Surgical ablation of atrial fibrillation in patients with heart failure

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With the aging of the population, the incidence of both atrial fibrillation (AF) and heart failure (HF) continues to increase, with a spiraling cost to health care services globally.^{2,3} AF and HF often coexist, promoting a vicious cycle that leads to worsening and often rapid deterioration in a patient's condition. AF is both a cause and consequence of HF, with complex interactions that can lead to impairment of systolic and diastolic function not present in sinus rhythm.³ AF is also associated with a 3-fold increased risk of HF. The EuroHeart Failure Survey reported that 25% of HF patients with reduced ejection fraction (left ventricular ejection fraction [LVEF] <40%) had chronic AF,⁴ with many likely having a component of tachycardia-induced cardiomyopathy (TIC).

With the restoration of sinus rhythm and improved heart rate control, left ventricle (LV) function can be expected to normalize in patients with TIC. However, even in the absence of a rapid ventricular rate in AF, an irregular ventricular rhythm has also been shown to lead to a reduction in LV function.⁵⁻⁸ Conversely, the neurohormonal and structural changes, including atrial and ventricular fibrosis observed in patients with HF, create a proarrhythmic environment that favors the initiation and maintenance of AF.⁹ Canine studies by our group and others have shown that left atrial dilation leads to a significant shortening of the atrial effective refractory period, and slower and more inhomogeneous conduction.^{10,11} These changes have been implicated in the initiation of AF in humans and an increased AF inducibility in canine models of mitral regurgitation.^{10,12}

Improvement in left ventricular function following stand-alone CMP IV. Reproduced with permission.¹

CENTRAL MESSAGE

Surgical ablation of AF can restore sinus rhythm in selected patients with reduced ejection fraction and is associated with significant improvement in left ventricular function and symptomatic relief.

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MEDICAL THERAPY AND CATHETER-BASED ABLATION

Regardless of which comes first, patients with concomitant AF and HF have a significantly worse prognosis.^{3,6} The goals of therapy are similar to other patients with AF: to prevent stroke, control the ventricular rate and rhythm, reduce symptoms, and improve functional status and quality of life. Unfortunately, pharmacologic rate and rhythm control strategies, which come with serious side effects, have not led to improvements in LV function, quality of life, or cardiovascular death.^{9,13}

In contradistinction, multiple studies have shown catheter ablation to be superior to medical therapy with improved quality of life, exercise capacity, LV function,

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and reduced AF burden.^{2,14-17} In 2018, Marrouche and colleagues¹⁶ reported a randomized controlled trial (Catheter Ablation for Atrial Fibrillation with Heart Failure) comparing patients with AF and HF who underwent catheter-based ablation ($n = 179$) to those with medical therapy alone (rate or rhythm control) ($n = 184$). Catheter-based ablation for AF in this patient population was associated with a significantly lower mortality rate from any cause or hospitalization for worsening HF. Catheter ablation was associated with significant improvement in LV function, exercise capacity, and a reduction in AF burden.¹⁶ Patients with an ejection fraction $\leq 35\%$ were enrolled. In the ablation group, 63.1% of patients in comparison to 21.7% in the medical therapy group ($P < .001$) were in sinus rhythm at the 60-month follow-up visit. The adjudicated rate of recurrence of AF in the ablation group among those who had actually undergone ablation and who were followed for up to 60 months was 50.0% (75 of 151 patients), with an average of 1.3 ± 0.5 ablation procedures per treated patient.¹⁶

In agreement with this randomized study, a subgroup analysis of patients with HF from the largest randomized controlled trial to date, Catheter Ablation Versus Antiarrhythmic Drug Therapy, was recently analyzed in a systemic review and showed that catheter ablation was associated with all-cause mortality benefit, improvement in ventricle function, and reduction in cardiovascular hospitalization and AF recurrence.^{18,19}

Lifelong maintenance of rate and rhythm control is crucial in these patients as recurrence of the arrhythmia is associated with the rapid development of symptomatic HF and worsening of left ventricular systolic function.¹ For this reason, for patients who develop HF as a result of AF, both the 2013 American College of Cardiology Foundation/American Heart Association guideline for the management of heart failure and the 2019 American College of Cardiology/American Heart Association/Heart Rhythm Society guideline for the management of patients with AF, recommend nonsurgical rhythm control strategies.^{20,21}

Despite improvements in technology and techniques, catheter-based ablation outcomes remain relatively poor, particularly in patients with chronic AF. In a study of 255 patients who underwent catheter ablation, of whom 43% had paroxysmal AF, the AF-free survival after a single ablation procedure was 32% for the overall cohort at 10 years (39% for paroxysmal vs 24% for nonparoxysmal AF [$P = .001$]). Allowing for multiple catheter ablations in those with failure improved the AF-free survival to 52% at 10 years (61% paroxysmal vs 44% nonparoxysmal [$P = .002$]).²² Several other studies have reported early- and midterm success rates after catheter ablations with equally disappointing results.^{23,24}

SURGICAL ABLATION

Owing to these disappointing results of catheter ablation, surgical ablation is generally the only treatment alternative to atrioventricular nodal ablation with permanent pacemaker implantation in symptomatic patients who are refractory to medical and catheter ablation therapy.²⁵ The most effective surgical technique for the management of AF has been the Cox maze procedure (CMP), introduced by James Cox and colleagues in 1987. The cut-and-sew version—CMP III—became the gold standard because long-term follow-up had $>90\%$ freedom from symptomatic AF.²⁶ In this procedure, surgical incisions were made in both atria to create lines of conduction block to prevent AF. However, due to its technical complexity, few surgeons adopted the procedure. In 2002, a modified version, CMP IV, was introduced by our group utilizing bipolar radiofrequency and cryoablation devices to replace most of the atrial incisions.²⁷ CMP IV is as effective as its predecessor at restoring sinus rhythm while also reducing operative morbidity and mortality.²⁸⁻³⁰ It is the only surgical operation to receive Food and Drug Administration indication for the treatment of AF. Additionally, in contradistinction to catheter ablation and more limited surgical lesion sets, CMP was found to be equally effective in patients with both paroxysmal and nonparoxysmal AF.^{29,30}

The Society of Thoracic Surgeons, The Heart Rhythm Society, European Heart Rhythm Association, and the European Cardiac Arrhythmia Society have recommended surgical ablation as a primary standalone procedure to restore sinus rhythm for patients who are refractory to class I or III antiarrhythmic drugs and/or catheter-based therapy (Class IIa, Level B, nonrandomized).^{31,32} Nonetheless, there is currently no consensus regarding the referral for surgical ablation of patients diagnosed with HF and AF. This is due to the paucity of clinical series and randomized trials in patients with HF undergoing surgical ablation. However, it can be assumed that with the higher efficacy of CMP, and its documented low morbidity and mortality, the results of the large catheter ablation trials summarized above would be applicable to the surgical ablation population, and can be used to justify a more aggressive surgical approach.

Several retrospective case series have shown improvement in LVEF after the restoration of sinus rhythm with surgical ablation in the general population of patients with AF. These studies had limited data regarding patients with severely depressed ejection and AF without structural or coronary heart disease.³³⁻³⁶ More recently, our group reported a series of patients with severely depressed LVEF $\leq 40\%$ who underwent standalone CMP IV. In this patient cohort, 85% of patients (29 out of 34) had clinical (New York Heart Association [NYHA] functional class II

or higher) HF symptoms. Restoration of sinus rhythm with CMP IV was associated with significant improvement in LVEF ($32\% \pm 8\%$ to $55\% \pm 8\%$; $P < .001$) (Figure 1, A). Additionally, patients' NYHA functional classification improved significantly from baseline to final follow-up (2.3 ± 0.8 to 1.3 ± 0.6 ; $P = .02$). At last follow-up, 91% of patients had NYHA class I or II symptoms ($P < .001$) (Figure 1, B).¹ The complications associated with surgical ablation in this patient population remained relatively low, as reported by our group and others.^{1,33-36}

In another similar study by Pozzoli and colleagues,³⁶ 39 highly symptomatic patients with reduced ejection fraction underwent standalone surgical ablation. At a mean follow-up of 29.4 ± 14.2 months, freedom from arrhythmias on or off antiarrhythmic drugs was 92% and 93% at 24 and 36 months, respectively. Ejection fraction normalized in all cases, from $51.3\% \pm 9\%$ to $61.1\% \pm 3\%$ ($P < .001$) overall, and from $37.0\% \pm 10\%$ to $60.3\% \pm 3\%$ ($P < .001$) when LVEF was $\leq 45\%$ preoperatively.³⁶

PATIENT SELECTION

Patient selection can be challenging (Figure 2). Identifying a suitable patient who can benefit from surgical ablation is extremely important in this cohort of patients. It is important to distinguish patients with reversible HF secondary to AF with or without concomitant structural or coronary heart disease (eg, tachycardia-induced cardiomyopathy), from those experiencing cardiomyopathies or other nonreversible forms of HF. At our center, all patients undergo an evaluation with echocardiography. Gadolinium-

enhanced cardiac magnetic resonance imaging (MRI) is also performed to assess for other causes of cardiomyopathy, myocardial viability, and fibrosis. If there is any abnormality on cardiac MRI or a high index of suspicion, endomyocardial biopsies are performed.¹ As discussed previously, sustained tachycardia may result in both atrial and ventricular fibrosis, which can influence the degree of ventricular function improvement.^{2,3,17} Recently, the Catheter Ablation versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction MRI study randomized patients with persistent AF and idiopathic cardiomyopathy (LVEF $\leq 45\%$) to medical treatment or catheter ablation. Randomization was done following cardiac MRI to assess the degree of LV fibrosis by late gadolinium enhancement. Compared with the medical group, the catheter ablation group had superior rhythm control and LV function improvement. However, the degree of ventricular fibrosis predicted the extent of LVEF recovery. On multivariate analysis, only the absence of late gadolinium enhancement was found to predict LVEF normalization.¹⁷ Thus, preoperative cardiac MRI should be strongly considered in all patients with a tentative diagnosis of TIC to help gauge the degree of improvement from a patient may gain from surgical ablation.

Additionally, patients with dilated cardiomyopathy should be identified. Patients with idiopathic dilated cardiomyopathy tend to have larger LV end-diastolic diameters than patients with TIC. Jeong and colleagues³⁷ reported that LVEF $\leq 45\%$ and LV end-diastolic dimension ≤ 61 mm is predictive of TIC with a sensitivity of 100% and a specificity of 71%. Furthermore, in patients with

FIGURE 1. Improvement in left ventricle (LV) function (A) in patients with a left ventricular ejection fraction (LVEF) $\leq 40\%$ or less at a median follow-up of 22 months after the standalone Cox-maze IV procedure. Left ventricular function improved from $32\% \pm 8\%$ to $55\% \pm 8\%$ (95% confidence interval, 0.51-0.58; $P < .001$). Improvement in New York Heart Association (NYHA) functional class (B) following the stand-alone Cox-maze IV procedure. At late follow-up, 30 of 33 patients (91%) had NYHA functional class I or II symptoms ($P < .001$). Reproduced with permission.¹

FIGURE 2. Management of patients with atrial fibrillation (AF) and heart failure (HF) at our institution. *CHA₂DS₂-VASc*, CHF or LVEF $\leq 40\%$, Hypertension, Age ≥ 75 , Diabetes, Stroke/TIA/Thromboembolism, Vascular Disease, Age 65 - 74, Female; *HAS-BLED*, Hypertension, Abnormal Liver or Renal Function, Stroke, Bleeding, Labile INR, Elderly (Age > 65), Drug or Alcohol; LAA, left atrial appendage; AV node, atrioventricular node; LGE-CMRI, late gadolinium enhancement cardiac magnetic resonance imaging; CMP-IV, Cox-maze IV procedure.

LVEF $< 30\%$, LV diastolic dimension ≤ 66 mm is predictive of TIC with a sensitivity of 100% and a specificity of 83%.³⁷ Lastly, when in doubt, medical management should be initiated, and cardioversion should be considered. If LVEF improved shortly after the restoration of sinus rhythm and when the rate is more adequately controlled, the diagnosis of TIC is more likely, and the patient is much more likely to benefit from surgical ablation.^{5,34} Patients with irreversible causes of HF (eg, LV fibrosis, amyloidosis, and ischemic and/or dilated cardiomyopathy) should not

be offered stand-alone surgical ablation. Despite the restoration of sinus rhythm, LV function often will not recover in these patients.

CONCLUSIONS

Given the exceptional outcomes of CMP, it should always be considered as an option in treating patients with AF and HF. When performed correctly, in selected patients with HF, it provides reversal of AF-related cardiomyopathy with excellent outcomes, symptomatic relief, and negligible

risk. Additionally, CMP IV is a better alternative to atrio-ventricular nodal ablation with permanent pacemaker implantation. The latter, although effective in controlling the ventricular rate, does not improve LVEF and exercise capacity as effectively as treatments that restore sinus rhythm.²⁵ Considering the excellent late outcomes of CMP, with more than 80% of patients free from recurrent AF at 5 years,^{38,39} the positive results from the catheter ablation versus medical management trials in the HF population, such as Catheter Ablation for Atrial Fibrillation with Heart Failure, should be translatable to the surgical population. Moreover, given the other potential long-term benefits of CMP IV, including increased overall survival and stroke reduction, concomitant surgical ablation should be considered in this surgically high-risk population, despite the longer operative time.^{1,30,39}

Although there have been only a few retrospective studies reporting the outcomes of surgical ablation for AF in patients with HF, it is our opinion that future guideline committees need to consider the addition of CMP IV to their recommendations for the management of patients with AF and HF who are undergoing cardiac surgery for another reason—or as a standalone operation in carefully selected patients. Although we need to create a better evidence base for surgical ablation in this population through the performance of prospective, multicenter clinical trials, there are ample published data establishing the important role of ablation in patients with AF and HF. Surgeons need to be aware that HF and the presence of TIC is a strong indication for proceeding with AF ablation in properly selected patients.

Conflict of Interest Statement

Dr Damiano has worked as a speaker and received research funding from AtriCure; as a consultant for Medtronic; and as a speaker for LivaNova, Inc, and Edwards Lifesciences. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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