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STATE-OF-THE-ART PAPER

Chronic Mitral Regurgitation and Aortic Regurgitation

Have Indications for Surgery Changed?

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The timing of surgery in patients with mitral regurgitation (MR) and aortic regurgitation (AR) continues to elicit uncertainty and considerable controversy. Some patients will incur myocardial structural changes, pulmonary hypertension, or arrhythmias before they manifest symptoms, with the risk that these adverse endpoints will not be reversible after valve repair or replacement. Imaging to assess valve morphology, severity of regurgitation, and left ventricular (LV) volume and function is firmly established, and the guidelines of the American College of Cardiology/American Heart Association and the European Society of Cardiology support this approach. However, with improvement in surgical technique and outcomes, there is momentum toward earlier intervention before patients reach class I indications of symptoms or LV systolic dysfunction, particularly in patients with degenerative MR who are candidates for mitral repair. In expert centers, mitral valve repair is achieved at low risk and with excellent long-term durability of repair, returning patients to a lifespan equivalent to that of the normal population. In AR, decision making is more complex because patients almost invariably require valve replacement. Prospective clinical trials are needed to provide the evidence base for more objective decisions regarding timing of surgery. Biomarkers and new methods to assess interstitial fibrosis and regional myocardial function have also evolved for clinical investigation and hold the promise of enhanced determination of those in whom early surgical intervention is warranted. (J Am Coll Cardiol 2013;61:693–701) © 2013 by the American College of Cardiology Foundation

Major advances in the evaluation and management of patients with valvular heart disease during the past half century have improved the survival and quality of life for patients with mitral and aortic valve disease. Enhanced diagnosis, understanding of natural history, and striking improvements in surgical valve repair and replacement have completely transformed the approach to patients with mitral regurgitation (MR) and aortic regurgitation (AR). The surgical windows have expanded to encompass both older patients with severe comorbidities and younger patients earlier in the natural history of their disease, to include even those who are asymptomatic. Rather than waiting to operate until patients are severely symptomatic and have impaired left ventricular (LV) function, which was the paradigm 50 years ago, current clinical strategies now emphasize earlier intervention in many patients before the onset of symptoms, LV dysfunction, and other adverse endpoints such as pulmonary hypertension and atrial fibrillation. These latter trends are especially pertinent in patients who have MR and AR because the chronic LV volume overload may lead to irreversible LV dysfunction before the onset of symptoms.

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The American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) practice guidelines for management of patients with valvular heart disease represent a major step toward improving and standardizing patients' quality of care (1,2). The ESC/EACTS guidelines were revised in 2012, and the ACC/AHA guidelines are currently undergoing revision. However, there are unique hurdles in developing and implementing guidelines in this field. There is a paucity of prospective clinical trials addressing management of valve disease, and the published literature primarily represents the retrospective experiences of single institutions in relatively small numbers of patients. Virtually all of the recommendations in both guidelines are based on expert consensus (Level of Evidence: C). In the ACC/AHA valve guidelines, only 1 of 320 recommendations (0.3%) was based on Level of Evidence: A data (3). It is thus remarkable that the ACC/AHA and ESC/EACTS guidelines are concordant in the majority of their recommendations.

Changes in clinical practice, with new imaging methods, greater surgical experience, and a trend toward earlier surgery in patients with regurgitant lesions, raise the question of whether the indications for surgical intervention have evolved beyond the current guidelines for some patients with valvular regurgitation. The answer clearly de-

Abbreviations and Acronyms

ACC = American College of Cardiology
AHA = American Heart Association
AR = aortic regurgitation
AVR = aortic valve replacement
CABG = coronary artery bypass graft
EACTS = European Association for Cardio-Thoracic Surgery
ESC = European Society of Cardiology
LV = left ventricular
MR = mitral regurgitation
MV = mitral valve
MVP = mitral valve prolapse
STS = Society of Thoracic Surgeons

pends on the experience of the referring cardiologist and the expertise of the surgical team. A "reasonable" Class IIa guideline recommendation has different interpretations and implications in various settings.

Degenerative MR

Class I recommendations for surgery in the ACC/AHA and ESC/EACTS guidelines (1,2) for patients with degenerative MR (predominantly mitral valve prolapse [MVP] from myxomatous disease and fibroelastic deficiency) include patients with symptoms and those with asymptomatic LV systolic dysfunction (Table 1). Because LV shortening may be enhanced in the setting of severe MR by the ability to unload into the low-impedance left atrium, LV dysfunction in severe MR is defined as an ejection fraction ≤60% or an elevated end-systolic dimension. Surgery is also reasonable (Class IIa) for patients who have pulmonary hypertension at rest or new-onset atrial fibrillation if they are candidates for mitral valve (MV) repair. Exercise testing is helpful in many situations (4) for determining if a patient is truly asymptomatic and in identifying those who develop pulmonary hypertension with exercise (>60 mm Hg) (1,2).

These indications for MV surgery are reasonable if a patient presents initially to the cardiologist with any of these findings. However, in the longitudinal management of asymptomatic patients with severe MR, would it be preferable for patients to undergo surgery before these endpoints develop, because LV dysfunction, pulmonary hypertension, or atrial fibrillation is not always reversible after surgery? This question frames the debate whether all asymptomatic patients with MVP and chronic severe MR should undergo elective MV repair. This dilemma can only be settled with a prospective randomized trial of elective MV repair versus a strategy of "watchful waiting."

Table 1 Guideline Recommendations for Surgery for Degenerative Mitral Regurgitation

Indication	ACC/AHA	ESC/EACTS
Symptomatic patients	Class I	Class I
Asymptomatic patients		
LV systolic dysfunction*	Class I	Class I
Pulmonary hypertension		
PASP >50 mm Hg at rest	Class IIa	Class IIa
PASP >60 mm Hg with exercise	Class IIa	Class IIb
Atrial fibrillation	Class IIa	Class IIa
Normal LV function, repair feasible	Class IIa	Class IIa†

This is a simplified table. See full guidelines (1,2) for complete recommendations. *Defined as ejection fraction ≤60% or elevated end-systolic diameter (≥40 mm in ACC/AHA guidelines; >45 mm in ESC/EACTS guidelines). †Specifically for patients with flail leaflet and end-systolic dimension ≥40 mm; there is a separate class IIb recommendation for such patients with left atrial volume index ≥60 ml/m^2.

ACC/AHA = American College of Cardiology/American Heart Association; ESC/EACTS = European Society of Cardiology/European Association for Cardio-Thoracic Surgery; LV = left ventricular; PASP = pulmonary artery systolic pressure.

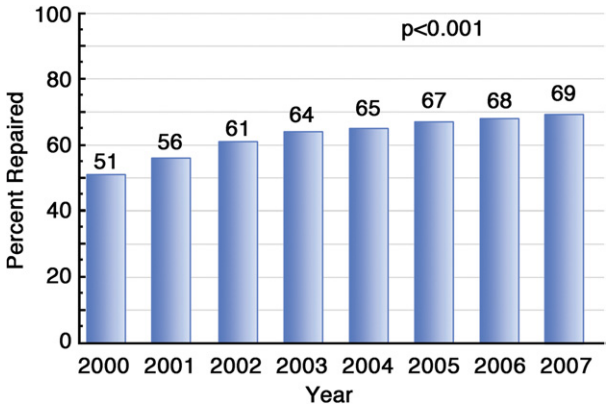

Figure 1 Mitral Valve Repair 2000 Through 2007

Percentage of patients in the Society of Thoracic Surgeons Database undergoing mitral valve repair for primary mitral regurgitation from 2000 through 2007. Data include 47,126 patients at 910 hospitals. Patients with mitral stenosis, endocarditis, previous cardiac surgery, shock, emergency surgery, and concomitant coronary artery bypass graft or aortic valve surgery are excluded. Reprinted, with permission, from Gammie et al. (5).

One concern about a broad recommendation for MV surgery in all asymptomatic patients with MVP and severe MR in the United States is that many might be subject to the long-term risks of prosthetic valves when they are excellent candidates for MV repair. According to the database of the Society of Thoracic Surgeons (STS) (5), the frequency of MV repair for patients with MR in North America, after excluding patients with mitral stenosis endocarditis, emergency surgery, previous heart surgery, and concomitant coronary artery bypass graft (CABG) or aortic valve surgery, has increased during the last decade but has plateaued at just <70% (Fig. 1). Because the great majority of such operations are for MVP or functional MR, one would anticipate that a higher percentage of patients are candidates for MV repair.

The frequency of repair is just one aspect of the issue; there are no data regarding the actual success rates of MV repair in the United States in terms of elimination of MR. Residual MR at hospital discharge has adverse implications regarding the longevity of the repair and the likelihood that additional surgery may be necessary (6). In addition, despite excellent durability of a successful repair in most patients, there is the risk of recurrent MR over the long term (6–9).

Assuming that a high-volume, high-quality surgical center can provide asymptomatic patients who have MVP and severe MR with successful repair more than 95% of the time