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EDITORIAL COMMENT

Reversing the Substrate for Atrial Fibrillation With CRT?*

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The importance of atrial function is progressively and rapidly being recognized in current cardiovascular research and clinical practice. It has been widely acknowledged that atrial fibrillation (AF) imposes a poor prognosis among patients with heart failure and that these conditions are often concomitant and indeed directly predispose one to the other (1). Recently developed tools have allowed us to improve the evaluation of atrial function and understand its implications in early heart failure or even in normal hearts (2). Accordingly, several studies have shown the central role of atrial (dys)function in the occurrence of symptoms and prognosis in cardiovascular disease.

The particular subgroup of patients with heart failure receiving cardiac resynchronization therapy (CRT) have worse outcomes when AF is present, with a lower rate of clinical and volumetric response in comparison with those in sinus rhythm (3). Nonetheless, appropriately selected patients benefit in relation to outcomes and reverse remodeling (4), if adequate pacemaker capture can be ensured by either antiarrhythmic drugs or atrioventricular node ablation (5).

Compared with those with diastolic dysfunction but no overt heart failure, patients with heart failure with either preserved or reduced left ventricular ejection fraction (LVEF) show reduced atrial strain, despite having similar left atrial (LA) size (6). Atrial dysfunction is even present in patients with sinus rhythm and a first episode of clinical heart failure; therefore, it seems likely that atrial dysfunction may contribute to symptom onset among patients with preserved LVEF (7). In patients with heart failure and preserved LVEF, AF and loss of atrial function have been also related to worse clinical outcome (8), impaired exercise capacity, and adverse cardiovascular outcomes (9).

SEE PAGE 99

In this issue of *iJACC*, Sade et al. (10) provide further evidence on the potential benefits of CRT beyond left ventricle (LV) reverse remodeling and clinical improvement, showing also potential prevention and reduction in the progression of AF. These researchers showed that CRT had favorable effects on LA size, reservoir, and contractile function and that this effect was independently related to AF-free survival, irrespective of LV reverse remodeling. These findings are in accordance with previous reports that CRT induced improvement in LV diastolic function and LA volumetric and functional reverse remodeling in patients with clinical improvement without ventricular reverse remodeling (11,12). Although the reported relative independence of improved atrial function from reverse remodeling of the LV is not surprising, it adds additional evidence of the hemodynamic benefits of synchronizing the mechanically uncoupled heart with CRT.

Cardiac remodeling includes the distortion of normal geometry, enlargement of cardiac chambers, and substitution of normal tissue by collagen or fibrotic tissue. The fundamental cause of cardiac remodeling is a response to myocardial contractile dysfunction to maintain stroke volume and adapt to overload. In the atria, remodeling might be induced by indirect chronic overload associated with elevated filling pressures. The remodeled atrium finally acts as the necessary substrate for the origin and for the perpetuation of AF. The work of Sade et al. (10) suggests that if the trigger for atrial remodeling is reversed (by improving filling pressures), and the remodeling process is still in a reversible stage, this

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tendency to proarrhythmia may be cured or at least delayed. LA functional improvement is associated with AF-free survival after CRT and correlates with long-term event-free survival after CRT, independent of LV volume response.

The development of deformation imaging—particularly speckle tracking—has enabled a better means of analysis and understanding of atrial function. As also mentioned by Sade et al. (10), atrial strain might be a more straightforward marker of structural changes in the atrial myocardium and therefore more sensitive than isolated geometric or size-based parameters. This fact has 2 implications among patients with heart failure who are potential candidates for CRT. First, it may be helpful to detect subclinical atrial dysfunction among patients consulting for heart failure symptoms, and second, it may help to define whether atrial changes are still reversible. Potentially, the recognition of contractile atrial reserve might be used to justify intensification of therapies aimed at maintaining sinus rhythm in these patients.

It might be anticipated that the assessment of atrial function will increasingly form part of clinical decision-making in patients with heart failure and in those with unexplained shortness of breath. A better understanding of pathophysiological processes will certainly lead to improved diagnosis and management of patients that will ultimately translate to better outcomes. We have the tools now, but we need to apply them and integrate the new parameters with our existing knowledge.

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