REVIEW

Catheter Ablation in Patients With Heart Failure: Current Data from Recently Published Randomized Trials

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ABSTRACT

Atrial fibrillation in patients with heart failure with reduced left ventricular ejection fraction is common and is associated with an increased risk of mortality, hospitalization and all-cause death. Rhythm control via medical treatment in these patients is restricted to use of amiodarone as the only suitable antiarrhythmic drug with the least proarrhythmic effect compared to other antiarrhythmic drugs for this population of patients. Over the last years there is a growing evidence that catheter ablation is beneficial in patients with heart failure since randomized clinical trials with hard endpoints have already been published. However, there are still unanswered questions about the patient categories that could benefit from the ablation procedures and the optimal ablation strategies in these patients. These issues are herein reviewed. ***Rhythmos 2018;13(4):75-77.***

Key Words: atrial fibrillation; heart failure; catheter ablation; antiarrhythmic drugs; rhythm control

Abbreviations: AAD = antiarrhythmic drug; AF = atrial fibrillation; CA = catheter ablation; CFAE = complex fractionated atrial electrograms; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; LGE = late gadolinium enhancement; LV = left ventric-le(-ular); LVEF = left ventricular ejection fraction; MRI = magnetic resonance imaging; NNT = number needed to treat; NYHA = New York Heart Association; PVI = pulmonary vein isolation

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in the general population and is associated usually with significant symptoms and high rates of hospitalization and mortality. The prevalence of AF in the general population is 1.0–1.5% increasing to 9.0% in patients aged ≥80 years.[1,2] Atrial fibrillation and heart failure (HF) frequently co-exist since there are common pathophysiologic pathways involved in both of them. Heart failure increases mean right and left atrial pressures promoting their progressive dilation. Data from the Framingham study demonstrated that in AF patients, occurrence of HF was associated with significant increase in mortality, while in HF patients, new-onset AF was associated with significant rise on mortality.[3]

Nowadays, catheter ablation (CA) has emerged as a more effective treatment strategy compared to antiarrhythmic drugs (AADs) especially for patients with paroxysmal AF. Many observational and randomized trials have compared CA with AADs in patients with HF and AF and the latest guidelines from the European Society of Cardiology (ESC) recommend CA in this population when it is performed by experienced operators and after careful consideration of the benefits over the possible complications.[4,5] Thus, there are unanswered questions regarding firstly the characteristics of the ideal patient with HF who should undergo CA and secondly the optimal CA strategy.

RANDOMIZED CLINICAL TRIALS OF CATHETER ABLATION IN PATIENTS WITH ATRIAL FIBRILLATION AND HEART FAILURE

Early clinical trials enrolled a small number of patients assessing end points such as left ventricle ejection fraction (LVEF) and quality of life but not hard clinical end points such as mortality. During the last years, a number of randomized clinical trials regarding the efficacy of AF ablation in patients with HF compared to AADs have been published.

Patients with persistent AF, symptomatic HF, and LVEF <50% were randomized to CA or medical rate control in the CAMTAF study. Totally 55 patients were finally enrolled with a high proportion of non-ischemic cardiomyopathy and persistent AF, and the primary end-point was the difference between groups in LVEF at 6 months. An improvement in LVEF, peak oxygen consumption and quality of life score was seen in the ablation group versus the medical rate control group.[6]

In the Ablation versus Amiodarone for Treatment of Atrial Fibrillation in Patients with Congestive Heart Failure and an Implanted Device (AATAC) study, CA (pulmonary vein isolation ± substrate modification) was compared with amiodarone, as rhythm control strategy, in patients with persistent AF, systolic LV dysfunction (LVEF<40 %) and NYHA Class II–III heart failure. The primary endpoint of this study was AF recurrence during the two years of follow up and the secondary endpoints included all-cause mortality and hospitalizations. The patients in the CA group had significantly higher rates of freedom from AF (70 %) compared with the amiodarone (34 %) group. It must be noted that all patients in both groups had a cardiac implantable device, pacemaker or defibrillator, which improved the reliability of the follow up process. Both all-cause mortality and hospitalizations were also reduced and LVEF was significantly improved

in patients who underwent CA. Moreover, the number needed to treat (NNT) to avoid one hospitalization or one death was 3.8 and 10 patients for CA versus amiodarone, respectively.[7]

The CAMERA-MRI trial (Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Heart Failure) randomized 68 patients with persistent AF and idiopathic cardiomyopathy (LVEF <45 %) to receive either CA or medical rate control. All patients underwent a cardiac magnetic resonance imaging (MRI) scan in order to assess LVEF and to evaluate the presence of ventricular fibrosis via late gadolinium enhancement (LGE). The primary endpoint of this study was the change in LVEF after a 6-month follow up period. Patients who were randomized to the ablation group showed improved LVEF compared with the medical rate control group. It is important to note that 58% versus 9% in both groups had a normal LVEF (≥50%) after 6 months. Moreover, the improvement in LVEF was significantly better in the ablation group patients with negative LGE at baseline compared to those with positive LGE. This indicates that restoration and maintenance of sinus rhythm in patients with reduced LV systolic function due to tachycardia – induced cardiomyopathy (without evidence of fibrosis) contributes to the improvement even in normalization of cardiac function.[8]

One of the most important trials in the field of CA in patients with AF and HF was the CASTLE-AF which randomized 363 patients (>3000 screened for eligibility) suffering from symptomatic AF (30% had paroxysmal AF) and systolic dysfunction with LVEF≤35%, NYHA class > II to either radiofrequency CA or medical treatment. All patients had an implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy-defibrillator (CRT-D) device and the median follow up period was 37.8 months. The great importance of this study is the fact that is the first one designed to provide an answer in clinical hard endpoints, such as composite of all-cause mortality or hospitalization for worsening HF. The composite endpoint of all-cause mortality and hospitalization for HF was significantly lower in the ablation group compared to the control group (28.5% vs 44.6%, p=0.006) and the NNT to prevent one primary endpoint event was 6 patients. Moreover, after 60 months of follow-up, LVEF in the CA group had increased by 9% compared with the medical therapy group. The ablation strategy in this study included pulmonary vein isolation plus additional lesions involving the cavotricuspid isthmus, and left atrium substrate modification according to the preferences of the operator.[9] A possible limitation of the CASTLE-AF study was the fact that the positive results of catheter ablation were observed in symptomatic patients without advanced HF the majority of whom had previously failed AAD treatment. Also, patients with LVEF<25% seem to derive no benefit from CA compared to other patients. With regards to the catheter ablation related complication rates in patients with HF, serious adverse events occurred in 7.8 %.[9]

CATHETER ABLATION IN PATIENTS WITH AF AND HF WITH PRESERVED EJECTION FRACTION

Few studies have examined outcomes of CA in patients with AF and heart failure with preserved ejection fraction (HFpEF). A retrospective study of 230 patients with HF who underwent AF ablation, including 133 with HFpEF was published recently evaluating symptoms and freedom from atrial arrhythmia at 12-months. There was no significant difference in adverse events and symptoms between patients with HFpEF compared to those with reduced LVEF with similar improvements in NYHA class in both groups.[10]

Another study enrolled patients with normal and abnormal LV function who underwent CA for AAD-refractory AF. Three groups of patients were compared: patients with systolic dysfunction (LVEF ≤40%); with isolated diastolic dysfunction and preserved LVEF ≥50%; and with normal LV function. The primary end point was freedom from AF at 1 year after ablation without AADs use. This was achieved in 62% of patients with systolic dysfunction, 75% of those with diastolic dysfunction, and 84% of controls (P=0.007). In the systolic dysfunction group, 49% experienced an increase in LVEF by ≥5% after ablation, of which 64% achieved normal LVEF. In the diastolic dysfunction group, 30% of patients demonstrated at least 1 grade improvement in diastolic dysfunction.[11]

WHICH IS THE IDEAL AF ABLATION STRATEGY IN PATIENTS WITH HF*?*

Patients with HF is more likely to suffer from persistent than paroxysmal AF. The ablation strategy in patients with persistent AF is not common across different electrophysiology centers and can include pulmonary vein isolation (PVI) alone or additionally linear ablation and/or ablation of complex fractionated atrial electrograms (CFAE). Besides, it is known from the Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II (STAR AF II) that no difference between these two strategies have been observed in patients with persistent AF. [12]All the studies mentioned above have had significant differences both in the ablation strategy adopted by each operator and in the population characteristics. A meta-

analysis of clinical and observational studies in patients with HF, showed similar percentages of sinus rhythm maintenance between a PVI approach versus extensive left atrial ablation (linear lesions or CFAE ablation).[13] On the other hand, the structural and the subsequent electrophysiological abnormalities in the left atrium of patients with HF enforce the adoption of different ablation strategies according to the primary atrial substrate and to the type of cardiomyopathy (e.g. ischemic vs. hypertophic cardiomyopathy). In a recent study, a more aggressive ablation with left atrial substrate modification additionally to PVI resulted in better outcomes in patients with HF compared to those without HF as regards the AF recurrences after one year follow up.[14] The optimal AF ablation strategy is different for each patient category and greatly depends on the degree of left or bi-atrial fibrosis. In this field, the contribution of MRI scan with LGE may give additional information about the left atrium characteristics and although it is not a widely used method for evaluation of CA outcomes, it may in the near future be more accessible in clinical practice. An ongoing study (DECAAF-II) will provide further data about the impact of targeting LGE-MRI detected atrial fibrosis during AF ablation to improve procedural outcomes.[15]

CONCLUSIONS

Atrial fibrillation ablation seems to have beneficial effects compared to medical treatment in selected patients with HF reducing the recurrences and the unplanned hospitalizations additionally to quality of life indexes. CASTLE-AF was a landmark randomized trial with hard end points such as death and hospitalization rates which showed superiority of CA to medical therapy, thus establishing CA as first line therapy in patients with HF with reduced LVEF. More data is required in order to identify the more appropriate patients with HF who could benefit from the CA procedures.

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