CHAPTER 48

DEGENERATIVE MITRAL VALVE DISEASE

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The normal mitral valve permits one-way blood flow from the left atrium to the left ventricle in an efficient, nearly frictionless fashion.[1] Although even a normal competent valve may allow a trivial amount of reversed flow, more than a trace of mitral regurgitation is considered pathologic.[2] Mild to moderate mitral regurgitation is tolerated indefinitely as long as it does not worsen. However, severe mitral regurgitation causes left ventricular remodeling reduced forward cardiac output, neurohumoral activation, left ventricular damage, heart failure, and ultimately death.[3] The natural history of mitral regurgitation depends intimately on its etiology, the severity of left ventricular volume overload as well as its contractile performance, and the appearance of overlapping clinical conditions secondary to reversal flow such as atrial fibrillation and pulmonary hypertension.[4] In this setting, myxomatous degeneration of the mitral valve, a very common pathologic substrate of mitral valve billowing (normal valve coaptation) and prolapse (deficient valve coaptation), is the most prevalent cause of isolated severe mitral regurgitation requiring surgical intervention in the United States.[5] The following is a review of the normal mitral valve anatomy as well as a summary of causes, consequences, and treatment of degenerative mitral valve regurgitation.

MITRAL VALVE ANATOMY

The mitral valve is located in the left atrioventricular groove, and allows unidirectional flow of oxygenated blood from the left atrium into the relaxed left ventricle during diastole. The mitral valve apparatus is a very complex three-dimensional assembly of separate anatomical components including the annulus, the leaflets and commissures, the chordae, the papillary muscles, and the ventricle.[6] During systole, a coordinated interaction of these anatomical components closes the valve against ventricular pressure. Therefore, its anatomy should be scrutinized systematically to identify the lesions (the abnormalities in valve structure) that lead to the valve's dysfunction (the alteration in closure that results in mitral regurgitation).[7]

MITRAL ANNULUS

The mitral annulus is a fibromuscular ring located in the left atrioventricular groove, which serves as an attachment and hinge point for the mitral valve leaflets. The mitral annulus is subjectively divided into anterior and posterior segments based on the attachments of the anterior and posterior mitral leaflets, but can also be segmented by location into septal and lateral components. The anterior portion of the mitral annulus is in continuity with the fibrous skeleton of the heart, defined by the right and left fibrous trigones and the aortic mitral curtain. This portion of the mitral annulus is thus fibrous in nature, and is much less prone to dilation in comparison to the posterior portion of the annulus (Fig. 48–1). Because the fibrous skeleton is discontinuous along the posterior portion of the mitral annulus, this portion dilates or increases its circumference in the setting of chronic mitral valve regurgitation with associated atrial and ventricular dilatation.[8] The resultant increase in mitral annular dimension tends make the annulus more circular in shape, compared to its normal "kidney-bean shape," which in turn compromises the coaptation of the mitral leaflets as a result of the increase in septal-lateral or anterior-posterior dimension. The hinge point of the posterior portion of the mitral annulus may become "atrialized" in long-standing posterior leaflet prolapse, and may also be affected by diffuse pathologic calcification. The normal mitral annulus also has a three-dimensional saddle shape, and the anterior portion of the annulus tends to bulge during systole to accommodate the aortic root. The overall circumference of the annulus may decrease by as much as 20% during systole, promoting central leaflet coaptation.[9]

MITRAL LEAFLETS AND COMMISSURES

The mitral valve has an anterior and posterior leaflet with similar surface areas but markedly different shapes.[10] The anterior leaflet is

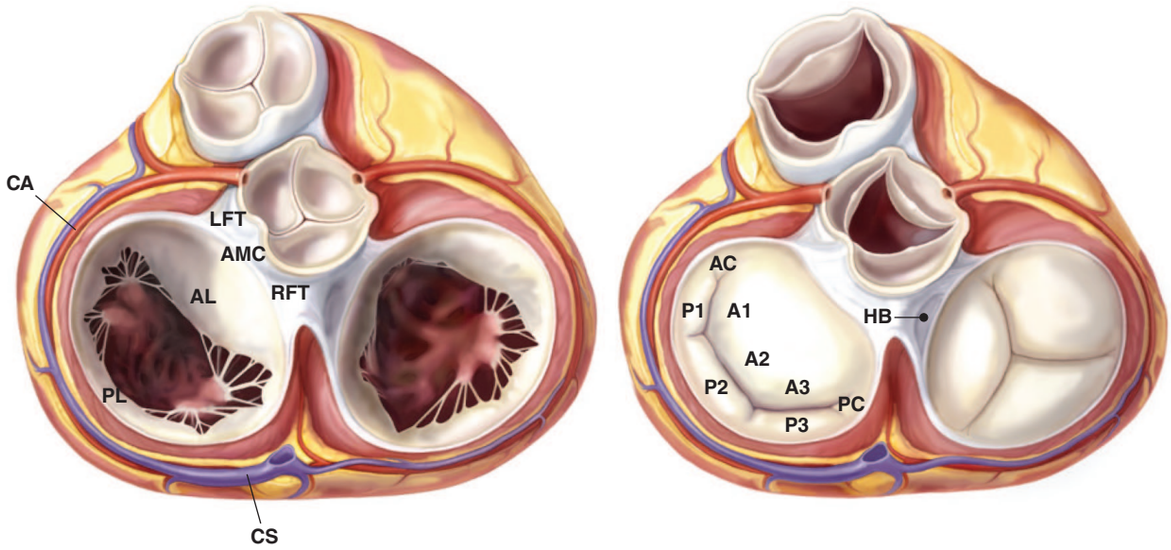


FIGURE 48–1. Anatomic view of the cardiac valves in diastole (left) and systole (right) with the left and right atrium cropped away and the great vessels transected. The illustration highlights the anatomical relations of the mitral valve, particularly its continuation with the aortic valve through the aorto-mitral curtain. AC, anterior commissure; AL, anterior leaflet; AMC, aorto-mitral curtain; CA, circumflex artery; CS, coronary sinus; HB, Hiss bundle; LFT, left fibrous trigone (anterolateral trigone); PC, posterior commissure; PL, posterior leaflet; RFT, right fibrous trigone (posteromedial). Modified from *Carpentier's Reconstructive Valve Surgery* by Carpentier AC, Adams DH, Filsoufi F (Saunders Elsevier, 2010).

taller than the posterior leaflet but with a shorter base, attaching to one-third of the annular circumference between the right and left fibrous trigones. During systole the anterior leaflet forms a portion of the left ventricular outflow tract through its continuity with the aorto-mitral curtain. The posterior leaflet is broader based, extending along the remaining two-thirds of the annulus, and has a shorter height. Despite their different shapes, the overall surface areas of the two leaflets are similar. The different orientations of the two leaflets ensures during systole the closure line of the mitral valve will be located in the posterior one-third of the valve orifice, which prevents systolic anterior motion of the tip of the anterior leaflet in into the outflow track. Both leaflets present two zones from its base to the free margin: *the body zone* (smooth and translucent) and the *coaptation zone* (thicker and rough as a result of the attachment of numerous chordae). During systole the coaptation zones of the respective leaflets join together to form a seal anywhere from a few millimeters to a centimeter, ensuring mitral valve competence (Fig. 48–2). The leaflets of the mitral valve can be "segmented" by location of the clefts or indentations in the posterior leaflet that subdivide it into individual "scallops." The middle scallop of the posterior leaflet is designated as P2 and adjacent lateral and medial scallops are designated as P1 or P3 (See Fig. 48–1). The anterior leaflet does not typically have natural indentations, but the corresponding areas of this leaflet are designated by opposition to the segments in the posterior leaflet as A1, A2, and A3.

In addition to anterior and posterior leaflet segments, the mitral valve has posterior medial and anterior lateral commissures, which represent small segments of leaflet tissue presenting at the insertional junction of the anterior and posterior leaflets. These distinct areas of leaflet tissue are supported by chordal fans, and are critical to insure a good surface of coaptation at the junctions of the two leaflets. The height of commissural leaflet tissue can vary from a few millimeters to over 1 cm.

CHORDAE TENDINAE

The chordae tendinae attach the mitral leaflets to the papillary muscles and left ventricle, creating a suspension system that allows full opening

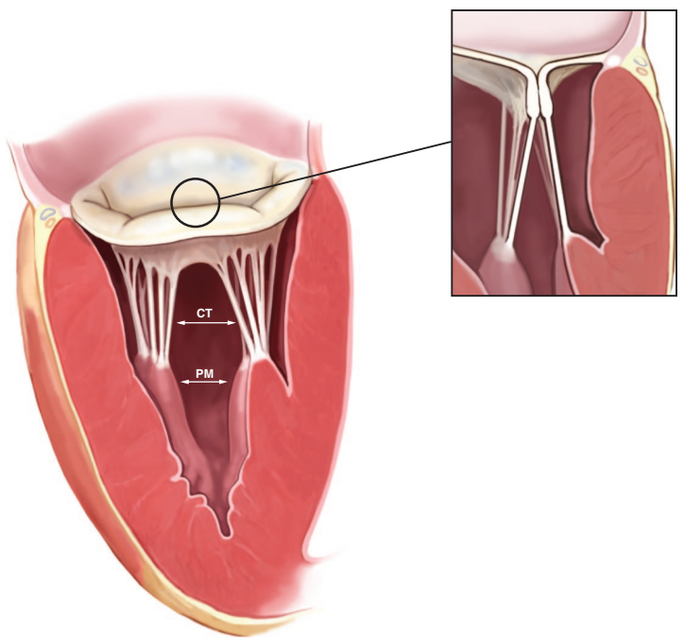


FIGURE 48–2. The mitral valve apparatus consists of the mitral leaflets, mitral annulus, chordae tendinae, papillary muscles, and left ventricle. Normal function of the mitral apparatus brings both leaflets together in systole and creates the coaptation zone. CT, chordae tendinae; PM, papillary muscles. Modified from *Carpentier's Reconstructive Valve Surgery* by Carpentier AC, Adams DH, Filsoufi F (Saunders Elsevier, 2010).

of the leaflets during diastole and prevents displacement of the leaflets above the annular plane during systole. Chordae tendinae are classified according to their attachment between the free margin and the base of the leaflets.[11] Primary or marginal chordae attach along the margin of the leaflets and are critical to prevent leaflet prolapse and to align the rough zones of the anterior and posterior leaflets during systole. Typically primary chordae insert every 3 to 5 mm along the margin of both leaflets. Secondary or body chordae, attach to the ventricular side of the body of the leaflets, provide ventricular annular continuity and balance of leaflet tension during systole. Tertiary or basal chordae, attached to the base of the leaflet hinge, providing additional linkage to the ventricle.[12]

PAPILLARY MUSCLES AND THE LEFT VENTRICLE

The mitral valve leaflets are attached by the chordae tendinae to the papillary muscles, which are a part of the left ventricle. The papillary muscles vary in the number of heads and exact position in the ventricle, but generally there are two main groups comprising the anterior and posterior papillary muscles. Each papillary muscle is identified according to the relationship to the valve commissures, and each provides a fan chord to its corresponding commissure as well as to both anterior and posterior leaflets. The anterior papillary muscle's blood supply can originate from both the left anterior descending artery as well as the circumflex artery, whereas the posterior papillary muscle is dependent primarily on the posterior descending artery. This explains the relative vulnerability of the posterior papillary muscle to ischemia, and subsequent involvement in localized remodeling in the setting of ischemic mitral valve regurgitation. The left ventricle supports the entire mitral apparatus by way of the papillary muscles, and thus ventricular dimensional changes in the setting of volume overload and remodeling can lead to leaflet tethering and mitral valve regurgitation irrespective of etiology.[13] This important relationship of volume overload and remodeling to mitral valve dysfunction has led to the common observation that "mitral regurgitation begets mitral regurgitation."

DEGENERATIVE MITRAL VALVE REGURGITATION

DYSFUNCTION

It is important to clarify the etiology and lesions that lead to clinically significant mitral valve regurgitation, as treatment options and long-term outcomes vary in different clinical scenarios. It is also useful to identify the valve dysfunction that results from the lesions of the mitral valve apparatus. The main dysfunctions, lesions, and etiologies that can result in mitral valve regurgitation are listed in Fig. 48–3. Carpentier described this pathophysiologic triad, and it is a useful tool in everyday practice when assessing patients with mitral valve regurgitation.[7]

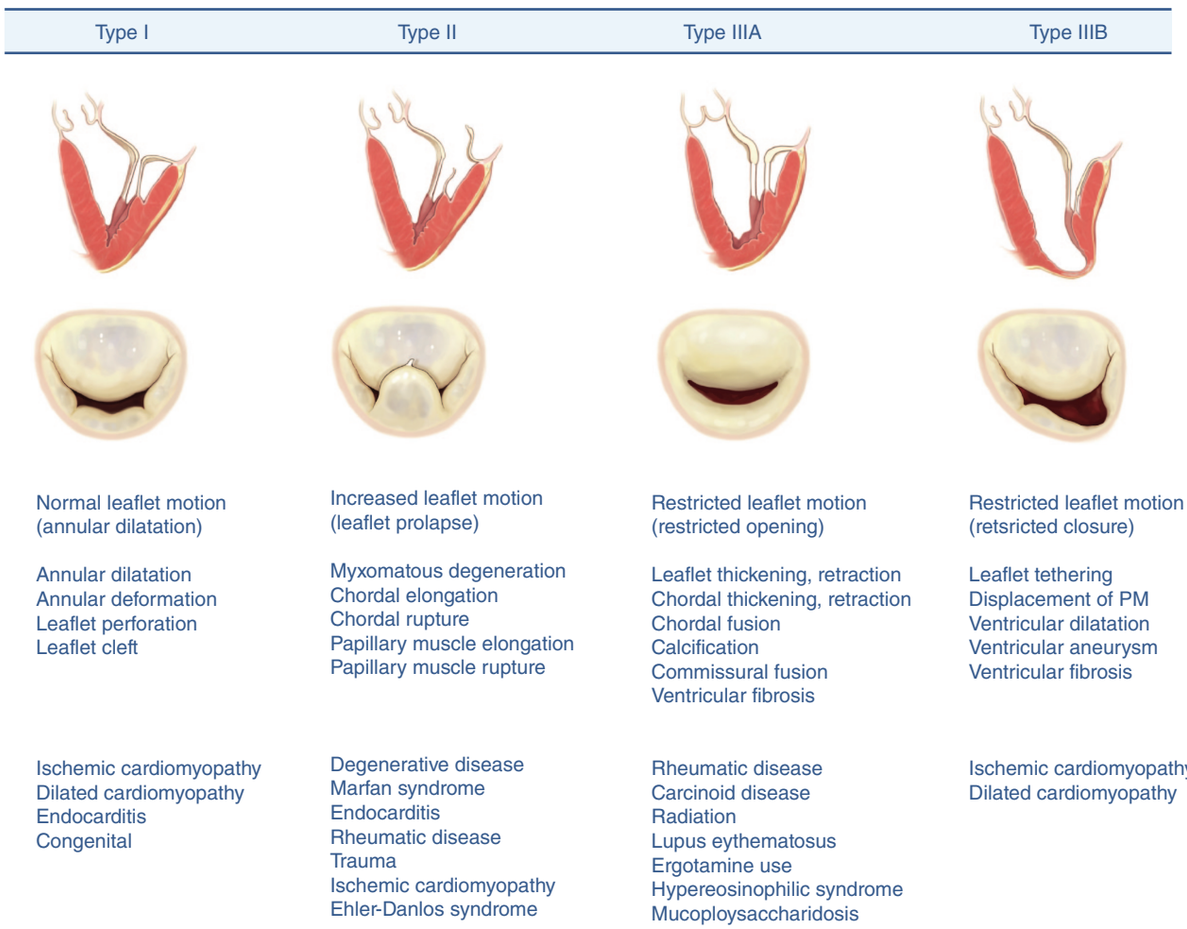


FIGURE 48–3. Pathophysiologic triad of mitral valve regurgitation composed of (top to bottom of each column): ventricular view, atrial view, leaflet dysfunction, valve lesions, and etiology.

Dysfunctions are classified on the basis of the position of the leaflet margins in relationship to the plane of the mitral annulus. Type I dysfunction implies normal leaflet motion, is the most common cause of significant mitral valve regurgitation, and often results from isolated annular dilatation or leaflet perforation; the former is common in the setting of primary atrial fibrillation. Type II dysfunction implies excess leaflet motion, and is most commonly associated with chordal elongation or rupture in the setting of degenerative mitral valve disease. Type IIIA dysfunction designates restricted opening and closing leaflet motion, and results typically from rheumatic valve disease or other inflammatory diseases that lead to chordal and leaflet scarring and calcification. Type IIIB dysfunction is associated with restricted leaflet motion in systole, and is most commonly associated with papillary muscle displacement and associated leaflet tethering in the setting of ischemic or nonischemic dilated cardiomyopathy. Some others have chosen to designate conditions associated with type I, II, and IIIA dysfunction as primary or organic mitral regurgitation, because the valve components (annulus, leaflets, and chords) are diseased, whereas type IIIB dysfunction is classified as secondary or functional mitral regurgitation, because it is caused by perturbations in ventricular geometry.[14]

ETIOLOGY AND LESIONS

Although rheumatic heart disease is still the most common cause of mitral regurgitation worldwide, it is no longer a common cause of mitral regurgitation in developed countries.[15] Ischemic mitral regurgitation resulting from myocardial infarction accounts for 10% to 20% of mitral regurgitation in developed countries, but earlier intervention in acute coronary syndromes may be limiting the number of such cases in the future.[16] In developed countries, degenerative mitral valve disease is now the leading cause of mitral valve disease and regurgitation.[17] Degenerative mitral valve diseases is defined by a spectrum of lesions, varying from simple chordal rupture involving prolapse of an isolated segment (particularly P2 or the middle scallop of the posterior leaflet) in an otherwise normal valve, to multisegment prolapse involving one or both leaflets in a valve with significant excess tissue and a large annular size (Fig. 48–4). This spectrum of degenerative disease is evident in clinical practice and carries important surgical and clinical implications. Furthermore, based on this spectrum of lesions, degenerative disease may be further divided into two main entities, fibroelastic deficiency and Barlow disease.[18-20] Other terms used to describe degenerative mitral valve disease include floppy valve syndrome, mitral valve prolapse, click-murmur syndrome, and parachute valve—a morass of terms causing much confusion. For instance, mitral valve prolapse can cause a click and murmur on physical examination, but the terms fail to clarify etiology.[21]

Fibroelastic deficiency usually occurs in patients over the age of 60 years[22] who have a relatively short history of valve disease, and their mitral regurgitation is usually holosystolic and severe. Fibroelastic deficiency describes a condition associated with fibrillin deficiency, which often leads to a rupture of one or more thinned and elongated chordae usually involving the middle scallop of the posterior leaflet. Chordal rupture is the most common lesion causing mitral regurgitation in fibroelastic deficiency. Leaflets are usually thin and translucent, although the prolapsing segment may show myxomatous degeneration with leaflet segment thickening and distension in long-standing regurgitation. The key characteristic of fibroelastic deficiency within the spectrum of degenerative disease is that the adjacent segments to

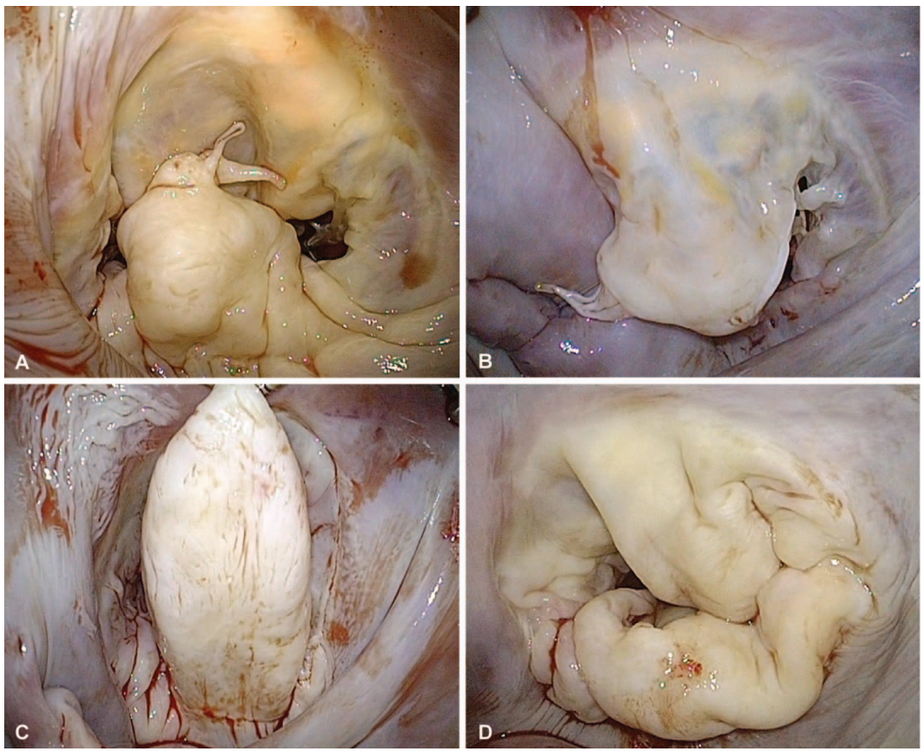


FIGURE 48–4. Valve lesions in degenerative mitral valve disease. **A.** Fibroelastic deficiency; isolated P2 prolapse secondary to chordal rupture and mild segmental thickening. **B.** Fibroelastic deficiency; anterior leaflet prolapse as a result of multiple ruptured chordae. **C.** Barlow disease; very tall and thickened P2 segment with otherwise normal P1 and P3 segments. **D.** Barlow disease; large valve with redundant, thick, bulky leaflets. Note the blurring of the junction between atrium and leaflet with fissures.

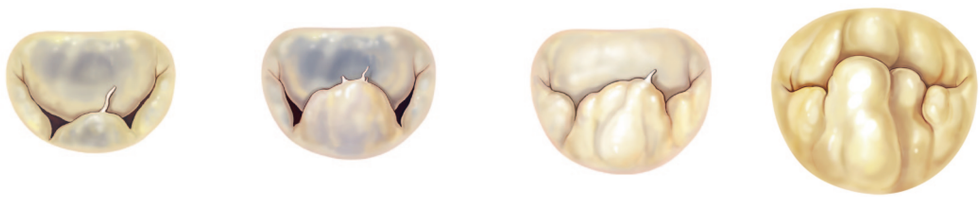
the prolapsing segment are generally normal in size, height, and character.[19,20,23] The valve annular size, as defined by anterior leaflet surface area, is generally ≤32 mm. In contrast, patients with Barlow disease are generally younger (<60 years of age) at the time of surgical referral, an often present with long history of follow-up for a murmur. Barlow valve disease causes a more diffuse and complex redundancy of the valve, producing prolapse and myxomatous degeneration of multiple segments in one or both leaflets. The most common lesions are excess leaflet tissue, leaflet thickening, and distention, with diffuse chordal elongation, thickening, and/or rupture. Severe annular dilatation with giant valve size is evident (>36 mm).[24] Additionally, varying degrees of annular calcification are often observed, as well as subvalvular fibrosis and calcification of the papillary muscles, in particular the anterior papillary muscle.[25] These extremes of the spectrum of lesions bracket a continuum of a more myxomatous form of fibroelastic deficiency and forme fruste disease, a term given to certain valves with some but not all pathologic features of Barlow disease (Fig. 48–5).

No specific cause of these lesions associated with abnormalities in the extracellular matrix, matrix metalloproteases, and subnormal leaflet and chordal strength has been identified (Fig. 48–6).[26] Some genetic abnormalities[27] have been described but no one genetic variation still fully explains the variation of pathology seen. It is likely that genetic abnormalities render the valve susceptible to the degenerative process and after mitral regurgitation develops it places progressively more hemodynamic stress on the valve perpetually worsening the disease. At present no useful strategies have emerged for preventing or slowing the progression of degenerative mitral regurgitation.

PATHOPHYSIOLOGY

Mitral regurgitation imparts a volume overload on the left ventricle because it must compensate for the volume lost to regurgitation. Mild to moderate mitral regurgitation is well tolerated, possibly for long periods of time, as long as the severity of mitral regurgitation does not increase. The grades of severity as suggested by the *AHA/ACC Guidelines for the Management of Valvular Heart Disease*[28] are listed in (Table 48–1). Although these are only guidelines, they stem in part from the fact that when regurgitant fraction has been calculated for patients requiring mitral valve surgery, the regurgitant fraction almost always exceeds 50%.

Severe mitral regurgitation can be subdivided into three stages: acute, chronic compensated, and chronic decompensated (Fig. 48–7). In acute mitral regurgitation as might occur from rupture of a marginal chordae tendinae, a small unprepared left ventricle is suddenly confronted with a large volume overload from blood returning from the pulmonary veins summed with the regurgitant volume from the left ventricle. The volume overload causes existing sarcomeres to stretch maximally, increasing end-diastolic volume and also stroke work through the Frank-Starling mechanism. The extra pathway for ejection into the left atrium unloads the left ventricle, reducing end-systolic volume. Increased preload,



	Fibroelastic deficiency	Fibroelastic deficiency +	Forme fruste	Barlow's disease
Age at diagnosis	>60 years old	Likely >60 years old	Likely <60 years old	<60 years old
History of MR	<5 years	Likely <5 years	Likely >10 years	>10 years
Annular dilatation	≤26 mm	Likely ≤32 mm	Likely 32 mm - 36 mm	≥36 mm
Leaflet tissue	Thin, translucent ○ ○ ○	Translucent, mild thickening ● ○ ○	Moderate excess ● ● ○	Diffuse excess ● ● ●
Segmental distribution	Single segment (P2)	Single segment (P2)	Posterior segments	Multisegmental
Chordae tendinae	Thin, ruptured	Thin, ruptured	Elongated, ruptured	Irregular, elongated
Degree of calcification	○ ○ ○	○ ○ ○	● ○ ○	● ● ●
Repair phylosophy	Respect tissue	Likely respect tissue	Small resection	Resection
Difficulty of repair	● ● ○	○ ○ ○	● ○ ○	● ● ●
Repair techniques	Chordal transfer PTFE neochordoplasty Loop techniques	Leaflet displacement Free edge plication Loop techniques Triangular resection	Leaflet displacement Triangular resection Limited quadrangular Annular plication Limited sliding plasty Posterior leaflet flip	Leaflet displacement Targeted resections Cleft closure Quadrangular resection Sliding plasty Commissuroplasty Posterior leaflet flip

FIGURE 48–5. Characteristic clinical and surgical differences between fibroelastic deficiency and Barlow disease.

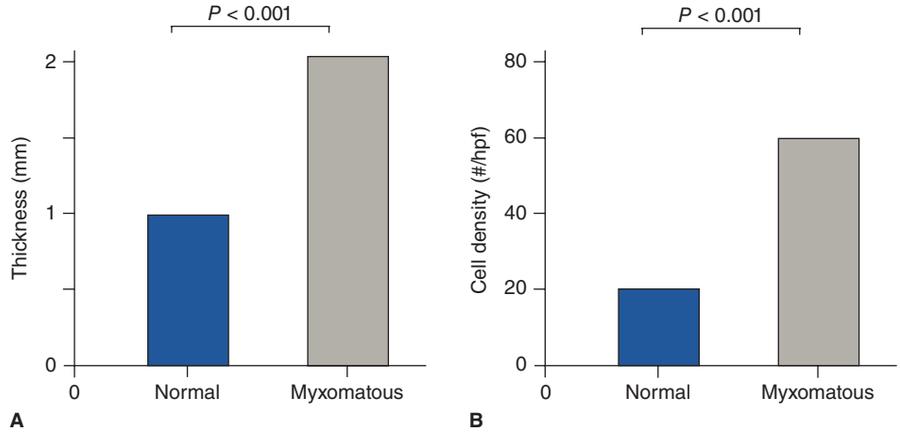


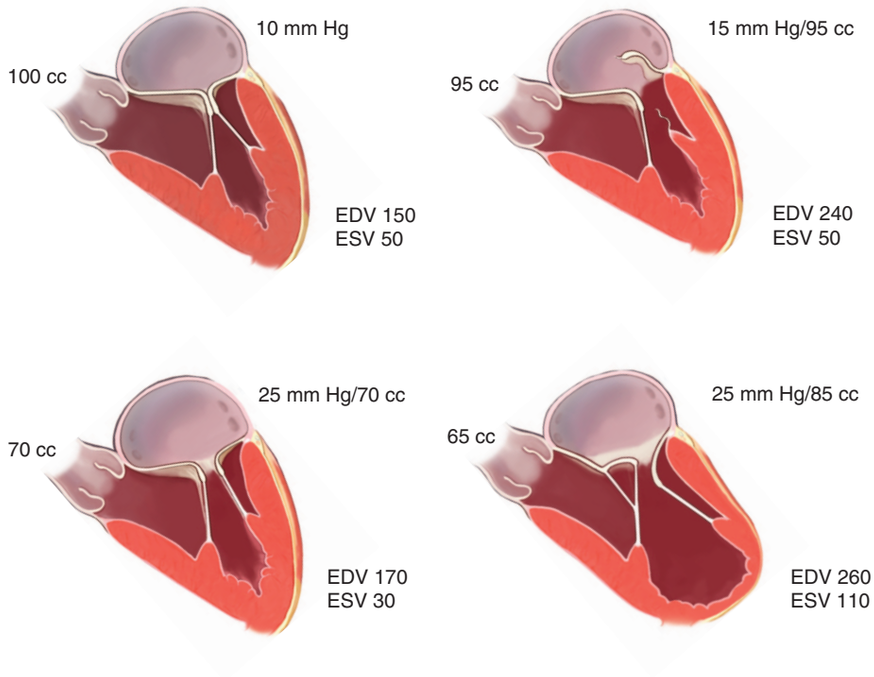
FIGURE 48–6. Quantitative analysis of mitral posterior leaflet tissue demonstrating significant thickening and increased cellularity of myxomatous valves. Adapted from Grande-Allen KJ, Griffin BP, Ratliff NB, et al. Glycosaminoglycan profiles of myxomatous mitral leaflets and chordae parallel the severity of mechanical alterations. *J Am Coll Cardiol*. 2003;42(2):271-277.

decreased afterload and a reflexive sympathetically mediated increase in contractility act in concert to increase total stroke volume and ejection fraction. However, because 50% or more of the total stroke volume is regurgitated into the left atrium, forward stroke volume and cardiac output are reduced. Additionally, the left atrium, of normal size and compliance, receives its very high total volume at high filling pressure, in turn leading to pulmonary congestion. Thus although left ventricular function is normal or even supernormal, the patient suffers the low output and pulmonary congestion typical of left ventricular failure. Many patients will require immediate corrective surgery at the time acute severe mitral regurgitation develops. In others there may be a more gradual progression to severe mitral regurgitation so that it is better tolerated. Such patients may enter a chronic compensated phase. In this phase eccentric hypertrophy develops, increasing left ventricular volume. Because the radius term in the Laplace equation for wall stress has increased (stress $\sigma = p \times r / 2th$, where p = LV pressure, r = radius, and th = thickness), afterload returns from subnormal to normal. However, increased preload and normal contractility permit a higher than normal ejection fraction of a large

TABLE 48–1. Stages of Primary Mitral Regurgitation

Grade	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of MR	• Mild mitral valve prolapse with normal coaptation • Mild valve thickening and leaflet restriction	• No MR jet or small central jet area <20% LA on Doppler • Small vena contracta <0.3 cm	• None	• None
B	Progressive MR	• Severe mitral valve prolapse with normal coaptation • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE	• Central jet MR 20%-40% LA or late systolic eccentric jet MR • Vena contracta <0.7 cm • Regurgitant volume <60 mL • Regurgitant fraction <50% • ERO <0.40 cm^2 • Angiographic grade 1-2+	• Mild LA enlargement • No LV enlargement • Normal pulmonary pressure	• None
C	Asymptomatic severe MR	• Severe mitral valve prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • Regurgitant volume ≥60 mL • Regurgitant fraction ≥50% • ERO ≥0.40 cm^2 • Angiographic grade 3-4+	• Moderate or severe LA enlargement • LV enlargement • Pulmonary hypertension may be present at rest or with exercise • C1: LVEF >60% and LVESD <40 mm • C2: LVEF ≤60% and LVESD ≥40 mm	• None
D	Symptomatic severe MR	• Severe mitral valve prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • Regurgitant volume ≥60 mL • Regurgitant fraction ≥50% • ERO ≥0.40 cm^2 • Angiographic grade 3-4+	• Moderate or severe LA enlargement • LV enlargement • Pulmonary hypertension present	• Decreased exercise tolerance • Exertional dyspnea

ERO, effective regurgitant orifice; IE, infective endocarditis; LA, left atrium/atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD; left ventricular end-systolic dimension; MR, mitral regurgitation. Adapted from Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63:2438-2488.



	Preload (SL)	*Afterload (ESS)*	*Contractile function*	*Ejection fraction*	*Regurgitant fraction*	*Stroke volume (cc)*
Control	2.07	90	N	0.67	0.0	100
Acute MR	2.25	60	N	0.82	0.5	70
Compensated MR	2.19	90	N	0.79	0.5	95
Decompensated MR	2.19	100		0.58	0.7	65

FIGURE 48–7. Normal physiology (control) is compared to that of acute mitral regurgitation (chordal rupture), compensated mitral regurgitation, and decompensated chronic mitral regurgitation. The sudden opening of a new pathway for regurgitant flow into the left atrium increases left atrial pressure and preload (sarcomere length), in turn mildly increasing end-diastolic volume because resting sarcomere length is still 90% of maximum length. Afterload (end-systolic stress) is decreased, allowing more complete left ventricular ejection fraction, reducing end-systolic volume. These changes in loading increase ejection fraction and total stroke volume, but because 50% of the total stroke volume is lost to regurgitation (regurgitant fraction), forward stroke volume is decreased. Therefore, despite normal contractile fraction and increased ejection fraction, the patient presents with the hemodynamics of congestive heart failure. In the presence of decompensated chronic mitral regurgitation, muscle damaged caused by prolonged severe volume overload reduces the effectiveness of ventricular ejection and end-systolic volume increases. There is a further increase in diastolic volume, which is not compensatory, resulting in a decrease in total and forward stroke volumes. EDV, end diastolic volume; ESS, end-systolic stress; ESV, end-systolic volume; MR, mitral regurgitation; SL, sarcomere length. Modified from Carabello BA. The current therapy for mitral regurgitation. *J Am Coll Cardiol*. 2008;52(5):319-326.

end-diastolic volume so that total stroke volume is greatly increased.[29] This permits forward stroke volume to return to normal. Left atrial size is now enlarged, permitting it to accept the large regurgitant volume at nearly normal pressure. Thus the patient now has a near normal cardiac output and filling pressure and is likely to be asymptomatic even during exercise. Although the patient may enjoy a period of compensation for years, eventually contractile dysfunction sustained from prolonged hemodynamic overload ensues and decompensation becomes manifest.[30] Impaired contractility causes increased end-systolic volume and reduced stroke volume and cardiac output. Filling pressure is re-elevated and the patient may develop heart failure symptoms. Although mitral regurgitation is usually thought to be a phenomenon that unloads the left ventricle, in decompensated mitral regurgitation, the increased radius term in the Laplace equation causes systolic wall stress to increase and afterload is greater than normal, contributing to left ventricular dysfunction.[31] In mitral regurgitation, increased left ventricular radius is not offset by increased thickness, leading to the increase in wall stress. Thus the relatively thin wall of the mitral regurgitant ventricle is beneficial to diastolic function and left ventricular filling but is detrimental to left ventricular systolic function because maladaptive left ventricular remodeling causes increased afterload.[32,33] It is important to note that ejection fraction may be held in the normal range by enhanced preload despite contractile dysfunction and afterload excess.

The left ventricular dysfunction caused by severe mitral regurgitation stems from multiple pathologic processes. At the cellular level there is loss of contractile elements in the endocardium in experimental models of mitral regurgitation and in the papillary muscles of humans.[34,35] This abnormality can be reversed by valve repair/replacement in the experimental animal and in man and also by administration of beta-blockers in the experimental animal.[36-38] These data suggest that sympathetic overdrive, present in both human and experimental mitral regurgitation, contributes to the cellular pathology of the disease.[39,40] In addition, the force-frequency relation of the mitral regurgitant ventricle is depressed but can be normalized by the administration of forskolin, suggesting that abnormalities in calcium handling contributes to left ventricular dysfunction.[41]

The left ventricular remodeling of mitral regurgitation is unique and probably dictated by the loading conditions present. Mitral regurgitation stands out as a pure volume overload.[42] In most other volume overloads such as anemia, heart block, and aortic regurgitation, the extra volume generated by the left ventricle is ejected into the aorta, where the high stroke volume generates a widened pulse pressure and an element of systolic hypertension. Thus most volume overloads are in fact a combination of volume and pressure overload and the left ventricle remodels accordingly. In aortic regurgitation, for instance, not only is left ventricular volume increased to compensate for the regurgitated volume but left ventricular thickness is also greater than normal.[43] Conversely, in mitral regurgitation the extra volume is ejected into the left atrium and systolic pressure is often low normal. In turn, left ventricular thickness is low normal, producing a thin-walled large left ventricle as noted earlier.

Several decades ago Grossman and coworkers proposed a paradigm for left ventricular remodeling wherein the increased systolic wall stress of pressure overload was transduced to generate new sarcomeres laid down in parallel such that myocyte thickness and left ventricular wall thickness increased.[44] Increased wall thickness in the denominator of the Laplace equation offset increased pressure term in the numerator,

keeping wall stress (afterload) normal, facilitating left ventricular ejection. On the other hand, the increased diastolic stress from the sarcomere stretch of volume overload led to new sarcomeres laid down in series, increasing myocyte length and ventricular volume, allowing the ventricle to increase stroke volume. In experimental acute pressure overload, a 35% increase in contractile protein synthesis occurs within 6 hours of the onset of the pressure overload.[45] Conversely, following the acute volume overload of mitral regurgitation and during chronic mitral regurgitation, no increase in protein synthesis was detected.[46] Because increased muscle mass can only accrue from either increased protein synthesis or decreased protein degradation, and because synthesis is not increased, it suggests that the hypertrophy of mitral regurgitation develops from a process opposite of that of pressure overload, that is, decreased protein degradation instead of increased protein synthesis. It might be that older contractile proteins are less robust, a factor in part responsible for the left ventricular dysfunction that ultimately develops.

As noted earlier, if mitral regurgitation is corrected before left ventricular dysfunction is long standing, ventricular function can recover dramatically both in the experimental animal and in humans. Recovery is marked by restoration of myocyte contractile elements and a reduction in adrenergic drive.

In summary, the pure volume overload of mitral regurgitation is compensated by eccentric left ventricular hypertrophy, which enables rapid left ventricular diastolic filling and an increase in stroke volume. However, this remodeling eventually encumbers systolic emptying. This maladaptive geometry together with the adrenergic over activation results in contractile protein loss, abnormal calcium handling, and a decrease in contractility. If mitral regurgitation is corrected in a timely fashion this pathophysiology can be reversed.

CLINICAL PRESENTATION

The typical symptoms of mitral regurgitation are those of left ventricular failure and include dyspnea on exertion, orthopnea, and paroxysmal nocturnal dyspnea. If pulmonary hypertension has developed, ascites and edema may also occur. Debate continues as to whether or not there is a mitral valve prolapse syndrome, that is, a group of symptoms associated with degenerative mitral valve disease. These symptoms are thought to include palpitation, fatigue, and chest pain, atypical of classic angina and syncope or pre-syncope.[47,48] These symptoms are very common in the general population, and whether they occur more frequently in patients with mitral valve prolapse continues to be a subject of controversy.

On physical examination the reduced forward stroke volume tends to reduce systolic blood pressure and pulse pressure, but this finding is quite variable and some patients are actually hypertensive. The apical beat is displaced downward and to the left in chronic severe disease owing to left ventricular dilatation. The typical murmur is holosystolic if the lesion is chordal rupture, and is heard best at the apex and radiates to the axilla. There is a weak positive correlation between mitral regurgitation severity and murmur intensity.[49] Severe mitral regurgitation is often accompanied by an S_3 produced by the emptying of the large left atrial volume under higher than normal pressure into the left ventricle. The presence of an S_3 is often evidence that the mitral regurgitation is severe rather than indicating that the patient is in heart failure.

Mitral valve prolapse in Barlow disease is sometimes referred to as click-murmur syndrome, indicative of the typical findings on physical examination of a mid-systolic click followed by a late systolic murmur. The click is generated as the elongated chordae are stretched taut. The valve leaflets then move past their coaptation point and the murmur ensues. Physical maneuvers that decrease left ventricular volume, such as standing or the Valsalva maneuver, cause the click and murmur to come earlier in systole and consequently to increase in intensity. This occurs because a decrease in left ventricular volume reduces tension on the mitral valve, in effect lengthening the valve apparatus. Maneuvers that increase left ventricular volume such as squatting or lying down may cause the opposite effect or may cause the click and murmur to disappear altogether. In some patients only the click or murmur is present, or mitral valve prolapse may occur without any physical findings. As the severity of mitral regurgitation worsens, the murmur becomes progressively more holosystolic and the click may disappear.

LABORATORY FINDINGS

The electrocardiogram and chest x-ray often demonstrate nonspecific abnormalities. The ECG may show evidence of left atrial enlargement and left ventricular hypertrophy, and T-wave abnormalities have been reported in the inferior leads in patients with prolapse. Because atrial fibrillation is common in patients with mitral regurgitation, a baseline ECG is important to have on file in case this arrhythmia occurs later. The chest x-ray may show cardiac enlargement and pulmonary congestion if heart failure has intervened.

Although the above studies are very modestly useful in diagnosing mitral regurgitation, the echocardiogram is indispensable.[50,51] Transthoracic images can demonstrate the pathoanatomy or lesions responsible for mitral regurgitation, the degree of severity of mitral regurgitation, and the effect of mitral regurgitation on left ventricular remodeling and function, and help clarify the likelihood of eventual valve repair.[52-54] Because the esophagus virtually abuts the left atrium, transesophageal echocardiograms usually produce clear images of the mitral valve and of the left atrium and ventricle.[55]

ECHOCARDIOGRAPHIC PATHOANATOMY

The typical echocardiography features of fibroelastic deficiency and Barlow disease are demonstrated in Fig. 48–8. In patients with fibroelastic deficiency, echocardiographic findings typically include an isolated segmental prolapse, with flail leaflet segment caused by chordal rupture leading to holosystolic mitral regurgitation. Conversely, echocardiographic findings in patients with Barlow disease include mid-systolic and frequently diffuse regurgitation with multiple jets consistent with chordal elongation effecting grossly thickened myxomatous leaflets. The posterior leaflet is often displaced towards the left atrium away from the ventricular hinge, resulting in a cul-de-sac along the posterior portion of the annulus, which potentially becomes a precipitating factor for the development of annular fissures and calcification.[56]

Real-time three-dimensional echocardiography replicates the "surgical view," the view of the mitral valve the surgeon will see upon opening the left atrium. Quantitative analysis using proprietary software also allows precise determination of prolapsing or restricted segments within the plan of the annulus.[57] As such this imaging technique is very useful in identifying the leaflet segments involved with disease and planning the surgical approach to repair the mitral valve.

ECHOCARDIOGRAPHIC SEVERITY ASSESSMENT

Transthoracic echocardiography provides most of the diagnostic data needed for baseline evaluation of patients with mitral regurgitation (MR). The role of imaging is twofold: (1) to determine the severity of MR and (2) to determine the etiology of the disease. The severity of MR is based on the integration of several quantitative parameters, including measurement of vena contracta width, regurgitant volume, regurgitant fraction, and effective regurgitant orifice area (Table 48–1, Fig. 48–9).[28,58,59] This helps minimize the effects of technical or measurement errors inherent to each method. In addition, TTE provides useful information about LV size and function, RV function, left atrial size, and pulmonary artery pressure.

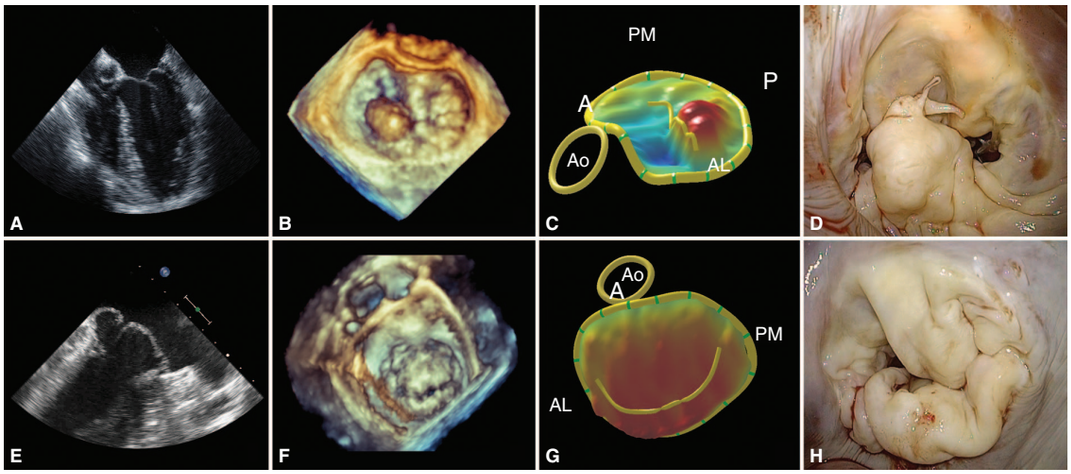


FIGURE 48–8. Transesophageal echocardiographic correlation of 2D and 3D in the differentiation of degenerative mitral disease. **A.** Fibroelastic deficiency with a ruptured chord to P2 (posterior middle scallop). **B.** 3D volume rendering of the same valve. **C.** 3D rendering using quantitative analysis (*red area* corresponds to prolapsing area). **D.** Surgical view. **E.** Barlow disease with multi-segment prolapse and excess leaflet tissue. **F.** 3D volume rendering of the same valve. **G.** 3D rendering using quantitative analysis (*red areas* correspond to prolapsing areas). **H.** Surgical view.

Etiologic differentiation of primary MR is crucial for guiding treatment and management decisions. Primary MR is characterized by abnormalities of the mitral valve itself and the majority of the structural abnormalities can be identified on transthoracic echocardiogram (TTE). Although transesophageal echocardiogram (TEE) is more accurate than TTE in locating the site and severity of structural abnormalities and quantifying the severity of MR, TEE during an initial diagnostic evaluation is only indicated in patients with inconclusive or technically difficult TTE

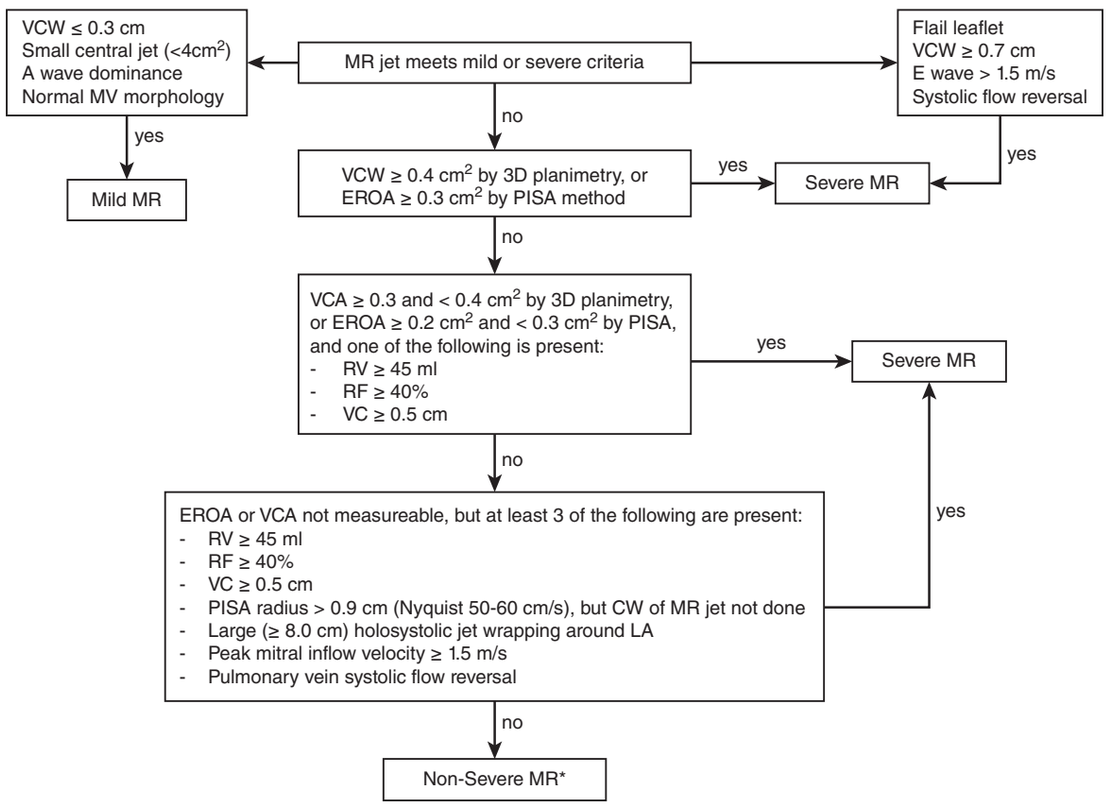


FIGURE 48–9. Algorithm for distinguishing severe from nonsevere mitral regurgitation (MR) in patients with clinically MR jets on color Doppler imaging. Severe MR corresponds to angiographic grades 3+ and 4+ per American College of Cardiology/American Heart Association guidelines. The first step is to determine whether MR severity is obviously mild or severe by American Society of Echocardiography/European Association for Echocardiography criteria (see text). If not, quantitative parameters are applied in a systemic, integrated fashion to determine whether MR is severe. Unless the MR is unequivocally mild in step 1, no attempt is made to distinguish mild from moderate MR (nonsevere), because studies comparing quantitative echocardiographic measures to an independent reference standard show substantial overlap. VCW, vena contracta width; MV, mitral valve; VCA, vena contracta area; 3D, 3-dimensional; EROA, effective regurgitant orifice area; PISA, proximal isovelocity surface area; RV, regurgitant volume; RF, regurgitant fraction; VC, vena contracta; CW, continuous-wave Doppler; and LA, left atrium. Adapted from Grayburn PA, Weissman NJ, Zamorano JL. Quantitation of mitral regurgitation. *Circulation*. 2012;126:2005-2017.

examinations. On the other hand, following a surgical consultation, TEE is routinely used in the perioperative period for confirming the mechanism of MR and guiding surgical planning. Recent advances in real-time 3D TEE technique allow accurate quantification of vena contracta area, regurgitant orifice area, and regurgitant volume. However, these techniques are relatively new, and their test-retest characteristics, prognostic value, threshold for severity classifications, and multicenter studies of accuracy and reproducibility require further standardization.[60]

Assessment of myocardial function is challenging for patients with MR. Left ventricular ejection fraction may remain in the normal or supernormal range for long periods of time, even if alterations in contractility develop. Moreover, a marked drop in LV ejection fraction can occur after surgery, even when the preoperative LV ejection fraction is normal. Therefore, earlier detection of LV contractile dysfunction is of pivotal importance so that surgical correction of chronic MR can be performed in a timely manner. There has been growing interest in using newer dedicated software that can track natural myocardial markers, or speckles in echocardiography images, for characterizing myocardial functional abnormalities beyond ejection fraction.[61] Several studies have suggested that assessment functional abnormalities of the LV in the longitudinal direction may provide windows for characterizing subclinical LV dysfunction in patients with severe MR.[62]

STRESS ECHOCARDIOGRAPHY

Exercise Doppler echocardiography can be used in asymptomatic patients with moderate to severe primary MR with preserved LV ejection fraction for immediate risk stratification and to guide the timing of mitral valve surgery, especially for those in whom the risk-to-benefit ratio of surgical intervention is uncertain or borderline.[63] Worsening of valvular regurgitation severity, exercise-induced pulmonary hypertension, impaired LV contractile reserve, inducible ischemia, and altered exercise capacity, together with the development of symptoms during exercise echocardiography, provide the clinician with information for a more accurate definition of the optimal timing of intervention in patients with valvular regurgitation. Exercise Doppler echocardiography can also be useful in patients with secondary MR in the following situations: (1) patients with exertional dyspnea out of proportion with the severity of resting LV dysfunction or MR; (2) patients with moderate MR in whom acute pulmonary edema occurs without an obvious contributing factor; (3) those with moderate MR before surgical revascularization; (4) those in whom individual risk stratification is requested; and (5) those operated on for mitral valve problems but with persistent postoperative pulmonary hypertension.[64]

COMPUTED TOMOGRAPHY AND CARDIAC MAGNETIC RESONANCE

Computed tomography and cardiac magnetic resonance techniques have been compared to echocardiography for MR assessment, but are not routinely recommended unless there are critical considerations regarding chamber remodeling, the presence of cardiac neoplasm, or coronary artery disease using viability assessments.[65,66] With the developments in transcatheter techniques for treating MR, there has been growing interest in using CT techniques for assessing the geometry and sizing of the mitral valve apparatus.[67] MRI of the valve apparatus may be useful in evaluating the amount of regurgitant flow with velocity encoding using model-independent measurements of stroke volumes of RV and LV with higher precision and accuracy than echocardiographic techniques.[68]

CARDIAC CATHETERIZATION

Once the mainstay of evaluation, invasive hemodynamic evaluation is now reserved for cases in which the diagnosis of the severity and impact of mitral regurgitation is uncertain. Although the exact mechanisms of dyspnea are not entirely understood, in cardiac disease, dyspnea correlates best with elevated left atrial pressure. Thus elevated left atrial or wedge pressure at rest or during dynamic or handgrip exercise during heart catheterization can demonstrate the hemodynamic underpinnings of a patient's symptoms. The presence of a large v-wave (twice the mean left atrial pressure) in the pulmonary capillary wedge or left atrial tracing may further indicate severe mitral regurgitation. Remembering that left ventriculography visualizes actual flow of blood from left ventricle to left atrium whereas color-flow Doppler only visualizes flow velocity, a well-performed ventriculogram can help clarify mitral regurgitation severity in some cases, provided a sufficient dye load is used.

MEDICAL THERAPY

INFECTIVE ENDOCARDITIS PROPHYLAXIS AND PREOPERATIVE DENTAL CLEARANCE

The risk of infective endocarditis is significantly increased in patients with mitral valve prolapse, especially in patients with thickened redundant valves.[69] Because of this risk, antibiotic prophylaxis was recommended prior to undergoing procedures that are known to cause bacteremia such as teeth cleaning, scaling, and colonoscopy. This recommendation was based upon the theory (with little proof) that prophylaxis was actually effective. Recently amid controversy, the AHA/ACC guidelines were changed and no longer make such prophylaxis mandatory.[28] The change was based in part upon the lack of proof of prophylaxis effectiveness and in part because bacteremia is a daily occurrence with eating and dental flossing yet antibiotic prophylaxis for these activities would be impossible. In the same context, the need of preoperative dental work, or in other words the need of preoperative dental clearance, also remains unclear.[70] Although general dental work is indeed not associated with an increased risk of endocarditis or preoperative mortality, tooth extraction or root treatment still is.[71] The indication for any dental work before mitral surgery should be clearly defined, and this is particularly true for dental extractions. Although poor dental hygiene might or might not need special attention, a periodontal infection (requiring extraction) and the presence of an apical abscess (requiring extraction and potential debridement) do. Therefore, individualization is mandatory upon decision making, focusing on stability of the patient (ie, flash pulmonary edema) and complexity of the potential procedure (concomitant coronary artery bypass grafting, valve or Maze procedure). Dental infections should not be neglected in the setting of valve disease, but complex dental interventions (especially extractions) should be performed by an oral surgeon and a cardiac anesthesiologist with familiarity with hemodynamic monitoring, anticoagulation or antiplatelet therapy, and intensive care.

VASODILATOR THERAPY

In acute severe mitral regurgitation, agents that reduce afterload such as vasodilators or even the intra-aortic balloon pump are effective in relieving heart failure.[72] Such therapy works by causing preferential flow away from the left atrium and into the aorta as resistance to flow into the aorta is reduced. Success of afterload reduction in acute mitral regurgitation led to trials of vasodilators in patients with long-standing mitral regurgitation. Although no large randomized trials have been conducted afterwards, the small trials that have been performed have been confusing but largely negative.[73] Although vasodilators and other agents should be used to treat hypertension in patients with mitral regurgitation there is no evidence that they will slow the need for eventual valve surgery.

β-ADRENERGIC BLOCKADE

Adrenergic overstimulation appears to be a significant detriment in the pathophysiology of mitral regurgitation and there is evidence of benefit to the use of beta-blockers in experimental mitral regurgitation.[74] There is also some observational data that patients with mitral regurgitation already receiving beta-blockers may have a better outcome than those not taking the drugs.[75] However, no trials exist to indicate that beta-blockers are effective therapy in mitral regurgitation other than as therapy for hypertension. Thus the use of beta-blockers to treat mitral regurgitation in normotensive subjects should be viewed as experimental only.

TIMING OF SURGERY

The 2014 guidelines introduced a new classification of the severity of valve lesions based on multiple criteria, including findings on the physical examination and their subsequent correlation with data from a comprehensive TTE.[28,76] Intervention in patients with degenerative mitral valve disease is dependent on (1) severity of mitral regurgitation; (2) presence or absence of symptoms (mainly shortness of breath or unusual limitations in exercise capacity); (3) ventricular response to chronic volume overload[77,78]; (4) impact of volume overload on pulmonary or systemic circulation[79]; and (5) new arrhythmias (likely atrial fibrillation from atrial enlargement).[80,81] The stages of degenerative mitral valve disease (primary mitral regurgitation) are (A) patients at risk of disease or with risk factors for development of the disease (mild prolapse or leaflet thickening with normal coaptation); (B) patients with progressive disease (moderate to severe prolapse with still normal coaptation); (C1) severe prolapse with loss of coaptation in an otherwise preserved ventricle; (C2) severe prolapse in a patient with left ventricular dysfunction; and (D) severe prolapse in a symptomatic patient (Fig. 48–10).[28]

STAGES A AND B: LESS THAN SEVERE MITRAL REGURGITATION

Currently there is no indication to intervene in less than severe mitral regurgitation, except in symptomatic patients where there is a high

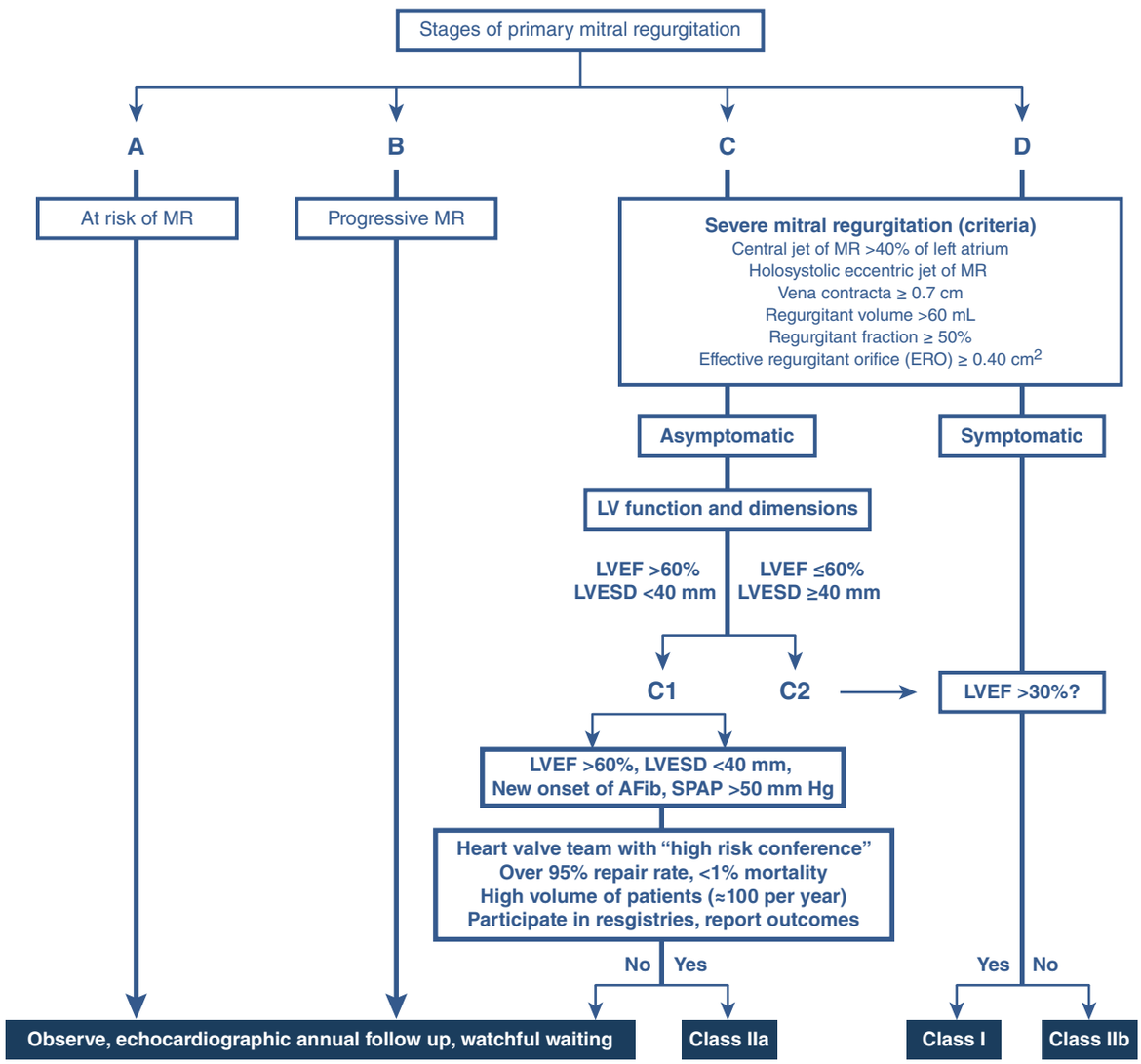


FIGURE 48–10. Proposed algorithm for the management of patients with degenerative mitral valve disease. AFib, atrial fibrillation; EF, ejection fraction; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; MR, mitral regurgitation; SPAP, systolic pulmonary artery pressure. Modified from Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: Executive summary: A report of the American College of Cardiology/American Heart Association task force on practice guidelines. *J Am Coll Cardiol*. 2014;63:2438-2488

suspicion that MR grade may be underestimated. In such patients, exercise testing as described above is useful to clarify the decision making.[82]

STAGE C1: ASYMPTOMATIC SEVERE MITRAL REGURGITATION WITH PRESERVED LEFT VENTRICULAR FUNCTION

Over the past decade, the management of mitral valve regurgitation has changed dramatically and there has been a shift towards a more aggressive approach in terms of surgical timing and of course interpretation of the natural history of the disease.[83,84] Nowadays, prompt correction of asymptomatic mitral regurgitation with preserved left ventricular function (class IIa), in other words before development of guideline triggers (class I), is based on several axioms: (1) severe MR is not a benign condition,[85] and if left uncorrected carries a significant excess mortality associated with increased rates of heart failure and atrial fibrillation[86]; (2) surgical correction in patients with severe MR is unavoidable; (3) patients with severe MR or/and ventricular dysfunction may or may not develop symptoms; and (4) mitral valve prolapse is a 100% repairable disease in reference centers with excellent operative outcomes (mortality and stroke rates <1%) and durability (Fig. 48–11).[87-89] However, in the setting of preserved left ventricular function (LVEF >60% and LVESD <40 mm), early surgery still remains solely based upon a major tenet.[90,91] This is that mitral valve repair will almost certainly be performed under at least a 95% probability of repair (based upon preoperative echocardiographic evaluation of the valve anatomy) with a mortality rate of <1%. Such outcomes mandate patient referral to a "reference center," which by definition should have a high volume of patients (≈ 100 per year), a heart valve team with "high-risk conference," and involvement in data registries with subsequent report of outcomes (data quality control) (see Fig. 48–10). If a mitral valve replacement with its higher operative risk and more morbid postoperative outcome were performed the unwarranted risk of early surgery would absolutely not be justified.[92] In the same context, stage C1 of degenerative mitral valve disease, the presence of pulmonary hypertension or the new onset of atrial fibrillation[93] are also considered class IIa triggers for mitral surgery in asymptomatic patients with preserved left ventricular function[94]. Pulmonary hypertension and exercise-induced pulmonary hypertension are frequent in asymptomatic patients with degenerative mitral valve disease.[95] Pulmonary hypertension and its severity have been demonstrated to be a strong independent predictor of exercise-induce pulmonary hypertension and in turn a predictor of survival.[96,97]

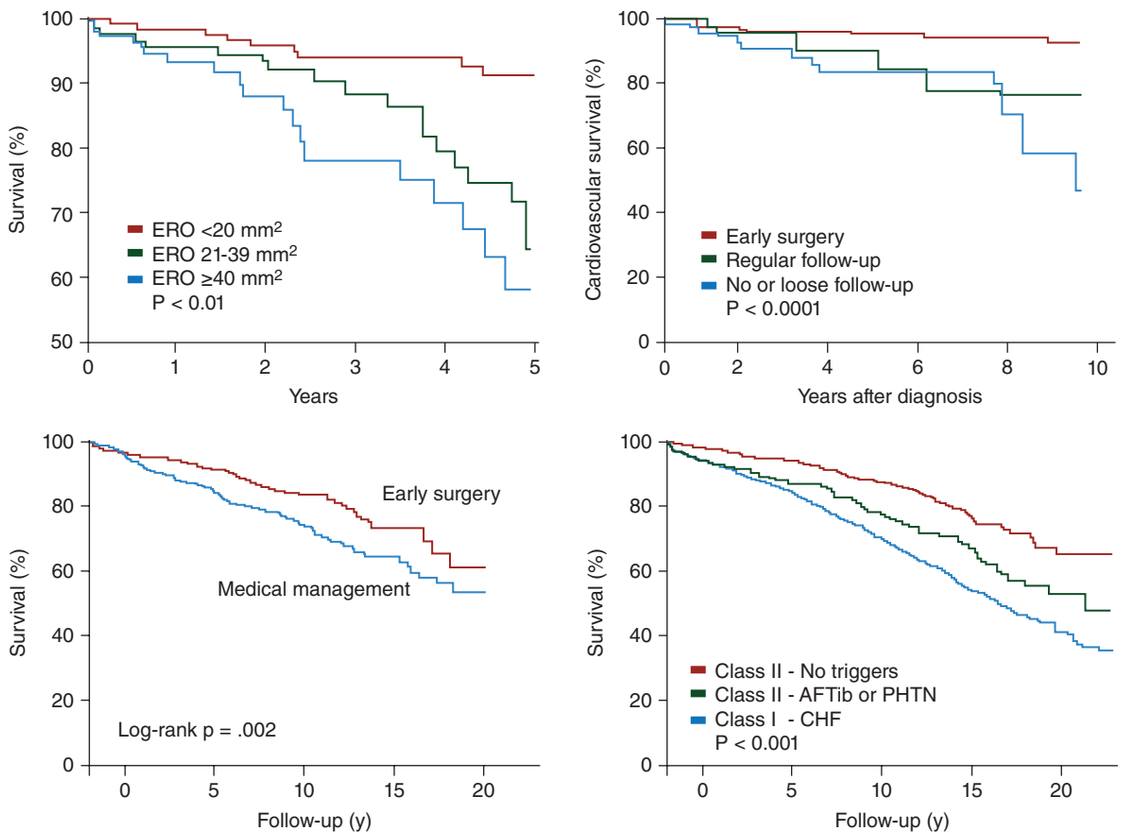


FIGURE 48–11. A. Rates of overall survival among patients with asymptomatic mitral regurgitation under medical management according to the effective regurgitant orifice (ERO); adapted from Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med*. 2005;352:875-883. **B.** Cardiovascular survival compared with patients having early surgery, those treated conservatively and followed regularly, or those treated conservatively and with irregular follow-up; adapted from Montant P, Chenot F, Robert A, et al. Long-term survival in asymptomatic patients with severe degenerative mitral regurgitation: A propensity score-based comparison between an early surgical strategy and a conservative treatment approach. *J Thorac Cardiovasc Surg*. 2009;138:1339-1348. **C.** Survival after diagnosis of mitral regurgitation caused by flail mitral leaflet according to initial treatment strategy in a propensity score-matched cohort; adapted from Suri RM, Vanoverschelde JL, Grigioni F, et al. Association between early surgical intervention vs watchful waiting and outcomes for mitral regurgitation due to flail mitral valve leaflets. *JAMA*. 2013;310:609-616. **D.** Enriquez-Sarano M, Suri RM, Clavel MA, et al. Is there an outcome penalty linked to guideline-based indications for valvular surgery? Early and long-term analysis of patients with organic mitral regurgitation. *J Thorac Cardiovasc Surg*. 2015;150:50-58.

STAGE C2: ASYMPTOMATIC SEVERE MITRAL REGURGITATION WITH LEFT VENTRICULAR DYSFUNCTION

The standard class I indications for mitral valve surgery are the onset of symptoms and/or of left ventricular dysfunction (Figs. 48–12 and 48–13).[28,98] As LV dysfunction develops in MR, many patients become symptomatic but some do not.[84,99] However, if MR is not corrected at that time, LV function will worsen and dysfunction may become permanent, leading to a poor surgical outcome and eventually to death.[30] In those patients lacking symptoms some other objective measure of LV function must be used to determine the need for mitral valve surgery.[100] Two accepted benchmarks indicating the onset of LV dysfunction are an ejection fraction ≤ 60% or a left ventricular end-systolic dimension ≥ 40mm.[101,102] When these indicators become evident on echocardiography mitral surgery should be undertaken.[63,103] Recent studies from the Mayo Clinic have suggested superior survival if the end-systolic dimension is <40 mm[102] and superior recovery of left ventricular function if the EF is ≥65% at the time of mitral surgery,[100] emphasizing the importance of timely identification of changes in left ventricular function in asymptomatic patients. Once a patient has been identified as having severe MR, follow-up with history, physical exam, and serial echocardiograms (or other imaging studies) should be conducted every 6 to 12 months to ensure that the best time for intervention is not overlooked.[104] The above measures of LV function though useful are imprecise and reflect changes in the LV after the negative impact of MR has already been realized. It is likely that more sophisticated measures of LV function (novel echocardiographic parameters) and the use of new markers indicating an adverse myocardial response to MR will help to better determine the optimum timing of surgery in a very near future. In this context, new potential triggers for surgical intervention in asymptomatic patients might include high brain natriuretic peptide (BNP) levels,[105] lower percent of age/sex-predicted metabolic equivalents or lower heart rate recovery

Guideline triggers for surgical referral of patients with degenerative mitral valve disease
2014 ACC/AHA guidelines for the management of heart valve disease

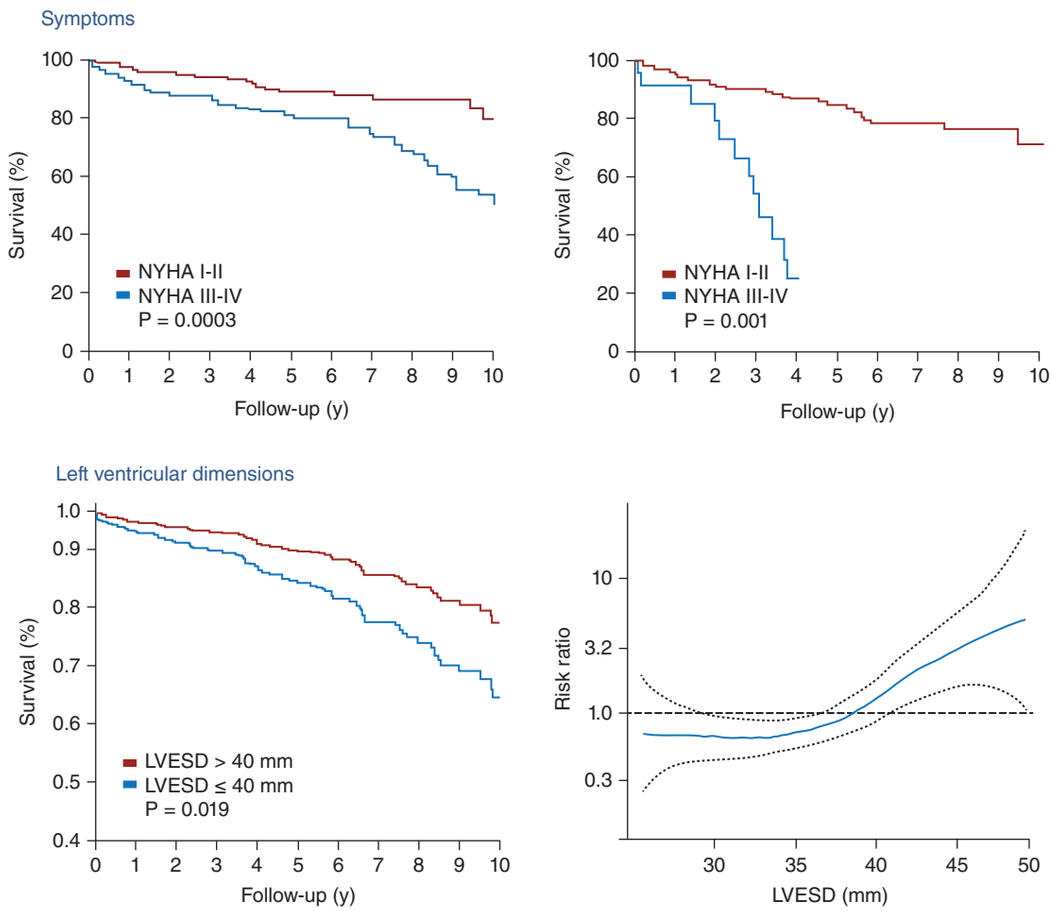


FIGURE 48–12. A. Overall postoperative survival compared for patients in New York Heart Association (NYHA) class I/II and those in class III/IV who had a preoperative left ventricular ejection fraction ≥60%; adapted from Tribouilloy CM, Enriquez-Sarano M, Schaff HV, et al. Impact of preoperative symptoms on survival after surgical correction of organic mitral regurgitation: rationale for optimizing surgical indications. *Circulation*.1999;99(3):400-405. **B.** Long-term survival with medical treatment, according to New York Heart Association class; Ling LH, Enriquez-Sarano M, Seward JB, et al. Clinical outcome of mitral regurgitation due to flail leaflet. *N Engl J Med*. 1996;335:1417-1423. **C, D.** Overall survival according to left ventricular end-systolic diameter (LVESD) in patients with organic mitral regurgitation; adapted from Tribouilloy C, Grigioni F, Avierinos JF, et al. Survival implication of left ventricular end-systolic diameter in mitral regurgitation due to flail leaflets a long-term follow-up multicenter study. *J Am Coll Cardiol*. 2009;54:1961-1968.

Guideline triggers for surgical referral of patients with degenerative mitral valve disease
2014 ACC / AHA guidelines for the management of heart valve disease

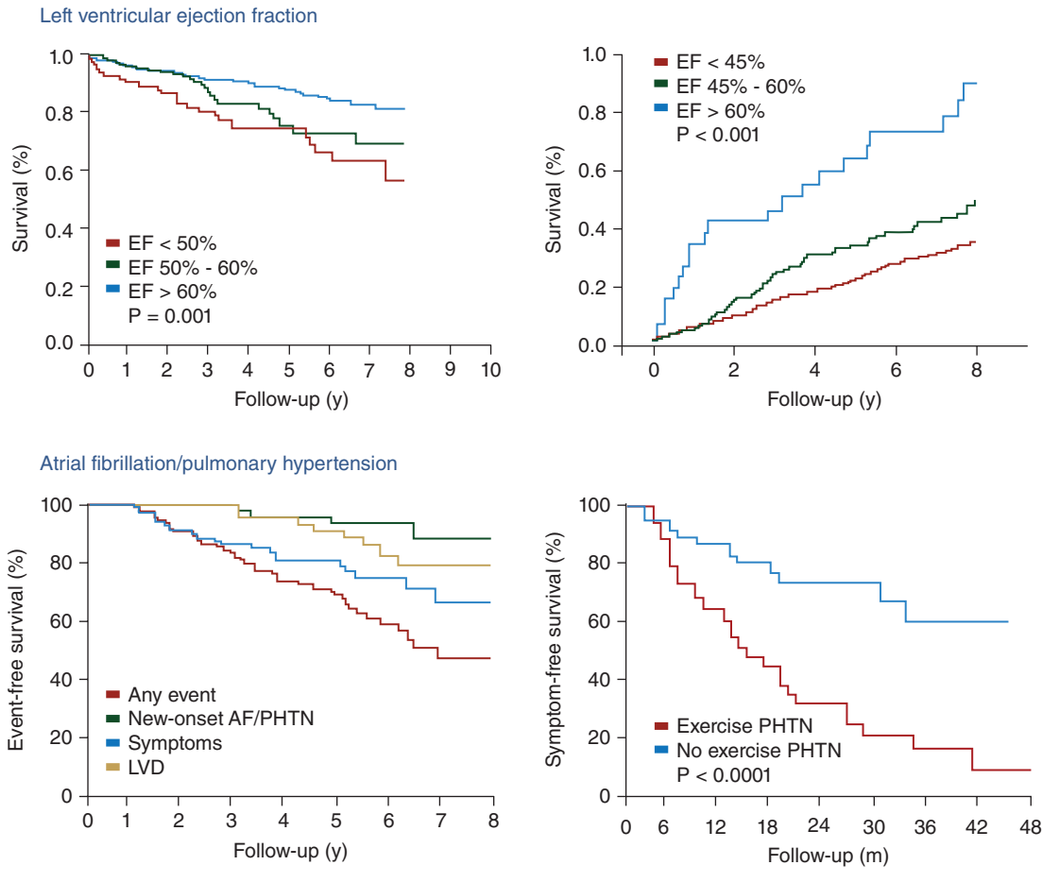


FIGURE 48–13. **A.** Late survival according to preoperative ejection fraction; adapted from Enriquez-Sarano M, Tajik AJ, Schaff HV, et al. Echocardiographic prediction of survival after surgical correction of organic mitral regurgitation. *Circulation*. 1994;90:830-837. **B.** All-cause mortality according to ejection fraction (EF) in patients with organic mitral regurgitation under conservative management; adapted from Tribouilloy C, Rusinaru D, Grigioni F, et al. Long-term mortality associated with left ventricular dysfunction in mitral regurgitation due to flail leaflets: A multicenter analysis. *Circ Cardiovasc Imaging*. 2014;7:363-370. **C.** Survival free of symptoms, survival free of asymptomatic LV dysfunction, and survival free of asymptomatic pulmonary hypertension or recurrent atrial fibrillation in patients under watchful waiting; adapted from Rosenhek R, Rader F, Klaar U, et al. Outcome of watchful waiting in asymptomatic severe mitral regurgitation. *Circulation* . 2006;113(18):2238-2244. **D.** Symptom free survival in patients with severe asymptomatic mitral regurgitation according to the development of exercise pulmonary hypertension; adapted from Magne J, Lancellotti P, Pierard LA. Exercise pulmonary hypertension in asymptomatic degenerative mitral regurgitation. *Circulation*. 2010;122:33-41.

after exercise,[82] the left ventricular ejection index,[106,107] and left atrial dimensions (Fig. 48–14).[108,109]

STAGE D: SYMPTOMATIC SEVERE MITRAL REGURGITATION

The occurrence of severe NYHA class III or IV preoperative symptoms confers a poor prognosis for patients postoperatively even if left ventricular function is preserved (see Fig. 48–12).[110-112] Thus it is important to correct mitral regurgitation at the onset of even mild symptoms because waiting for symptoms to progress appears dangerous. In fact the onset of symptoms represents a change in cardiac physiology as the mitral regurgitation has begun to affect cardiac output and left atrial filling. In addition there may be a small risk of sudden death in patients who have developed symptoms.[113,114] Thus symptom onset is a clear indication for mitral valve surgery. Although guidelines currently contemplate mitral valve replacement as an acceptable option, mitral valve repair should be the only option in patients with mitral valve prolapse.

ADHERENCE TO GUIDELINES IN REAL WORLD PRACTICE

Several studies have suggested discordance with timely referral of patients with chronic mitral valve regurgitation for surgical intervention despite the presence of one or more accepted guideline indications for surgery. A substudy of the *Euro Heart Survey* showed that 49% of patients with symptomatic severe mitral regurgitation of various etiologies were not referred for surgery, and that clinicians were placing too much emphasis on age and ejection fraction in their decision to not offer patients surgery.[115] Another study involving a large number of Canadian cardiologists in either university-based or community-based practice suggested that nearly half were unfamiliar with even class I indications for surgical intervention in patients with severe mitral regurgitation.[116] A separate recent study at the University of Michigan similarly found that over one-third of patients with degenerative disease and a guideline indication for surgical intervention were not referred for surgical evaluation, despite the fact that no high-risk patients were turned down for surgery during the study period, and surgical results in

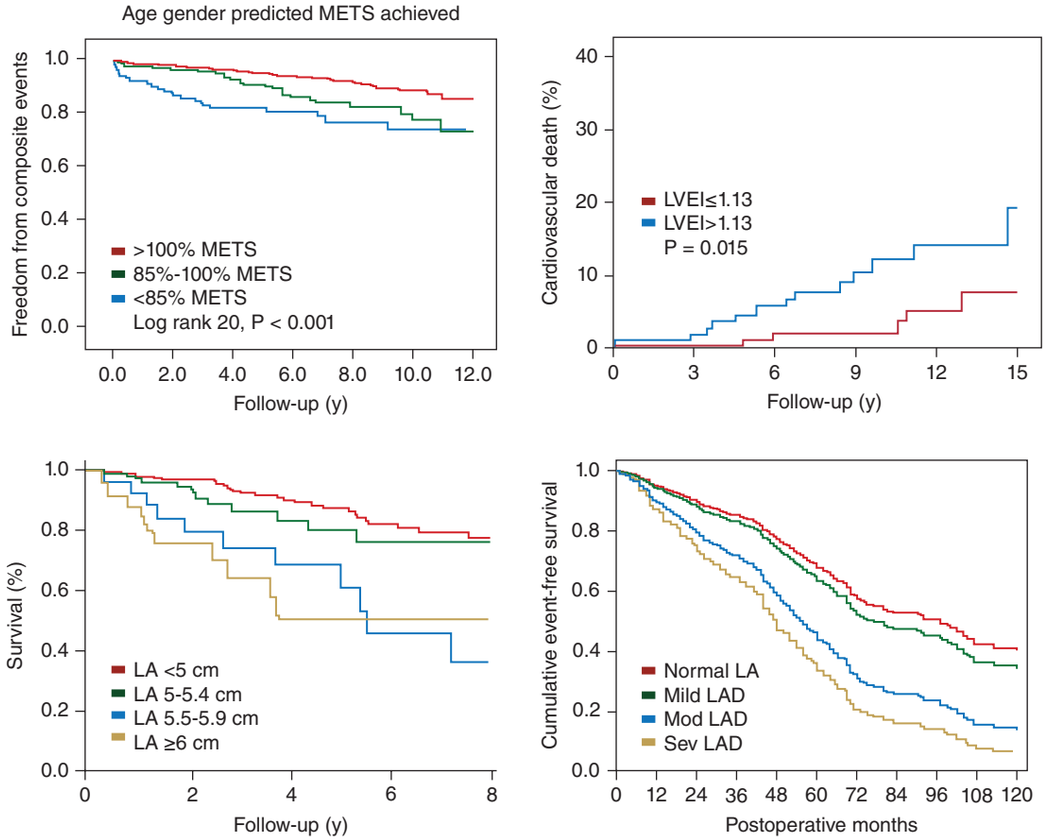


FIGURE 48–14. A. Freedom from composite events (death, myocardial infarction, stroke, and progression to congestive heart failure) according to METS; adapted from Naji P, Griffin BP, Asfahan F, et al. Predictors of long-term outcomes in patients with significant myxomatous mitral regurgitation undergoing exercise echocardiography. *Circulation*. 2014;129:1310-1319. **B.** Cardiovascular death according to left ventricular ejection index; adapted from Magne J, Szymanski C, Fournier A, et al. Clinical and prognostic impact of a new left ventricular ejection index in primary mitral regurgitation because of mitral valve prolapse. *Circ Cardiovasc Imaging*. 2015;8:e003036. **C, D.** Survival and event-free survival according to leaft atrial dimensions or degree of dilatation; adpated from Rusinaru D, Tribouilloy C, Grigioni F, et al. Left atrial size is a potent predictor of mortality in mitral regurgitation due to flail leaflets: Results from a large international multicenter study. *Circ Cardiovasc Imaging*. 2011;4:473-481; and Athanasopoulos LV, McGurk S, Khalpey Z, et al. Usefulness of preoperative cardiac dimensions to predict success of reverse cardiac remodeling in patients undergoing repair for mitral valve prolapse. *Am J Cardiol*. 2014;113:1006-1010.

this subgroup were excellent.[117] Thus it appears that "perceived risks" of surgical intervention in real world practice are often overestimated, suggesting the need for continued education of practicing clinicians regarding current guidelines and best practice outcomes.[118]

MITRAL VALVE REPAIR FOR DEGENERATIVE DISEASE: A SUBSPECIALTY

Severe mitral valve regurgitation in the setting of degenerative mitral valve disease is a mechanical problem with an only definitive mechanical solution; at this time the only definitive treatment is mitral valve repair.[119] As mentioned before, all prolapsing valves are repairable and mitral valve replacement should not be an option if appropriate referral patterns are followed.[120] Degenerative mitral valve disease along with annular dilatation is the most repairable form of surgical mitral valve disease, and repair should be recommended. Mitral valve repair is favored over replacement for several reasons, including a lower perioperative risk, improved preservation of left ventricular function, improved event-free survival in the majority of operated patients, and greater freedoms from prosthetic valve-related complications such as thromboembolism, anticoagulant-related hemorrhage, and endocarditis (Fig. 48–15).[121-123] Although no randomized trials comparing outcomes of mitral valve repair versus replacement exist (and it seems very unlikely that such trials would be conducted, particularly in the setting of degenerative mitral valve disease), the vast majority of available retrospective data strongly support the long-term advantage of mitral valve repair.

MITRAL VALVE REPAIR IN THE ELDERLY

The risk-adjusted advantage of mitral valve repair versus mitral valve replacement is also patent in the elderly (Fig. 48–16).[124,125] The prevalence of mitral valve disease increases with age and around 10% of patients above 75 years who require hospitalization have significant mitral regurgitation, predominantly caused by fibroelastic deficiency.[16] However, surgery is often contraindicated in elderly patients with multiple comorbidities such as coronary artery disease, renal failure,[126] or neurological impairments.[124] In a recent series, Chikwe and associates analyzed a consecutive series of 322 octogenarian patients with degenerative mitral valve disease (most of them with fibroelastic deficiency) and showed that 30-day mortality was 2.5-fold higher in those patients who underwent mitral valve replacement. Later on, Badhwar and associates conducted a retrospective study that involved over 14,000 patients over 65 years of age from the STS National Cardiac Registry and US Medicaid. The authors reported an overall 2.6% mortality with a 68% 5-year survival.[127] Finally, Dodson and coworkers interrogated

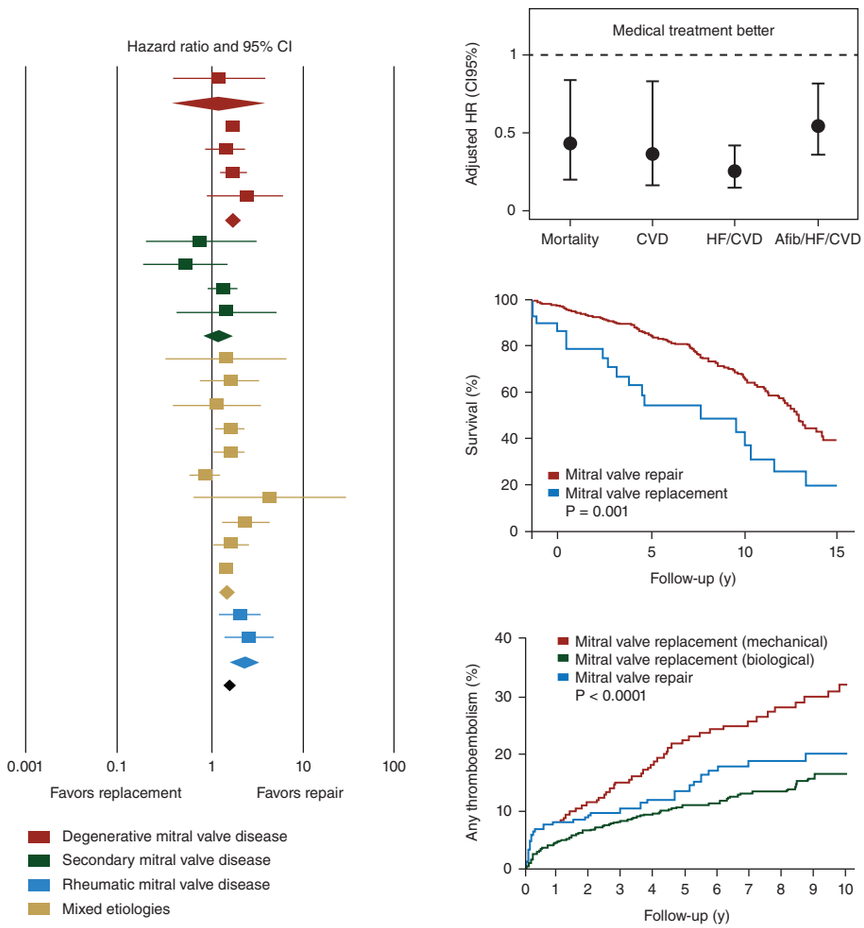


FIGURE 48–15. Superiority of mitral valve repair over valve replacement in patients with degenerative mitral valve disease. **A.** Adapted from Shuhaiber J, Anderson RJ. Meta-analysis of clinical outcomes following surgical mitral valve repair or replacement. *Eur J Cardiothorac Surg*. 2007;31:267-275. **B.** Adapted from Grigioni F, Tribouilloy C, Avierinos JF, et al. Outcomes in mitral regurgitation due to flail leaflets a multicenter european study. *JACC Cardiovasc Imaging*. 2008;1:133-141. **C.** Adapted from Suri RM, Schaff HV, Dearani JA, et al. Survival advantage and improved durability of mitral repair for leaflet prolapse subsets in the current era. *Ann Thorac Surg*. 2006;82:819-826. **D.** Adapted from Russo A, Grigioni F, Avierinos JF, et al. Thromboembolic complications after surgical correction of mitral regurgitation incidence, predictors, and clinical implications. *J Am Coll Cardiol*. 2008;51:1203-1211.

the National Medicare database to elucidate outcomes of isolated mitral valve surgery among patients above 65 years. This study, the largest to date, demonstrated that the proportion of patients undergoing mitral valve repair significantly increased from 24.7% to 46.9% (versus bioprosthetic valve replacement 23.8% to 33.0%). Although the latest data clearly suggest that elderly patients with degenerative mitral valve disease benefit from the better success rates and numerous advantages of mitral valve repair, the reality is that surgeons, especially those at low-volume centers, are often reluctant to attempt repair because of the potential need for longer bypass times or a more likely conversion to standard sternotomy.[128] In addition, the integration of quality of life and functional scoring systems seems to be important in order to assess surgical benefit versus futility.[129] In this context, novel transapical techniques may become an alternative therapeutic option only for patients who are not eligible for any surgical approach until transcatheter techniques[130] show proof of better efficacy.[131,132] This is an important point in patients with degenerative mitral valve disease, because residual moderate mitral regurgitation has been demonstrated to be associated with poorer outcomes in survival and symptom relief, and with greater recurrence.[129]

HOSPITAL AND SURGEON PROCEDURAL VOLUME AS A QUALITY METRIC

Surgical management of degenerative mitral valve disease has evolved considerably and so have the quality metrics to assess outcomes. Now that there is quorum among surgical leaders about the superiority of mitral valve repair over replacement and the need for repair in every single patient with mitral prolapse, attention has been shifted to nonpatient factors that influence feasibility of repair and operative mortality such as hospital teaching status, surgeon procedural volume, and hospital procedural volume.[133]

Although mitral valve repair rates have risen throughout the last decade, and currently approach 70% in the Society of Thoracic Surgery Database,[134] its application remains quite variable with some surgeons performing five or fewer mitral operations per year with repair rates of less than 30%, particularly for more complex scenarios such as anterior or bileaflet prolapse (Fig. 48–17).[135] In Europe, an analysis of over 5000 mitral valve operations from the United Kingdom mandatory adult cardiac surgical database suggests a significant impact of surgeon volume on mitral valve repair rates.[136] Even in high-volume centers, the repair rates can be low; in patients with degenerative mitral regurgitation, repair rates at high-volume centers were as low as 36%, and only three high-volume centers had repair rates above 85%.[136] One of the first institutional reports to demonstrate the implications of surgeon volume in mitral valve repair rates was published in 2008.[137] Gillinov and coworkers observed that some surgeons were independent predictors of mitral valve replacement in patients with degenerative mitral valve disease. Since then, several authors have emphasized the exponential correlation between surgeon volume and mitral valve repair rates, repair quality, and shortened cross-clamp times (Fig. 48–18).[138-140] The most recent analysis of the Nationwide Inpatient Sample (NIS) including over 50,000 patients showed that although hospital volume accounted for 11% of the surgeon volume effect on increased mortality for low-volume surgeons, surgeon volume accounted for 74% of the hospital volume effect on increased mortality in low-volume hospitals.[141] Furthermore, significant trends were observed in regard to repair rates, with increasing surgeon volume demonstrating stronger correlation with the odds of repair than hospital volume, thus highlighting the importance of learning curves in mitral valve repair.[142]

FEASIBILITY AND DURABILITY OF MITRAL VALVE REPAIR

Carpentier's repair philosophy and techniques are the foundation of contemporary mitral valve repair strategies.[7] A "lesion-specific approach" addresses leaflet, chordal, and annular pathology according to the wide spectrum of lesions encountered in patients with degenerative mitral valve disease. After systematic analysis, mitral valve repair should be performed following a sequential approach such as (1) annuloplasty sutures, (2) repair of the posterior leaflet, (3) annuloplasty, (4) leaflet resuspension when required, and (5) repair any prolapse of the anterior

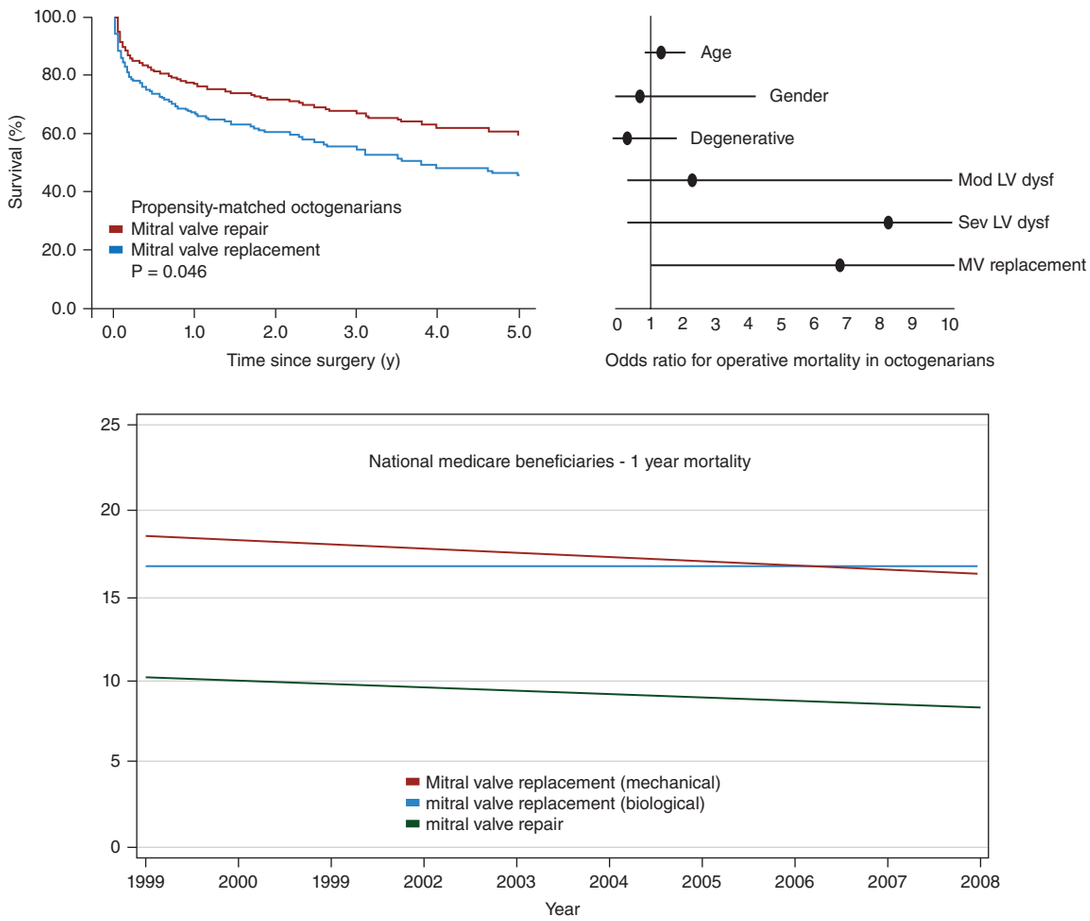


FIGURE 48–16. Superiority of mitral valve repair over valve replacement in elderly patients with degenerative mitral valve disease. **A.** Adapted from Chikwe J, Goldstone AB, Passage J, et al. A propensity score-adjusted retrospective comparison of early and midterm results of mitral valve repair versus replacement in octogenarians. *Eur Heart J*. 2011;32:618-626. **B.** Adapted from Nloga J, Henaine R, Vergnat M, et al. Mitral valve surgery in octogenarians: Should we fight for repair? A survival and quality-of-life assessment. *Eur J Cardiothorac Surg*. 2011;39:875-880. **C.** Adapted from Dodson JA, Wang Y, Desai MM, et al. Outcomes for mitral valve surgery among medicare fee-for-service beneficiaries, 1999 to 2008. *Circ Cardiovasc Qual Outcomes*. 2012;5:298-307.

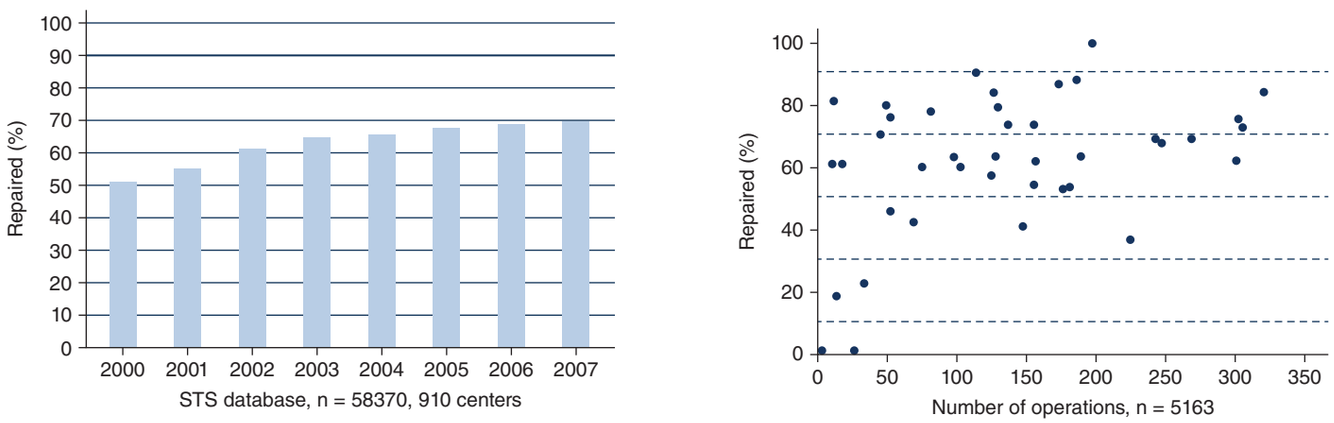


FIGURE 48–17. Mitral valve repair rates in the United States (Society of Thoracic Surgery) and United Kingdom (mandatory adult cardiac surgical database). **A.** Adapted from Gammie JS, Sheng S, Griffith BP, et al. Trends in mitral valve surgery in the united states: Results from the society of thoracic surgeons adult cardiac surgery database. *Ann Thorac Surg*. 2009;87:1431-1437; discussion 1437-1439. **B.** Adapted from Anyanwu AC, Bridgewater B, Adams DH. The lottery of mitral valve repair surgery. *Heart*. 2010;96:1964-1967.

Impact of hospital and surgeon volume on operative outcomes in mitral valve surgery

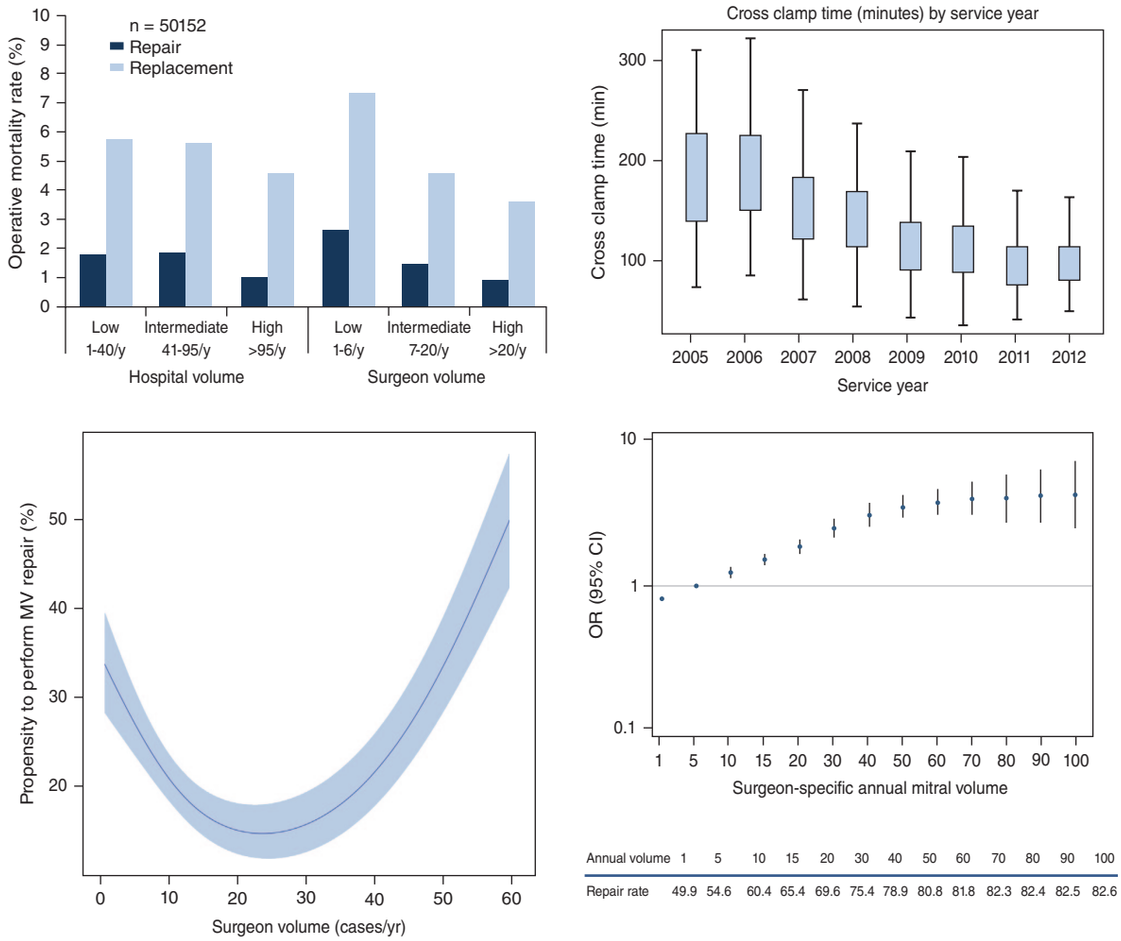


FIGURE 48–18. Impact of hospital volume and surgeon volume on the feasibility of mitral valve repair. **A.** Adapted from Kilic A, Shah AS, Conte JV, et al. Operative outcomes in mitral valve surgery: Combined effect of surgeon and hospital volume in a population-based analysis. *J Thorac Cardiovasc Surg*. 2013;146:638-646. **B.** Adapted from Weiner MM, Hofer I, Lin HM, et al. Relationship among surgical volume, repair quality, and perioperative outcomes for repair of mitral insufficiency in a mitral valve reference center. *J Thorac Cardiovasc Surg*. 2014;148:2021-2026. **C.** Adapted from LaPar DJ, Ailawadi G, Isbell JM, et al. Mitral valve repair rates correlate with surgeon and institutional experience. *J Thorac Cardiovasc Surg*. 2014;148:995-1003; discussion 1003-1004. **D.** Adapted from Bolling SF, Li S, O'Brien SM, et al. Predictors of mitral valve repair: Clinical and surgeon factors. *Ann Thorac Surg*. 2010;90:1904-1911; discussion 1912.

leaflet or commissures after inspection of the line of closure during a saline test (Fig. 48–19). An optimal mitral valve repair should meet the following criteria: (1) the valve is competent on saline testing, (2) there is good surface of coaptation, (3) the closure line is symmetric and located where the anterior leaflet occupies at least 80% of the valve area, (4) there is no residual leaflet billowing, and (5) there is no tendency to systolic anterior motion.[143,144]

The most frequent lesion encountered in degenerative mitral valve disease is posterior leaflet prolapse, which accounts for about 70% of patients. In this scenario, triangular resection and leaflet resuspension (if the adjacent native chords do not look totally healthy or in light of further disease progression) remain the most popular techniques.[145] Most centers would report repair rates above 90% in patients with isolated posterior leaflet prolapse. However, repair rates fall drastically in the presence of more complex lesions such as severe annular dilatation, involvement of three or more segments, anterior leaflet prolapse, various degrees of calcification, scarcity of leaflet tissue, and opposite dysfunction. Regardless of the leaflet and chordal approach, essentially all mitral valve repairs should include an annuloplasty,[146] which reshapes the annulus and addresses posterior annular dilatation that is always present in long-standing severe mitral valve regurgitation (Fig. 48–20).[147-149]

As a fast-growing number of asymptomatic patients with degenerative mitral valve disease are expected to be referred for surgery, it seems mandatory to ensure mitral valve repair rates above 95% with minimal perioperative risk and optimal long-term outcomes. This goal has been proved to be feasible at reference centers with specialized valve teams that include cardiologists, anesthesiologists, intensivists, and surgeons. From a surgical point of view, the use of a systematic surgical strategy that embraces a broad armamentarium of techniques (as opposed to subscribing to a single technique or philosophy) should lead to achieve very high repair rates in experienced hands. On the other hand, the role of a multidisciplinary heart team approach is crucial to achieve

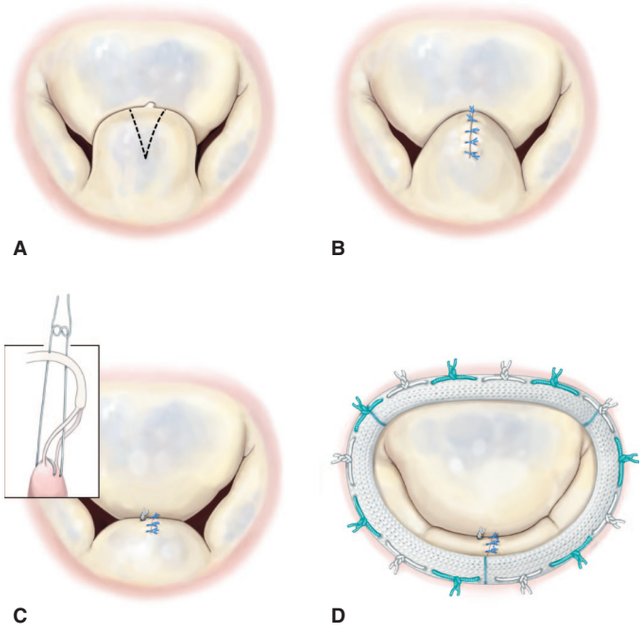


FIGURE 48–19. The current most applied techniques in mitral valve repair are triangular resection and leaflet resuspension with a polytetrafluoroethylene neochord.

contemporary benchmarks. In this context, the presence of advanced myxomatous degeneration, long-standing regurgitation with ventricular dysfunction, calcification, or previous failed repairs might require longer cross-clamp times to perfect the repair, which in turn might make postoperative management and recovery more difficult.

Mortality after mitral valve repair in patients with degenerative disease correlates with age, with an average risk of 1% for patients below 65 years (estimated risk for all comers in high-reference centers regardless of age), 2% for those aged 65 to 80 years, and 4% for octogenarians.[150] Some of the identified independent predictors of postoperative survival include severe symptoms (NYHA class III or IV), LV dysfunction (EF<60% or LVESD >40 mm), a regurgitant orifice area ≥40 mm^2, left atrial dimensions (left atrial index ≥60mL/m^2 or LA >55 mm), or the presence of pulmonary hypertension or long-standing atrial fibrillation. It is important to highlight that those patients referred to surgery with severe symptoms will have greater postoperative risk despite symptom relief as a result of the absence of ventricular remodeling,

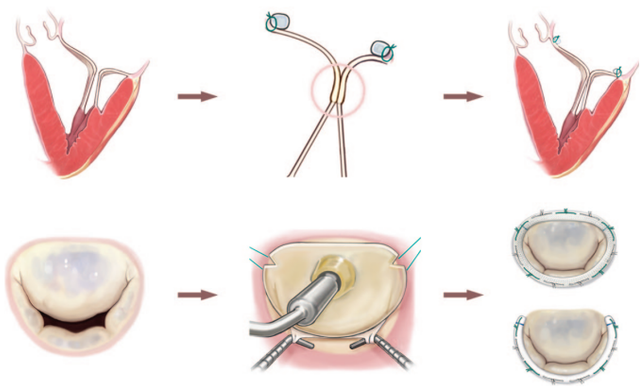


FIGURE 48–20. Annuloplasty with a complete ring or a posterior band.

particularly if the EF is <50%. Repair durability, strictly defined as echocardiographic freedom from moderate or greater mitral regurgitation (as opposed to freedom from symptoms or reoperation), has been reported to be around 90% at 10 years in reference centers such as the Mayo Clinic, the Cleveland Clinic, Toronto General Hospital, and Mount Sinai Hospital, with a recurrent rate of 1% per year up to 20 years after the procedure (Fig. 48–21).[151-154] When durability rates are stratified according to leaflet involvement,[155] patients with bileaflet or isolated anterior leaflet prolapse have slightly lower repair durability, ranging from 75% to 85% at 5 years.[120,156] Additional factors that impact durability of repair include failure to use an annuloplasty device or the use of chordal shortening techniques (which are now abandoned).[157] Although technical failures account for residual and some early repair failures,[158] progression of disease with new pathology is the most common cause of long-term failure.[159]

SURGICAL ACCESS

Mitral valve surgery has progressively evolved over the past decade, particularly in patients with degenerative mitral valve disease. Without doubt, surgical indications, repair techniques. and approaches represent the most important[160] aspects of an already established best practice revolution in mitral valve repair. Regarding the latter aspect, the current gold standard and still most popular approach is median sternotomy, which allows central cannulation and assures good myocardial protection (direct cardioplegia), and most importantly, permits direct access if a complication occurs. The trend towards more cosmetic incisions has triggered the adoption of very limited median incisions as small as 7 to 9 cm in selected patients.[161] However, the term "minimally invasive" in today's cardiac surgery is understood as a video-assisted approach including right thoracotomy and robotic surgery.[162] In this context, cardiopulmonary bypass is accomplished through peripheral cannulation (most commonly via femoral artery and vein-retrograde arterial perfusion). Although traditionalists have claimed that minimally invasive mitral valve surgery is technically more complex (thus potentially affecting mitral valve repair rates) and implies a learning curve that not every surgeon overcomes,[142] even in high-volume centers, the reality is that extraordinary outcomes from a few experienced high-volume centers have challenged their opinions.[156,163,164] This is also true[165] even in complex scenarios such as Barlow disease or anterior leaflet prolapse.[166,167]

The most important goal for patients with degenerative mitral valve disease and the physicians involved in their care (referring cardiologist and surgeons) is to achieve not only a competent repair of the mitral valve but a durable one, as emphasized by the new guidelines. In ideal conditions, these axioms should be met in all prolapsing valves regardless of the surgical approach and the final cosmetic outcome. We are convinced that as technology advances, minimally invasive techniques will expand. However, at this time, the average repair rates dictate that the use of these techniques should be restricted to selected, high-volume, specialized centers.

CONCOMITANT TRICUSPID VALVE REPAIR IN PATIENTS WITH DEGENERATIVE MITRAL VALVE DISEASE

Tricuspid valve disease affects around 1% of the general population, and most patients remain asymptomatic despite having moderate to severe degrees of tricuspid regurgitation. However, increasing attention has been given to the tricuspid valve in parallel to a better understanding of the negative impact of right-sided heart failure on the clinical outcome of patients regardless the presence or severity of left-sided valve disease.[168] Although primary tricuspid regurgitation is

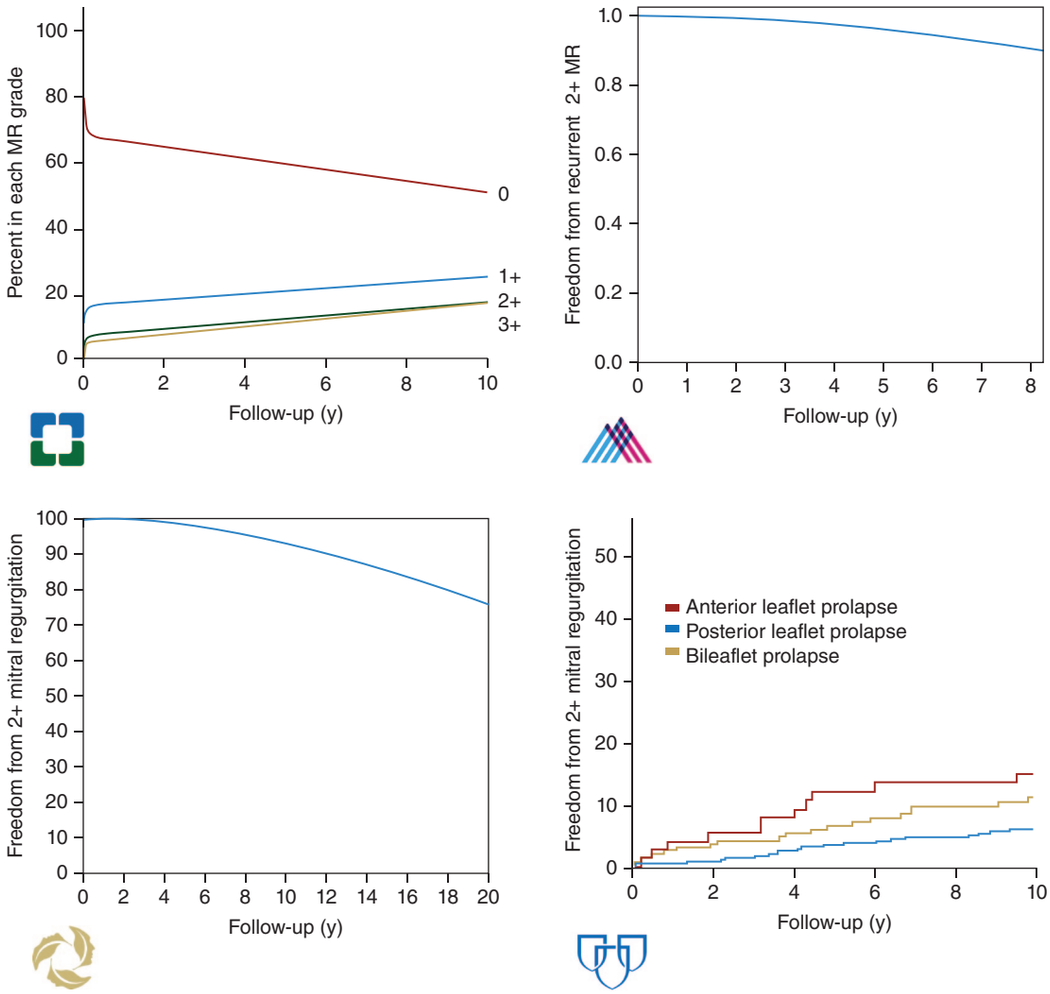


FIGURE 48–21. Freedom from moderate MR in reference centers. **A.** Adapted from Gillinov AM, Mihaljevic T, Blackstone EH, et al. Should patients with severe degenerative mitral regurgitation delay surgery until symptoms develop? *Ann Thorac Surg*. 2010;90:481-488. **B.** Adapted from Castillo JG, Anyanwu AC, Fuster V, et al. A near 100% repair rate for mitral valve prolapse is achievable in a reference center: Implications for future guidelines. *J Thorac Cardiovasc Surg*. 2012;144:308-312. **C.** Adapted from David TE, Armstrong S, McCrindle BW, et al. Late outcomes of mitral valve repair for mitral regurgitation due to degenerative disease. *Circulation*. 2013;127:1485-1492. **D.** Adapted from Suri RM, Clavel MA, Schaff HV et al. Effect of recurrent mitral regurgitation following degenerative mitral valve repair: Long-term analysis of competing outcomes. *J Am Coll Cardiol*. 2016;67:488-498. Adapted from David TE, Armstrong S, McCrindle BW, et al. Late outcomes of mitral valve repair for mitral regurgitation due to degenerative disease. Circulation. 2013;127:1485-1492. D. Adapted from Suri RM, Clavel MA, Schaff HV et al. Effect of recurrent mitral regurgitation following degenerative mitral valve repair: Long-term analysis of competing outcomes. J Am Coll Cardiol. 2016;67:488-498.

rare (often seen in patients with pacemakers, chest trauma, or endocarditis), secondary (functional) tricuspid regurgitation as a result of pulmonary hypertension and right ventricular dilation as a result of left-sided valve disease is common. However, although the number of tricuspid procedures has double over the last decade,[169] the management of secondary tricuspid regurgitation remains as one of the most heated debates, particularly in regard to the best surgical option in patients with severe tricuspid regurgitation and whether concomitant "prophylactic" tricuspid procedures are necessary in patients with mild to moderate tricuspid regurgitation.[170,171]

At the present time, there are two opposing schools of thoughts regarding the need for concomitant tricuspid valve repair at the time of mitral repair in patients with degenerative valve disease, both of them supported by leading experts in mitral valve repair. The main explanation for these contrary opinions is the difficulty in accurately assessing the degree of tricuspid regurgitation as a result of the significant dependence of the right ventricle on preload conditions. In order to avoid this bias, many authors have suggested an annular dilatation of 40 mm or 21 mm/m^2 as an independent criterion for tricuspid intervention. Recently, our group demonstrated that this strategy, applied in two-thirds of patients undergoing mitral valve repair, does not lead to a difference in mortality, morbidity, or requirement of a permanent pacemaker.[172] An even more recent paper from De Bonis and colleagues confirmed these findings and also noted that half of the untreated patients presented with either severe tricuspid regurgitation or a progression of at least two grades of tricuspid regurgitation 7 years after the procedure.[173] On the other hand, only around 10% of patients receive concomitant tricuspid annuloplasty at Toronto General Hospital or the Mayo Clinic. Objectively, we can assert that preoperative functional class (as a surrogate of ventricular dysfunction) should play a major role in decision making. Those patients in NYHA class III or IV, who have not developed at least moderate TR at the time of surgical intervention, will most likely not develop TR after mitral valve repair. Likewise, patients with preserved left ventricles and none

or mild degrees of tricuspid regurgitation are also unlikely to develop tricuspid regurgitation. It may be that earlier the mitral valve repair will lead to fewer patients requiring tricuspid intervention.

Overall, secondary or functional tricuspid regurgitation is the most common etiology of TV disease, and thorough interrogation is mandatory in patients undergoing mitral valve repair. Concomitant tricuspid valve repair does not carry a significant additional surgical burden and might lead to improved perioperative outcomes, functional class, and survival. Tricuspid regurgitation does not always regress after correction of left-sided valve disease[174] and reoperations for residual or recurrent tricuspid regurgitation are associated with a higher mortality risk in experienced centers (up to 15%).[175] The final decision should be guided not only by the degree of regurgitation (≥ moderate) but also by annular dimensions (diameter ≥7 cm from anteroseptal to anteroposterior commissures, or 40 mm when measured by echocardiography); leaflet coaptation or mismatch between leaflet and annulus on direct inspection; and presence of atrial fibrillation, pulmonary hypertension, right ventricular dysfunction, and/or left ventricular dysfunction. As for the type of repair, the authors favor the use of a disease-specific open ring with a rigid component located in the region corresponding to the right ventricular free wall aspect of the annulus (remodeling) with flexible open ends for wider accommodation of the conduction system to reduce iatrogenic injury.[176]

PERCUTANEOUS APPROACHES TO MITRAL VALVE REPAIR AND REPLACEMENT

At present there are over 20 investigational devices for repair or replacement of the mitral valve. Some make use of the proximity of the coronary sinus to the mitral annulus, wherein devices cinch the coronary sinus, thereby reducing annular dimension and reducing MR. Percutaneous valve replacement is in its infancy with a large number of valve designs being tested.[130,177]

Currently the MitraClip is the only device approved in the United States and is employed for treatment of inoperable patients with primary MR. The device is inserted transeptally and clips the two mitral leaflets together in their mid-portions, substantially reducing MR, usually from severe to moderate degrees of regurgitation. Five-year follow-up is now available and demonstrates both persistent reductions in MR as well as persistent symptomatic improvement.[178]

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