Filling the Gap Between Guidelines and Current Surgical Practice: Is Early Surgery Justified in Patients With Asymptomatic Severe Aortic Regurgitation With Normal Left Ventricular Function?

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The optimal timing for surgery in patients with asymptomatic aortic regurgitation (AR) associated with normal left ventricular ejection fraction (LVEF ≥ 50%) remains controversial. The most recent 2014 American Heart Association/American College of Cardiology (AHA/ACC) guidelines on valvular heart disease recommend a Class II indication: patients with a preserved LVEF ≥ 50% with severe LV dilatation (LV end-systolic dimension [LVESD] > 50 mm) or indexed LVESD (iLVESD) >25 mm/m^2 (Class IIa) or LV end-diastolic dimension (LVEDD) >65 mm (Class IIb) in addition to Class I indication including symptoms and impaired LVEF <50%.[1] However, most of the studies used as the foundation for the guideline recommendations were more than a decade old and were based on relatively small sample sizes and limited follow-up periods.

Recent studies from the Mayo Clinic and the Cleveland Clinic with large patient cohorts question these guidelines. Although symptoms (Class I) are the most common indicators for AVR, they were strong predictors of all-cause mortality.[2,3] In contrast, 30-day mortality values among Class II patients[2,3] were only 0.3−0.6%, and survival benefits among these patients were extended up to 5−10 years after surgery.[2,3] Despite surgical mortality in Class II patients being reduced to very low levels, supporting the concept of earlier operations, the question remains as to how can we precisely define the optimal timing for decision-making among patients who are asymptomatic and have normal LVEF (>50%) values.[4]

In this issue of *Seminar in Thoracic and Cardiovascular Surgery*, Maeda et al clarified the short- and long-term outcomes of asymptomatic patients with preserved LVEF >50% who underwent isolated AVR for severe chronic AR. They included 162 patients in Class II who have been operated upon for 2 decades (1991−2010) and compared the outcomes between the early-stage C group (iLVESD ≤ 25 mm/m^2 and LVEDD < 65 mm [periodic monitoring recommendation]) and the late-stage C group (iLVESD > 25 mm/m^2 and LVEDD > 65 mm). In their study, AVR survival was excellent over 10 years after surgery and did not differ between the 2 groups. Overall survival of these patients was not statistically different from that of the age- and gender-matched general population of Japan. Interestingly, however, a subanalysis of their study indicated that the 10-year survival for late-stage C patients was inferior to that of the age- and gender-matched general population.[5] Since late outcomes of a majority of other studies were limited up to 10 years, their observation of inferior survival beyond 10 years in the late-stage C group is worthy of attention and provides incentives for further investigation regarding earlier surgical intervention. However, major limitations of this study include the rather small number of over 10-year survivors and missing important

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Central Message

Isolated AVR for severe AR in asymptomatic patients with preserved LV function can currently be performed with very low perioperative risk and excellent short- and long-term outcomes.

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postoperative factors including cause of death, major morbidities, reoperation-free date, and echocardiography findings. Although these factors are part of the inherent nature of a retrospective observational study, they also make it difficult to draw any definitive conclusions. Interestingly, the authors recommended AVR for a sizable number of asymptomatic severe AR patients before the introduction of the 2006 valvular heart disease guidelines, which advised that severe AR patients with advanced symptoms be referred for AVR.[6]

One critical message from the studies by the Mayo Clinic,[2] Cleveland Clinic,[3] as well as that by Maeda et al[5] is that isolated AVR for severe AR in asymptomatic patients with preserved LVEF can currently be performed with a very low perioperative risk and better short- and long-term outcomes in patients satisfying the Class II criteria or recommended for periodic monitoring. Moreover, large-scale retrospective studies from the 2 most experienced centers indicated that iLVESD was the only LV criterion linked to all-cause mortality, and the risk of death increased gradually when iLVESD reached 20 mm/m^2, a cutoff lower than that recommended by the current guidelines.[1]

These results suggest that at least modest intrinsic myocardial dysfunction occurs before significant symptoms and impairment of LVEF develop. As a result, remodeling of the left ventricle becomes irreversible, which leads to persistent myocardial dysfunction even after surgery.[7] Accordingly, further investigation is needed to determine the optimal timing for surgical referral by searching for ideal imaging conditions and sensitive subclinical markers. LV volume determinations based on cardiac magnetic resonance, transesophageal echocardiography, or computed tomography angiography may provide an accurate measurement of remodeled left ventricle size.[1,8] Reduced global longitudinal strain, abnormal gadolinium enhancement on cardiac magnetic resonance, and serum biomarkers may be useful tools for detecting early changes that may serve to identify the optimal referral timing for surgery.[9,10] Finally, larger prospective studies including intensive medical supervision, echocardiographic measurement on both the pre- and postoperative periods, and rigorous long-term follow-up may enable risk assessment for early surgery. Randomized control trials of early AVR vs watchful waiting in asymptomatic AR with preserved LV function would be desirable for determining the best treatment strategy and for providing solid data for revision of future clinical practice guidelines. Filling the gap between guidelines and current surgical practice is challenging but achievable only through a high-quality meta-analysis and prospective randomized trials.

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