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EDITORIAL COMMENT

Atrial Secondary Mitral Regurgitation

Often Overlooked, But Never Forgotten*

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Functional or secondary mitral regurgitation (SMR) is typically characterized by normal mitral structure in the setting of impaired left ventricular (LV) systolic function and/or dilatation. It is regarded as a predominantly ventricular problem, the result of imbalanced tethering forces and reduced closing force of the LV. However, this classic understanding of SMR could not explain the etiology of mitral regurgitation (MR) in a growing subgroup of patients with atrial fibrillation/ flutter (AF) and normal LV function or heart failure with preserved ejection fraction (1,2). Unlike patients with SMR of ventricular origin, these patients usually have normal mitral leaflet motion (Carpentier Type I), as well as preserved LV size and function. In these patients, SMR is believed to be of atrial origin, as evidenced by marked left atrial (LA) dilatation, impaired LA function, and mitral annular dilatation. It is thus termed atrial SMR, as opposed to simply "SMR," which implies MR with restrictive leaflet motion (Carpentier Type IIIb) and LV dysfunction.

The term "atrial SMR" was first coined by Gertz et al. (3), who studied patients with moderate to severe degree of MR undergoing AF catheter ablation. These patients had normal LV function, which set them apart from the conventional SMR. The restoration of sinus rhythm resulted in significant MR reduction, suggesting a causal relationship between AF and MR, rather than AF being a mere confounder or consequence of significant MR.

Many subsequent studies, most in patients with AF, have established that atrial functional MR represents a unique clinical entity. Atrial SMR was present in 4% to 8% of patients with AF (3,4), and the prevalence increased with the duration of AF, up to 28% in patients with lone AF for more than 10 years (4). In an epidemiology study of community patients in Olmstead County, Minnesota, the prevalence of atrial SMR was high, at 27% among patients with isolated moderate to severe MR (5). AF and idiopathic annular dilatation were identified as the predominant etiologies of atrial SMR.

Various mechanisms of atrial SMR have been proposed. Several authors have suggested that atrial SMR in patients with AF could be mediated through annular dilatation (3,6), whereas others found that isolated mitral annular dilatation was insufficient to cause significant MR in patients with AF (4). Silbiger et al. (7) proposed the concept of atriogenic leaflet tethering, in which MR was a result of LA remodeling, displacement of the posterior mitral annulus, and tethering of the posterior mitral leaflet. Kim et al. (4) hypothesized that insufficient mitral leaflet adaptation commensurate with the degree of annular dilatation contributed to atrial SMR. Other etiologies of atrial SMR include, but are not limited to, abnormal mitral annular saddle shape and contractility.

In this issue of *iJACC*, Mesi et al. (8) presented the clinical characteristics, echocardiographic features, management options, and outcomes of patients with severe atrial SMR. The study positioned itself as the largest study to date on atrial SMR confirmed by transoesophageal echocardiogram. Its main focus was on the clinical aspects of severe atrial SMR, a selective subgroup at the advanced end of the disease spectrum, although it would have been more informative if the entire spectrum of atrial SMR (i.e., those with mild and moderate severity) were also presented, given the aim of the study was to provide clinical insights. Patients with severe atrial SMR were compared against those with severe primary MR and normal ejection fraction. Patients with functional MR

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of ventricular origin or primary MR with impaired ejection fraction were not studied.

Patients with severe atrial SMR more frequently had long-standing AF, hypertension, diabetes, diuretic use, prior nonmitral cardiac surgery, pacemaker implantation and New York Heart Association function class III/ IV symptoms at presentation compared with patients with severe primary MR. In terms of echocardiographic findings, more patients with atrial SMR had concomitant dilated right chambers, moderate to severe tricuspid regurgitation, and a raised right ventricular systolic pressure. Diastolic function and peak LA strain were worse in patients with atrial SMR compared with those with primary MR, underscoring the role of atrial function and synchrony in the development of atrial SMR.

Most patients with severe atrial SMR had predominantly central MR jet. Twenty-three percent had posteriorly directed MR jet, which was associated with a shorter posterior leaflet, increased anteroposterior annular dimension, and a larger effective regurgitant orifice area compared with those with central MR jet. Although these findings are not novel per se, they offer important clinical perspectives and real-world clinical correlations to the previously proposed mechanisms of atrial SMR (1,4).

Among patients with severe atrial SMR, 41% underwent mitral intervention. Although this figure was lower than those with severe primary MR at 84%, it is still much higher than patients in the community. In a recent study of Olmsted County patients with isolated moderate to severe MR, only 3% of patients with atrial SMR received mitral valve repair or replacement in their lifetime (5). The disparity could be due to patient selection. The study by Mesi et al. (8) included only patients with severe MR, whereas the community study comprised mainly patients with moderate MR and only 10% had severe MR (5). Also, the reason for referral for echocardiography was persistent symptoms, with 74% of the study population being symptomatic (New York Heart Association functional class ≥II) at presentation.

This study has some limitations inherent to its study design. It is a retrospective, single-center cohort study. Patients in the group that received mitral intervention and those who did not were not propensity matched, although this could be due to the small number of study patients, rendering matching technically difficult. A matched cohort would have been instructive at understanding the effect of mitral intervention on clinical outcomes. Poor outcomes in patients with conservatively treated atrial SMR could be a function of higher burden of comorbidities, rather than the result of nonintervention. Apart from mitral valve interventions, this study did not address the role of other treatment options, such as rhythm control, which have been shown to effectively reduce atrial SMR in the context of AF (5).

To date, there is no uniform diagnostic criteria for atrial SMR. Although it has mostly been described in patients with AF, many studies, including the present one, have shown that this disease entity can be present in patients with sinus rhythm and LA remodeling. Also, most studies of atrial SMR were conducted in patients with normal LV size and function, for the ease of distinguishing it from ventricular SMR. Such approach inevitably precludes patients with atrial SMR with mildly impaired systolic function or borderline dilated LV, either as a result of tachycardia-induced cardiomyopathy or volume overload from chronic severe MR. Future studies should expand on the definition and cutoff values of LA, LV, and mitral annular dimensions, as well as function for a uniform diagnosis of atrial SMR.

Thus far, the treatment options of patients with atrial SMR include that of mitral valve intervention, mainly surgical repair or replacement, and for patients with AF, rhythm control (direct current cardioversion or AF ablation). The role of heart failure therapy in the treatment of atrial SMR has yet to be determined. Given the growing prevalence of heart failure with preserved ejection fraction globally and its association with atrial SMR, HF therapy is an area of interest that warrants further research. Also requiring further study is the role of percutaneous mitral valve intervention in the treatment of atrial SMR. Currently, there is still a lack of recognition and inclusion of these patients in percutaneous intervention trials. It is therefore not surprising that only 1 patient with severe atrial SMR underwent percutaneous mitral repair in this study despite available expertise. In view of the heterogeneity of disease mechanisms, the treatment of patients with atrial SMR should be tailored individually. The goal of treatment should be multipronged, addressing both the downstream valve problem and the underlying triggers.

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