EDITORIALS

# Paradigm Shift for Treatment of Atrial Fibrillation in Heart Failure

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Congestive heart failure and atrial fibrillation often coexist. Up to 50% of patients who present with new-onset congestive heart failure have atrial fibrillation; conversely, among those patients with new-onset atrial fibrillation, close to one third have congestive heart failure.[1] It is difficult to sort out which is cause and which is effect, yet it would seem logical that being in atrial fibrillation is not ideal for patients with congestive heart failure and that maintenance of normal sinus rhythm would probably improve functional status and possibly reduce mortality in this population.

In the absence of congestive heart failure, the data to support the clinical benefits of maintenance of normal sinus rhythm in patients with atrial fibrillation as compared with a rate-control strategy are sparse.[2] In patients with congestive heart failure, randomized, controlled trials (RCTs) of amiodarone and dofetilide have shown an increase in the time for normal sinus rhythm but failed to show a benefit in left ventricular ejection fraction (LVEF) or a decline in the rate of hospital admissions for heart failure or in mortality.[3,4] More recently, a number of small RCTs conducted in patients with congestive heart failure with atrial fibrillation have shown the superiority of ablation over antiarrhythmic drugs in the maintenance of normal sinus rhythm and in outcomes such as improved performance in a 6-minute walking test, LVEF, and quality of life.[5,6] Results even hint that hospitalization rates and mortality may decline.[7]

In this issue of the *Journal*, Marrouche et al. present the data from a large trial of ablation for atrial fibrillation in patients with heart failure.[8] Patients with atrial fibrillation, New York Heart Association class II, III, or IV heart failure, and a left ventricular ejection fraction (LVEF) of 35% or less were randomly assigned to catheter ablation for atrial fibrillation (179 patients) or pharmacologic control (medical therapy) (184 patients). After a median follow-up of 37.8 months, patients who were assigned to ablation were less likely to meet the primary composite end point of death from any cause or heart-failure–related admission or the secondary end points, which included death from any cause and death from cardiovascular disease. At 60 months, the LVEF had increased by 8% in the ablation group as compared with no increase in the medical-therapy group ($P=0.005$). In addition, 63% of patients in the ablation group were in sinus rhythm, as compared with 22% of those in the medical-therapy group ($P<0.001$).

The strengths of this trial are the large number of patients enrolled, which allowed for reasonable power to detect an end point of death, the low crossover rates, the excellent adherence to guideline-directed medical therapy, and the continuous monitoring for atrial fibrillation. In addition, the end points of death and admission for heart failure are both objective and clinically relevant. Further, the secondary end points of walking distance at 6 minutes and LVEF allowed for a full characterization of response. Finally, the relatively long follow-up period allowed for the detection of the benefit related to mortality, a finding that was not apparent until year 3.

These findings must be interpreted conserva-

tively given the relatively small sample size, specific criteria for patient selection, lack of blinded randomization and treatment allocation, and the fact that the procedures were performed by experienced operators in high-volume medical centers, a circumstance that probably reduced complication rates. Despite these limitations, this trial builds on and adds to the accumulating evidence that the use of ablation to maintain normal sinus rhythm in patients with atrial fibrillation and congestive heart failure not only results in fewer admissions for heart failure and decreased mortality but also leads to reverse remodeling, as indicated by an improvement in LVEF.

In the current trial, it is notable that ablation did not completely eliminate atrial fibrillation in all patients but rather decreased the time in atrial fibrillation to roughly 25%, whereas the time in atrial fibrillation among patients who received medical therapy was 60%. This decrease in the burden of atrial fibrillation — as opposed to its elimination — has also been observed in other trials in which there were positive outcomes for the use of ablation to treat atrial fibrillation in patients with congestive heart failure. In these trials, the atrial fibrillation burden after ablation remained at 20 to 30%.[5,7,9] Together these trials show that "cure" of atrial fibrillation is not necessary to improve outcomes in heart failure. A reduction in the amount of time in atrial fibrillation may be sufficient for clinical benefit. Longer-duration normal sinus rhythm may improve outcomes by means of a number of mechanisms, including better average rate control, regularity, and greater atrial emptying, all of which translate into improved cardiac output. In addition, ablation for atrial fibrillation may have a beneficial effect on the autonomic nervous system, an effect that may improve outcomes irrespective of atrial-fibrillation response. Ablation may also homogenize the spotty atrial fibrosis caused by atrial fibrillation. A better understanding is needed as to why a decrease in density, but not complete elimination of atrial fibrillation, is sufficient for reverse remodeling. Such an understanding may lead to additional therapeutic measures in these patients.

Where to now? Can we increase the success of the ablative procedure, and would that increase translate into further improvement in reverse remodeling and further reductions in rates of heart failure and mortality? If a reduction in the density of atrial fibrillation to 25% improves outcomes in this trial, what could be accomplished with reductions to 5% or even with elimination? All that is for the future. For the present, it seems reasonable to be more aggressive in offering ablation for atrial fibrillation in patients who also have congestive heart failure.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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DOI: 10.1056/NEJMe1714782