Heart Failure, Atrial Fibrillation, and Catheter Ablation

Are We There Yet?*

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Contemporary cardiological practice places great emphasis on the availability of an evidence base to justify and refine indications for treatment. This is particularly apposite to the field of catheter ablation for atrial fibrillation (AF), where almost 2 decades of research at an increasingly frenetic pace has delivered us a potentially curative treatment in carefully selected patients. In drug refractory patients, there is now consensus that catheter ablation is recommended in paroxysmal AF, reasonable in persistent AF, and might be considered in longstanding persistent AF (1,2). It is also deemed reasonable to consider catheter ablation in all AF patient groups before a trial of drug therapy (2).

Heart failure (HF) and AF are often referred to as the twin epidemics of cardiovascular disease and frequently coexist in the same patient. Robust epidemiological and pathophysiological evidence clearly implicates AF in the development and/or exacerbation of left ventricular dysfunction, whereas conversely, HF promotes atrial electrical and structural change that serves to facilitate the perpetuation of AF, once initiated. For the arrhythmia, the therapeutic goal would seem self-evident—to seek to prevent or reverse the development of AF in all patients with HF and in particular in those for whom no identifiable cause has been found. Nevertheless, well-designed and executed studies of rhythm versus rate control therapy in normal left ventricular function (3) and HF patients (4) have not demonstrated an important advantage in favor of the former, citing the potential dangers of antiarrhythmic medication as a sink for any beneficial effect of sinus rhythm restoration. It is against this heartscape that many electrophysiologists see a potentially key role for catheter ablation as an important option for antiarhythmic drug-free rhythm control.

There are precious few prospective randomized controlled trials in the field of AF ablation, with our practice influenced greatly by well-executed cohort experiences in patients with HF, many of which demonstrate a positive impact of catheter ablation on outcome measures such as ejection fraction (5). The 3 randomized studies that do exist offer starkly different experiences—Hsu et al. (6) demonstrated convincingly that AF ablation resulted in a remarkable improvement in ejection fraction; Khan et al. (7) demonstrated superiority of ablation over atrioventricular node ablation and biventricular pacing in a mixed paroxysmal and persistent AF population when using a composite endpoint of ejection fraction, 6-min walk distance, and Minnesota Living with Heart Failure Questionnaire score; whereas a more recent smaller study by MacDonald et al. (8) did not show any impact on magnetic resonance-derived ejection fraction, N-terminal pro–B-type natriuretic peptide, 6-min walk, or quality of life.

In this issue of the Journal, Jones et al. (9) report their findings from a single center, prospective randomized trial of catheter ablation versus stringent rate control in an HF population with persistent AF. Over almost 4 years, they were able to randomize 52 patients who met the demanding inclusion criteria of persistent AF, New York Heart Association functional class II to IV symptoms on a regimen of optimal HF therapy, and left ventricular ejection fraction $\leq 35\%$, while excluding patients with cardiovascular implantable electronic device insertion within 6 months. In addition to conventional cohort characterization measures, the investigators included B-type natriuretic peptide, radionuclide ventriculography, cardiopulmonary exercise testing, Minnesota Living with Heart Failure Questionnaire score, and a 6-min walk test. Rate control was achieved in 88% of patients by 3 months, and 24 of 26 patients in the rate control group remained in AF throughout the study, representing a true test of rhythm versus rate control. Although a stepwise catheter ablation strategy was employed, the rate of redo procedures was substantially lower than that previously reported for this technique (10), perhaps related to the intentionally short follow-up of 12 months—by which time 69% of patients were arrhythmia-free after a single ablation and off medication regimen, climbing to 92% after multiple procedures.

Although these figures are impressive, of greater relevance perhaps is the attention paid to the physiological impact of catheter intervention. By the end of follow-up, the primary endpoint of peak oxygen consumption had increased significantly in the ablation arm and decreased in the rate control arm, with close attention paid by the investigators to exclude any influence of subject motivation by incorporating the respiratory exchange ratio to standardize exercise effort. For each of the secondary endpoints, a catheter ablation strategy repeatedly showed a more markedly positive response from baseline than a rate control
strategy although not always reaching statistical significance. Therefore, the investigators can reasonably conclude that rhythm control by catheter ablation in their laboratory is more effective than good rate control in the studied population of patients with medically optimized HF.

How readily can these results be generalized to the ever-increasing population of patients with symptomatic HF and AF? The investigators openly acknowledge some important limitations of their study. For example, their small cohort is young, and two-thirds of patients have a nonischemic etiology for their HF. Over the course of the trial, only 52 of 101 patients referred for participation underwent randomization, with no mention of the denominator of the HF population from which the studied cohort was recruited. It might be seen as unusual that neither a failed trial of cardioversion nor inadequate rate-control were specified as inclusion criteria. It is common clinical practice to offer a therapeutic trial of sinus rhythm by means of cardioversion or to demonstrate an inability to achieve adequate pharmacological rate control before embarking on what is likely to be more than 1 catheter ablation procedure in such a challenging population. In fact, only 14 of 26 (54%) of the ablation arm and 15 of 26 (58%) of the rate control arm had undergone a previous cardioversion. Similarly, 14 of 26 (54%) rate control patients were already rate-controlled at baseline and required no further change in medication throughout the study. In defense of the investigators, however, this was designed as a trial of rate versus rhythm control as pre-specified strategies for symptomatic patients with no further treatment needed for adequately rate-controlled patients at inclusion.

As always, the issue of procedural complications merits emphasis. These were very extensive ablation procedures (333 ± 61 min), with high fluoroscopy (80 ± 19 min) and ablation (82 ± 20 min) times. One patient required a sternotomy for tamponade, and 3 other significant complications were reported, giving a reported complication rate of 4 in 30 procedures (13%). Although the reported maintenance of sinus rhythm at 1 year is high, gradual attrition will likely occur, as has been widely reported for patients with persistent AF (11), necessitating a very frank and thorough discussion with patients at the outset about the potential risk and unproven long-term benefits of such an aggressive interventional strategy.

Conventional rhythm control strategies have not been shown to offer a mortality benefit over rate control in HF (4). A recently published substudy of the AF-CHF (Atrial Fibrillation and Congestive Heart Failure) trial demonstrated a modestly greater improvement in quality of life scores with a rhythm compared with rate control strategy and a greater likelihood of New York Heart Association functional class improvement associated with a higher prevalence of sinus rhythm (12). The electrophysiology and HF communities eagerly await the outcome of the CASTLE-AF (Catheter Ablation Versus Standard Conventional Treatment in Patients With Left Ventricular Dysfunction and Atrial Fibrillation) and RAFT AF (A Randomized Ablation-based Atrial Fibrillation Rhythm Control Versus Rate Control Trial in Patients With Heart Failure and High Burden Atrial Fibrillation) trials, both due to complete in 2016, and both of which address the role of catheter ablation versus medical therapy for management of AF in substantially larger numbers of HF patients than reported in the current study. Although this is a challenging group of patients, it is also potentially the group that stands to gain the most in terms of morbidity and perhaps even mortality. In the meantime, the advice must remain to assess each HF patient on an individual basis when considering a nonpharmacological rhythm control strategy. The study by Jones et al. is to be enthusiastically commended for extending our evidence base to persistent AF and in particular for embracing a study design that has clearly been jointly informed by experts in electrophysiology and HF medicine.

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