Physiologic Basis for the Surgical Treatment of Ischemic Mitral Regurgitation

Farzan Filsoufi, MD; Parwis B. Rahmanian, MD; Anelechi Anyanwu, MD; David H. Adams, MD

Ischemic mitral regurgitation (MR) can complicate severe coronary artery disease and myocardial infarction. Ischemic MR results from left ventricular remodeling after myocardial infarction and can also accompany acute myocardial ischemia. The most common mechanism of ischemic MR is Carpentier’s type IIIb dysfunction due to an apical and lateral displacement of papillary muscles leading to a tethering of the mitral leaflets. This apical tenting of the leaflets prevents the free margin from reaching the plane of the annulus, significantly reduces the surface of coaptation, and causes MR. Recent advances in imaging studies have led to a better understanding of the pathophysiology of this condition as well as to the development of innovative surgical approaches to treat this disease. Current research efforts have mainly focused on 2 directions: (1) percutaneous approaches to correct MR, and (2) surgical therapy to address the ventricular component of the disease. In this article, the authors define ischemic MR and review its pathophysiology, current management strategies, and future directions. ©2006 Le Jacq

Mitral regurgitation (MR) resulting from prior myocardial infarction (MI) is now recognized as an important clinical entity that negatively impacts patients’ long-term survival. The pathophysiology of this condition is now better understood, and much clinical interest is currently directed toward a better determination of surgical indication as well as a better definition of the optimal management strategy of patients with ischemic MR. This review will describe current concepts relating to the pathophysiology of and surgical therapy for this condition.

Definition of Ischemic MR and Carpentier’s Functional Classification

Significant coronary artery disease, particularly in the setting of MI, can be complicated by MR. Ischemic MR often results from either left ventricular remodeling following MI or, occasionally, from acute myocardial ischemia. This disease should be distinguished from ischemic cardiomyopathy and associated MR due to other etiologies such as rheumatic disease and degenerative mitral valve disease.

Carpentier’s functional classification is useful to describe the mechanism of MR and to determine the lesion responsible for this condition regardless of the etiology. This classification is based on the opening and closing motion of the mitral leaflet (Figure 1). Patients with type I dysfunction have normal leaflet motion, with MR due to isolated annular dilatation. In patients with type II dysfunction, there is an increased leaflet motion, with the free edge of the leaflet overriding the plane of the annulus during systole (leaflet prolapse). The most common lesions for type II dysfunction are chordal elongation or rupture and papillary muscle elongation or rupture. Patients with type IIIa dysfunction have a restricted leaflet motion during both diastole and systole. The most common lesions for type IIIa dysfunction are chordal thickening/retraction, chordal thickening/shortening, and commissural fusion, often observed in rheumatic heart disease. The mechanism of MR in type IIIb dysfunction is restricted leaflet motion during systole due to left ventricular enlargement and papillary muscle displacement. Ischemic MR can result from type I, II, or IIIb dysfunction. Type I dysfunction, with annular...
dilatation, is observed in basal MI and accounts for about 5% of cases of ischemic MR. Type II dysfunction is due to either papillary muscle rupture (acute MI and partial or complete rupture of the posterior papillary muscle) or papillary muscle elongation (chronic fibrotic transformation of the papillary muscle following MI). Carpentier's type IIIb dysfunction is the most common form of ischemic MR, with apical and lateral displacement of papillary muscles following MI and ventricular remodeling, and is the main focus of this review (Figure 2).

**Pathophysiology of Type IIIb Ischemic MR**

The mitral valve is a complex structure with multiple components: leaflets, annulus, subvalvular apparatus with chordae and papillary muscles, and the left ventricular posterolateral wall. The normal function of each component is a sine qua non of a competent mitral valve. Several anatomic and physiologic changes affecting these components following an ischemic event lead to the onset of MR. Following an MI, the left ventricle becomes less elliptical and more spherical. This increase in sphericity leads to an apical and lateral displacement of papillary muscles (mostly the posteromedial papillary muscle), producing a tethering of the mitral leaflets. This apical tenting of the leaflets prevents the free margin from reaching the plane of the annulus, significantly reduces the surface of coaptation, and causes MR (type IIIb dysfunction). Because of the systolic restricted leaflet motion, the 2 leaflets coapt below the plane of the annulus. The coaptation depth, which is defined by the distance between the annular plane and the plane of coaptation, is therefore increased in patients with type IIIb dysfunction, and its severity reflects the degree of leaflet tethering. In addition, tethering of secondary chordae can lead to a deformation of the body of the leaflets (effet de mouette), further impairing their mobility and thus reducing the surface...
of coaptation. Recent studies using 3-dimensional echocardiography further refined the analysis of restricted leaflet motion in ischemic cardiomyopathy. Kwan et al have shown that the pattern of mitral valve deformation from the posteromedial to the anterolateral commissure was asymmetric in ischemic MR. They reported a significant tethering of both leaflets on the posteromedial side (A3 and P3 segments), whereas the tethering was less pronounced on the anterolateral segments of the valve (A1 and P1). These findings have a significant clinical relevance, emphasizing the fact that surgical treatment modalities should particularly focus on this region of the valve to achieve a perfect mitral valve repair.

Ischemic MR typically occurs after infarction in the posterior (inferolateral) territories. Recently, it is becoming increasingly appreciated that anterior infarction is also a significant contributor in the etiopathology of ischemic MR. In anterior infarction, leaflet tethering tends to be more symmetric, compared with posterior infarction. The areas of stress and tenting are also different, with a more uniform distribution of stress and a greater area of tenting in anterior infarction compared with the concentration in the P3 region seen in classical ischemic MR.

Mitral annular dilatation or deformation is a secondary lesion often observed in patients with type IIIb ischemic MR contributing to worsen this condition. Several experimental studies have shown that isolated annular dilatation does not necessarily lead to MR. Timek et al, in an acute ischemic model following the occlusion of the left anterior descending or left circumflex artery, have reported mild degrees of annular dilatation that did not cause MR. Therefore, annular dilatation is not considered the primary lesion in the pathogenesis of type IIIb ischemic MR. Another interesting finding is that in patients with ischemic MR, the grade of annular dilatation can vary and does not necessarily correlate with the severity of MR. Annular dilatation results in an increased anteroposterior (septolateral) diameter, which becomes greater than the transverse diameter of the mitral orifice. Although annular dilatation is predominant along the posterior segment of the annulus, several recent studies have also demonstrated an augmentation of the transverse annular diameter (intercommissural distance). Furthermore, in an ovine model of chronic ischemic MR, Gorman et al have shown that not only were all segments of the mitral annulus dilated, but that this dilatation was asymmetric and more accentuated at the postero medial portion of the annulus (P2–P3 region). Similarly, in a magnetic resonance imaging study using 3-dimensional reconstruction among 38 patients with previous inferior or posterior infarction, Kaji et al demonstrated that patients with chronic ischemic MR (≥2+) had greater septolateral and commissure–commissure mitral annular dimension, larger intertrigonal distance, and a flattened saddle shape of the mitral annulus.

Once the process of negative left ventricular remodeling is initiated, it becomes self-perpetuating as resultant MR leads to ventricular dilatation (increase in sphericity index), which, in turn, leads to further papillary muscle displacement, annular enlargement, and then further MR (Figure 3).

**Surgical Treatment of Type IIIb Ischemic MR**

**Coronary Artery Revascularization.** Most patients with ischemic MR present with severe multivessel coronary artery disease; therefore, coronary revascularization, either surgically or percutaneously, is an important component of their treatment. Recent studies have shown, however, that in most patients coronary revascularization alone does not correct MR. In a study from our group, 136 patients with moderate ischemic MR underwent isolated coronary artery bypass grafting. Postoperative transthoracic echocardiography showed no improvement of MR in 90% of patients; 40% of patients were left with moderate or severe (3+ and 4+) residual MR, whereas 50% had mild (2+) residual MR. Fewer
than 10% of patients had significant improvement, with no more than trace (0–1+) residual MR. More recently, Campwala et al.\textsuperscript{12} reported a series of 92 patients with 3+ and 4+ ischemic MR undergoing isolated coronary artery bypass grafting. In postoperative echocardiographic follow-up, nearly half of these patients still had 3+ or 4+ MR. The authors also reported a trend toward a higher mortality in this group of patients compared with patients with regression of MR. Similarly, Ellis et al.\textsuperscript{13} demonstrated the impact of MR in a cohort of patients undergoing percutaneous coronary artery angioplasty. The 3-year survival rate ranged between 46% and 76% and was dependent on severity of MR and left ventricular function. Patients with moderate-to-severe MR and ejection fraction <40% had a 50% mortality rate at 3 years despite successful percutaneous revascularization (Figure 4).

**Mitral Valve Reconstruction.** Mitral valve annuloplasty is the appropriate surgical procedure for the treatment of type IIIb ischemic MR. The goal of mitral annuloplasty is to restore a large surface of coaptation and to remodel the annulus while preserving leaflet mobility.\textsuperscript{1} In most instances, the prosthetic ring is undersized to create a larger surface of coaptation by significantly reducing the anteroposterior (septolateral) diameter of the annulus. The optimal technique of annuloplasty and the choice of prosthetic ring have been the subject of controversy for a long period of time. During the past years, several types of prosthetic rings and bands have been used to treat ischemic MR. Residual or recurrent MR following some of these techniques became a major concern,\textsuperscript{14} and multiple clinical and experimental studies were undertaken to better understand the mechanism of repair failure and attempt to provide an adequate response.

Flexible bands mainly reduce the circumference of the posterior segment of the annulus and do not significantly alter the anteroposterior diameter and the intercomissural distance. Recently, Bhudia et al.\textsuperscript{15} reported from the Cleveland Clinic Foundation that mitral annuloplasty with Cosgrove-Edwards (Edwards Lifesciences, Irvine, CA) flexible posterior annuloplasty bands in the setting of type IIIb MR was associated with a 30% incidence of recurrent MR at midterm follow-up. Similarly, in patients...
with ischemic MR undergoing mitral valve repair, the use of flexible and deformable rings is associated with a high failure rate. Tahta et al\(^{16}\) reported the outcome of 100 patients undergoing combined coronary artery bypass grafting and mitral annuloplasty using a Duran (Medtronic, Minneapolis, MN) flexible ring. They reported a 29% rate of >2+ recurrent MR at a mean follow-up of 36 months.\(^{16}\)

Remodeling annuloplasty using completely rigid or semirigid rings restores both the size and the shape of the annulus with a significant reduction of the anteroposterior diameter. Currently, the use of these rings is favored in patients with type IIIb dysfunction. In a series of 51 patients with preoperative 3+ or 4+ ischemic MR undergoing remodeling annuloplasty using the Carpentier-Edwards Physiologic (Edwards Lifesciences), Bax et al\(^{17}\) reported absent or trivial recurrent MR in all patients at 2-year follow-up. Despite the good early results, recurrent MR, predominantly localized at the postero-medial portion of the valve, has also been reported several years after this procedure in 10%–15% of patients.

A better understanding of the pathophysiology of ischemic MR (pronounced P2–P3 leaflet tethering and asymmetric annular dilatation) led to the development of a disease-specific prosthetic ring. The Carpentier-McCarthy-Adams (CMA) IMR ETlogix (Edwards Lifesciences) annuloplasty ring combines the principles of undersizing while addressing the specific asymmetric deformation observed in type IIIb ischemic MR. This new design leads to increased leaflet coaptation due to the reduced anteroposterior dimension. In addition, the asymmetric 3-dimensional design with reduced P2–P3 curvature allows for a better accommodation of tethered P2–P3 segments (Figure 5).\(^{18}\) In a recent multicenter study, Daimon et al\(^{19}\) reported the outcome of patients with type IIIb ischemic MR who underwent mitral annuloplasty using the CMA ring. Postoperative echocardiography showed a significant reduction of mitral annulus diameter, leaflet tenting area, and tenting height in all patients. Ninety-seven percent of patients had an MR grade 0–1+ and only 2 patients had a 2+ residual MR on postoperative echocardiography.

**Adjunct Procedures.** Mitral valve reconstruction with a remodeling annuloplasty in combination with coronary artery revascularization produces satisfying results in a large number of patients with ischemic MR. Additional adjunct procedures may be useful to improve leaflet mobility and to increase the surface of coaptation in select patients.

The posterior leaflet can be extended, particularly at the P2–P3 segment, with a pericardial patch to improve mobility and available surface of coaptation. This technique may be challenging, however, because leaflet tissue is often fragile and thin in these patients.\(^{20}\) Other studies have focused on altering the subvalvular apparatus to improve leaflet mobility. Resection of secondary chordae may be indicated in select patients with significant leaflet tethering due to a large secondary chordae attached to the body of the leaflet. In an experimental study of a chronic inferobasal infarction, Messas et al\(^{21}\) reported that the resection of secondary chordae can improve coaptation and reduce chronic ischemic MR without impairing left ventricular function. Papillary muscle repositioning is another approach in ischemic MR that has been used to reduce leaflet tethering.\(^{22}\) The papillary muscle sling technique, joining the papillary muscles using a Gore-Tex (WL Gore & Associates Inc, Newark, DE) tube, addresses leaflet tethering caused by papillary muscle displacement. This technique was shown to have an immediate effect on mitral leaflet mobility.\(^{23}\)

Finally, the edge-to-edge repair (attaching the free margins of both leaflets together) has also been reported in the setting of ischemic MR. Timek et al\(^{24}\) have shown in an ischemic MR animal model that this technique did not alter the annular, subvalvular,
or leaflet geometric configuration. In addition, this procedure did not prevent the occurrence of ischemic MR. Furthermore, without annuloplasty, edge-to-edge repair is associated with a high failure rate; even the addition of annuloplasty rings may not significantly improve the results. Bhudia et al have shown that flexible posterior annuloplasty bands in combination with edge-to-edge repair resulted in a 30% incidence of recurrent MR after 18 months' follow-up. Finally, in the clinical setting, the use of an undersized annuloplasty combined with edge-to-edge repair may significantly increase the risk of mitral stenosis. Currently, the use of this technique in patients with ischemic MR has not gained a broad application.

Although correction of MR by annuloplasty can halt the vicious cycle of ischemic MR and produce remodeling of the ventricle, some studies suggest that ventricular dilatation and papillary muscle displacement continue in spite of annuloplasty, resulting in recurrent regurgitation. It is true that until a recent date, most therapeutic approaches had focused on the valvular dysfunction seen in ischemic MR and had neglected the primary ventricular component. During the past few years, significant efforts

**Figure 6.** External ventricular constraint device (Acorn Cardiovascular, Inc, St Paul, MN). Adapted from Oz et al.

**Figure 7.** Effect of the Coapsys device (Myocor Inc, Maple Grove, MN). Left: mitral regurgitation results from annular dilatation or papillary muscle (PM) displacement. Right: the Coapsys device increases leaflet coaptation and repositions the papillary muscles. AML indicates anterior mitral leaflet; PML, posterior mitral leaflet. Adapted from Fukamachi et al.
have been made to address the ventricular disease, with the goal of discontinuing the ventricular remodelling. Surgical restoration of ventricular geometry, as in the Dor procedure, can reduce papillary muscle displacement and subsequent MR. Ischemic MR can be reduced by placing an epicardial ventricular restraint device that prevents further ventricular expansion (Figure 6). In experimental settings, this device has been shown to reduce adverse remodelling and MR. In a recent clinical study, Acker has reported on the use of external ventricular constraints at the time of mitral valve repair. This procedure has been associated with the prevention of further ventricular dilatation and its negative consequences. Another epicardial approach to ventricular reshaping was introduced with the Coapsys device (Myocor Inc, Maple Grove, MN). This device consists of 2 epicardial pads connected by a flexible cord that is passed through the left ventricle and then tightened to improve leaflet coaptation and stabilize the ventricular wall (Figure 7). Early clinical experience suggests that the Coapsys device not only corrects MR effectively, but also has a reverse remodelling effect on the left ventricle. In a study reported by Grossi et al., the implantation of the Coapsys device was associated with a significant reduction of the basal, mid, and apical left ventricular diameter from 4.8 cm to 3.6 cm, 4.9 cm to 3.6 cm, and 4.4 to 3.4 cm, respectively. Another epicardial approach was recently reported by Hung et al., with the fixation of an external balloon in the region of an inferior infarction that could reposition the papillary muscle and therefore reduce tethering of the mitral leaflet, thus correcting MR.

The percutaneous approach for the treatment of ischemic MR is in an early phase of development. The current strategies have adapted the concept of mitral valve annuloplasty. A mitral annular constraint device is placed in the coronary sinus located at the posterior portion of the mitral valve. The successful implantation of these devices has been reported in small experimental studies with short-term follow-up. Due to their localization at the posterior segment of the annulus, these devices do not address either anterior annular dilation or the asymmetric dilation of the postero medial annular area and, therefore, may provide suboptimal long-term results in patients with type IIIb ischemic MR. In the future, less invasive percutaneous approaches may combine coronary angioplasty and mitral valve annuloplasty through coronary sinus or other approaches to correct valvular regurgitation.

REFERENCES


