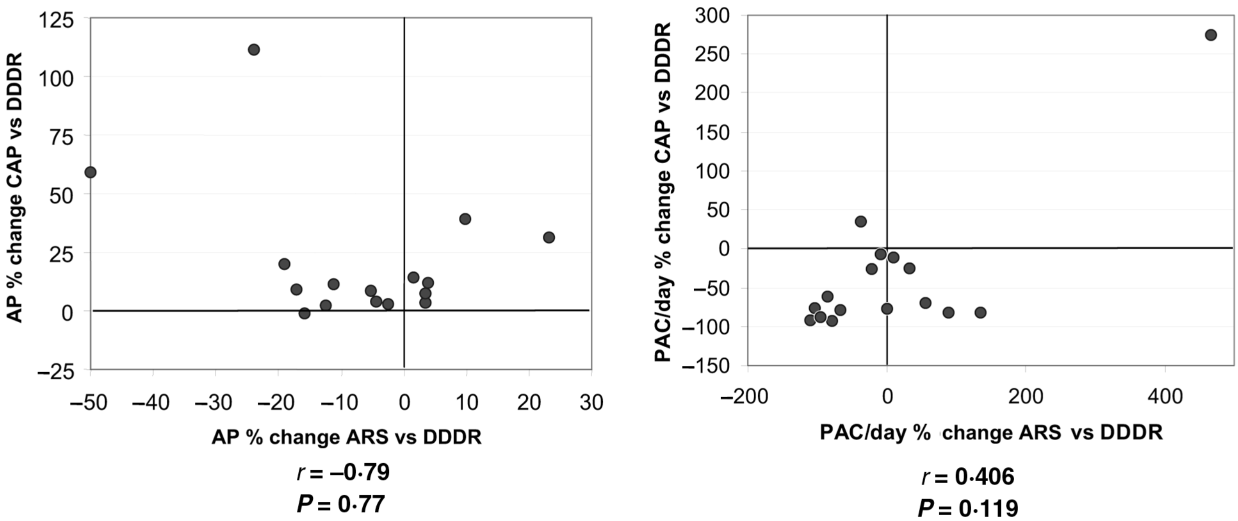

Figure 6 **Correlation between the observed changes in percentage of atrial pacing (AP%; left) and in number of premature atrial complex (PACs) per day (right) during consistent atrial pacing (CAP) versus DDDR and during atrial rate stabilization (ARS) versus DDDR.**

asymptomatic AF recurrences, various strategies have been proposed. These include alternative pacing sites for the atrial lead, such as the inter-atrial septum[24] or Bachmann's bundle[25], and dual-site[26] or biatrial pacing[27,28]. Moreover, special algorithms for AP have been proposed for suppressing AF[14,15,18–20]. No data are yet available in the literature on direct comparisons of the ability of different pacing algorithms to suppress AF.

This is the first study to compare two different pacing algorithms in the same patients, and it was designed to evaluate the effects on AF episodes of CAP and ARS in comparison with DDDR pacing. According to the present study, the effects of ARS and CAP algorithms are heterogeneous, both with regard to AF prevention and AF burden. In comparison with DDDR pacing, however, a significant reduction (>50%) in AF burden and mode switch episodes was obtained in 44% and 56% of patients on ARS mode pacing, respectively, and in 31% and 56% of the patients on CAP mode pacing, respectively. These results are noteworthy in comparison with previous reports on other pacing algorithms[14] or in comparison with recent experience with multisite atrial pacing performed in patients without bradycardia[29,30]. The heterogeneity in patient response to the two tested pacing algorithms suggests the possibility of paradoxical increases both in AF episodes (as revealed by mode switch count) and in AF burden, although this phenomenon was observed only in a few patients. In the population as a whole, however, both CAP and ARS were associated with a significant reduction in AF burden in comparison with DDDR pacing. A reduction in AF burden is currently considered an important end-point in AF treatment[31].

In the present study significant correlations were found between changes in AF burden and in mode switches during ARS and CAP in comparison with DDDR pacing (Fig. 4). This finding may indicate that the changes induced by these algorithms do not occur randomly; in other words, the arrhythmia incidence at baseline influences the effects that may be achieved by special pacing algorithms. Moreover, a significant correlation was found between atrial premature beats and both AF episodes and AF burden during DDDR pacing and pacing using the ARS algorithm. The same correlations were not found for the CAP algorithm, and this might be explained by the different and independent effects of CAP in comparison with ARS on two important variables: PACs and AP percentage (Fig. 6).

According to the findings of the present study, evaluation of two simple parameters (i.e. PACs and AP percentage) that are simply retrievable through the pacemaker diagnostics, is of practical interest because AF burden during DDDR and ARS (but not during CAP) can easily be predicted by equations that include those two variables. This may allow us to follow the evolution of arrhythmia incidence in individual patients, as well as time-dependent or seasonal changes in AF occurrence[32].

The role of PACs in conditioning AF burden and AF recurrence is highlighted by the present study, at least during DDDR and ARS pacing. It is known that PACs are the triggers of AF in most patients[33], and this has been explained by induced slowing of conduction and unidirectional block in the atrial tissue, with subsequent initiation of a re-entrant excitation leading to AF. The role of PACs as triggers of AF is the basis of ablation interventions that are aimed at suppressing AF by eliminating the ectopic foci that trigger and maintain AF[34,35]. A study by Papageorgiou *et al*.[36] showed that the ability of an atrial depolarization to propagate and induce an AF episode strictly depends on the site of initial depolarization (or of pacing) and on the site of origin of the premature atrial beat. Consistent overdrive pacing has been show to reduce PACs[13,20] and the present study confirms those findings. Atrial pacing may prevent the effects of PACs by accelerating the pacing rate after a sensed PAC, by preventing short–long cycles, or by consistent overdrive.

Those distinct effects were achieved by the two algorithms tested here. Indeed, the lack of correlation between the changes induced by the CAP and ARS algorithm on PACs and AP percentage suggests that the effects of these two algorithms are consistently different in every patient. In clinical practice the availability of different algorithms for AP, such as ARS or CAP, within the same device will allow us to individualize pacing in order to improve the efficacy of the device in preventing AF recurrence and in reducing AF burden.

In the present study the effects of different pacing sites (inter-atrial septum versus right atrial appendage) did not appear to be associated with a unique pattern of response. In patients with the atrial lead implanted in the inter-atrial septum and in those with the atrial lead implanted in the atrial appendage, pacing algorithms induced different variations in AF burden and AF episodes, ranging from a significant reduction to a paradoxical increase. The present study was not designed to compare the two different pacing sites, however, and future prospective evaluations of this aspect will be of great clinical interest.

Study limitations

In the present study the effects of CAP and ARS algorithms were evaluated using the diagnostic processes of the device, without a definitive evaluation of symptoms associated with AF episodes. The diagnostic processes of the device used in the present study were validated in previous evaluations[13,21,22]. Moreover, as shown in a previous report in a similar patient population[13], the ratio between symptomatic and asymptomatic AF episodes in patients implanted with a DDDR pacemaker with automatic mode switch has a mean value of 1:22. Recently, the risk for embolic complications associated with clinically silent AF has been stressed[37].

The diagnostic data provided by the pacemaker were analyzed, considering every episode of mode switch as an episode of paroxysmal AF. Data from previous studies[21] have shown that the algorithms of the Thera device are highly reliable in this type of patient population. In a recent study[22] the diagnostic features of the Thera DR pacemaker were found to be highly reliable in appropriately detecting paroxysmal AF, with a rate of false-positive detections of only 2·9%. The telemetric functions of the device are limited by the maximum number of recorded mode switch episodes, which is 255. Overall, seven out of the 16 patients studied (43·8%) reached the maximum number of recorded mode switch episodes. In four of those seven the mode switch episode counter saturated in all three periods of study; in the remaining three patients, the mode switch episode counter saturated in DDDR and CAP modes, but not in ARS. However, this bias is not necessarily in favour of the algorithms.

The study was conducted in a selected population of patients with frequent self-terminating episodes of AF in the setting of brady-tachy syndrome, and the data cannot be extrapolated to the treatment of AF occurring without any detectable association with bradycardia[29,30]. Another possible limitation of the present study is that selection of the pacing algorithm was not based on evaluation of the atrial substrate in each individual patient; this electrophysiologically guided approach to AF therapy is currently under evaluation[19].

Conclusions

In patients with a DDDR pacemaker implanted for recurrent paroxysmal AF in the setting of brady-tachy syndrome, the response to different pacing algorithms, such as ARS and CAP, is heterogeneous, both with regard to AF episode prevention and reduction in AF burden. In 31–69% of the patients a significant reduction in AF burden and/or mode switch episodes was obtained by using ARS or CAP algorithms; however, in a few patients an increase in AF episodes and/or AF burden occurred. In the population as a whole, pacing with CAP was associated with a significant reduction in AF burden in comparison with DDDR pacing.

The changes induced by ARS with regard to PACs and AP percentage, in comparison with DDDR pacing, are quite different from those induced by CAP. However, evaluation of these two simple parameters (i.e. PACs and AP percentage), which are simply retrievable through pacemaker diagnostics, is of practical interest because AF burden during DDDR and ARS mode pacing (but not during CAP) can easily be predicted by equations that include these two variables.

Availability in the same device of different algorithms for atrial pacing, such as ARS or CAP, may allow us to individualize pacing in order to improve the efficacy of these devices in preventing AF recurrences and in reducing AF burden.

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