

Mechanistic Insights into Ischemic Mitral Regurgitation: Echocardiographic and Surgical Implications

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Ischemic mitral regurgitation is a common complication of the healing phase of myocardial infarction. A number of mechanisms have been invoked in its pathogenesis, including alterations of papillary muscle position, annular dynamics, and intraventricular synchrony. The echocardiographic hallmark of ischemic mitral regurgitation is systolic tethering of the mitral valve leaflets away from the annular plane. A number of leaflet tethering parameters have been described (tenting height and area, leaflet angles) that provide insight into the mechanism of tethering as well as prognostic information about the durability of mitral valve repair. Restrictive annuloplasty and coronary artery revascularization promote reverse remodeling and remain the most common surgical treatment. Innovative subannular therapies and a number of percutaneous interventions are under investigation. (*J Am Soc Echocardiogr* 2011;24:707-19.)

Keywords: Echocardiography, Ischemic mitral regurgitation, Papillary muscle dysfunction, Myocardial infarction, Mitral annulus, Mitral annuloplasty, Cardiac Resynchronization therapy

Ischemic mitral regurgitation (MR) is a complication of the chronic healing phase of myocardial infarction (MI). As the left ventricle remodels after MI, the normal geometry of the mitral apparatus becomes distorted, resulting in incomplete leaflet closure and valvular regurgitation.¹ Unlike degenerative and infectious disorders, however, the structural integrity of the leaflets and chords remain intact.

Ischemic MR occurs commonly after MI, with an estimated prevalence of 20% to 50%,^{2,3} and its presence has been shown to significantly worsen prognosis independent of ejection fraction.³ Indeed, a stepwise increase in mortality can be demonstrated as effective regurgitant orifice area (ROA) increases (Figure 1). It is also worthwhile noting that even subjects with otherwise clinically insignificant amounts of MR (effective ROA < 20 mm²) have excess mortality rates.³

Despite considerable interest in this disorder, the pathogenesis of ischemic MR remains incompletely understood, and the optimal surgical approach remains largely controversial. Echocardiography has helped facilitate much of our current understanding of the mechanisms involved in ischemic MR and is emerging as a useful tool for surgical planning. In this review, I discuss the pathogenesis, echocardiographic diagnosis, and surgical treatment of this disorder.

PATHOGENESIS OF ISCHEMIC MITRAL REGURGITATION

Alterations of Left Ventricular (LV) Geometry

In 1963, Burch *et al.*⁴ wrote that “during periods of angina pectoris, reduction in the circulation to a papillary muscle (PM) may result in total or

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partial failure of the PM to contract producing a murmur of MR. When the circulation is restored, the PM...gradually regains its function and the murmur...slowly disappears.” The long-held notion that ischemic MR is due to PM dysfunction has a sound physiologic basis. In the normal heart, PM contraction prevents the mitral valve leaflets from falling back into the left atrium during systole. When the left ventricle contracts, the annulus descends toward the apex. Were it not for simultaneous contraction of the vertically oriented fibers of the PMs, slackening of the chords might otherwise permit the leaflets to prolapse into the left atrium as the annulus descends. Instead, a constant distance is maintained between the mitral annulus and the tips of the PMs, thereby preventing MR.⁵ Notwithstanding these observations, animal models of isolated PM infarction fail to produce MR⁶. The finding that MR does occur when muscle adjacent to the PM is infarcted^{6,7} is significant, particularly in light of the observation that such muscle readily deforms in response to increases in afterload.⁸ Taken together, these findings suggest an alternative mechanism for ischemic MR unrelated to myocardial ischemia, providing insight into why ischemic MR worsens with exercise despite the absence of inducible ischemia.^{9,10} It has been proposed that the increase in afterload attending exercise worsens MR through geometric distortion of the infarcted PM-bearing segments, shifting them away from the annular plane. Increased chordal traction, in turn, tethers the leaflets, which become effaced, resulting in incomplete mitral valve closure and worsening regurgitation.¹

Several additional lines of evidence support the notion that ischemic MR is more related to dynamic changes in loading conditions than to the effects of reversible myocardial ischemia. One study demonstrated that despite surgical revascularization, hemodynamically significant MR persists postoperatively in as many as 40% of patients.¹¹ Additional evidence suggesting that load plays a role in the pathogenesis of ischemic MR comes from the often-made clinical observation that diuretics and afterload reducing agents, commonly used in the treatment of these patients, reduce MR severity.¹² Reduced afterload during general anesthesia also decreases MR severity, and for this reason, echocardiographic evaluation of ischemic MR should ideally precede valve repair.¹¹ Not uncommonly, patients with

Abbreviations

AML = Anterior mitral leaflet
CRT = Cardiac resynchronization therapy
LV = Left ventricular
MI = Myocardial infarction
MR = Mitral regurgitation
PM = Papillary muscle
ROA = Regurgitant orifice area

ischemic MR complain of significant effort intolerance but exhibit only minimal MR when studied at rest. Stress echocardiography can be especially useful in such patients and may unmask higher grades of MR from the increased afterload attained with exercise.^{9,10} One study found that an exercise-related increase in effective ROA of $\geq 0.13 \text{ cm}^2$ significantly worsens prognosis.¹³

Mitral valve closure is a dynamic process in which two opposing forces, a tethering force and a closing force, act simultaneously on the leaflets determining their instantaneous position throughout systole. The tethering force, imparted by the PMs and chords, pulls the leaflets away from the annular plane, and the closing force, generated by LV contraction, drives them in the opposite direction (Figure 2). Ischemic MR results from an imbalance between these forces, tipped in favor of the former. As the left ventricle remodels after MI, increased tethering impairs the systolic excursion of the leaflets toward the annulus,^{1,14-16} and valvular competence becomes increasingly dependent on closing forces.¹⁴ Figure 3 depicts the dynamic interaction of closing and tethering forces in ischemic MR. Note that the ROA becomes substantially reduced in midsystole, when LV pressure (closing force) is maximal, whereas in early and late systole, when LV pressures are lower, tethering forces are less opposed, allowing the ROA to increase.^{15,16} Excess tethering results in leaflet deformation, producing a characteristic tented appearance readily recognized echocardiographically.¹⁷⁻¹⁹

Alterations of Mitral Annular Mechanics

The mitral annulus is thin fibrous membrane separating the left heart chambers. Its shape has been likened to a saddle, with peaks located anteriorly (at the "riding horn") and posteriorly, and valleys located medially and laterally, at the commissures.²⁰ This nonplanar shape significantly reduces the stress exerted on the leaflets during ventricular systole.²¹ The annulus undergoes conformational changes during the cardiac cycle, reducing its area through dorsiflexion of its fibrous anterior portion and by sphincteric contraction of its muscular posterior portion (Figure 4). Because the annulus is intrinsically noncontractile, its motion is determined by that of the structures surrounding it.^{20,22} Hence, annular flexion results from posterior displacement of the aortomitral curtain as the aortic root expands during systole.²³⁻²⁶ Sphincteric contraction of the posterior annulus, which begins in late diastole,²³⁻²⁹ is caused by shortening of atrial fibers encircling the annulus. With the onset of ventricular systole, shortening of helical LV fibers causes further contraction, with annular area reaching its nadir in midsystole.²²⁻²⁶ These changes in size and shape bring the free margins of the mitral leaflets into contact, and as systolic pressure increases, the leaflets become pressed together, creating a competent overlapping coaptation length,^{30,31} which normally measures about 1 cm (Figure 5).³²

The annulus undergoes a number of structural changes in ischemic MR, becoming larger and flatter (Figure 6).³³⁻³⁵ An increase in size causes effacement of the mitral leaflets compromising coaptation length. In vitro models³⁶ predict that the coaptation length is sufficiently redundant, permitting an increase in annular area of approxi-

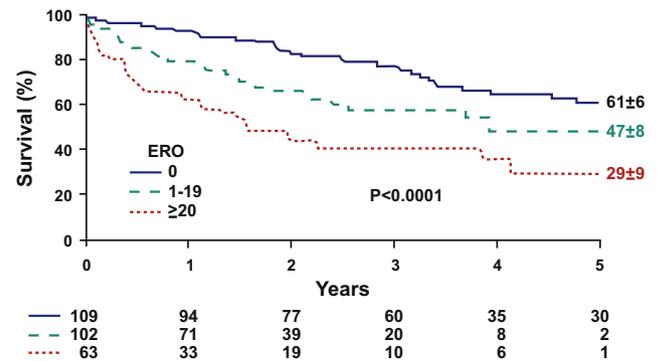


Figure 1 Survival after MI according to degree of MR graded by effective ROA (ERO). Reproduced with permission from *Circulation*.³

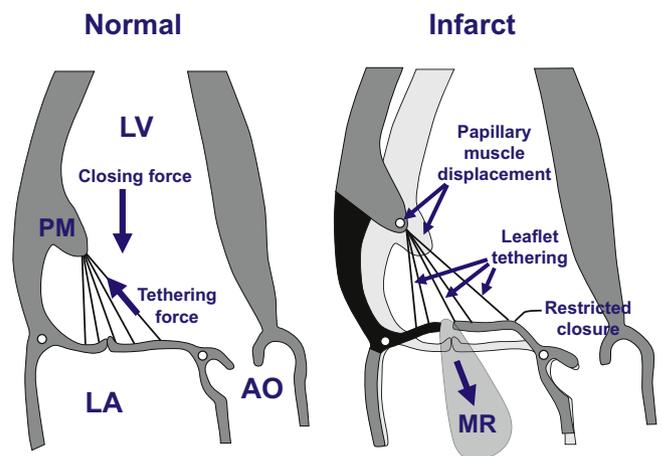


Figure 2 Figures depict closing and tethering forces in the normal ventricle (left) and after inferior MI (right). In the normal ventricle, the mitral leaflets reach the annular plane during systole. PM displacement after infarction increases tethering forces, which pull the mitral leaflets away from the annular plane resulting in incomplete mitral leaflet closure. Ao, Aorta; LA, left atrium. Reproduced with permission from *Circulation*.⁸¹

mately 1.8 times before MR develops. As the annulus enlarges, exposure of interscallop slits on the posterior mitral leaflet may create additional sites of regurgitation.^{37,38} It has also been shown that the annulus becomes more nonplanar in ischemic MR.^{25,35} This has important pathophysiologic effects, increasing the systolic closing stresses imposed on the mitral leaflets.³⁹ Alterations in annular contraction, which could interfere with leaflet coaptation, have been described in patients with ischemic MR. Three-dimensional imaging reveals a reduction in the total extent of annular contraction and prolonged contraction extending through late systole.⁴⁰ It is important to note that the relative contribution of annular enlargement and dysfunction to the overall regurgitant burden in patients with ischemic MR is minor compared with that imparted by augmented leaflet tethering forces.^{15,41,42}

Dyssynchronous LV Contraction

Dyssynchronous LV contraction is an important determinant of ischemic MR. In fact, hemodynamically significant MR is nearly twice as common among patients with QRS durations >130 msec compared

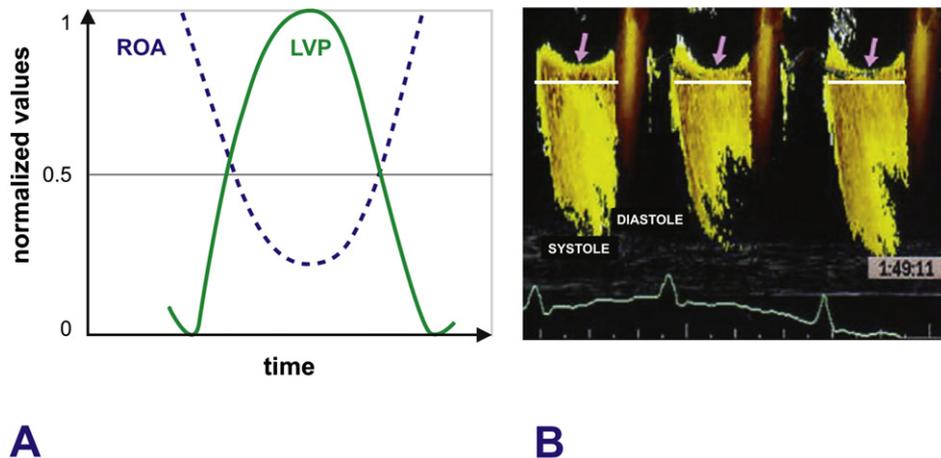


Figure 3 (A) Superimposed graphs of ROA (blue) and LV pressure (LVP) (green) during systole. Note that ROA reaches its nadir in midsystole, when LVP (closing force) is maximal. In early and late systole, when LVP is lower, tethering forces are less opposed, allowing ROA to increase. Reproduced with permission from *J Am Coll Cardiol*.⁴⁴ (B) Color M-mode tracing obtained by interrogation of the proximal convergence zone (PCZ) in a patient with ischemic MR. Note that the radius of the PCZ reaches its nadir in midsystole (arrow) coincident with peak LVP. Reproduced with permission from Otsuji Y, Levine RA, Takeuci M, Sakata R, Tei C. Mechanism of ischemic MR. *J Cardiol* 2008;51:145–56.

with those with normal QRS durations.⁴³ A number of mechanisms have been invoked to account for this. Delayed activation of the lateral PM causes uncoordinated contraction of the PMs, resulting in malalignment of the mitral valve leaflets⁴⁴ (Figure 7). Additionally, uncoordinated contraction of the musculature at the base of the left ventricle impairs sphincteric contraction of the posterior mitral annulus,⁴⁵ which can interfere with leaflet coaptation. Dyssynchronous LV contraction also blunts the rate of pressure generation (dp/dt) by the left ventricle. The resultant decrease in closing force leaves tethering forces relatively unrestrained, increasing leaflet deformation.⁴⁶ Cardiac resynchronization therapy (CRT) has been shown to reverse a number of these abnormalities and is discussed below.

Adaptations to Ischemic MR

Despite comparable amounts of geometric distortion of the left ventricle, significant patient-to-patient differences in MR burden are observed clinically. Several mechanisms can be invoked to account for this heterogeneity. Studies have shown that the mitral valve is capable of remodeling after MI, with adaptive increases in leaflet surface area developing in response to increased tethering forces.⁴⁷ This tissue response reduces MR by restoring coaptation length,⁴⁸ and it is conceivable that individual variability in the extent of such adaptive leaflet remodeling may account, in part, for the differences in MR severity seen among patients.

Adaptive changes in PM morphology and function may also occur after MI.^{7,49,50} It has been observed that MR can be attenuated by PM remodeling, with an increase in length from tip to base. Paradoxical systolic elongation of the PMs may further reduce leaflet tethering forces, as depicted in Figure 8.

Ischemic MR usually worsens in response to the increased tethering forces attending exercise, but patients with preserved contractility of the musculature of the basal inferoposterior segments frequently demonstrate a decrease in MR during exercise.¹⁵ It has been proposed that such patients are able to compensate by recruiting contractile reserve within these myocardial segments, increasing sphincteric contraction of the posterior mitral annulus.^{15,51} In this respect, individuals with separate coronary artery blood supplies to the mid

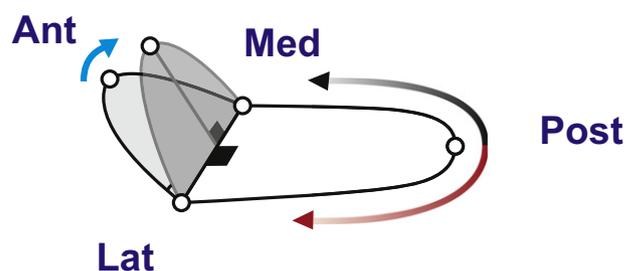


Figure 4 Figure depicting the saddle-shaped mitral annulus and its conformational changes. The anterior (Ant) annulus undergoes a folding motion (curved blue arrow) along its mediolateral (intercommissural) axis. The muscular posterior (Post) annulus undergoes sphincteric contraction, indicated by the curved red and black arrows. Lat, Lateral; Med, medial. Reproduced with permission from *J Thorac Cardiovasc Surg*.²⁶

inferoposterior segments, overlying the PMs, and to the basal inferoposterior segments, adjacent to the posterior annulus, may be at some teleologic advantage.

ECHOCARDIOGRAPHIC RECOGNITION OF ISCHEMIC MITRAL REGURGITATION

Echocardiography plays an important role in the evaluation of ischemic MR. Localized or diffuse changes in LV size and shape due to post-MI remodeling can be readily appreciated. Echocardiography is also useful in characterizing deformational changes in the mitral leaflets caused by tethering.

Post-MI Ventricular Remodeling

Ischemic MR is a disease of the left ventricle. As the ventricle remodels after MI, the normal geometric relationship of the PM and mitral valve becomes altered, resulting in increased leaflet tethering and MR. Early after transmural MI, the necrotic myocardium of the

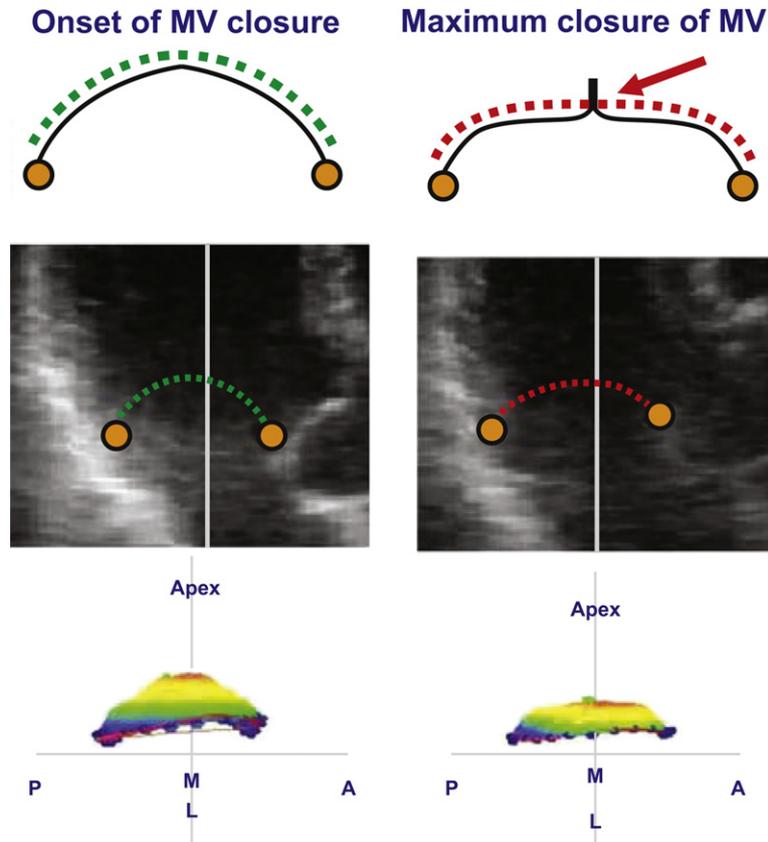


Figure 5 Coaptation length. Conformational changes within the annulus bring the mitral leaflet tips into contact (*left*). As systolic pressure increases (*right*), the leaflet bodies become pressed together forming an overlapping a zone of coaptation. Coaptation length (*arrow*) can be measured by subtracting the length of the traced red surface from that of the traced green surface. MV, Mitral valve. Reproduced with permission from *J Cardiol*.³⁰

affected region thins and enlarges (infarct expansion).⁸ Ventricular remodeling, however, frequently does not remain confined to the region of infarction. Echocardiographic studies have demonstrated dilatation of noninfarcted myocardial segments remote from the site of infarction.⁵² Such remote remodeling can result in marked and diffuse LV enlargement, thought to represent an adaptive response (using the Frank-Starling mechanism) to maintain stroke volume in the face of lost contractile elements.⁸ It is important to recognize that it is the site of LV remodeling, more than its extent, that is the more important determinant of whether ischemic MR will develop. LV dilatation, even when marked, may not cause MR unless accompanied by geometric distortion in the region of the PM. This explains the high prevalence of ischemic MR in patients with localized infarction of inferior wall.⁵³ Ischemic MR can also develop in the absence of any echocardiographically evident scar, presumably from highly localized remodeling limited to the region of the PM.

Echocardiographic Parameters of Leaflet Tethering

A number of echocardiographic parameters of leaflet tethering have been described (Figure 9). Besides providing quantitative information about leaflet deformation, these offer insight into the mechanism of tethering as well as prognostic information about the durability of mitral valve repair (discussed in the subsequent section). *Tenting height*^{7,9} is the vertical distance between the mitral annulus and the leaflet coaptation point. The region bound by the

annulus and the mitral valve leaflets is referred to as the *tenting area*.^{7,9} *Tenting volume*, measured by three-dimensional echocardiography, is less susceptible to foreshortening and therefore correlates better with ROA in patients with ischemic MR.⁵⁴ It is important to recognize that all three tenting indices reflect the global tethering burden imposed on the mitral valve, because they integrate a number of otherwise independent geometric factors (i.e., anterior leaflet tethering, posterior leaflet tethering, annular size, and the leaflet coaptation point⁵⁵). Information about regional leaflet tethering can, however, be obtained by measuring individual mitral leaflet angles. A wide *posterior leaflet angle* indicates posterior leaflet restriction. Widening of the *basal anterior leaflet angle* implies restriction limited to the basal portion of the anterior mitral leaflet (AML). The combined effects of tethering of both the basal and distal portions of the AML can be determined by measuring the *distal anterior leaflet angle*.^{9,55-57}

The area of the mitral annulus can be estimated by measuring orthogonal annular dimensions assuming an ellipsoid shape.⁵⁸ This geometric assumption can be avoided with three-dimensional imaging,²⁴⁻²⁶ which also provides dynamic information about annular folding, contraction, and translation. It should be emphasized that echocardiography measures the projected area of the annulus, not its actual nonplanar surface area. Normal indexed diastolic annular area is approximately 5 cm²/m², decreasing by about 25% by midsystole.⁵⁹ *Coaptation length*, a measure of coaptation reserve, can be measured echocardiographically,^{30,32} as shown in Figure 5.

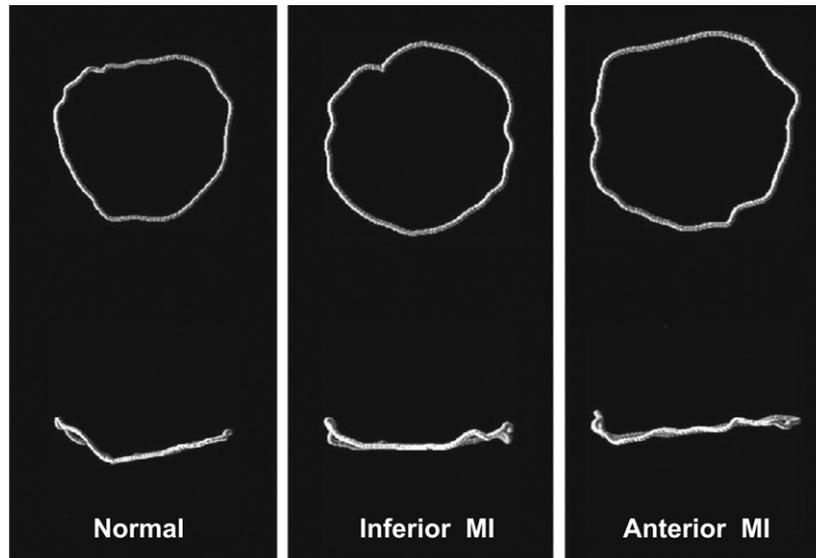


Figure 6 Three-dimensional echocardiographic reconstructions of the mitral annulus viewed en face (*above*) and in profile (*below*). Note the increased annular area and nonplanarity after MI. These changes are more prominent after anterior infarction. Reproduced with permission from *Circulation*.³⁵

Echocardiographic Tethering Patterns

Tethering is characterized echocardiographically by displacement of the mitral valve leaflets away from the annular plane during systole^{17,60} and is best appreciated in the apical four-chamber view. Traction exerted by the basal chords on the body of the AML creates a characteristic angulation or “bent knee” appearance. The tension within the basal chords is transmitted from their point of attachment at mid leaflet⁶¹ down to the leaflet base, rendering the proximal portion of the leaflet more or less immobile.

Two echocardiographic tethering patterns have been described, asymmetric and symmetric, on the basis of the disposition of the mitral leaflets with respect to their point of coaptation^{17,60} (Figure 10). With asymmetric tethering (Figures 10B and 11, Videos 1A and 1B [view video clips online]), the anterior leaflet coapts against the atrial surface of the posterior leaflet, creating a “pseudoprolapse” appearance. This is caused by disproportionately greater tethering of the posterior leaflet.⁶² The MR jet associated with asymmetric tethering is typically eccentric, oriented along the posterior wall of the left atrium.¹⁷ A symmetric tethering pattern (Figures 10C and 12, Video 2 [view video clips online]) results when there is balanced tethering of both leaflets such that the coaptation point remains at the leaflets’ tips, albeit displaced apically.^{17,60} The MR jet associated with symmetrical tethering is typically oriented centrally.¹⁷

TREATMENT OF ISCHEMIC MITRAL REGURGITATION

Restrictive Mitral Annuloplasty

Restrictive mitral annuloplasty combined with coronary revascularization is currently the conventional approach for the surgical treatment of ischemic MR. Insertion of an undersized annuloplasty ring restores valve competence by decreasing the anteroposterior dimension of the annulus.⁶³ It is important to recognize, however, that restrictive annuloplasty alters the normal closing mechanism of the mitral valve.⁶⁴ By hoisting the posterior annulus anteriorly, undersizing increases the distance between the tip of the PM and the posterior annulus, augment-

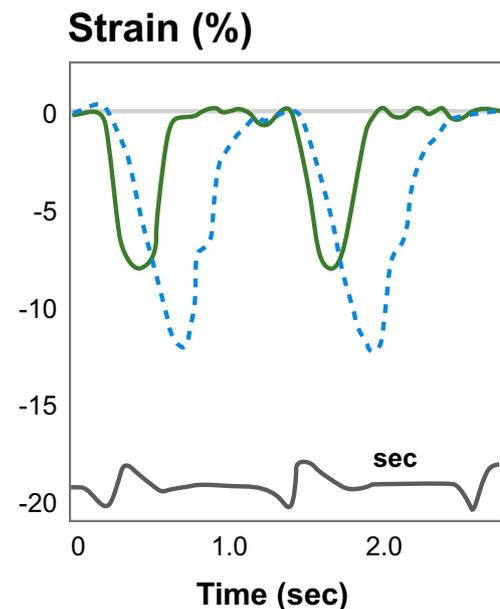


Figure 7 Doppler strain tracings obtained by interrogation the medial (*green*) and lateral (*blue*) PMs in a patient with intraventricular dyssynchrony and ischemic MR. Note the significant time offset in peak developed strain. These tracings were not recorded simultaneously but are depicted as such for clarity. Reproduced with permission from *J Am Coll Cardiol*.⁴⁴

ing posterior leaflet tethering. Excess tethering substantially widens the posterior leaflet angle such that valve closure becomes entirely dependent on the AML, which must span the annulus to maintain competence^{65,66} (Figure 13, Video 3 [view video clips online]).

Restoring the anteroposterior diameter of the annulus with restrictive annuloplasty may not be sufficient to relieve MR, and adjunctive procedures that reduce leaflet tethering may be necessary. Strut chord transection (chordal cutting) has recently been proposed as a strategy

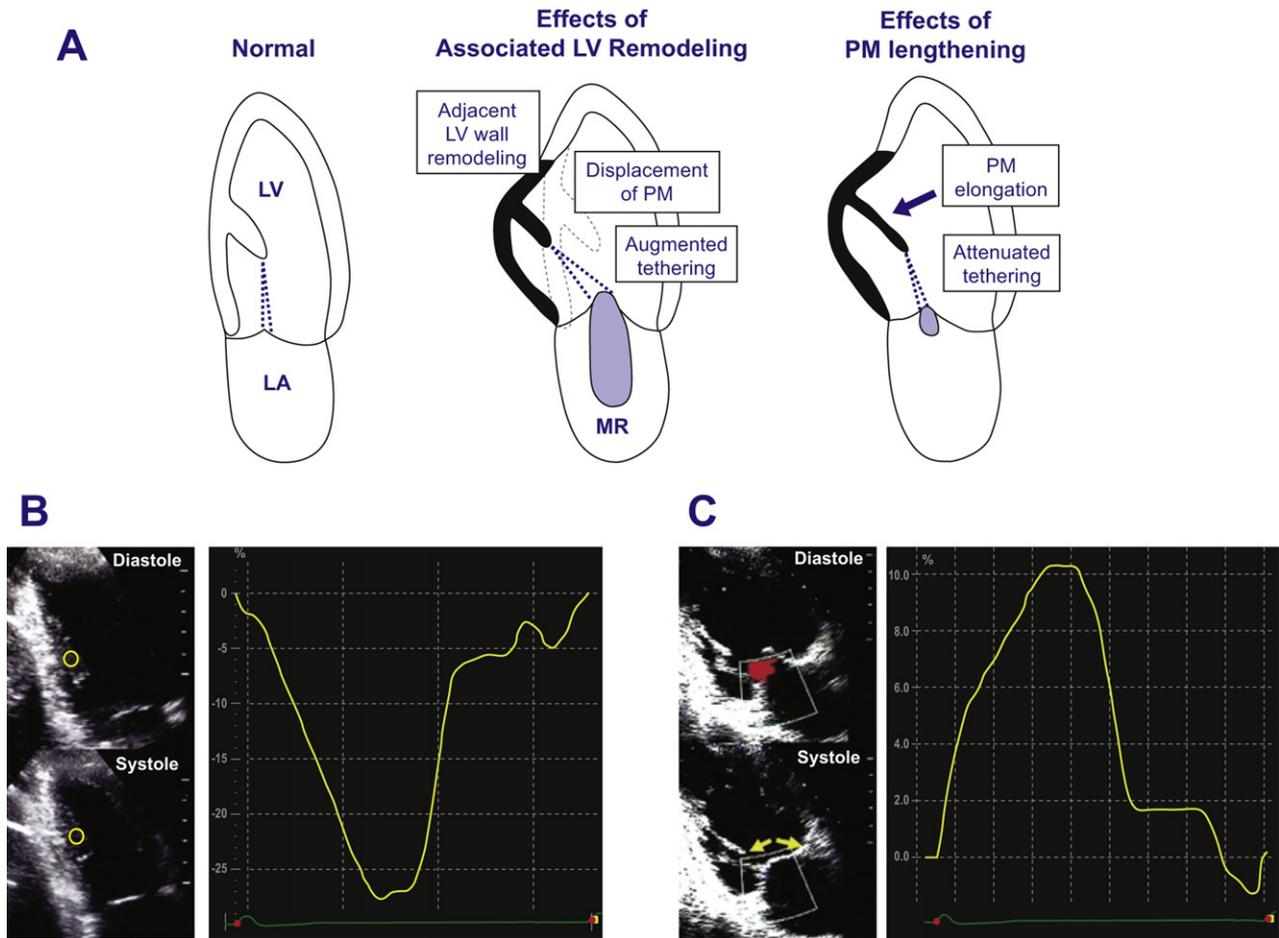


Figure 8 (A) Illustration depicting how PM remodeling attenuates leaflet tethering after inferior infarction. (B) Doppler strain tracing of a normal PM developing negative systolic strain. (C) Doppler strain tracing showing positive systolic strain resulting from paradoxical elongation of the PM. Elongation decreases the tethering distance between the tip of the PM and the anterior annulus (yellow arrows). LA, Left atrium; LV, left ventricle. Reproduced with permission from *J Am Coll Cardiol*.⁴⁹

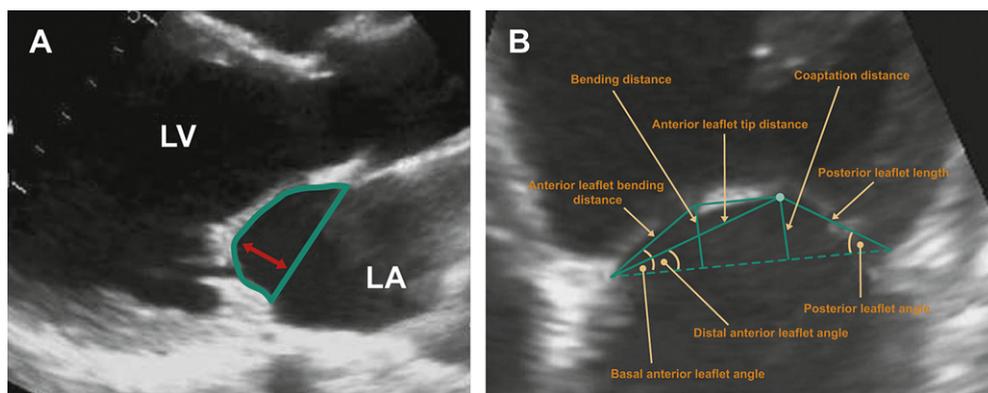


Figure 9 Leaflet deformation indices. (A) Parasternal long-axis view. The tenting area is outlined in green. The tenting height (red arrow) extends from the annulus to the coaptation point. (B) Apical four-chamber view demonstrating leaflet angles. The proximal anterior leaflet angle is formed by the intersection of the annulus (dashed line) and the anterior leaflet bending distance. The distal anterior leaflet angle is formed by the intersection of the annulus and the posterior leaflet tip distance. The posterior leaflet angle is formed by the intersection of the annulus and the posterior leaflet length. The green dot represents the point of leaflet coaptation. LA, Left atrium; LV, left ventricle. Reproduced with permission from *Am J Cardiol*.⁵⁶

for alleviating excess tethering of the AML.⁶⁷ The strut chords are the most prominent (i.e., thickest and longest) of the basal chord attached to the AML.⁶¹ By increasing the surface area available for coaptation,

strut chord transection helps restore coaptation length (Figure 14). There continues to be controversy, however, regarding the safety of this procedure. The strut chords constitute the anatomic interface

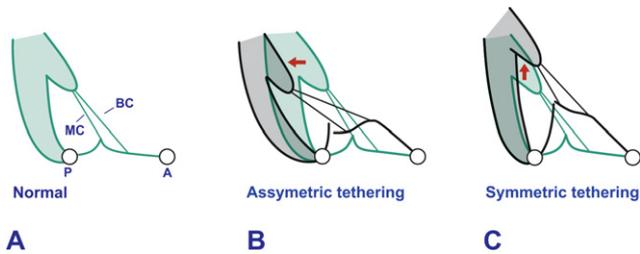


Figure 10 Tethering patterns. **(A)** Normal leaflet coaptation: the bodies of both mitral leaflets are in the annular plane, and their coaptation point is located just above it. Marginal chords (MC) attach to the anterior leaflet's tip, and basal chords (BC) attach at mid leaflet. **(B)** Asymmetric tethering: the point of coaptation is located on the atrial surface of the posterior leaflet, creating a "pseudoprolapse" appearance. Note that the predominant tethering vector is oriented posteriorly (arrow). **(C)** Symmetric tethering: both leaflets coapt along their free margins at a significantly increased distance above the annular plane. The predominant tethering vector is oriented apically (arrow). Note that the bend of the anterior leaflet is less prominent with symmetric tethering due to apical tethering at the leaflet's tip by the MC. A, Anterior annulus; P, posterior annulus. Reproduced with permission from *Circulation*.⁵⁵

between the musculature of the LV myocardium (at the PM) and the mitral annulus (at the fibrous trigones), maintaining so-called annular-papillary or ventricular-valvular continuity.⁶⁸ From their insertion at the base of the left ventricle, epicardial fibers descend along the anterior wall toward the apex, gradually becoming subendocardial, where they give rise to the PM.^{69,70} The strut chords emerging from the PM attach to a dense collagen network of the AML,^{71,72} which provides fibrous continuity that ultimately terminates at the fibrous trigones (completing the ventricular-valvular loop). During systole, the strut chords, much like stretched rubber bands, remain under tension, which is transmitted to the PM and fibrous trigones.^{73,74} The tension in the strut chords is made evident from the retraction of the PM that follows their division. It has been proposed that loss of this tension is transmitted from the PM to the vertical epicardial

fibers, with which they form a continuous syncytium, resulting in perturbations in LV function and geometry.⁷⁵⁻⁷⁷ This remains controversial, however, as a number of studies⁷⁸⁻⁸⁰ have failed to demonstrate any significant LV remodeling or deterioration of LV function after strut chord transection.

PM repositioning is an alternative approach used to reduce leaflet tethering. Repositioning the PM closer to the annular plane increases chordal slack allowing for more physiologic coaptation. A number of innovative approaches have been developed, including the creation of a PM sling⁸¹ and infarct plication.⁸² The Coapsys device (Myocor Inc., Maple Grove, MN; Figure 15) consists of two epicardial pads interconnected by a cord that spans the LV cavity. As the chord is shortened, not only are the PM repositioned, but annular distortion is also corrected.⁸³ A complete discussion of the various procedures used for PM repositioning is beyond the scope of this article, and the interested reader is referred to a recent review of the subject.⁸⁴

Despite advances in the surgical treatment of ischemic MR, recurrence of significant MR after ring annuloplasty continues to be problematic. Rates as high as 30% have been reported in the past,⁶³ although it has been suggested that innovative ring designs^{85,86} and novel subannular procedures⁸⁴ have substantially reduced this figure.⁸⁴ The mechanism underlying recurrent MR is thought to be continued LV dilatation from adverse remodeling. Persistence of even minor amounts of MR postoperatively may be significant, because MR serves as both the cause and the result of adverse remodeling and can incite a vicious cycle inexorably leading to LV dilatation and failure.⁸⁷ Surgical elimination of ischemic MR halts the progression of adverse remodeling, instead setting into motion molecular and cellular processes that promote a reverse LV remodeling phenotype.⁸⁸ Several studies have demonstrated significant reductions in LV size after annuloplasty,^{89,90} although reverse remodeling is less likely once LV end-diastolic dimension has exceeded 6.5 cm.⁹¹ It should be noted that although recurrent MR is widely attributed to adverse LV remodeling, it can occur in its absence, presumably because of subtle and highly localized remodeling not detectable echocardiographically.⁹²

A number of echocardiographic predictors of persistent and/or recurrent MR after mitral annuloplasty have been identified^{55,57,93-96} and are listed in Table 1. Among these, tenting height > 1.0 cm and

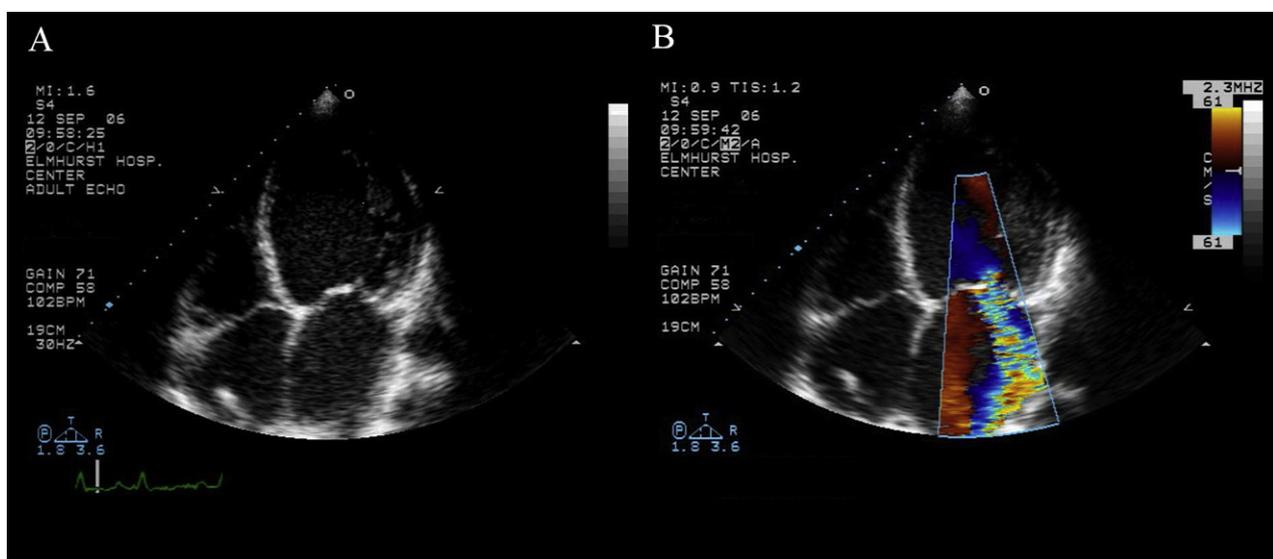


Figure 11 Asymmetric tethering. **(A)** Systolic frame in an apical four-chamber view. See Video 1A. **(B)** Color Doppler image showing a posteriorly oriented jet of MR. See Video 1B.

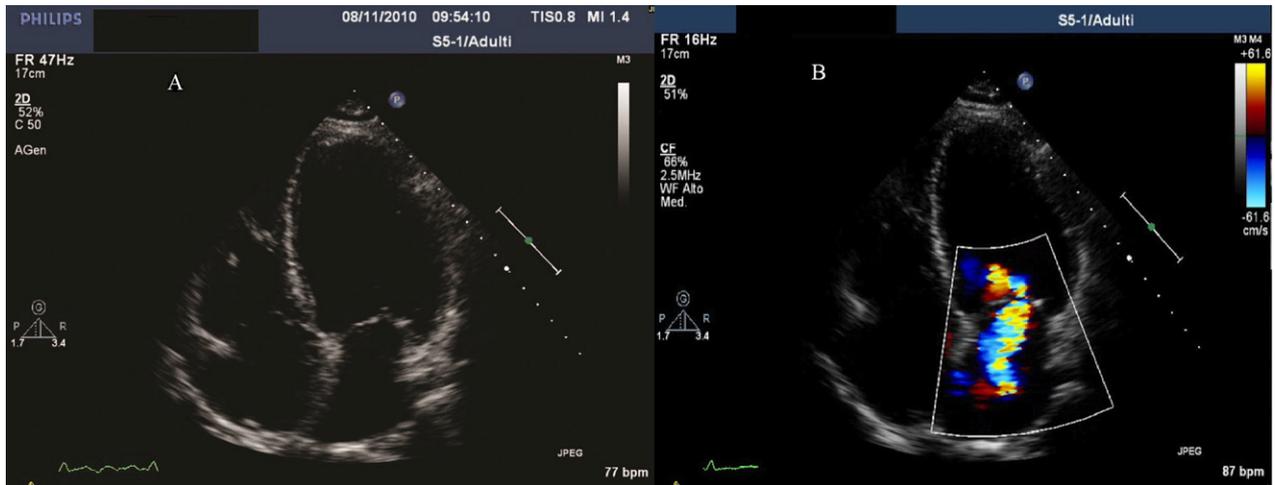


Figure 12 Symmetric tethering. **(A)** Systolic frame in an apical four-chamber view. See Video 2. **(B)** Color Doppler image showing a centrally oriented jet of MR. Images courtesy of Dr. Eustachio Agricola.

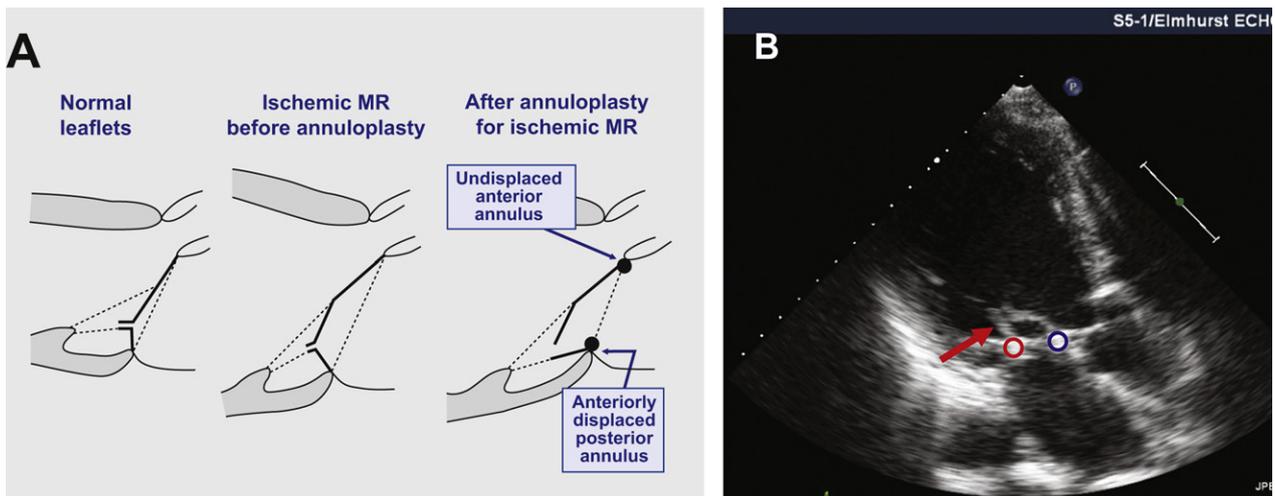


Figure 13 **(A)** The undersized annuloplasty ring hoists the posterior annulus anteriorly, increasing the distance between the PM tip and the posterior annulus. Increased tethering of the posterior leaflet widens the posterior leaflet angle, rendering it immobile. Reproduced with permission from *Circulation*.⁶⁶ **(B)** Apical long-axis image after undersized ring annuloplasty. Note the anterior annulus (blue circle) and the anteriorly displaced posterior annulus (red circle). The posterior mitral leaflet (arrow) is excessively tethered with substantial widening of the posterior leaflet angle. See Video 3.

tenting area $> 2.5 \text{ cm}^2$ were found to be highly specific but relatively insensitive for predicting postoperative MR.⁵⁷ By contrast, a posterior leaflet angle $> 45^\circ$,⁵⁷ as well as a distal anterior leaflet angle $> 25^\circ$,⁵⁵ are highly sensitive and specific. Postoperative MR is more common in patients with symmetric tethering compared with those with asymmetric tethering.⁵⁵ These guidelines may be helpful in identifying high-risk patients in whom adjunctive therapies (chord cutting, PM repositioning) or mitral valve replacement might be considered.

Novel Percutaneous Therapies

A number of percutaneous approaches to the treatment of ischemic MR have recently been developed. Percutaneous mitral valve repair is an adaptation of the surgical Alfieri stitch,⁹⁷ in which the A2-P2 scallops are approximated with a clip (e.g., MitraClip; Evalve Inc., Menlo Park, CA) instead of suture material, creating a double-orifice configuration (Figure 16). Notwithstanding the reduction in orifice area,

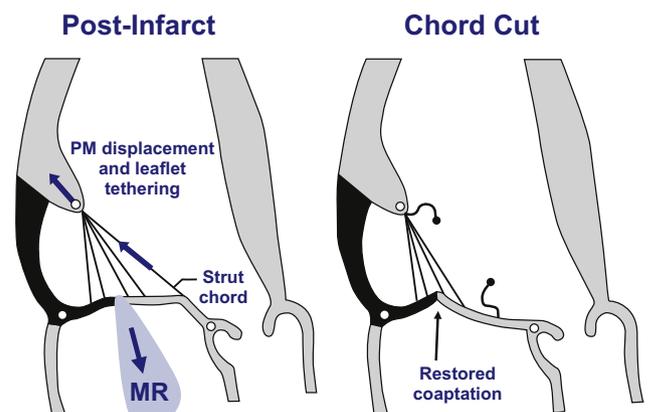


Figure 14 Strut cord transection. Note that the untethered leaflet has more surface area available for coaptation. Reproduced with permission from *Circulation*.⁶⁷

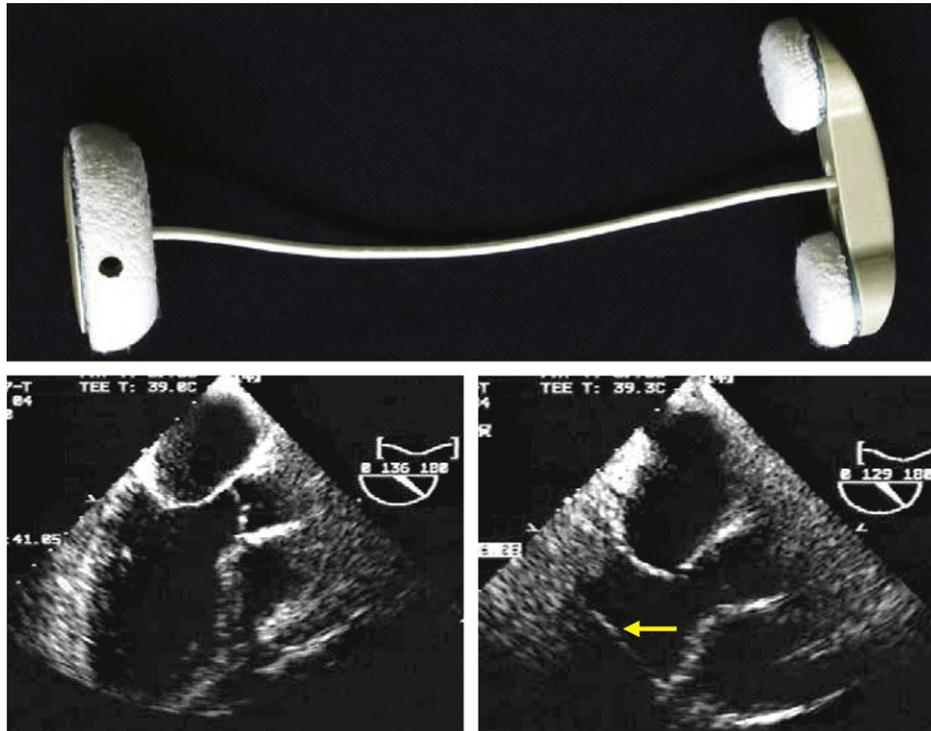


Figure 15 Coapsys device. Echocardiographic images obtained before (left) and after (right) insertion of a Coapsys device (arrow). Note the reduction in LV internal dimension after insertion. Reproduced with permission from Mishra YK, Mittal S, Jaguri P, Trehan N. Coapsys mitral annuloplasty for chronic functional ischemic MR: 1-year results. *Ann Thorac Surg* 2006;81:42-6.

Table 1 Echocardiographic predictors of persistent and/or recurrent MR

Predictor	Source
Leaflet deformation indices	
Tenting height ≥ 1.0 cm	Magne et al ⁵⁷
Tenting height ≥ 1.1 cm	Calafiore et al ⁹⁴
Tenting area ≥ 2.5 cm ²	Magne et al ⁵⁷
Tenting area ≥ 1.6 cm ² *	Kongsaerepong et al ⁹³
Posterior leaflet angle ≥ 45	Magne et al ⁵⁷
Distal anterior leaflet angle > 25	Lee et al ⁵⁵
Annular size	
Mitral annular dimension ≥ 3.7 cm*	Kongsaerepong et al ⁹³
MR jet characteristics	
Grade > 3.5 *	Kongsaerepong et al ⁹³
Central or complex	McGee et al ⁶³
LV factors	
Systolic sphericity index ≥ 0.7	Gelsomino et al ⁹⁵
LV end systolic volume ≥ 145 mL	Gelsomino et al ⁹⁵
Restrictive LV diastolic filling pattern	Eremiene et al ⁹⁶

*Measurements made by intraoperative transesophageal echocardiography.

hemodynamically significant mitral stenosis does not appear to be a problem.⁹⁸ The Endovascular Valve Edge-to-Edge Repair Study (EVEREST) II⁹⁹ followed patients with hemodynamically significant functional and degenerative MR who underwent percutaneous mitral valve clipping. At 1 year, almost two thirds were free from death, mitral valve surgery, or MR $> 2+$. A randomized comparison with conventional surgical repair or replacement is currently under way. It should

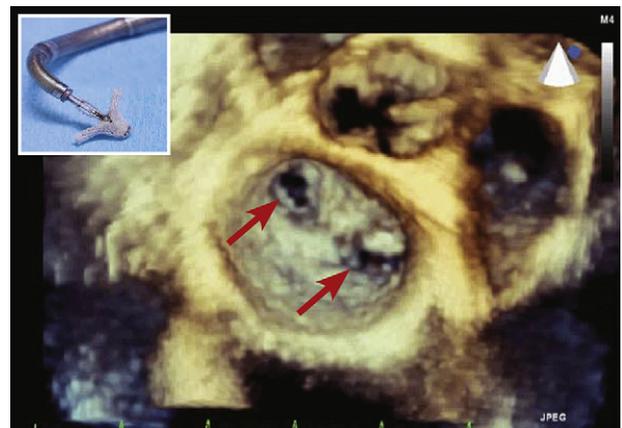


Figure 16 Three-dimensional echocardiographic image of the mitral valve after the insertion of a MitraClip device (insert). A characteristic double orifice is seen (arrows). Reproduced with permission from *J Am Coll Cardiol*.⁹⁹

be noted that the EVEREST II trial only enrolled patients with MR jets originating centrally (at A2-P2), and it remains to be determined whether percutaneous valve repair is broadly applicable to the full anatomic spectrum of tethering patterns in ischemic MR. The investigators of this study observed that anteroposterior annular diameter did not increase during 12 months of follow-up, suggesting stabilization by the tissue bridge formed as a result of healing around the MitraClip device. LV dilatation might also be limited by this tissue bridge through enhanced ventricular-valvular continuity.⁹⁹

Percutaneous ring annuloplasty devices take advantage of the anatomic relation of the coronary sinus to the posterior mitral annulus.

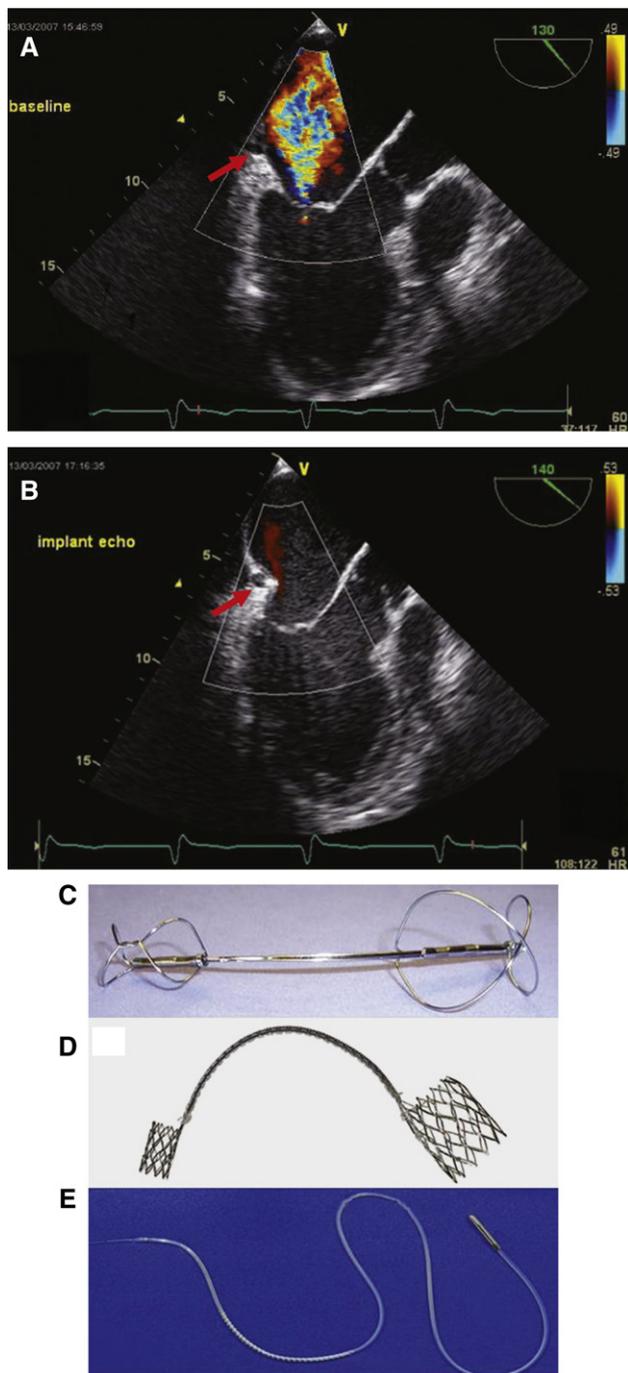


Figure 17 Echocardiographic images obtained **(A)** before and **(B)** after percutaneous coronary sinus annuloplasty. Note the marked reduction in MR after implantation. The red arrows are pointing to the coronary sinus. Various percutaneous annuloplasty devices are shown. **(C)** CARILLON (Cardiac Dimensions, Kirkland, WA). **(D)** MONARC (Edwards Lifesciences, Irvine, CA). **(E)** Percutaneous Transvenous Mitral Annuloplasty Device (Viacor Inc., Wilmington, MA). Reproduced with permission from *Circ Cardiovasc Interv.*¹⁰⁴

Although this spatial relationship is variable,¹⁰⁰ this does not appear to affect procedural outcomes.¹⁰¹ Percutaneous ring annuloplasty devices reduce the anteroposterior dimension of the annulus, and acute improvements of one MR grade (3+ to 2+) have been demonstrated¹⁰²

(Figure 17). Because the coronary sinus frequently crosses the left circumflex artery, arterial occlusion remains a barrier to use in patients with unsuitable coronary anatomy. The published data¹⁰²⁻¹⁰⁴ on percutaneous annuloplasty reflect preliminary observations, and additional research into the safety and efficacy of this procedure is needed.

Cardiac Resynchronization Therapy

Restoration of intraventricular synchrony with CRT has been shown to have a number of salutary effects in patients with ischemic MR. Acute reductions in MR have been attributed to restoration of PM⁴⁴ and annular¹⁰⁵ synchrony. CRT has also been shown to offset otherwise excessive tethering forces by increasing LV dP/dt (closing forces).^{46,106} It is interesting to note that restoring mechanical synchrony blunts exercise-induced increases in ROA.¹⁰⁷ Over the long term, CRT is thought to reduce MR through reverse remodeling. However, it should be emphasized that in this respect, the response to CRT is more robust in functional MR than ischemic MR.¹⁰⁸

CONCLUSIONS

Ischemic MR is a complex disorder for which echocardiography remains an invaluable investigative and diagnostic tool. As our understanding of its pathogenesis continues to evolve, additional insights will undoubtedly lead to the development of innovative therapies in the future.

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