Antiarrhythmic drugs and ablation in patients with atrial fibrillation: New perspectives

Giuseppe Boriani[1], Jacopo Francesco Imberti[1], Davide Antonio Mei[1, 2]

[1]Cardiology Division, Department of Biomedical, Metabolic, and Neural Sciences, University of Modena and Reggio Emilia, Policlinico di Modena, Modena, Italy
[2]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy

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Correspondence to:
Prof. Giuseppe Boriani, MD, PhD, Cardiology Division, Department of Biomedical, Metabolic, and Neural Sciences, University of Modena and Reggio Emilia, Policlinico di Modena, Via del Pozzo 71, Modena, 41121, Italy, phone: +39 059 422 58 36, e-mail: giuseppe.boriani@unimore.it

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Since the introduction of quinidine and digoxin more than 200 years ago, antiarrhythmic drugs (AADs) have been the main tool adopted by physicians for controlling atrial fibrillation (AF) and other atrial tachyarrhythmias, with the aim to improve symptoms and reduce the risk of adverse outcomes, in combination with anticoagulants for stroke prevention [1–3].

Amiodarone is an iodine-rich benzofuran derivative that was initially employed for control of coronary angina, due to its multiple pharmacological activities including a reduction of sympathetic tone, but it was soon adopted as an AAD, effective both on atrial and ventricular tachyarrhythmias [1]. The risk of adverse events of AAD (a significant problem with long-term amiodarone) coupled with a limited adherence to AAD regimens and an overall limited efficacy in maintaining sinus rhythm at follow-up conditioned and promoted the search for non-pharmacological treatment. Consequently, pulmonary vein isolation was tested and validated as an effective treatment for appropriately selected patients with AF, with an efficacy in maintaining sinus rhythm currently around 75%–85% at 1 year for paroxysmal AF and around 50%–60% at 1 year for longstanding persistent AF [4–7].

In the current issue of *Polish Heart Journal*, Pytkowski et al. [8] report an interesting retrospective study that evaluated a strategy for rhythm control based on pre-treatment with oral amiodarone applied to patient with persistent AF in the weeks before a planned ablation combined with pre-procedural electrical cardioversion targeted to allow ablation with pulmonary vein isolation in sinus rhythm. In a median follow-up of 39.5 months, patients treated with amiodarone were free from AF (detected clinically and/or through 3-day Holter electrocardiography) in 45.9% of cases as compared to 15.8% of patients not treated with amiodarone. This favorable outcome was associated with a higher proportion of patients with conversion from persistent to paroxysmal AF. Although derived from a retrospective study, these results are interesting, and they should be evaluated in the perspective of a potential synergetic effect of drugs and ablation for more effective rhythm control.

The onset and maintenance of AF is associated, along with time, with a progressive atrial and structural remodeling recently reported as "atrial cardiomyopathy", which markedly condition the possibility to restore and maintain sinus rhythm [9–11]. Importantly, the patients enrolled in this study were affected by persistent AF. Therefore, the overall lower efficacy of AF ablation strategies (even including additional ablation lines) as compared with paroxysmal AF justifies the use of amiodarone to maximize the potential effective rhythm control, at least for the period necessary to achieve some degree of reverse-remodeling of the atrial electrophysiological derangement [1, 9].

The most significant limitation of amiodarone is its tolerability long-term [1, 12]. Because a series of toxicities may occur, careful monitoring is required and should be specifically focused to avoid the risk of thyroid, hepatic, and pulmonary toxicity [1, 12]. Amiodarone is the most effective AAD in the case of persistent

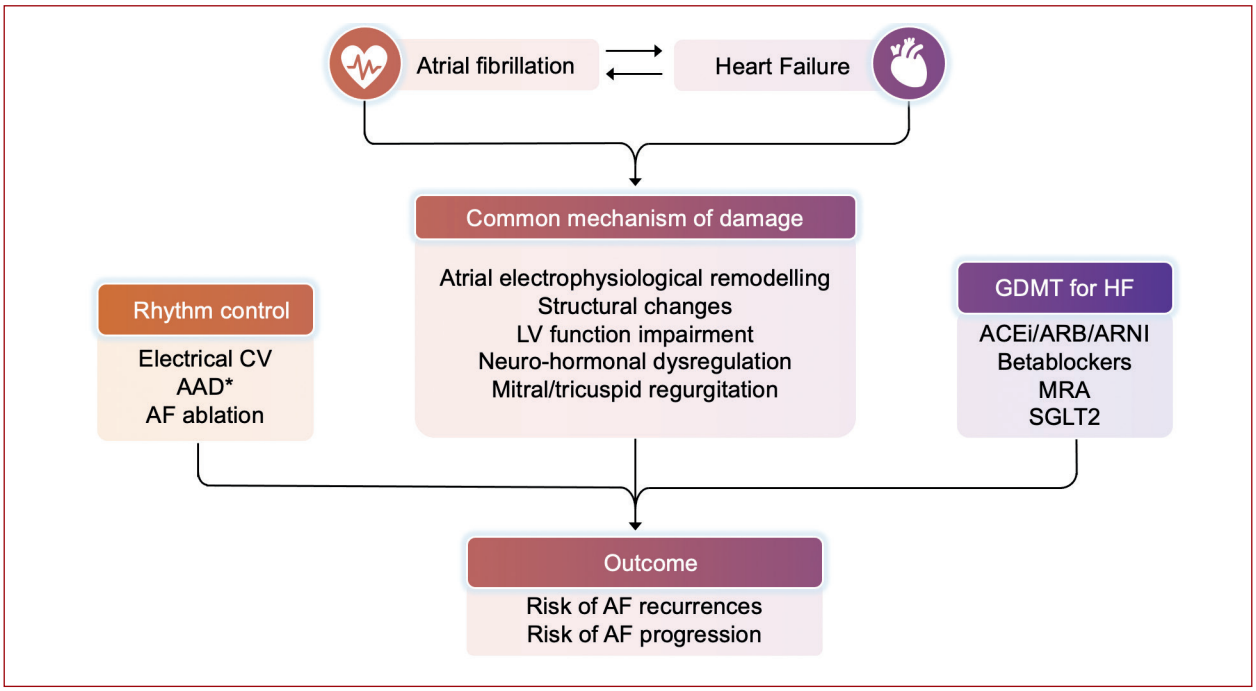

Figure 1. Relationship between AF and HF: mechanism of heart damage and role of rhythm control and optimized therapy for HF
*With monitoring of tolerability and adverse effects

Abbreviations: AAD, antiarrhythmic drug; ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; CV, cardiovascular; HF, heart failure; LV, left ventricle; MRA, mineralocorticoid receptor antagonist; SGLT, sodium-glucose co-transporter

AF, but in consideration of its toxicity, its use has declined in recent years, with much wider access to AF ablation, as supported by consensus and guidelines [2, 3, 13].

To reduce its risk of toxicity, a derivative of amiodarone was developed and clinically tested, with favorable results both in terms of sinus rhythm maintenance and patient outcomes in terms of cardiovascular deaths and hospitalizations [1, 10]. However, strict regulations for monitoring the risk of hepatic toxicity strongly limit its use in Europe, where a wide variability is observed in its prescription in daily practice [13, 14].

Unfortunately, the use of dronedarone is not advised in patients with heart failure (HF) with reduced ejection fraction, in whom amiodarone is the drug of choice [1, 2]. In the article by Pytkowski et al. [8] HF was present in the form of tachycardiomyopathy (a form of HF that can be reversed through rhythm control or even rate control), as well as associated comorbidity.

The association of AF and HF has many pathophysiological interactions and a growing epidemiological impact. Consequently, AF ablation has gained a primary role in managing AF in HF, in consideration of the negative outcome implication of AF [2–4]. It is noteworthy that in this study AF ablation was associated with an improvement in left ventricular ejection fraction of around 10% overall, but 17% in patients who maintained sinus rhythm during the follow-up [8]. Optimized drug therapy for AF plays an additional synergistic role, as reported in Figure 1. The current clinical approach is to offer rhythm control to all patients with AF with a reasonable possibility to maintain sinus rhythm, especially when there is HF, and this becomes a mandatory choice when tachycardiomyopathy is suspected [2, 3]. In this scenario, drugs and specifically amiodarone should be viewed in a new role and no longer considered as the alternative to "AF ablation". Conversely, AAD may constitute an integration to AF ablation, for potentiating the success, as suggested in this study, but also to reduce symptoms and improve quality of life [1, 3]. As is known, the efficacy of AF ablation is not 100%, as reported by this study, in line with the literature [4]. Moreover, although some recurrences may occur after ablation, clinical benefit may be achieved in relation with conversion from persistent to paroxysmal AF, thus avoiding or slowing progression towards permanent AF, or a benefit may derive from improvement of AF symptoms, a target frequently achieved with AF ablation with or without AAD [4].

As a matter of fact, in daily practice up to 40%–45% of patients are prescribed AAD after AF ablation for various reasons, such as preventing AF recurrences during the blanking period, or maximizing the efficacy of ablation in terms of outcomes [15]. This use of AAD should not be criticized or censored and should be individualized according to patient status, age, associated comorbidities, risk of AF recurrences, occurrence of prior ablation, and type of AF (paroxysmal vs. persistent), and it may be planned for a variable time-period, with periodic reassessment of advantages and disadvantages, also taking into account the patient's view. The recent guidelines on AF of the

European Society of Cardiology have proposed the AF-CARE pathway, where E means "evaluation and dynamic re-assessment" [2, 3], and all these clinical considerations and evaluations should be applied to individual patients. This is an absolute requirement considering the complexity of AF management in specific settings, as reported even if some recurrences occur after ablation [6], with need for a holistic integrated personalized care.

Article information

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