

Why Do Mitral Valve Repairs Fail?

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In this issue of *JASE*, Magne et al¹ continue their previous work using echocardiography to analyze outcomes of mitral valve repair for ischemic mitral regurgitation, demonstrating that continued adverse left ventricular (LV) remodeling may not be a prerequisite for recurrent mitral valve regurgitation in patients who had undergone initially successful repairs. They observed a group of 26 patients selected from a larger group who had undergone surgical repair for ischemic mitral regurgitation and noted that 10 patients developed recurrent mitral regurgitation within a mean of 18 months after surgery. In those 10 patients, recurrent regurgitation was ascribed to continued adverse LV remodeling in 5 patients, while the other 5 did not have detectable changes in ventricular volumes. The authors did note increased tethering of the anterior leaflet in the latter group of patients and suggested that recurrent regurgitation was due to localized LV remodeling in the vicinity of the papillary muscle. Does this finding represent an advance in our understanding of ischemic mitral valve repair? Have alternate explanations for recurrent regurgitation been excluded? To help put these findings in perspective, it is necessary to review the pathophysiology of ischemic mitral valve regurgitation and to separate the issue of residual or recurrent mitral regurgitation that results from surgical technical failure, as opposed to that due to the progression of the underlying disease process.

PATHOPHYSIOLOGY OF ISCHEMIC MITRAL VALVE REGURGITATION

Ischemic mitral valve regurgitation is often characterized as “a ventricular disease,” as opposed to a “primary valve disease”; this is because the valve structures often have a normal appearance, in contradistinction to degenerative or rheumatic mitral valve disease, in which the leaflets and/or subvalvar structures are visibly abnormal. In ischemic mitral valve disease, the predominant lesions are leaflet tethering and annular dilatation and distortion, due to inferior and lateral papillary muscle displacement. Because the inferior wall of the heart and thus the posteromedial papillary muscle is supplied predominantly by the posterior descending artery, it is particularly susceptible to infarction and injury in the setting of atherosclerotic coronary disease. Post-infarction ventricular remodeling leads to displacement of the posteromedial papillary muscle, with resultant mitral leaflet tethering and varying degrees of mitral valve regurgitation. In cases of inferior wall infarction, the predominant tethering involves the P3 area of the valve, whereas the tethering of multiple leaflet segments (both anterior and posterior) occurs after anterior infarction, which is

associated with more diffuse and symmetric ventricular remodeling.² Associated annular dilatation is common in ischemic mitral valve regurgitation and is most often the target of surgical repair strategies. Because leaflet tethering causes a decrease in the amount of leaflet surface available for coaptation, it is now generally accepted that a downsized complete rigid or semirigid annuloplasty ring should be implanted to accommodate for tethered leaflets and thus maximize leaflet coaptation. It is important to note that the concept of downsizing was not introduced until the mid-1990s,³ and the possible influence of annuloplasty type in ischemic repair was not appreciated until the mid-2000s.⁴ Hence, several series that reported poor outcomes with ischemic mitral valve repair included patients operated on in the 1990s and early 2000s, before restrictive annuloplasty became an accepted strategy to overcome leaflet tethering.⁴⁻⁶ More recently, the poor results of flexible rings or bands compared with semirigid or rigid complete rings have led a majority of surgeons to abandon the use of flexible annuloplasty devices in the setting of ischemic mitral regurgitation. Adjunct techniques such as chordal cutting,⁷ cleft closure, papillary muscle relocation,⁸ and leaflet augmentation⁹ help ensure a good initial surface of leaflet coaptation and are becoming increasingly prevalent. These techniques further reduce leaflet tethering and may potentially yield better midterm results. The current standard surgical strategy to repair ischemic mitral valves should therefore include a downsized rigid or semirigid annuloplasty, with the use of adjunctive procedures as appropriate.

Although traditionally, the outcomes of mitral valve repair were assessed by long-term freedom from valve reoperation, freedom from residual or recurrent mitral regurgitation by echocardiography has now superseded reoperation rates as the gold standard for evaluating outcomes of mitral valve repair. This arose after two large studies showed that with systematic echocardiography, the freedom from recurrent mitral regurgitation at 10 years for degenerative disease was approximately 70%, whereas the freedom from reoperation rates was 94%, implying that many patients with recurrent regurgitation do not undergo reoperation.^{10,11} Systematic echocardiography to evaluate for the onset of moderate or greater regurgitation, therefore, provides the key to understanding the durability of valve repair for various etiologies and various surgical techniques. The occurrence of moderate or greater regurgitation indicates a failure of repair. Echocardiography is also critical to understanding mechanisms for failure of repair, as demonstrated by the current study by Magne et al.¹

Mitral valve repairs, regardless of underlying etiology and the surgical techniques used to effect repair, can fail for 3 reasons: a deficient surgical technique causing immediate failure, a delayed failure of surgical technique, or the progression of native disease.

DEFICIENCIES IN SURGICAL TECHNIQUE

To measure the long-term outcomes of any surgical technique requires that the technique was applied optimally at initial surgery.¹² Suboptimal technique predisposes to poor outcomes. Indeed, in studies of ischemic mitral valve repair, a common factor in several studies showing high frequencies of midterm failure is the use of less effective repair techniques, which are associated with a higher frequency of recurrent regurgitation.¹³ Specifically, flexible rings, which were

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popular over the past decade, are associated with a higher frequency of residual and recurrent regurgitation.¹⁴ In contrast, centers that have consistently applied downsized rigid or semirigid annuloplasty rings have achieved more durable results.^{15,16} For degenerative valves, surgical factors such as failure to use an annuloplasty ring and the use of techniques such as chordal shortening have been predictive of long-term failure.¹⁷ Unless present at initial surgery, it is somewhat difficult to make assertions on the adequacy or quality of the mitral repair operation, but there are some indicators that are useful surrogates for quality in a repair team. Most notably, because the objective of mitral valve repair is to eliminate mitral valve regurgitation, one should expect the vast majority of patients to leave the operating room with this goal met. Where mitral regurgitation has not been eliminated, the explanation would be advanced pathology, such as in complex Barlow's disease (which should have a finite known frequency), random chance (which should be rare), or suboptimal repair. Provided that patients have been selected properly and that the surgical team is well versed in mitral valve repair, we believe no more than 5% of patients should leave the operating room with residual mitral regurgitation. Advanced pathology limiting repair quality should be rare, because it usually is possible to tell the complexity of the required repair on examination of the preoperative echocardiogram. If the surgeon makes an assessment as to whether he or she has the skills or ability to effect a repair on the basis of the preoperative echocardiogram, it would be rare that the surgeon is unexpectedly faced with a repair that is beyond his or her technical ability. When the surgical team feels that they do not have a high probability of repairing the valve, they should consider referral to a reference center¹⁸ or discuss planned mitral valve replacement; the latter, although not ideal in most scenarios, is preferable to a failed mitral repair.

The data presented by Magne et al¹ raise questions as to the adequacy of the mitral valve repairs in their patients. Although they did use a downsized remodeling complete ring strategy, their results were not optimal. The 26 patients studied were part of a larger group (number not specified) who underwent mitral valve repair in the same period; several patients were excluded from study for various reasons. Seven patients were excluded because of residual mitral regurgitation on immediate postoperative echocardiography, suggesting intraoperative failure of the mitral valve repair in $\geq 20\%$ of patients; a prior study by Magne et al¹⁹ also found recurrent regurgitation in 11 of 51 (22%) patients who underwent restrictive annuloplasty. This high incidence of residual regurgitation is in contrast to contemporary series, which have shown near complete absence of residual mitral regurgitation on initial postoperative echocardiography after ischemic mitral repair with a downsized remodeling complete ring strategy.^{15,20,21} The finding of such a high frequency of residual mitral regurgitation by Magne et al¹ raises particular questions regarding the adequacy of their repair strategies, as residual regurgitation should have been infrequent, given that the authors stated that patients who had mild or greater regurgitation in the operating room underwent further downsizing or valve replacement.

Magne et al¹ also excluded patients who underwent a second bypass run for revision of the repair or valve replacement and, by virtue of their study criteria, early postoperative deaths. They also excluded patients who sustained perioperative myocardial infarctions, which is notable given that perioperative infarction is an inherent risk with valve repair surgery and may indeed be a contributor to failures of mitral valve repair. Although it may well be that our current techniques of ischemic valve repair are inadequate, it is difficult to determine so with incomplete patient cohorts. As we have suggested previously,¹² valve repair studies should be reported on an intention-

to-treat basis, because information (even just raw numbers) on patients who did not complete the planned repair, or who had repair but were excluded from analysis, can be of critical value in understanding the reported practice and outcomes.

DELAYED FAILURE OF SURGICAL REPAIR

Every valve repair technique has an inherent failure rate. In ischemic repair, the modality of failure is usually related to annuloplasty dehiscence or errors in the sizing of annuloplasty; in degenerative or rheumatic repair, any of the sutures used for leaflet reconstruction or support can disrupt. Inadequate choice of device (such as a flexible band in myopathic ventricles) will also predispose to late failures. Adjunctive procedures used in ischemic repair, such as cleft closure, papillary repositioning, and surgical ventricular remodeling, also have intrinsic failure rates.

Additionally in ischemic repair, a seemingly adequate repair can fail shortly after surgery if the patient leaves the operating room with a minimally coapting valve, even if there was no mitral regurgitation observed intraoperatively, because the valve will have a propensity to leak once the ventricle resumes more physiologic loading conditions. A shorter length of coaptation is associated with a greater propensity for residual mitral regurgitation.²² One study found that patients with postoperative residual or recurrent regurgitation had an indexed coaptation length of 1.9 mm/m², compared with 4.5 mm/m² in those who did not have recurrent regurgitation and 5.2 mm/m² in controls without history of regurgitation.²³ Inadequate length of coaptation is a possible alternative explanation for recurrent regurgitation in the 5 patients in whom the ventricles did not remodel further, and it cannot be excluded, because Magne et al¹ do not provide information on the length of the coaptation at the conclusion of repair. Leaving the operating room with an adequate length of coaptation is possibly as critically important as leaving the operating room without mitral regurgitation. The length of coaptation can be easily observed during the repair.²⁴ Indeed, Braun et al¹⁵ (who reported excellent midterm results with ischemic mitral valve repair) defined criteria for a successful mitral valve repair as the absence of residual mitral regurgitation and a leaflet coaptation length of ≥ 8 mm at the A2-P2 level on postrepair echocardiography; if either is not met on postbypass transesophageal echocardiography, cardiopulmonary bypass is reinstated, and the annuloplasty is further downsized.

The choice of ring size can itself contribute to delayed surgical failure. Too large a ring can result in an inadequate length of coaptation. Too small a ring can induce mitral stenosis. Indeed, Magne et al²⁵ recently studied 24 patients who had ischemic mitral repairs and did not have recurrent regurgitation and found mean mitral gradients of 6 mm Hg at rest and 8 mm Hg during exercise, suggesting that functional mitral stenosis can occur after successful restrictive mitral annuloplasty. In the current study,¹ however, the authors found a mean gradient of only 2 mm Hg in the subset of patients who did not have recurrent regurgitation. It is not clear how the current cohort differs from that of the previous study; although the patient characteristics and surgical strategy are reported to be the same in both studies, the results, published 1 year apart, are very different. Such discordant results from the same team suggest some undocumented change in surgical technique, selective subgroup analysis, or chance (due to small numbers), any of which would reduce the robustness of the findings in both studies.

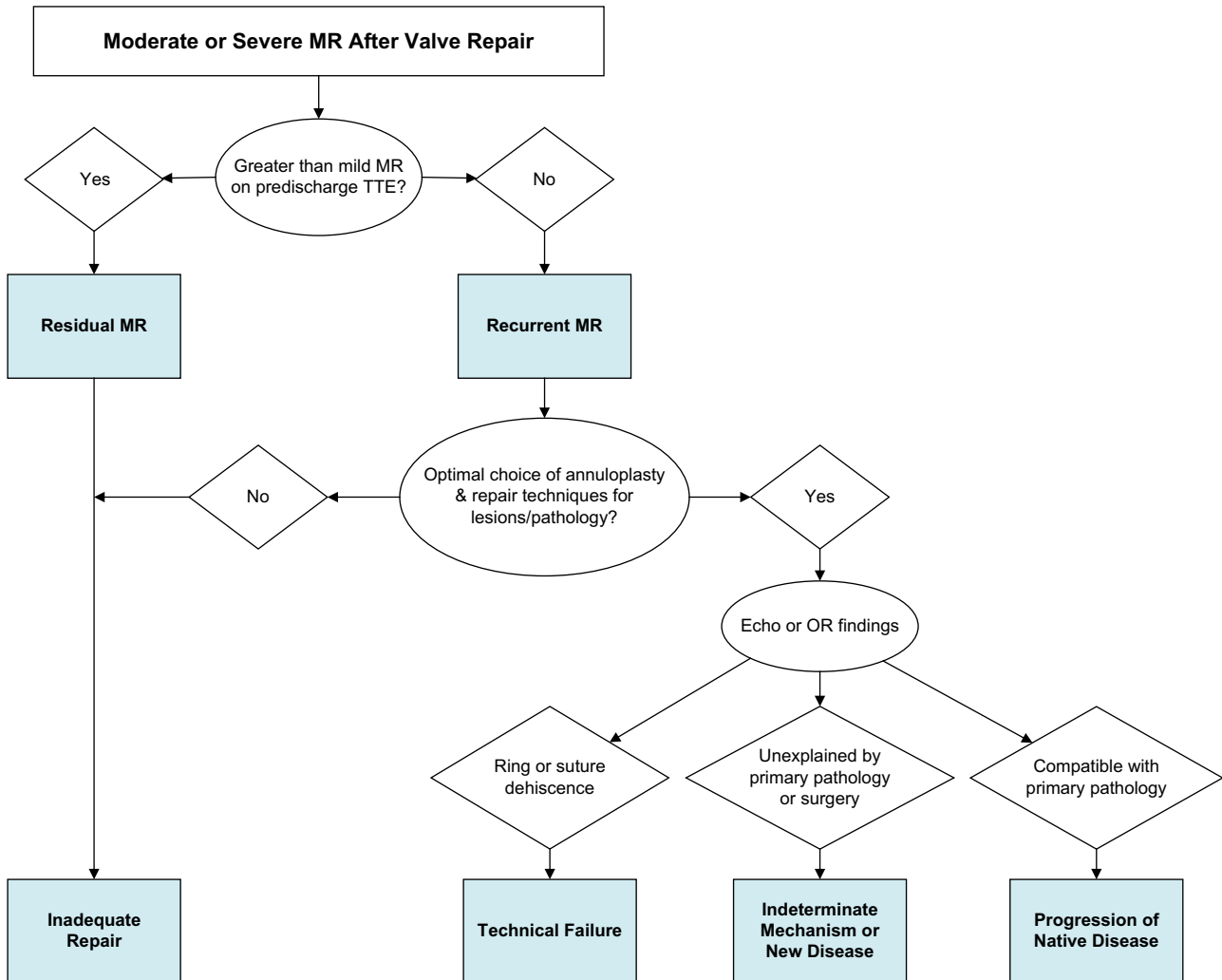


Figure 1 Algorithm for ascribing the cause of mitral regurgitation (MR) occurring after mitral valve repair. *TTE*, Transthoracic echocardiography; *OR*, operating room.

PROGRESSION OF NATIVE VALVE DISEASE

The progression of ventricular disease generally gets the blame for the failure of ischemic mitral repair. Scrutiny of the published literature, however, shows that attempts were not made in most instances to first exclude mechanisms of failure related to surgical technique. The progression of native valve disease is observed as a frequent mechanism of failure in degenerative mitral valve repair and is related often to prolapse of new segments due to new chordal elongation or rupture; this progression may explain the relatively linear recurrence rate of regurgitation of about 2% to 4% per year after degenerative mitral valve repair.^{10,17} In rheumatic disease, new chordal or leaflet fibrosis or calcification is the usual mechanism for recurrent regurgitation.²⁶

For ischemic disease, this progression has typically been linked to continued adverse LV remodeling and is particularly pronounced in those ventricles with severe dilatation at the time of surgical repair.^{15,21} This mechanism was observed in 5 of the 10 patients with recurrence in Magne et al's¹ series. The absence of continued adverse remodeling in the other 5 patients led the authors to seek an alternative explanation for recurrent regurgitation. Although the authors postulate that some form of localized LV remodeling may

selectively tether the anterior leaflet, they do not provide any direct evidence for such a mechanism. Alternative explanations may exist. For example, the early occurrence of recurrent regurgitation (average follow-up was 18 months) makes it plausible that operative rather than disease factors were in play, such that those unexplained recurrences could actually be technical failures. Alternatively, it is possible that remodeling may indeed have taken place, but echocardiography was not sensitive enough to detect it.

Considering that regional or global LV remodeling is the initiating factor in ischemic mitral regurgitation, it would be most likely that the same mechanism must be responsible for failures attributed to the progression of native disease. Indeed, a recent study suggests that combining surgical ventricular restoration with ischemic mitral repair in dilated ventricles halts the remodeling process and yields good midterm survival,²⁷ suggesting that a dilated or remodeled ventricle is critical to the persistence of ischemic mitral regurgitation. These findings reinforce that recurrent mitral regurgitation is uncommon in the absence of continued LV dilatation and raise further intrigue as to how half of the patients in the current study by Magne et al¹ developed recurrent severe mitral regurgitation despite the absence of remodeling.

IMPLICATIONS FOR FURTHER STUDIES

We have previously outlined the essential criteria required to evaluate outcomes of mitral valve repair.¹² Studies looking at the failure of repair must first consider surgical factors, including inadequate surgical technique, as the source of residual or recurrent mitral valve regurgitation. Indeed, the progression of disease should generally not be a consideration early in the time course of postrepair mitral valve regurgitation. A good initial surgical result is documented by the absence of more than trivial mitral regurgitation on postoperative transthoracic echocardiography in an awake and extubated patient (not intraoperative echocardiography, which may underestimate regurgitation because of loading conditions). Once early postoperative echocardiography has excluded mitral regurgitation, any newly documented regurgitation is now defined as recurrent (Figure 1). With recurrent regurgitation, however, one must still consider surgical factors related to inadequate technique, as well as the progression of disease, as potential causes of new mitral valve regurgitation: study of the operative report and the echocardiogram will usually enable this distinction to be made (Figure 1). Sometimes the mechanism of regurgitation will be indeterminate. Further investigation is then required to first exclude technical factors and to exclude alternative etiology; if neither is present, alternative mechanisms of recurrent regurgitation should be sought. This distinction is important as we try to define outcomes and durability for currently used mitral repair techniques, particularly so that we may understand which techniques are more likely to yield durable repairs. Despite the questions raised by their study, Magne et al¹ are to be applauded for their continued work on the echocardiographic assessment of ischemic mitral repair. Once again, they have reminded us that our understanding of the pathophysiology of ischemic mitral regurgitation, and also the treatment strategies we use, are far from certain and should continue to remain the subjects of future research and study.

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