Mitral Valve Repair in Asymptomatic Patients With Severe Mitral Regurgitation: Pushing Past the Tipping Point

Rakesh M. Suri, MD, DPhil, Hartzell V. Schaff, MD, and Maurice Enriquez-Sarano, MD

Degenerative mitral valve regurgitation (MR) is the one of the most frequent valvular heart conditions in the Western world and is increasingly recognized as an important preventable cause of chronic heart failure. This condition also represents the most common indication for mitral surgery and is of particular interest because the mitral valve can be repaired in most patients with very low surgical risk. Historical single-center studies have supported the performance of "early mitral valve repair" in asymptomatic patients with severe degenerative MR to normalize survival and improve late outcomes. Emerging recent evidence further indicates for the first time that the prompt surgical correction of severe MR due to flail mitral leaflets within 3 months following diagnosis in asymptomatic patients without classical Class I indications (symptoms or left ventricular dysfunction) conveys a 40% decrease in the risk of late death and a 60% diminution in heart failure incidence. A 10-point rationale based on the weight of rapidly accumulating clinical data, supports the performance of early mitral valve repair even in the absence of symptoms, left ventricular dysfunction, or guideline-based triggers; when effective operations can be provided using conventional or minimally invasive techniques at very low surgical risk.

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INTRODUCTION

Degenerative mitral valve regurgitation (MR) is a frequent cause of heart valve disease in young, otherwise healthy patients (1%-3% of the Western population) and is being increasingly recognized as an important preventable cause of chronic heart failure.[1] This condition represents the most frequent indication for mitral surgery in contemporary practice and is unique among heart valve lesions in that the degenerative mitral valve (ie, flail or prolapse) can be surgically repaired in most patients. Mitral valve repair of degenerative MR not only ameliorates and prevents heart failure symptoms but has also been proven to restore normal life expectancy.[2-5] However, despite a growing body of evidence, discordance persists in mainstream clinical practice regarding the timing of recommendation and performance of surgery following the initial diagnosis of severe MR,[6-8] particularly in patients without Class I indications for mitral surgery, that is, those with no or minimal symptoms and absence of overt left ventricular (LV) dysfunction.

Mayo Clinic College of Medicine, Rochester, Minnesota

Address reprint requests to Rakesh M. Suri, MD, DPhil, Division of Cardiovascular Surgery, Mayo Clinic, 200 First St. SW, Rochester, MN 55905. E-mail: suri.rakesh@mayo.edu

The recent 2014 AHA/ACC guidelines indicate that surgical mitral valve repair is reasonable (Class II a) in asymptomatic patients with chronic severe primary MR with preserved LV function (LV ejection fraction [EF] $>60\%$ and LV end systolic dimension [LVESD] <40 mm) in whom the likelihood of a successful and durable repair without residual MR is more than 95% with an expected mortality rate of less than 1% when performed at a Heart Valve Center of Excellence.[9,10] In contrast, European consensus statements have relegated repair under these circumstances to Class IIIb (not favored) status.[11] The disagreement centers on differing understanding of the natural history of severe uncorrected MR. Some clinicians believe that severe MR in asymptomatic individuals is a benign condition that is best managed by "watchful waiting." This recommendation is based largely on a small study of outcomes in young patients with MR and near-normal ventricular dimensions who had strictly mandated follow-up at 1 center.[12] Recent studies have exposed the excess mortality associated with severe uncorrected MR under medical management alone along with an increase in associated adverse consequences such as heart failure and atrial fibrillation.[1]

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THE ROOT OF THE DEBATE

The rationale for the "early" performance of mitral valve repair predicates the justification for surgery on the diagnosis and echocardiographic quantification of severe MR. Historical studies, largely using semi-quantitative methods at times either underestimated or overestimated MR severity, which in essence, relegates the debate regarding timing of surgery to a pseudoscience. Accurate determination of effective regurgitant orifice area and regurgitant volume in contemporary practice allowed cardiologists and surgeons to link the correction of severe MR to restoration of survival for the first time. These findings have subsequently been confirmed in studies from Korea (Kang et. al., Ref 4) and Belgium (Montant et al.[13]). However, despite the availability of this evidence debate persists because of (1) differing methods of MR quantification, (2) the derivation of evidence from small single-center studies, and (3) the comparison of outcomes derived from highly disparate populations.

Recently, the weight of evidence for the performance of evidence has recently progressed to beyond the "tipping point" largely because of (1) emerging long-term outcomes data indicating that valve repair is highly predictable with surgical risk that is well less than 1% and (2) recognition that "rescue surgery" following the onset of symptoms or ventricular dysfunction is associated with significantly increased rates of long-term death and heart failure.[6,14] In contrast to historical disparities in the performance of mitral valve repair, high-quality mitral valve sparing operations have become increasingly standardized and more widely available (at least regionally) in the current era. Furthermore, despite the concern by some that level I evidence might be lacking to support the recommendation of early surgery, the reality is that such trials are costly, logistically difficult,[15] and unnecessarily place patients at risk of sudden death and adverse cardiac remodeling while definitive surgical therapy is withheld.[14] The current reality is that owing to the widely acknowledged deleterious consequences of uncorrected chronic severe MR caused by leaflet prolapse, it is unlikely that sufficient enthusiasm exists among clinicians to randomize patients to either watchful waiting or early surgery strategies in numbers necessary to permit successful execution of a multicenter randomized clinical trial.

THE "OPPORTUNITY COST" OF WATCHFUL WAITING

A single historical small single-center study[12] suggested that young asymptomatic patients with normal ventricular dimensions and severe MR could be clinically followed up in a regimented fashion according to a "watchful-waiting" strategy and only operated on when guideline-based triggers were met. The study population was skewed to a young and necessarily highly compliant subgroup in a single country at a single center in a prior surgical era and thus is not reflective of mainstream contemporary cardiac valve practices worldwide. Yet, this small and difficult-to-generalize study is often used as the centerpiece for fomenting the watchful-waiting "rebellion". The reality in mainstream clinical practice is that rigorous protocolized lifestyle-limiting echocardiographic surveillance of otherwise healthy, active, financially productive patients cannot routinely be mandated or performed outside of clinical trials, and if it is done, then only in certain circumstances where financial reimbursement is provided and accepted by the patient in lieu of the not insignificant "opportunity" cost of being medically watched and not treated. The individual and institutional financial burdens associated with such an unusually intense level of scrutiny of asymptomatic and high-performing individuals have curtailed the ability to mandate such surveillance schemes beyond this small European experience to date. Our recent study addressed this limitation by examining a multinational cross section of patients receiving routine standard care in large valve practices worldwide, at the discretion of the likely varied clinical protocols of personal cardiologists.[1] The generalizability of these real-world results obtained under current international guidelines is thus improved and diminishes the likelihood of bias mediated by studying the proclivities of a small single-center practice. The notion that watchful waiting conveys "no survival disadvantage" is clearly dispelled by latest evidence. The liabilities of medical management alone in patients with confirmed severe MR have become evident not just in a single institution but across a broad multicenter experience. An ethical responsibility thus exists for cardiac care professionals to discuss evidence with patients describing the "opportunity benefit" of safe and effective surgical therapy for severe MR when modern surgical techniques are used.

CONTEMPORARY MITRAL REPAIR OUTCOMES

The results of contemporary mitral valve surgery continue to improve in the modern era. Mitral valve repair for leaflet prolapse without calcification or restriction can be performed with greater than 95%-99% certainty in high-volume centers using standardized techniques (Fig. 2).[16-18] Mortality associated with this operation is very low (<0.3%) and