ATRIAL FIBRILLATION ABLATION IN HEART FAILURE

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Abstract

Atrial Fibrillation (AF) and Heart Failure (HF) commonly coexist in the same patient and either condition predisposes to the other. Several mechanisms promote the pathophysiological relationship between AF and HF, reducing quality of life, increasing the risk of stroke and worsening HF progression.

Although restoration and maintenance of sinus rhythm would be ideal for those patients, several trials comparing rhythm and rate control failed to show a benefit of rhythm control strategy, achieved with pharmacological therapy, in terms of hospitalization for HF or death.

Caheter ablation is a well-established option for symptomatic AF patients, resistant to drug therapy, with normal cardiac function. Several recent studies have shown an improvement in clinical outcomes after AF ablation in HF patients highlighting the emerging role of the invasive approach in this subset of patients. However, several concerns regarding patients' selection and standardization of the procedure still remain to be addressed.

Atrial Fibrillation (AF) and Heart Failure (HF) frequently coexist in the same patient, often promoting the course of each other. Left Ventricular (LV) dysfunction is found in about 30% of patients with AF. Conversely, AF can deteriorate LV function determining the occurrence and favouring the progression of HF [1]. Several mechanisms may promote this relationship, including loss of atrial systole, high ventricular rate and irregular ventricular filling with time impairment of myocardial function. Finally, persistently elevated left atrial pressure and chronic neuro-hormonal upregulation may lead to atrial fibrosis favouring AF in patients with HF.

In the past decade, several studies have evaluated the role of rhythm control strategies for improving the outcome of patients with AF and HF. Although restoration of sinus rhythm in patients with AF and HF is attractive, several trials using antiarrhythmic drugs to restore sinus rhythm failed to result in a significant improvement in clinical outcomes. Herein, we review the current knowledge, unanswered questions and future perspectives of AF ablation in HF patients.

Rate versus Rhythm control

Large prospective randomized trials have identified AF as an independent risk marker of mortality and HF progression in patients with left ventricular dysfunction [2]. The coexistence of the two conditions is associated with reduced quality of life, worsened HF progression and increased risk of stroke. Therefore, it is common practice to attempt at restoration and maintenance of steady sinus rhythm in patients with AF and HF. Several studies were performed to investigate the effectiveness of rhythm versus rate control strategy in AF patients showing similar outcomes [3]. Of these, the AF-CHF trial investigated patients with clinically documented HF. In this study, patients with symptomatic HF (NYHA II-IV) and a LVEF <35% were randomized to pharmacological rate versus rhythm control (in the latter group mainly based on amiodarone administration). The study showed no differences of death from cardiovascular causes in the two groups [4]. It is well known that QT prolongation, conduction block, proarrhythmia effect and non-cardiac side effects are associated with the use of AADs. In the HF population, selection of an AAD is mainly based on amiodarone and its use is associated with an increased risk of thyroid, neurologic, skin, eye and pulmonary toxicity due to the progressive accumulation of the drug in the tissues, especially in case of chronic use, sometimes requiring treatment discontinuation [5]. In summary, the adverse events related to the use of AADs may potentially neutralize the benefit of restoring and maintaining sinus rhythm in patients with HF. In these patients, permanent restoration of sinus rhythm using methods other than drug therapy may provide an optimal model to test the true impact of rhythm control on clinical outcome [3].

Catheter ablation of atrial fibrillation in patients with heart failure

Catheter ablation of AF has emerged as a potential strategy in patients with HF. Initial results of catheter ablation versus rate control in HF patients were reported in small studies and early Randomized Clinical Trials (RCTs), although the small number of patients included and the design of the studies limited the strength of data [6-9]. A recent meta-analysis of prospective randomized clinical trials comparing catheter ablation versus rate control strategies in patients with HF and AF showed a significant improvement in Left Ventricular Ejection Fraction (LVEF), quality of life and functional capacity. Data from this meta-analysis indicate AF burden reduction as a possible cause of functional improvement since 22% to 50% of patients had AF episodes after ablation [3,6,7,9].

More recently, the Ablation vs Amiodarone for Treatment of Atrial Fibrillation in Patients with Congestive Heart Failure (AATAC) study aimed to evaluate a rhythm control strategy in both arms by comparing AF catheter ablation versus pharmacologic rhythm control with amiodarone [10]. The study enrolled HF patients with LVEF < 40%, a NYHA class II-III, persistent AF and an implantable defibrillator (ICD) provided with an atrial lead (tab. I). The study showed a superiority of catheter ablation in achieving freedom from AF recurrences compared to amiodarone therapy, with a favorable effect on rates of death and unplanned hospitalization. During 24-month follow-up, 70% of patients in the ablation arm (95% CI, 60%-78%) and 34% in the control arm (95% CI, 25%-44%) remained free from arrhythmia recurrences. Permanent restoration of sinus rhythm was associated with functional improvement suggestive of a direct role of stable sinus rhythm on cardiac contractility. In this study, the presence of a transvenous atrial lead provided accurate monitoring of arrhythmia episodes. The high selectivity of the population, the median time in AF before enrollment, the high discontinuation rate of amiodarone and the lack of uniformity of the ablation procedure have raised some criticism about the applicability of AATAC results in daily practice [11].

The recent Catheter Ablation versus Standard Conventional Therapy in Patients with Left Ventricular Dysfunction (CASTLE-AF) trial assessed for the first time the impact of AF catheter ablation compared to medical therapy (rate or rhythm control) on mortality and progression rates in patients. The study enrolled symptomatic paroxysmal or persistent AF with a NYHA class II-IV, LVEF <35% and an implanted device. In this population, catheter ablation was associated with a significant reduction of the composite of death and hospitalization compared to medical therapy (HR 0.62; 95% CI, 0.43-0.87) (tab. I). Moreover, a benefit in all cause mortality alone, mainly driven by a reduction of cardiovascular deaths, was described in the ablation group [12]. The study added important results to the current literature regarding hard endpoints such as mortality and hospitalization after AF catheter ablation in HF patients.

The continuous monitoring to check for AF recurrences and the secondary endpoints of 6 minutes walking distance and LVEF allowed an extensive characterization of the response after ablation compared to medical therapy. Similar to what previously reported, the clinical benefit was correlated with a reduction in the burden of recorded AF. A potential limitation of CASTLE-AF stems on the observation that procedures were performed by experienced operators in high-volume medical centers. In addition, there was a large heterogeneity in the ablation technique by the different operators.

Current guidelines recommend catheter ablation of AF in symptomatic patients with HF in order to improve symptoms and cardiac function, in particular when tachycardiomyopathy is suspected [13]. However, several questions remains to be answered regarding success rate on those patients after a single procedure, selection of appropriate patients, type and timing of procedure.

Selection of candidates to catheter ablation, procedural features, complication and success rates

Abnormalities in atrial electrophysiological properties, such as increased

Table I - Principal studies on AF ablation in HF published within the last ten years.

Study	*Patients*	*Aetiology and features of HF*	*AF pattern*	*Ablation strategy*	*Medical strategy*	*Ablation success rate*	*Results*	*Median Follow-up*
PABA-CHF[9]	81	73% ischemic CM EF<40% NYHA II-III	49% paroxysmal 51% persistent	PVI ± additional linear lesions	AV node ablation + CRT	88%	↑ EF, 6MWT and QoL in ablation arm	6 months
MacDonald et al.[10]	41	50% ischemic CM EF<35% NYHA II-IV	100% persistent	PVI ± additional linear lesions	Medical rate control	50%	No differences in EF 6MWT and QoL in ablation arm	6 months
ARC-HF[8]	52	33% ischemic CM EF<35%	100% persistent	Step wise: PVI, linear ablation at roof and mitral isthmus, CFE ablation	Medical rate control	88%	↑ Exercise performance and BNP in ablation arm	12 months
CAMTAF[7]	50	26% ischemic CM EF<50%	100% persistent	PVI ± linear lesions ± CFE ablation	Medical rate control	73%	↑ EF, exercise performance and QoL in ablation arm	12 months
AATAC[11]	203	62% ischemic CM EF<40% ICD or CRTD	100% persistent	PVI ± linear lesions ± CFE ablation	Amiodarone	70%	↓ AF recurrences ↑ Mortality and unplanned hospitalization in ablation arm	24 months
CAMERA-MRI[16]	68	100% idiopathic CM EF<45%	28% paroxysmal 72% persistent	PVI ± additional linear lesions	Medical rate control	75%	↑ EF, in ablation arm, greater in LGE negative	6 months
CASTEL-AF[13]	363	46% ischemic CM EF<35% NYHA II-IV ICD or CRT	30% paroxysmal 70% persistent	PVI ± additional linear lesions	Medical rate control	63.1%	↑ Mortality and HF hospitalization in ablation arm	37 months

Legenda: CM= CardioMyopathy; EF= Ejection Fraction; ICD= Implantable Cardioverter Defibrillator; CRT= Cardiac Resynchronization Therapy; PVI= Pulmonary Vein Isolation; CFE= Complex Fractionated Electrograms; 6MWT= 6 Minute Walking Test; QoL= Quality of Life; BNP= B-type Natriuretic Peptide; LGE= Late Gadolinium Enhancement.

atrial refractory period, increased atrial conduction time along the low lateral right atrium and coronary sinus and function delay at the crista terminalis and at the Bachmann bundle, may cause more complex arrhythmia manifestations in HF patients. Pre-procedural risk stratification tools to identify patients who might benefit more from catheter ablation, could avoid unnecessary procedures or offer different approaches in these subset of patients. In the Catheter Ablation versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction (CAMERA-MRI) study, patients with idiopathic cardiomyopathy and persistent AF were all studied with cardiac magnetic resonance (MRI) and randomized to catheter ablation or rate control therapy. A significant improvement in LVEF was found in patients after catheter ablation compared to patients randomized to medical therapy despite optimal rate control. In the ablation group, patients without evidence of Late Gadolinium Enhancement (LGE) had better results on ventricular function after the procedure compared to LGE positive patients, suggesting that cardiac MRI could identify HF patients who may benefit more from catheter ablation. Moreover, the study highlights the positive impact of sinus rhythm on ventricular function compared to an optimal rate control (tab. I) [14]. As summarized in table I, in all studies the ablation strategy was left to best operator judgment which led to a large heterogeneity of techniques.

Although many tools were introduced in the last decade to improve the efficacy of AF ablation, a standardized approach for the procedure is currently lacking. A recent meta-analysis from clinical trials and observational studies of AF ablation in HF patients found no difference in sinus rhythm persistence between PVI alone approaches versus extensive left atrial ablation [15]. Therefore, since a more extensive ablation could be preferred in this subset of patients and considering the potential need of additional procedures in up to 40-50% of the patients increasing the risk of complications, the selection of the appropriate candidate for AF ablation should be considered a substantial element to increase success and safety in HF patients [16].

In summary, catheter ablation in patients with AF and HF appears promising. Several concerns remain regarding patients' selection and standardization of the ablation approach to best weight risks and benefits of the procedure in this population.

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