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REVIEW

Catheter ablation of atrial fibrillation in patients with left ventricular dysfunction

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ABSTRACT

There is a complex interplay between atrial fibrillation and congestive heart failure. These two clinical entities often coexist, resulting in significant morbidity, affecting prognosis and rendering their management even more challenging. New nonpharmacologic therapies are emerging and may alter the management of these patients. Among them, catheter ablation of atrial fibrillation seems to be a promising therapeutic approach as it leads to improvement of cardiac function, symptoms, exercise capacity, and quality of life. This article reviews the role of catheter ablation in contemporary management of atrial fibrillation among patients with left ventricular dysfunction.

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice and it is responsible for substantial morbidity and mortality [1,2]. It occurs very often in patients with congestive heart failure (CHF) and the prevalence increases with the severity of the disease. AF is present in about 10% of patients in New York Heart Association (NYHA) functional class I, and up to 50% in patients with more advanced disease [3,4]. These two conditions seem to be linked together, and CHF may either be the cause or the consequence of AF [5]. An increase in the prevalence of these two clinical entities is occurring in part because of the demographic shift toward an ageing population [6,7].

Despite the clinical implications of AF in CHF, the reasons for its high prevalence are poorly understood. In a recent elegant study, Sanders et al. addressed the reason for the higher prevalence of AF in patients with CHF. Patients with CHF exhibited atrial remodelling characterized by anatomic and structural changes including, atrial enlargement, increased refractoriness and sinus node dysfunction, abnormalities of conduction, a greater number and duration of double potentials associated with areas of low voltage and electrical silence. These abnormalities were associated with an increased inducibility and sustainability of AF and may be responsible in part for the increased incidence of atrial arrhythmias in patients with CHF [8]. Once AF has started, it may worsen CHF because of faster heart rate with shortened filling time, absence of atrial contribution to cardiac output, and irregularity of the ventricular rhythm, leading to further hemodynamic deterioration [9]. Atrial dilation also plays an important role in the occurrence AF [10]. A recent subanalysis of the RACE study is consistent with these findings, suggesting partial reversibility of atrial and ventricular

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anatomical and functional characteristics after prolonged AF periods. Rhythm control was associated with a significant reduction of left atrial size, especially if sinus rhythm was maintained. Improvement of left ventricular fractional shortening was significant only in the case of maintenance of sinus rhythm [11].

The independent impact of AF on the prognosis of CHF patients has been examined in several studies but remains a subject of controversy. However, a plethora of epidemiological surveys and large clinical trials in CHF provides strong evidence that AF is a marker of increased mortality [12-16].

RHYTHM CONTROL VERSUS RATE CONTROL

Based on its pathophysiological and epidemiological background, it had long been believed that rhythm control for AF, was the preferable type of management, however the results of recent randomized controlled trials have cast doubt on whether rhythm control should be routinely applied in patients with AF [17-21]. All of these trials should be limited in the application of their results to the entire AF patient population. The subset of patients with AF and CHF was underrepresented (<9% of patients) in the largest of these trials (AFFIRM). A subgroup analysis of AFFIRM, revealed a benefit conferred by rhythm control in patients with CHF or left ventricular (LV) dysfunction, which was a prespecified subgroup in AFFIRM. Furthermore, the "on-treatment" analysis of AFFIRM showed that presence of sinus rhythm predicted a considerably lower risk of death [22]. Moreover, a substudy of the RACE trial reported a survival benefit in CHF patients who were able to maintain sinus rhythm. CHF patients assigned to the rhythm-control group who maintained in sinus rhythm throughout the study demonstrated a cardiovascular mortality rate of 0%, compared with 9.5% in patients who reverted back to AF. Mortality benefits were also observed in the DIAMOND study in CHF patients who maintained sinus rhythm on the antiarrhythmic drug dofetilide [23,24]. However, fewer than 50% of patients on an antiarrhythmic regimen remained in sinus rhythm at the end of 1 year [25]. These trials also did not include patients with highly symptomatic AF who might not be candidates for rate control. In particular, patients with diminished diastolic compliance (for example, long-standing hypertension and hypertrophic cardiomyopathy) may not tolerate loss of atrial function and benefit immensely from maintenance of sinus rhythm [26,27]. The question of rate versus rhythm strategy in patients with CHF remains unanswered and is currently being addressed in the Atrial Fibrillation and Congestive Heart Failure (AF-CHF) trial [28].

ABLATE AND PACE THERAPY

Inadequate rate control is associated with the development of tachycardia-induced cardiomyopathy [29]. Atrioventricular (AV) junction ablation with pacing is indicated for patients who cannot achieve adequate rate control with AV nodal blocking drugs or do not tolerate the doses of these medications that are required for adequate rate control. A meta-analysis of 21 mostly nonrandomized studies, including 1181 patients, showed a uniform improvement of quality of life and of health care utilization with ablation and pacing in patients with refractory atrial tachyarrhythmias [30]. These results were confirmed in randomized studies in patients with permanent, as well as paroxysmal AF [31,32]. However, AV junction ablation creates dependence on an implanted pacemaker. There is also a finite risk of sudden death due to torsade de pointes or ventricular fibrillation [33]. Furthermore, recent data suggest that mandatory right ventricular pacing may sometimes result in impaired ventricular function and CHF [34,35]. This was also highlighted in the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial in patients with underlying left ventricular (LV) dysfunction (LV ejection fraction [EF] ≤40%), in which RV pacing increased the risk of death or heart failure hospitalization [36]. Of note, in 3 recent prospective, randomized trials of ablate and pace therapy, the LVEF following AV node ablation showed only a modest improvement or no change in patients with LV dysfunction prior to the procedure [37-39]. Data from the Left Ventricular-based Cardiac Stimulation Post AV Nodal Ablation Evaluation (PAVE) showed that biventricular pacing is the preferred modality of pacing in patients undergoing AV node ablation and pacemaker implantation [40].

CATHETER ABLATION OF AF

In theory, a therapy that restores and maintains sinus rhythm while avoiding the adverse effects of antiarrhythmic drugs would improve survival. One such therapy is catheter ablation to eliminate AF. In contrast to antiarrhythmic (AAD) drug therapy, catheter ablation seems to have minimal long-term cumulative risk after the periprocedure period.

Since the pivotal role of the pulmonary veins (PV) in the genesis of AF was first discovered by Haissaguerre et al. several PV-based catheter ablation strategies have been developed. Currently, the techniques used for ablation of AF include one or a combination of the following techniques: isolation of the PVs (segmental or circumferential approach) with or without demonstration of pulmonary vein left atrial conduction block, left atrial linear ablation (mitral isthmus, roof, and posterior wall), ablation of the complex fractionated electrograms, and ablation of the autonomic ganglions [41-44].

These procedures either use a circular mapping catheter under fluoroscopic guidance to electrically isolate the PVs from the left atrium or create radiofrequency lesions encircling the PVs under the guidance of a three-dimensional electroanatomic mapping system [45-47]. The aim of catheter ablation is to "cure" AF, but much of the available data have come from small studies with relatively short periods of follow-up. Based on these data, success rates range from about 60-90% and were improved to a varying degree by the use of AADs. A second procedure was necessary in 20-30% of patients. Success rates for persistent or permanent AF or in patients with markedly dilated atria are lower [48-58].

In the largest of these trials Pappone and his colleagues analyzed the impact of catheter ablation of AF compared with drug therapy for sinus rhythm maintenance [59]. The study was prospective but not randomized and included a relatively diverse patient population with prevalent structural heart disease. Ablation therapy was associated with reductions in the risk of death (54%), major adverse events (55%), and recurrence of AF (70%). Of note, they reported that maintenance of sinus rhythm as a time-dependent variable also reduced the risk of death and adverse events regardless of treatment strategy. The results reported in this study contradict the conclusions drawn by the rate versus rhythm control trials [60]. In a large worldwide survey of centers performing AF ablation, 52% of patients who were not taking antiarrhythmic medications were asymptomatic, and another 24% were successfully treated with antiarrhythmic medications after ablation [61]. In addition, there was a high rate of maintenance of sinus rhythm among those patients who underwent a repeat procedure. The overall incidence of major complications was 6% [62]. Very recently, some investigators have reported that catheter-based AF ablation seems to be more effective than AADs for the treatment of paroxysmal and permanent AF. Wazni et al showed that pulmonary vein isolation as first-line therapy in patients with symptomatic AF was associated with improved clinical outcomes compared with initial AAD therapy [63]. The Catheter Ablation for the Cure of Atrial Fibrillation (CACAF) trial was an open, prospective, randomized, multicenter study which demonstrated that patients with treatment-resistant paroxysmal or persistent AF who were treated with a single session of catheter ablation therapy in combination with AADs were significantly less likely to experience recurrence of AF than patients treated with AADs alone. Importantly, investigators found that the long-term efficacy of ablation therapy was independent of drug therapy [64]. Oral et al reported that ablation was superior to amiodarone for the maintenance of sinus rhythm in patients with persistent AF [65]. Ablation for Paroxysmal Atrial Fibrillation (APAF) trial, which randomized patients to AADs or pulmonary vein ablation, showed a marked difference in freedom from recurrent arrhythmia in favor of the ablation group [66]. However, catheter-based AF ablation is a relatively new technique, and while the studies report high success rates from high-volume centers, most centers currently have limited experience. Additionally, the long-term follow-up of patients after ablation is limited, and given the natural history of AF, it is quite possible that the long-term success rates of this procedure will taper off significantly. Furthermore, these studies did not focus on patients with structural heart disease although the majority has included some proportion of patients with structural heart disease.

CATHETER ABLATION OF AF IN THE SETTING OF LV DYSFUNCTION

A central question in treating patients with AF and congestive heart failure (CHF) is whether maintaining normal sinus rhythm per se affects mortality, morbidity or quality of life. Recent evidence from the AFFIRM investigators, in addition to confirming the adverse prognostic effects of congestive heart failure, highlights the potential benefit of maintaining sinus rhythm if it could be achieved without the adverse effects of antiarrhythmic drugs [67]. There is preliminary evidence to support that catheter ablation may become a routine clinical approach to AF in patients with heart failure. There have been three published studies and several abstracts so far addressing this issue (Table 1) [68-73]. The outcomes of catheter ablation in patients with LV dysfunction were impressive. There was a consistent improvement in LVEF in these patients, which in the majority of studies reached statistical significance and although the AF recurrence rate in impaired LVEF patients was higher than in normal LVEF subjects, a significant percentage of patients with LV dysfunction remained AF-free. In a nonrandomized study Chen et al examined the effect of catheter ablation of AF in patients with LV dysfunction. The study included 377 consecutive patients over a 19-month period, a control group of 283 patients was compared with a study group of 94 patients with an LVEF below 40%. Patients were selected on the basis of the presence of symptoms and drug resistance. Circumferential ostial mapping and radiofrequency "cooled tip" ablation for PV isolation was "classically" guided

TABLE 1. Trials of AF in Heart Failure

	n	Success rate	Increase in EF	p
Chen [69]	94	96%	36±7 41±6	0.1
Hsu [68]	58	78% (on AAD)	35±7 56±13	0.001
Pappone [71]	95	81% (on AAD)	31±9 44±6	<0.05
Gentlesk [73]	53	90% (on AAD)	42±8 57±8	<0.01
Cha [72]	19	68% (on AAD)	34±6 51±7	0.003
Tondo [70]	40	87% (on AAD)	33±2 47±3	<0.01

Abbreviations: AAD: antiarrhythmic drugs, Increase in EF: values pre, post-ablation

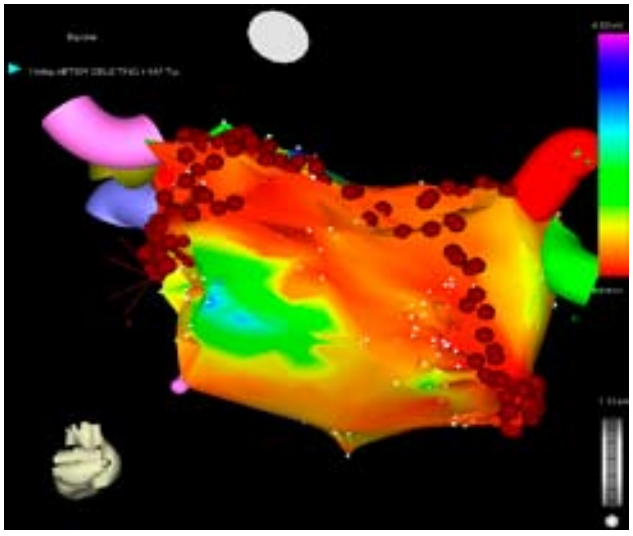

FIGURE 1. Circumferential ablation around pulmonary vein ostia. Shown is a posterior projection of a 3-dimensional replica of the left atrium as constructed with an electroanatomic mapping system. Brown tags represent points at which radiofrequency energy was delivered. The left- and right-sided pulmonary veins are encircled. The mitral valve isthmus and roof lines are also shown.

by angiography in the first 56 patients and by intracardiac ultrasound in the last 321. The latter allowed for monitoring of tissue overheating and impending impedance rise. A minority of patients underwent associated cavotricuspid isthmus ablation, but no additional linear lines were performed. Overall, the excellent results of this series fit with the best-published data on PV ablation techniques. Of note patients with impaired LVEF had a significantly worse outcome compared with controls after a first procedure but identical outcome after the second procedure. These results were obtained without significantly greater complications, although there was a trend toward a higher rate of cerebrovascular accident in the low LVEF group. Pulmonary vein ostial size measured by intracardiac echocardiogram was significantly larger in low LVEF patients than in those with normal LV function. There was a nonsignificant (5%) increase in LVEF after ablation. However, using the Short Form-36 Questionnaire, both normal and low-LVEF patients experienced a clear improvement in quality of life [69]. In a prospective non-randomized study Hsu et al evaluated 58 consecutive patients with CHF and a LVEF of less than 45% who were undergoing catheter ablation for AF and compared them with 58 patients without CHF who were undergoing ablation for AF, matched for age, sex, and classification of AF. The investigators evaluated 58 consecutive patients with CHF and a LVEF of less than 45% who were undergoing catheter ablation for AF and compared them with 58 patients without CHF who were undergoing ablation for AF, matched for age, sex, and classification of atrial fibrillation. After a mean of 12±7 months, sinus rhythm was maintained in 78% of the patients with CHF and in 84% of the controls (P= .34). Sinus rhythm persisted without use of AADs in 69% and 71% of patients, respectively. In the group with CHF, there were improvements in exercise capacity, symptoms, quality of life, LVEF (LVEF increased by 21%±13% and fractional shortening increased by 11%±7%; P<.001 for both comparisons), and left ventricular dimensions (diastolic diameter decreased by 6±6 mm; P=.03; and systolic diameter decreased by 8±7 mm; P<.001). The LVEF improved significantly not only in patients without concurrent structural heart disease (24±10 percent, P<0.001) and those with inadequate rate control before ablation (23±10 percent, P<0.001), but also in those with coexisting heart disease (16±14 percent, P<0.001) and adequate rate control before ablation (17±15 percent, P<0.001). The striking improvement in LV function after restoration of sinus rhythm in 92% of the patients who had inadequate rate control without coexisting heart disease suggests that CHF was attributable primarily to tachycardia-mediated cardiomyopathy in this group of patients [68]. Further evidence for the role of catheter ablation of AF in patients with left ventricular dysfunction has been demonstrated in a recent study by Tondo et al [70]. One hundred and five consecutive patients who underwent PV vestibule ablation for the control of AF were studied. The population comprised 40 patients affected by LV dysfunction with LVEF <40% and 65 patients with normal LV function. After 14±2 months, 87% of patients with impaired LV function and 92% of patients with normal LV function were in sinus rhythm, with or without AADs. A significant improvement in LVEF and fractional shortening was documented in patients with LV dysfunction. Evaluation of exercise capacity and quality of life documented better improvements in patients with impaired LV function compared to patients with normal LV function.

Cardiac resynchronization therapy (CRT) with biventricular pacing is an effective therapy in symptomatic, drug-refractory CHF patients with prolonged QRS and low LVEF. However, CRT may be ineffective in the setting of AF due to inhibition of resynchronization therapy by the rapid intrinsic AV nodal conduction. Thus, an important issue remains whether CRT in patients with chronic AF should be accompanied by AV node ablation. PABA CHF study was the first randomized trial to directly compare pulmonary vein antrum isolation versus AV node ablation and biventricular pacing in CHF patients with drug-resistant AF. Pulmonary vein isolation improved LVEF, 6-minute walk distance, and quality of life compared with the use of AV node ablation and biventricular pacing. It was also demonstrated that patients treated with pulmonary vein ablation were significantly more likely to be free of AF at 6 months than those treated with AV node ablation and biventricular pacing [74,75].

Catheter ablation in patients with LV dysfunction seems

to be a promising technique for non-pharmacologic treatment and cure of AF. Despite a relatively lower success rate, it is not associated with higher procedural complications, and provides a significant improvement in LV performance, symptoms, and quality of life during follow-up. Longer term follow-up and larger randomized trials are required.

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