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EDITORIAL COMMENT

Resynchronization therapy in patients with atrial fibrillation: What are the results?☆

Terapêutica de ressincronização em doentes com fibrilhação auricular: que resultados?

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Cardiac resynchronization therapy (CRT) is an established treatment for heart failure (HF) with left ventricular (LV) dysfunction and contraction dyssynchrony associated with intraventricular conduction disturbance, particularly complete left bundle branch block. In CARE-HF,[1] the largest published study, in 813 patients and with a mean follow-up of 29 months, there was a reduction in the primary endpoint (death from any cause or hospitalization for a major cardiovascular event) from 55% in the control group to 39% in the CRT group (hazard ratio 0.63, $p<0.001$) and in overall mortality from 30% to 20% (hazard ratio 0.64, $p<0.002$). Compared to medical therapy, CRT also reduced end-systolic volume and severity of mitral regurgitation, increased LV ejection fraction (LVEF), and improved symptoms and quality of life. These findings, confirmed in various studies[2] and meta-analyses,[3,4] led medical societies to classify CRT as a class I recommendation, level of evidence A.[5]

In clinical practice HF is frequently associated with atrial fibrillation (AF), the incidence of which is proportional to the severity of functional class and the degree of LV dysfunction. However, patients with AF are underrepresented in studies on CRT and there is therefore less evidence of its benefit in this population. Theoretically, in the presence of AF, CRT is likely to be less effective, since it is impossible to optimize the atrioventricular delay, and the chronotropic response needs to be carefully controlled in order to obtain a high percentage of biventricular pacing (ideally over 98%). A substudy of the RAFT trial[6] showed that in patients with AF, implantation of a CRT defibrillator was not associated with benefits in terms of morbidity or mortality compared to an implantable cardioverter-defibrillator. However, only half the patients in the study had biventricular pacing $\geq$90% of the time and only a third had $\geq$95% biventricular pacing. Accordingly, the guidelines give CRT a class IIa recommendation, level of evidence B, for AF patients, with the express reservation that measures should be taken to ensure a high percentage of biventricular pacing (generally by atrioventricular [AV] node ablation) or to achieve reversion to sinus rhythm (SR).[5]

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The study by Abreu et al.[7] published in this issue of the *Journal* is another contribution to our understanding of the role of CRT in the treatment of patients with HF and AF. It is a prospective study of 101 patients treated by CRT that compares baseline clinical characteristics and response to CRT at three and six months in two groups: 66 patients in SR and 35 in AF. The authors defined three types of therapeutic response: clinical (improvement of at least one functional class), echocardiographic (a minimum absolute 5% increase in LVEF), and functional (an absolute increase of >1 ml/kg/min in peak oxygen consumption [VO_2max] on exercise testing). Patients in the AF group were older and had larger atrial volume and lower baseline tolerance on exercise testing and lower VO_2max. In this group, only 5.7% underwent AV node ablation to achieve >95% biventricular pacing. At six-month follow-up, both groups had benefited from CRT, with similar clinical and echocardiographic improvements, while those with AF showed greater functional improvement, probably because their baseline functional capacity had been very low. The SR group also presented reductions in ventricular mass and left atrial size. These results indicate that CRT is of significant benefit in patients with AF, leading to symptomatic improvement, positive ventricular remodeling and increased functional capacity.

Notwithstanding these conclusions, some aspects of the study that are not fully clarified or are debatable require closer analysis, particularly the low proportion of patients who underwent AV node ablation to achieve appropriate chronotropic control, which was significantly lower than in most published studies,[3] in which it ranges between 20% and 100%. According to Abreu et al.,[7] the percentage of biventricular pacing was determined by device counters and by ECG and Holter in doubtful cases. However, it has been reported that in the context of AF, device counters may give inaccurately high readings due to fusion and pseudofusion beats, thereby overestimating the percentage of biventricular pacing. Several studies have shown that AV junction ablation reduces mortality in these patients compared to pharmacological therapy alone.[8,9]

Furthermore, although this was a ''real-life study'', no information is provided on complications arising from device implantation, either acute or during follow-up, or the type of programming used in either the AF or the SR groups. Also, no details are given of how pharmacological therapy was optimized, only that the AF group were prescribed beta-blockers, digoxin or amiodarone when necessary to ensure chronotropic control.

As stated above, the incidence of AF in HF patients is directly related to clinical severity, and it is thus plausible that the AF group had more advanced disease and hence cardiac dysfunction. For such patients, new methods for optimizing CRT have been described, including triple-site pacing, in which two sites in the right ventricle (the high septum and the apex) are stimulated as well as the left ventricle, and which has shown benefits both acutely[10] and during follow-up,[11] including achieving a significant percentage of super-responders.

In conclusion, CRT is useful and effective in patients with permanent AF, with similar benefits to those seen with patients in SR, as shown in the study published here. We also believe that it is especially important to obtain optimal chronotropic control in these patients by means of AV node ablation, which helps achieve a high percentage of biventricular pacing, as well as to adopt new CRT technologies that will ensure the best possible clinical response.

Conflicts of interest

The author has no conflicts of interest to declare.

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