Role of cardiac resynchronization therapy and atrioventricular junction ablation in patients with permanent atrial fibrillation

Károly Kaszala and Kenneth A. Ellenbogen*

Department of Medicine, Virginia Commonwealth University School of Medicine and the Hunter Holmes McGuire VA Medical Center, Richmond, VA, USA

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This editorial refers to ‘Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial†', by M. Brignole et al., on page 2420

State of the art treatment of atrial fibrillation in an individual patient may follow different, complex avenues depending on symptoms, clinical circumstances, and patient preferences. Management may become particularly challenging when atrial fibrillation is associated with other co-morbidities, especially heart failure. Epidemiological studies have shown that heart failure with New York Heart Association (NYHA) functional class II–IV may be complicated by atrial fibrillation in up to 50% of cases, and this association carries a worse prognosis. In these cases, while ventricular rate control may be the first objective based on results of large, multicentre studies, adequate doses of vasoactive medications may not be tolerated and antiarrhythmic medications or ablation to help with rhythm control may be contraindicated or ineffective. In these challenging cases, atrioventricular (AV) junction ablation and cardiac pacing is an alternative treatment option. AV junction ablation, by slowing and regularizing the ventricular rate, has been shown to improve symptoms, quality of life, and cardiac function, as judged by both physiological and structural measurements. It has been recognized that while rate control is achieved with AV junction ablation, ventricular dyssynchrony caused by chronic right ventricular (RV) pacing may adversely affect heart function and impede the salutary effects of rate control and rate regularization. It has been suggested that biventricular pacing may further improve exercise capacity, especially in patients with reduced LV function.

Data from large clinical trials have indicated that cardiac resynchronization therapy (CRT) improves heart failure symptoms and exercise tolerance, halts the progression of cardiomyopathy, and decreases heart failure hospitalization and mortality in NYHA class II–IV patients with left ventricular ejection fraction (LVEF) ≤35%, and a QRS duration >120–130 ms. However, most landmark trials only studied patients in sinus rhythm. AV filling cannot be controlled during atrial fibrillation, and biventricular pacing percentage is often suboptimal because the ventricular rate may increase above the programmed pacing rate, limiting the benefits of CRT. Furthermore, a study from Steinberg et al. has shown that pacing counters frequently overestimate the percentage of biventricular pacing in patients with atrial fibrillation. More recently, observational data from a large European registry showed that during a median follow-up of 34 months, mortality was similar in patients who underwent CRT regardless of the presence of underlying atrial fibrillation as long as biventricular pacing was maintained over 85%. A subgroup of patients, who underwent AV junction ablation in order to achieve this goal, had improved symptomatic relief and survival compared with those who were rate controlled using medical therapy. Small, prospective and retrospective studies as well as a meta-analysis drew similar conclusions, whereas other studies suggested that AV junction ablation may not be necessary. Evidence from randomized, controlled trials to guide therapy, however, remains scarce, and the role of AV junction ablation in CRT has not been assessed. All this information has led to the need for a prospective evaluation of this important issue.

The study by Brignole et al. is a welcome and important addition to our understanding of CRT in atrial fibrillation. The Ablate and Pace in Atrial Fibrillation trial recruited patients who were referred for AV junction ablation either for treatment of symptomatic atrial fibrillation or for a rate control strategy as part of CRT implantation for heart failure. A total of 186 patients were randomized to RV or biventricular pacing following AV junction ablation. The choice of implantable device back-up was left to the discretion of the implanter and was utilized in 67% of patients with EF ≤35% and 14% with EF >35%. RV leads were placed in...
the RV apex, and the target LV lead position was the posterolateral wall (91%). LV to RV timing was optimized in all patients using tissue Doppler imaging. The primary objective of the study over a median follow-up of 20 months was to compare the composite endpoint of death or hospitalization due to heart failure or worsening heart failure between the pacing groups. The primary composite endpoint (‘clinical failure’) occurred in 11% in the CRT group and in 26% in the RV group [hazard ratio 0.37, 95% confidence interval (CI) 0.18–0.73, \( P = 0.005 \)]. Similar benefit was shown in subgroups who would be considered eligible for CRT as a class IIa indication by the current European guidelines and recommendations \(^1\) \((\text{LVEF} \leq 35\% ; \text{QRS} \geq 130 \text{ ms or paced}; \text{NYHA class} \geq III)\) as well as in those (65–75% of enrolled patients) who fell outside of these guidelines.

How should we interpret these results and should we change our strategies for management of atrial fibrillation? The study by Brignole et al. represents an important contribution to the literature. It provides further evidence that CRT is effective in patients with atrial fibrillation and provides further support for AV junction ablation with CRT in control of symptomatic heart failure and atrial fibrillation. There are several cautionary notes to consider before the proposed strategy is widely accepted and disseminated. While the patient selection criteria mirror common clinical situations, the patient population was diverse and some of the conclusions may not hold true for all subgroups of the study population. Particularly important to note is that while the study was initiated before the current guidelines were published, 46% of all patients had abnormal LV function at baseline (EF < 35%) and the majority of these patients would currently be treated with a CRT device. This may have influenced the treatment effect, and it is conceivable that most events occurred in this higher risk group. Moreover, although a clinically significant composite endpoint was chosen, events were driven primarily by ‘soft’ heart failure endpoints. As the study was not powered to assess the differences in survival, future multicentre adequately powered randomized trials should examine the effects on mortality and confirm the main findings of the study, especially in patients with preserved LV function. Another limitation is that widespread reproducibility and value of tissue Doppler imaging in guiding RV–LV timing has been heavily debated. Finally, long-term consequences of irreversible AV junction ablation should be considered which may not be appropriate for all patient subgroups. Our approach to these patients is summarized in Figure 1.

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**References**


