Subvalvular Techniques for Ischemic Mitral Regurgitation

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Abstract

Surgical treatment of ischemic mitral regurgitation with reduction ring annuloplasty is the current standard of practice, yet recurrence in a third of patients limits the benefit of this approach. In an effort to improve outcomes, attention has turned to understanding the contribution of leaflet tethering in this disease process. Subvalvular techniques to alleviate leaflet restriction have been shown to be safe, and in the appropriate patient population decrease recurrence of ischemic mitral regurgitation when combined with reduction annuloplasty. We describe our preferred technique of posterior papillary muscle repositioning. Further understanding of the preoperative parameters that predict recurrence, and deployment of concomitant subvalvular repair techniques in this subset of patients will be the next important breakthrough in the surgical treatment of ischemic mitral regurgitation.

Keywords

Heart failure • Ischemic mitral regurgitation • Mitral repair • Tricuspid repair • Cardiomyopathy

Pathophysiology

The term functional mitral regurgitation is used to describe mitral regurgitation in the absence of any "organic" lesions of the mitral valve. It includes mitral regurgitation (MR) that results from dilated cardiomyopathy and also mitral regurgitation caused by ischemic dysfunction of the ventricle and subvalvular apparatus. Using the Carpentier pathophysiologic triad ischemic MR has an *etiology* of known coronary artery stenosis with

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evidence of prior myocardial infarction with regional or global left ventricular dysfunction. The primary l*esion* causing regurgitation in this setting is tethering of the mitral valve leaflets often combined with some degree of annular dilation. The resulting *dysfunction* in the case of chronic ischemic MR is most frequently Carpentier type IIIb dysfunction caused by restricted leaflet motion which occurs in response to ventricular remodeling after myocardial infarction. Carpentier type I dysfunction, or MR resulting from annular dilation with a lack of leaflet coaptation despite normal leaflet motion, may occur in the setting of basal infarction but accounts for less than 10% of ischemic MR cases and should be easily repairable with a reduction ring annuloplasty. Carpentier type II dysfunction, or leaflet prolapse, may occur with complete or partial rupture of the posteromedial papillary muscle but is rare in the current era of percutaneous early revascularization for myocardial infarction.

The normal mitral valve function involves a complex interaction among the valve leaflets, annulus, subvalvular apparatus, and left ventricle. In ischemic mitral regurgitation, the leaflets are spared but each of the other components of the normally functioning mitral valve are differentially affected. Annular dilation and distortion is present, dilation and increased sphericity of the ventricle occurs, and with these changes the papillary muscles of the subvalvular apparatus are displaced. All of these changes combine to cause leaflet tethering and therefore poor coaptation, creating a regurgitant valve. It is commonly and accurately stated that ischemic mitral regurgitation is a disease of ventricle, not a disease of the valve, and understanding it in this manner is necessary when pursuing effective and durable repair techniques.

Breaking down the changes in the valve components that lead to the final common pathway of Carpentier IIIb MR caused by leaflet tethering we can start with the most important changes which occur in the left ventricle. Myocardial ischemia or infarction with remodeling leads to regional distortion and ultimately poor leaflet coaptation. Watanabe and colleagues have shown that in patients with inferior infarction, tethering was more localized in the medial posterior leaflet, while anterior infarction results in more widespread tethering of both leaflets [1]. This observation confirms the crucial role that regional ventricular geometry and function play in the pathophysiology of ischemic MR and helps explain why some patients with only mildly impaired LV function develop severe ischemic MR. Indeed, the geometry of ventricle as it remodels in response to ischemia and infarction seems to be more important determinant of ischemic MR than the LV volume or ejection fraction.

Annular dilation is common in chronic ischemic MR however the degree of annular dilation does not necessarily correlate with the degree of MR. Some patients have severe MR with very little annular dilation while others with significant annular dilation have only mild regurgitation. Several studies have noted that the degree of septolateral (SL) dilation seems more important in the pathophysiology of ischemic MR than the commisure-commisure (CC) dilation [2, 3]. In severe cases of ischemic MR the SL dimension can approach the CC dimension which results in a circular annulus instead of the usual elliptical one. Most often, the majority of the dilation occurs in the posterior annulus, particularly in the region of the posterior commissure [4, 5].

When examining the role of the subvalvular apparatus, it is clear that papillary muscle displacement plays a critical role in the development of ischemic MR. On the contrary, papillary muscle dysfunction itself does not seem to significantly contribute to ischemic MR [6, 7]. Carpentier and colleagues demonstrated in sheep studies in the 1980s that formaldehyde injection in the posterior papillary muscle did not produce MR [8]. Instead, MR could only be produced by extending formaldehyde injection into the adjacent myocardium resulting in regional wall motion abnormality. The pattern of papillary muscle displacement necessary to yield ischemic MR is complex and involves displacement of the muscle tips posterolaterally and apically away from the anterior annulus and away from each other. The tethering distance has been shown experimentally to correlate with the severity of ischemic MR [9]. Displacement of both papillary

muscles is likely necessary to induce severe MR but particularly displacement of the posteromedial muscle usually predominates.

The combination of regional LV dysfunction and sphericity, annular dilation, and papillary muscle displacement all create a tethering force that leads to apical tenting of the mitral valve leaflets and Carpentier IIIb MR. Tethering of the primary chordae leads to restricted motion of the free margins of the leaflets which prevents them from rising to the plane of the annulus during systole with resultant poor coaptation and regurgitation. In addition, tethering of the secondary chordae can result in deformation of the body of the leaflet which also contributes to impaired coaptation.

Therapeutic targets for correction of ischemic MR include the coronary arteries, mitral annulus, subvalvular apparatus, valve leaflets, and the ventricle itself. Any surgery for ischemic MR should include full coronary artery revascularization. To date, the most common surgical treatment for ischemic MR involves coronary revascularization and a reduction ring annuloplasty which restores leaflet coaptation but fails to address the underlying tethering component in the pathophysiology of ischemic MR. This failure may explain why about a third of patients develop recurrent MR within a year of successful reduction annuloplasty. The remainder of this chapter will focus on surgical approaches to management of the subvalvular apparatus via varying techniques of papillary muscle relocation and several techniques of chordal modification in an effort to obtain a more durable correction of ischemic MR that is more resistant to continued ventricular remodeling and tethering. In rare cases, a simultaneous ventricular remodeling procedure such as a Dor operation may be indicated or necessary but this will be discussed elsewhere.

Principles of Treatment

To determine which patients are appropriate candidates for mitral valve repair with the employment of adjunctive subvalvular techniques, a thorough understanding of the latest data on ischemic MR is necessary. Traditional mitral valve repair for ischemic MR involves revascularization of ischemic myocardium along with a reduction ring annuloplasty as first described by Bolling and Bach in 1995 [10]. This repair technique is simple and has demonstrated a large degree of success over the past two decades but as alluded to earlier, this approach addresses the annulus only and ignores the underlying contributions of ventricular dysfunction and changes in geometry of the subvalvular apparatus to the development of ischemic mitral regurgitation. Not surprisingly, the rates of recurrent MR after reduction ring annuloplasty have been shown to be higher than 30 %.

As mentioned previously, results from the recent Cardiothoracic Surgical Trials Network (CTSN) randomized study on mitral valve repair versus replacement for severe ischemic MR [11] suggest that this approach alone is inadequate for some patients. In this trial, 251 patients with severe ischemic MR were randomized to mitral valve repair or chordal-sparing mitral valve replacement with a primary endpoint on left ventricular end-systolic volume index (LVESVI) and secondary endpoints of major adverse cardiac and cerebrovascular events, mortality, degree of residual MR, functional status, and quality of life. The vast majority of mitral valve repairs in this trial were done with reduction ring annuloplasty of 1–2 sizes. At 1 year, there was no significant difference between repair and replacement in either the primary or any secondary outcome. Notably, the rate of recurrent moderate or severe MR at 1 year in the repair group was 32.6 % vs. only 2.3 % in the replacement group ($P < 0.001$). Of those undergoing repair, the LVESVI was 64.1 ± 23.9 ml/m^2 in those with recurrent MR versus 47.3 ± 23.0 ml/m^2 in those without recurrent MR ($P < 0.001$) suggesting that if a durable repair can be achieved, there likely remains an advantage to repair over replacement.

In order to further investigate the question of whether failure of mitral valve repair can be predicted by certain preoperative characteristics, the CTSN investigators have performed a recent posthoc analysis of the 116 patients who were randomized to and received mitral valve repair

in the Severe MR trial with 2-year follow-up [12]. Logistic regression was used to determine baseline echocardiographic and clinical characteristics that predict failure of repair or death and a predictive model based on 10 factors (age; gender; race; body mass index; NYHA class; effective regurgitant orifice; basal aneurysm/dyskinesia; and history of coronary artery bypass grafting, percutaneous coronary intervention, or ventricular arrhythmias) was developed with a favorable area under the receiver operating characteristic curve of 0.82. Those patients who suffered from recurrent moderate/severe MR or who died were older, had a lower frequency of NYHA class III or IV, and had a higher frequency of basal aneurysm/dyskinesis. Of the ten variables, the standout predictor of recurrent moderate or severe MR, or death, was basal aneurysm/dyskinesia; reflecting a severe form of preoperative LV ischemic remodeling with the abnormalities of papillary muscle displacement, leaflet tethering, and annular dilation. It stands to reason that in these patients with preoperative basal aneurysm/dyskinesia, mitral repair with a downsized annuloplasty ring alone is insufficient and that either upfront replacement or additional subvalvular repair techniques are necessary for a durable result.

Techniques of Repair

No large randomized study exists to confirm the benefit of subvalvular techniques for repair of ischemic MR however multiple smaller studies support the adoption of various subvalvular techniques. Papillary muscle relocation to alleviate leaflet restriction was first reported one decade ago [13]. The original technique consisted of passing a prolene suture through the posterior papillary muscle and then through the mitral annulus immediately posterior to the right fibrous trigone prior to reduction annuloplasty. In the initial study, echocardiographic follow-up revealed restoration of a more physiologic configuration of the relocated posterior papillary muscle and no patient had recurrence of MR 2 months after repair. There were no mortalities and relocation of the papillary muscle, easily visualized through a standard left atriotomy, was demonstrated to be a safe and simple additional procedure. However, this technique requires a fibrotic posterior papillary muscle.

These encouraging initial results prompted further revisions in the technique of papillary muscle relocation, including a sling to anchor the bases of the papillary muscle together [14] and direct approximation of the tips of the two papillary muscles together [15]. Years after papillary muscle relocation, the majority of patients in these studies remain free from recurrent mitral regurgitation with evidence of reversal in left ventricular remodeling and improvement in both ejection fraction and New York Heart Association functional class. One recent study highlighted the importance of papillary muscle approximation in limiting further posterior leaflet tethering following reduction ring annuloplasty. Often reduction annuloplasty can worsen posterior leaflet tethering but Manabe et al. demonstrated decreased posterior leaflet restriction with papillary muscle approximation [16].

In 2013, results of the first retrospective study directly comparing outcomes after reduction annuloplasty alone versus concomitant papillary muscle relocation were published [17]. In this study, both papillary muscles were reapproximated to the mitral annulus using a CV-4 Gore-Tex suture placed through the head of each papillary muscle and tied to the ipsilateral mitral annulus. Postoperatively, patients who underwent this combined procedure had significantly decreased mean tenting area and coaptation depth as well as decreased left ventricular end systolic and diastolic diameter over a mean follow-up of 32 months. Recurrent mitral regurgitation was significantly decreased with the addition of papillary muscle relocation. There were no differences in early or late mortality and patients who underwent papillary muscle relocation had a decreased incidence of late cardiac events.

Concomitant procedures involving the chordae tendinae have also been reported in attempts to mitigate leaflet restriction. Chordal cutting has been met with resistance due to the potential for disruption of the valvular-ventricular continuity

and concern for progressive left ventricular modeling. However, these procedures target the secondary chordae and leave the basal and marginal chordae intact. In one recent study, addition of bileaflet secondary chordal cutting to reduction annuloplasty resulted in increased leaflet mobility which significantly decreased the severity of recurrent MR [18]. Importantly, reversal in left ventricular remodeling was also observed without adverse effect on left ventricular function.

Severity of distal anterior leaflet tethering, mediated by secondary chordae, has been found to be a risk factor for recurrent mitral regurgitation after reduction annuloplasty. This tenting effect results in the characteristic seagull sign of the anterior leaflet in ischemic mitral regurgitation, and the angle between the two segments of the anterior leaflet is known as the bending angle. One group recently stratified patients with excessive tethering of the anterior leaflet, as measured by a bending angle less than 145°, to undergo concomitant cutting of all secondary chordae to the anterior leaflet from both papillary muscles [19]. Compared with patients who underwent reduction annuloplasty alone, patients who underwent chordal cutting had significantly decreased recurrent or persistent mitral regurgitation and improved New York Heart Association functional class at a mean follow-up of 33 months. There were no deaths attributable to cardiovascular causes, and ejection fraction increased to a more significant degree after chordal cutting.

To preserve all aspects of the subvalvular apparatus, chordal reimplantation has been reported as an alternative procedure to chordal cutting. In a recent retrospective study, patients with chronic ischemic mitral regurgitation and severe leaflet restriction underwent detachment and reimplantation of secondary chordae to a primary position along the anterior mitral leaflet [20]. In addition to this cut-and-transfer technique, these patients underwent posterior papillary muscle relocation and a subset underwent infarct plication of the lateral left ventricular wall, maneuvers both intended to realign the displaced subvalvular apparatus to a more physiologic configuration under the mitral valve. The majority of patients were free of recurrent mitral regurgitation at 1 year, with echocardiographic and clinical findings revealing a significant improvement in ejection fraction and New York Heart Association functional class at follow-up. Based on these results, chordal procedures represent a valid option in our current armamentarium of concomitant subvalvular techniques in the treatment of ischemic mitral regurgitation.

Surgical Operative Technique

Our preferred subvalvular technique for repair of ischemic mitral regurgitation is well established and has been previously described [13, 21, 22]. This type of repair is appropriate for treatment of Carpentier IIIb MR and we have achieved excellent durable results utilizing these techniques. After standard preoperative preparation, intraoperative transesophageal echocardiography is performed to carefully assess the mechanism of MR. We typically repair greater than 2+ MR and this determination should be made based on the preoperative surface echo rather than in the operating room when afterload reduction may mask clinically significant MR. Conduit harvesting for coronary artery bypass is performed and cardiopulmonary bypass is established using standard aortic and bicaval cannulation with antegrade and retrograde cardioplegia. Distal coronary anastomoses are performed first before turning attention to the mitral valve. Caval tapes are placed and elevated to help facilitate exposure of the mitral valve which is obtained through a standard left atriotomy utilizing a Cosgrove self-retaining retractor.

Systematic valve inspection is performed to confirm the echocardiographic findings. In the typical case of A3/P3 regurgitation due to posteromedial papillary muscle tethering, we proceed with posterior papillary muscle relocation. First, circumferential mitral annular horizontal mattress stitches are placed and the mitral valve is sized using the inter-trigonal distance. We typically downsize by 1 to 2 sizes which generally results in a 26- or 28-mm semi-rigid complete annuloplasty ring. The annular stiches are passed through the sewing ring at appropriate

intervals to produce an even annular reduction and the ring is lowered onto the annulus and sutures tied. The valve is re-tested and if significant residual MR is detected then the tethering of the posterior papillary muscle and dysfunction of the subvalvular apparatus must be addressed.

A 3-0 polypropylene suture is placed through the fibrotic papillary muscle and the two ends are then passed through the annulus behind the previously placed ring in the area posterior to the right fibrous trigone. The suture is tied over a felt pledget and adjusted to restore the posterior papillary muscle to a more anatomic position. This adjustment correlates to the degree of tethering visualized on intraoperative transthoracic echocardiography. Prior to locking the suture, valve function is again tested with the saline test to assure no residual regurgitation and necessary adjustments are made. The atriotomy is then close as standard, deairing measures are performed and any proximal coronary conduit anastomoses are completed. Further deairing, removal of the aortic cross-clamp, and weaning from bypass are performed per routine. Transesophageal echocardiography is used to confirm adequacy of the repair. MR <1+ is deemed acceptable but MR ≥1+ necessitates further repair or valve replacement.

Patient Selection

The next step in subvalvular repair techniques is to more accurately determine those patients who will derive maximal benefit from these techniques. In a report published last year, a subset of patients undergoing reduction annuloplasty for ischemic MR was selected to undergo a concomitant subvalvular procedure [23]. Patients with significant left ventricular dilatation and increased tethering angles of the anterior and posterior mitral leaflets were selected to undergo papillary muscle approximation and suspension as well as left ventricular restoration. One year after surgery, bileaflet tethering angles were significantly increased in the group that did not undergo subvalvular repair and recurrent MR occurred only in this group. These results suggest that incorporating subvalvular techniques into repair in patients with left ventricular dilation and leaflet tethering impedes further left ventricular remodeling, papillary muscle displacement, leaflet tethering, and recurrent MR. Nevertheless, we have not perfected the identification of those patients who will depend on concomitant subvalvular procedures for a durable repair.

The recent efforts of the CTSN investigators to develop a risk model for prediction of recurrent MR after repair of ischemic MR offers a step in the right direction toward evidence-based treatment of ischemic MR and deployment of select subvalvular repair techniques in the setting of predicted failure of reduction annuloplasty alone. As described previously, the standout predictor of recurrent MR or death in this model, was basal aneurysm/dyskinesia. While the presence of a basal aneurysm/dyskinesia is a helpful predictor of repair failure using reduction annuloplasty alone, it is likely just a reflection of a severe form of preoperative LV ischemic remodeling with accompanying papillary muscle displacement, leaflet tethering, and annular dilation. As of yet, no data exists to completely predict repair failure for ischemic MR. Similarly, defined preoperative characteristics that guide which adjunctive subvalvular techniques are most appropriate in a given patient have not been fully elucidated. Our understanding of this complex pathophysiology has improved, as well as our ability to safely perform complex subvalvular repair maneuvers, but the systematic and appropriate deployment of these valuable techniques must be further investigated through rigorous collaborative investigation.

Conclusion

We have discussed the pathophysiology of ischemic mitral regurgitation and the principles of treatment with particular attention to techniques addressing the subvalvular apparatus. What must be understood beyond all else is that ischemic MR is a disease of the ventricle, not of the valve, and must be treated as such. With this in mind, it should not be surprising that the rate of recurrent mitral regurgitation after simple reduction annuloplasty for ischemic MR is high. The ventricle

continues to remodel after ring annuloplasty with further displacement of the papillary muscles and subsequent leaflet tethering and regurgitation. To correct this problem, the underlying dysfunction in each patient must be addressed. We have detailed a technique of posterior papillary muscle repositioning that we have found to be particularly effective in treating patients with typical Carpentier IIIb ischemic MR but this technique is not intended as a cure-all. Additional subvalvular adjunctive repair techniques such as chordal cutting and papillary muscle reapproximation are promising. Despite this promise, there is poor data to direct which technique to employ and only an early understanding of which patients may benefit from these approaches. Determination of those patients whose outcomes depend on these concomitant techniques of subvalvular repair will be the next important breakthrough in the surgical treatment of ischemic mitral regurgitation.

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