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Complexity of Defining Severe "Stenosis" From Mitral Annular Calcification

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There has been a gradual transition in the epidemiology of mitral stenosis (MS) in the Western world, with rheumatic disease in rapid decline and an increasing recognition of degenerative mitral annular calcification (MAC)–related MS in the elderly. In both diseases, the patient will present with dyspnea and an elevated transmitral gradient, but the anatomy and pathophysiology differ substantially. With the emerging advent of catheter-based therapies for the mitral valve,[1] it is clinically important to understand these differences.

RHEUMATIC MS VERSUS MAC: MORE DIFFERENT THAN THE SAME

In rheumatic MS, there is fusion of the commissures, with greatest narrowing at the leaflet tips, resulting in a funnel-shaped stenosis. In contrast, MAC primarily involves the annulus and base of the leaflets, resulting in circular narrowing that progresses from the outer annulus circumference inward, with relatively unrestricted leaflet tip motion. Therefore, in rheumatic MS, there is true leaflet impedance to left atrial (LA) emptying that is reflected in a blunted LA y descent, along with persistent diastolic separation of LA and left ventricular (LV) pressures.[2] In contrast, patients with MAC stenosis consistently have an unusually high LA v wave, and after mitral valve opening, there is a rapid y descent coupled with rapid equilibration of the LA-LV pressure gradient. These findings indicate minimal valvular impedance to flow, which suggest that factors other than inflow obstruction contribute to the elevated transmitral gradient in MAC MS.

In rheumatic MS, percutaneous mitral balloon valvotomy or surgery is highly effective in reducing LA pressure by opening the fused commissures and directly addressing the underlying pathology. In contrast, surgical replacement in MAC MS is technically challenging, and percutaneous valvotomy is not helpful because of the unrestricted leaflet tips and lack of commissural fusion. There is now an increasing interest in transcatheter valve replacement,[3,4] but we must understand the inherent differences between rheumatic MS and MAC MS before proceeding with high-risk interventions.

COMPLEXITIES OF EVALUATING THE PATIENT WITH MS

The transmitral gradient is an important parameter used to evaluate the severity of MS. In rheumatic MS, an elevated mean gradient is highly specific for severe MS and predicts symptom improvement with intervention. However, in the typical elderly patient with MAC, comorbidities are often present that are similar to those associated with heart failure with preserved ejection fraction. Thus, LV diastolic dysfunction is frequently present, which can result in a large LA

Key Words: mitral stenosis ■ valvular heart diseases

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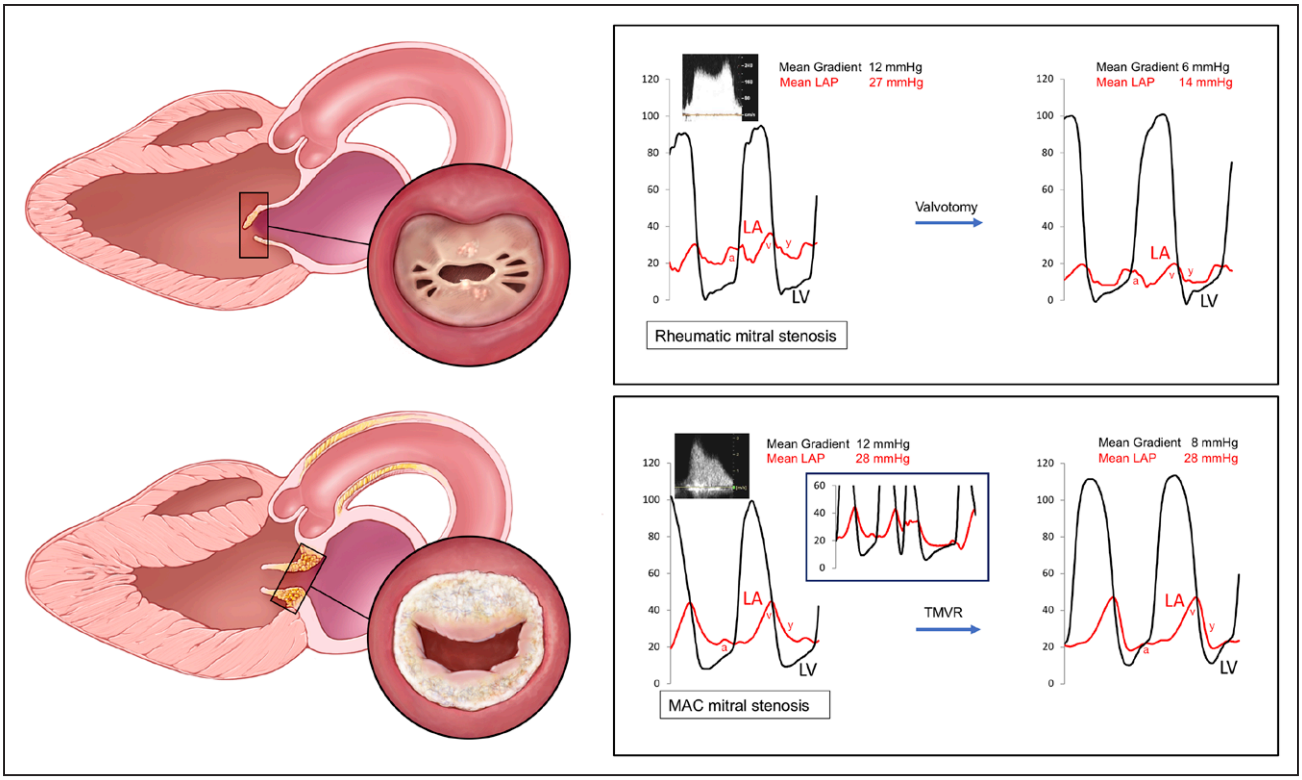

Figure. Contrast between mitral annular calcification and rheumatic mitral stenosis.
Note greatest narrowing at leaflet tips in rheumatic mitral stenosis (MS) leading to stenosis. In contrast, patients with mitral annular calcification (MAC) have annular calcification with narrowing at leaflet base and annulus, with relatively unrestricted leaflet tip motion, resulting in minimal valvular impedance. Note the brisk left atrial (LA) y descent and rapid equalization of left ventricular (LV) and LA pressure in MAC stenosis on a longer RR interval, suggestive of low valvular impedance (inset). The LV end-diastolic pressure is also elevated in MAC MS, in contrast to a normal LV end-diastolic pressure in rheumatic MS. After intervention, there is a drop in mean gradient for both rheumatic and MAC mitral stenosis; however, there is a lowering of the mean LA pressure (LAP) only after intervention for rheumatic stenosis, and no drop in mean LAP after transcatheter mitral valve replacement (TMVR) in MAC stenosis, because of a persistent large v wave in the LAP, as well as an increase in LV diastolic pressure.

v wave from abnormal atrioventricular coupling with poor operative LA compliance. This will increase the initial transmitral gradient, and if superimposed on coincidental MAC with only modest stenosis, will result in a high mean gradient, overestimating the degree of true valvular obstruction (Figure). Inertial/local acceleration forces can also result in an early diastolic inertial gradient, wherein a pressure gradient can be generated because of rapid local acceleration of blood without true valve obstruction.[5] Additionally, a stiff LA syndrome and mitral regurgitation can also independently increase the v wave and early diastolic gradient without true stenosis. Because of these MS-independent confounders to the mean gradient from both a large v wave and inertial gradient in MAC, the presence of an elevated pressure gradient alone may not imply severe mitral valvular obstruction.

The calculated valve area also presents problems in quantifying obstruction in MAC. The original Gorlin equation for calculation of valve area assumes a fixed, steady-state flow rate across the mitral valve, when in fact mitral flow is pulsatile and time varying, with most flow occurring in early diastole (particularly with a large v wave in MAC MS). Furthermore, the valve area calculation (cardiac output/$\sqrt{}$mean gradient) is heavily weighted and directly proportional to flow. Potential coexisting myocardial disease such as heart failure with preserved ejection fraction can independently decrease stroke volume and lower the calculated valve area irrespective of underlying MS severity. Therefore, neither a high transmitral gradient nor a small valve area calculation is sufficiently diagnostic for severe MS in MAC.

Doppler echocardiography is currently used to define severe stenosis when an elevated mean transmitral gradient is present. However, it is important to examine the contour of the transmitral flow velocity curve, which reflects the relative time-varying pressure gradient between the LA and LV. In rheumatic MS, there is a slow fall in velocity, reflecting the valvular impedance to passive flow, along with equal E and A velocities. Alternatively, in MAC there may be a high initial E velocity, a rapid fall in velocity, and a high E:A ratio, which raises caution about calling severe stenosis despite a high gradient. In this case, cardiac catheterization may be indicated to determine absolute LA and LV pressures, the contour of the v wave and y descent, and response to provocative maneuvers such as exercise or nitroprusside, which will highlight the relative contribution from

the mitral valve versus abnormal LV filling to the elevation in LA pressure.

TREATMENT FOR PATIENTS WITH MAC MS

In addition to the uncertainty over defining severe stenosis from MAC, there are no randomized trials showing a benefit of intervention, either with surgical or catheter-based mitral valve replacement. Although a reduction in mean gradient has been reported in an observational study,[3] ultimately the therapeutic goal is to lower the LA pressure, not the gradient. It is plausible that many of these patients have abnormalities related to heart failure with preserved ejection fraction that contribute to the elevation in exertional LA pressures (and thus symptoms of dyspnea), with possibly only a minimal contribution from inflow obstruction. Thus, even if the inflow obstruction can be relieved from mitral valve replacement, there may still be a significant elevation of LA pressure and no symptomatic benefit (Figure). Although there certainly will be a subset of patients who will benefit from intervention on the mitral valve, it is important to determine the contribution to the elevated LA pressure from the inflow obstruction versus the poorly compliant LA and LV, the latter of which will not be treated with mitral valve replacement. Other novel treatment options, such as atrial septostomy to unload the high LA pressure, may be more effective than valve replacement. Until we have further data on the direct hemodynamic benefit of these procedures, and given the prohibitive mortality and uncertain long-term benefit for intervening on these valves,[3,4] we would advocate that intervention only be performed after detailed invasive hemodynamic evaluation, and preferably within the realms of randomized clinical trials.

ARTICLE INFORMATION

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Disclosures

None.

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