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Options for Incidental Mitral Regurgitation Found During Aortic Valve Surgery for Aortic Regurgitation: An Evidence-Based Clinical Update for the Perioperative Echocardiographer

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THE COMMON ETIOLOGIES of chronic aortic regurgitation (AR) in the developed world include congenital bicuspid aortic valve, calcific aortic valve disease, and aortic root dilation.[1-3] In the developing world, chronic AR typically is due to rheumatic heart disease.[3] Although less common, infective endocarditis remains an important etiology of AR, even though its clinical presentation and microbiology have evolved.[3] Dilation of the aortic root results from pathologic processes such as dissection and aneurysm that may be due to an associated aortopathy such as Marfan syndrome.[4] Although chronic, severe AR may require aortic valve (AV) replacement, it frequently is amenable to durable repair, especially when analyzed in terms of the functional aortic annulus concept.[5] This expert review outlines the stages of and management guidelines for chronic AR as a platform for a further focus on the clinical approach to incidental mitral regurgitation in this setting because eventually this complex scenario likely will be encountered by every perioperative echocardiographer in adult cardiovascular practice.

STAGES OF CHRONIC AORTIC REGURGITATION

Chronic AR generally is a slowly progressive disease recently characterized by 4 stages (stages A to D) in the 2014 American College of Cardiology/American Heart Association (ACC/AHA) valvular heart disease guidelines.[6] The ACC/AHA stage A for chronic AR includes patients at risk for AR who may have bicuspid AV, diseases of the sinuses of Valsalva or ascending aorta, endocarditis, and sclerotic aortic valves.[6] The ACC/AHA stage B for chronic AR consists of patients with progressive mild-to-moderate AR, defined echocardiographically with respect to jet width, vena contracta, regurgitant volume, regurgitant fraction, and effective regurgitant orifice area.[6] The ACC/AHA stage C for chronic AR includes patients with severe AR who still are asymptomatic and has 2 subgroups, depending on left ventricle (LV) geometry and ejection fraction (EF). Stage C group C1 includes patients with normal LV function (LVEF $>50\%$) and mild-to-moderate LV dilation (LV end-systolic diameter <50 mm).[6] Stage C group C2 are those stage-C patients with LV dysfunction (LVEF $<50\%$) or severe LV dilation (LV end-systolic diameter >50 mm or indexed LV end-systolic diameter >25 mm/m^2).[6] The ACC/AHA stage D for chronic AR includes patients with symptomatic severe AR defined echocardiographically by the aforementioned parameters with a focus on LV function and dilation.[6] This classification of chronic AR defines the indications for AV intervention that are reviewed in the following section.

AORTIC VALVE INTERVENTION FOR CHRONIC REGURGITATION

Surgical AV intervention (repair or replacement) has been strongly recommended for stage C2 (LV dysfunction) and stage D chronic AR (class-I recommendation; level of evidence B).[6-10] Furthermore, in patients with severe AR (stages C and D), AV intervention also has been strongly recommended in the setting of cardiac surgery for another leading indication (class-I recommendation; level of evidence C).[6,11] In ACC/AHA stage C2 (LV dilation) chronic AR, AV intervention has been recommended as reasonable (class-IIa recommendation; level of evidence B).[6,11] In ACC/AHA stage B chronic AR, AV intervention has been recommended as reasonable in the setting of cardiac surgery for another reason (class-IIa recommendation; level of evidence C).[6,11] Lastly, in the setting of ACC/AHA stage C1 chronic AR, AV intervention may be considered in the setting of progressive LV dilation (LV end-diastolic diameter >65 mm) if surgical risk is low (class-IIb recommendation; level of evidence C).[6]

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The management of concomitant, incidentally discovered valvular heart disease in patients undergoing surgical AV intervention poses significant intraoperative therapeutic challenges, ranging from issues of patient consent to surgical considerations such as prolonged bypass and aortic cross-clamp times. This expert review now examines the management of incidental secondary mitral regurgitation in this setting.

MITRAL REGURGITATION

Chronic mitral regurgitation (MR) may be classified as primary or secondary.[6] In primary MR, the structural disturbance of one or more mitral valve (MV) components (leaflets, chordae tendineae, papillary muscles, annulus) results in systolic regurgitation of blood from the LV into the left atrium.[12,13] The etiologies of primary MR include mitral valve prolapse, rheumatic heart disease, infective endocarditis, cleft mitral valve, connective tissue disorders, and radiation heart disease.[6,11] In primary MR, the surgical correction of the MR is curative, demonstrating that the MR is the primary pathologic process.

In secondary chronic MR, the MV apparatus typically is normal, leading to its common alternative name, "functional MR." The primary pathologic process in secondary MR is altered LV geometry that may be due to coronary artery disease, aortic regurgitation, or idiopathic causes.[6,14] This primary LV pathologic process produces LV displacement of the papillary muscles, mitral leaflet tethering, and secondary MR (Carpentier type-III lesion).[12-15] The hallmarks of secondary MR are normal leaflet anatomy in the setting of impaired coaptation due to geometric alterations in ventricular size and sphericity. Secondary chronic MR of a significant degree also ultimately can result in pulmonary hypertension and heart failure. The therapy for secondary MR is aimed at the primary disease process, most commonly ischemic heart disease. Surgical correction of mitral leaflet coaptation in this setting is not by itself curative because the MR is only a part of the primary disease process.[16,17]

The distinction between primary and secondary MR also is important. Significant primary MR that is organic in etiology typically will necessitate surgical intervention at the time of AV intervention—the management in this scenario is clear and thus will not be discussed further because it has been discussed in depth not only in the guidelines but also in the *Journal*.[6,11-13] On the other hand, the management for incidental secondary MR in the setting of surgical AV intervention remains controversial and is the focus of the remainder of this expert review.

SECONDARY MITRAL REGURGITATION IN PATIENTS WITH SIGNIFICANT AORTIC REGURGITATION

Concomitant secondary MR in patients undergoing AV procedures often is not corrected due to an assumption that it will improve downstream in the setting of a competent AV.[18] A natural history study (n = 884) looking at the outcome of patients with secondary MR in this setting demonstrated that patients with more severe MR were older, had decreased LVEF, and experienced atrial fibrillation, all of which were significantly associated with an increased mortality risk.[19] Although secondary MR was common, it had no independent association with mortality. Patients with moderate-to-severe secondary MR in the setting of severe aortic insufficiency (AI) with an LV end-systolic diameter <45 mm were independently at significant risk for a composite outcome of heart failure, death from heart failure, and downstream mitral intervention (hazard ratio, 4.0; $p = 0.02$).[19]

In a second natural history trial (n = 756; from 1993-2007), mortality was examined as a outcome of secondary MR severity in patients with severe AR.[20] In this trial cohort, the prevalence of moderate or severe secondary MR was 45%, and there was a significant decrease in survival with increasing MR severity ($p < 0.0001$).[20] In the setting of secondary severe MR, survival was significantly increased with AV replacement ($p = 0.02$) and concomitant MV repair (hazard ratio, 0.29; $p = 0.02$).[20] The investigators concluded that severe secondary MR occured in 25% of patients with severe AR, that it independently predicted reduced survival, and that its onset should prompt AV replacement and MV repair.[20]

In a third, smaller clinical trial (n = 190; from 1993-2006; AV replacement for either aortic stenosis [AS] and/or AR), moderate secondary MR at the time of AV intervention was demonstrated to improve downstream without surgical intervention and did not independently predict downstream mortality.[21] In a fourth clinical trial of comparable size (n = 193; from 1993-2007; AV replacement for either AS and/or AR), mild-to-moderate secondary MR did not affect actuarial survival but did independently predict downstream heart failure (odds ratio, 3.8; $p = 0.012$).[22] The investigators concluded that concomitant mitral intervention was indicated in this setting to improve functional outcome downstream.[22] In a fifth clinical trial (n = 118; from 2000-2009; AV replacement for AS and/or AI), secondary MR was common, and if persistent after AV replacement, predicted diminished survival in the long term (77.8% *v* 93.1%; $p = 0.036$).[23] Multivariate analysis identified right ventricular systolic pressure as an independent predictor for persistent secondary MR after AV replacement (odds ratio, 1.037; 95% CI, 1.003-1.072; $p = 0.035$).[23] Although these trials were limited by small sample sizes and mixed AV disease populations, they tended to suggest that significant secondary MR in the setting of severe AR is clinically common and important.

In an effort to focus on secondary MR in AV replacement for severe AR, a recent dedicated analysis (n = 155; from 1996-2011) identified mild MR in 65% and moderate MR in 35% of this sample.[24] During a mean follow-up period of 4.5 ± 3.9 years, the secondary MR improved in 88% of patients. Multivariate analysis identified LV end-diastolic area reduction after AV replacement as the only independent predictor for improvement in functional MR (hazard ratio, 0.927; 95% CI, 0.881-0.977; $p = 0.004$).[24] Concomitant mitral annuloplasty did not significantly reduce the risk of persistent secondary MR after AV replacement for AR ($p = 0.35$). Although persistent secondary MR in this trial cohort did not predict lower survival, it did predict a greater risk of heart failure ($p < 0.001$).[24] The investigators concluded that secondary MR in this setting was common, but that it typically improved, except when the LV remodeling was suboptimal. In this cohort with persistent LV dilation, the investigators suggested meticulous medical management, given the additional risk for heart failure events downstream.[24]