

Evaluation of the Severity of Valvular Heart Disease and Timing of Surgery

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A better knowledge of the natural history of valvular disease and the advances in surgical techniques are allowing to improve the prognosis of patients with valvular heart disease.

At presente, imaging techniques, particularly Doppler-echocardiography, is the main tool to determine the diagnosis and prognosis of patients with valvular heart disease. Consequently, decision making in valvular heart disease is nowadays based on a combination of symptomatic status and echocardiographic findings. The main applications of Doppler-echocardiography with this purpose are summarized in this article. Therapeutic algorithms for patients with valvular heart disease are proposed, as well as the potential application of new imaging modalities appeared in the last years. The state of the art of clinical practice guidelines are also reviewed.

Key words: *Valvular heart disease. Doppler-echocardiography. Valve surgery. Outcome.*

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Evaluación de la severidad y decisiones quirúrgicas en las valvulopatías

En los últimos años, el mejor conocimiento de la historia natural de las enfermedades valvulares, y los avances en las técnicas quirúrgicas han permitido mejorar el pronóstico de los pacientes con enfermedad valvular cardíaca.

El diagnóstico por la imagen, específicamente la ecocardiografía Doppler, constituye en la actualidad la técnica de elección para establecer el diagnóstico y el pronóstico de los pacientes valvulares. En consecuencia, hoy día, la toma de decisiones clínicas en las valvulopatías se basa en gran medida en la combinación del estado sintomático y de los hallazgos ecocardiográficos. En el presente artículo se resumen las principales aplicaciones de la técnica con este objetivo y se proponen algoritmos terapéuticos en las principales enfermedades valvulares. Asimismo, se propone la posible aplicación de las nuevas técnicas de imagen surgidas en los últimos años y se revisa el estado actual de las normas de actuación clínica.

Palabras clave: *Valvulopatías. Ecocardiografía Doppler. Cirugía cardíaca. Pronóstico.*

VALVULAR STENOSIS

Aortic stenosis

Aortic valve stenosis in adults is due to calcific changes of a normal trileaflet or congenital bicuspid valve. Rheumatic disease is uncommon and is invariably accompanied by mitral valve involvement. The classic physical findings of severe aortic stenosis such as diminished amplitude and rate of rise of the carotid upstroke may not be seen in elderly patients

due to superimposed atherosclerotic vascular disease. The loudness of the murmur is not a reliable indicator of disease severity and although a clearly split S2 excludes severe aortic stenosis, a single S2 is associated with a range of disease severity. The chest x-ray may show calcification in the aorta and in end stage disease may show left ventricular (LV) enlargement, but in general is not very helpful. Likewise the electrocardiogram (ECG) shows LV hypertrophy once the stenosis is severe and otherwise is non-specific.

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Evaluation of cause and disease severity

Two-dimensional (2D) transthoracic echocardiography combined with Doppler is the main tool employed to determine the presence, severity, and etiology of aortic stenosis. In addition, potential

consequences of aortic stenosis such as reduced ejection fraction, left ventricular hypertrophy, left atrial dilation, and secondary pulmonary hypertension are easily quantified by echocardiography. Despite the fact that surgical timing is usually based on symptoms, serial echocardiography is useful, as it is known that the Doppler derived valve area typically decreases by 0.1 to 0.2 cm² per year^{1,2} and serial studies provide reasonable estimates of when symptoms are likely to develop.

Although it may be difficult to identify the number of valve leaflets in adults with aortic stenosis, 2D echocardiography can identify the degree of valve calcification, an important prognostic factor for predicting the rate of disease progression and for clinical decision-making in difficult cases. Doppler echocardiography is the standard approach for assessment aortic stenosis severity including measurement of maximum velocity, calculation of the maximum instantaneous and mean transaortic pressure gradient, and calculation of valve area using the continuity equation.

The maximum left ventricular to aortic gradient is determined by the modified Bernoulli equation as:

$$\text{Maximum pressure gradient} = 4V^2$$

The mean gradient is determined by averaging the pressure gradient over the systolic ejection period. In general, gradients measured by Doppler correlate well with those determined by left heart catheterization both for mean gradient and the maximum instantaneous gradient. Note that there is no Doppler echocardiography equivalent to the «peak to peak» valve gradient, that is the peak left ventricular to peak aortic gradient obtained by catheterization, as these two pressures do not occur at the same time (Figure 1).³⁻⁵

The velocity across the aortic valve and hence the Bernoulli equation derived peak and mean gradients are elevated in the presence of significant aortic regurgitation, or underlying high cardiac output states like anemia, thyrotoxicosis, sepsis, and severe hepatic disease. This is a normal physiologic elevation in velocity, without valve stenosis, caused by an elevated volume flow rate across the valve. Conversely, patients with a low transaortic flow rate, such as with concurrent left ventricular dysfunction, may have relatively a low velocity and pressures gradient despite severe stenosis. In both these situations, calculation of valve area provides a more accurate measure of disease severity.

The continuity equation measures aortic valve area (AVA) based on the principle of continuity of volume flow rate from the left ventricular outflow tract (LVOT) into the stenotic aortic (AS) valve. Volume flow rate is calculated as the cross-sectional area of

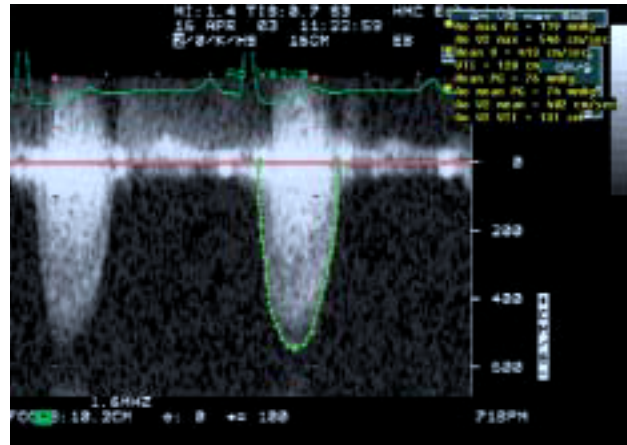


Fig. 1. Example of a continuous wave spectral Doppler assessment of the velocity across the aortic valve. Note the corresponding peak and mean gradients.

flow (CSA) times the velocity time integral (VTI) of flow at each site. Thus:

$$CSA_{LVOT} \times VTI_{LVOT} = AVA \times VTI_{AS}$$

And solving for aortic valve area (AVA):

$$AVA = (CSA_{LVOT} \times VTI_{LVOT}) / VTI_{AS}$$

with the circular LVOT cross-sectional area calculated from the LVOT diameter (D) as:

$$LVOTa = \pi (D/2)^2 \text{ where } D = \text{LVOT diameter}$$

In clinical practice, the time velocity integrals can be replaced with maximum velocities.

The major error in echocardiographic evaluation of aortic stenosis is underestimation of severity due to failure to obtain a parallel intercept angle between the Doppler beam and aortic jet. Careful evaluation with a dedicated continuous wave Doppler probe with optimal patient positioning in an experienced laboratory is needed to avoid this problem. Another potential error in the continuity equation is measurement of the LVOT diameter, an error with magnified significance since that dimension is squared in the formula (Figure 2). For patients with images too poor to accurately measure this diameter, the ratio of outflow tract to aortic velocity provides a dimensionless measure of severity, where 1.0 is normal, 0.5 indicates a valve area 50% of normal and so forth. When the LVOT to AS velocity ratio is less than 0.25, severe aortic stenosis is almost always present.

Although less flow dependent than velocities and pressure gradients, valve area can change with transaortic volume flow rate. An extreme example of this phenomenon is the patient with a very low cardiac output when even normal aortic valve leaflets open only partially resulting in a small orifice area. The



Fig. 2. Measurement of the left ventricular outflow tract. The measurement should be the internal diameter between the junction of the anterior aortic cusp and the interventricular septum to the junction of the posterior aortic cusp and the anterior mitral leaflet.

effect of volume flow rate on aortic valve area becomes a clinical problem in the patient with valve calcification and left ventricular dysfunction. In these cases, dobutamine stress echocardiography may allow differentiation of severe stenosis with a fixed valve area from reduced leaflet motion due to left ventricular dysfunction. However, stress echocardiography for evaluation of aortic stenosis severity should only be performed at experienced centers.

Aortic stenosis severity is best evaluated by transthoracic Doppler echocardiography. Although some centers advocate planimetry of valve area on transesophageal images, this approach has limitations due to the non planar valve orifice and ultrasound artifacts related to valve calcification. It is difficult to adequately evaluate aortic stenosis by Doppler methods from the transesophageal approach due to inability to align the Doppler beam parallel with the aortic jet from most views, although this usually can be accomplished from deep gastric views. Intraoperative evaluation of aortic stenosis severity should be avoided. Aortic stenosis usually is managed without determination of catheter-derived gradients and valve area, although hemodynamic evaluation may be helpful when the clinical symptoms or physical examination are discrepant with the Doppler data. Coronary angiography is indicated prior to surgical intervention in most adults with aortic stenosis to evaluate for concurrent coronary artery disease.

Timing of intervention

The timing of surgical intervention for aortic stenosis is based on the patient's symptoms (Figure 3). Quantitative evaluation of disease severity is used to confirm that symptoms are likely due to valve disease

and that surgery would result in improved hemodynamics. In general, surgical intervention is indicated in adults with symptoms consistent with aortic stenosis and hemodynamic evidence of severe obstruction (aortic jet velocity >4.0 m/s or valve area ≤ 1.0 cm²). However, if symptoms are present with no other explanation, valve surgery should be strongly considered even when stenosis is only «moderate» in severity. In the asymptomatic patient, surgery is not indicated unless there is evidence for left ventricular systolic dysfunction.

In the patient undergoing cardiac surgery for other reasons, aortic valve replacement should be considered for moderate to severe asymptomatic aortic stenosis because of the high likelihood of progression to severe disease within a few years and the higher risk of reoperation at that time.^{6,7} Despite success in the pediatric population and young adults without calcification, percutaneous balloon aortic valvuloplasty is not a useful procedure for the majority of adults with calcified valves.⁸

MITRAL STENOSIS

Mitral stenosis in the adult population is nearly always due to rheumatic heart disease, although rare cases of severe mitral annular calcification extending towards the tip of the mitral leaflets are seen.

Evaluation of cause and disease severity

Transthoracic echocardiography (TTE) is the mainstay for the diagnosis of mitral stenosis as well as for determining severity at baseline and on serial follow-up exams. Two-dimensional echocardiography demonstrates the classic diastolic doming of the anterior mitral leaflet in diastole, best demonstrated in the parasternal long axis view (Figure 4). The parasternal short axis view allows evaluation of the fusion and degree of calcification of the medial and lateral commissures.

The mean diastolic gradient is the most applicable gradient across the mitral valve and can be obtained by tracing the continuous wave Doppler signal for integration of instantaneous pressure gradients over the diastolic filling period (Figure 5).

Measurement of mitral valve area is performed with two-dimensional TTE echocardiographic by planimetry of the orifice in short axis view as well as indirectly with spectral Doppler. The 2D valve area is measured in a short axis view, taking care to identify the minimum orifice at the leaflet tips and tracing the black-white interface on the image (Figure 6). 2D mitral valve area has been well validated compared to direct measurement at surgery.⁹ Three-dimensional

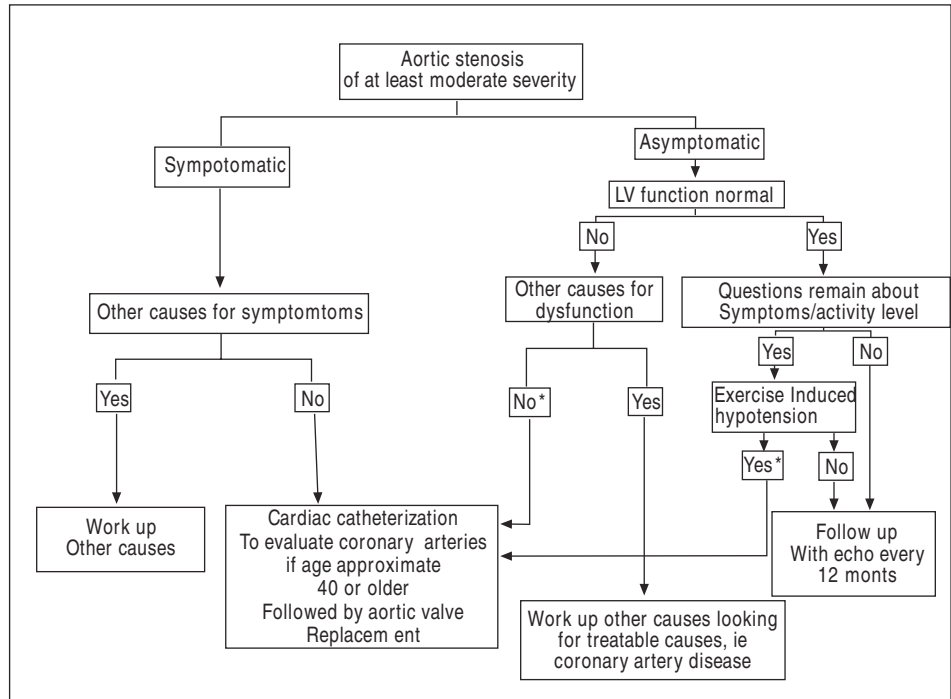


Fig. 3. Algorithm for management of aortic stenosis. LV indicates left ventricle. *IIa indication for referral to surgery.

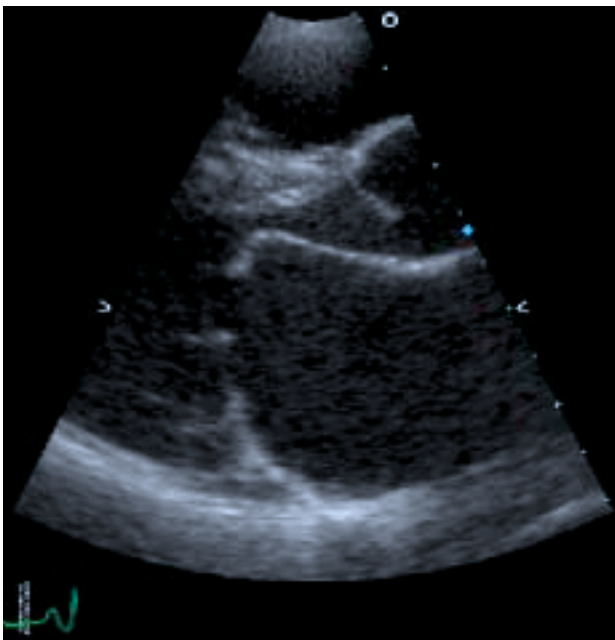


Fig. 4. An example of the bowing or «hockey stick appearance» to the anterior leaflet of the mitral valve in mitral stenosis.

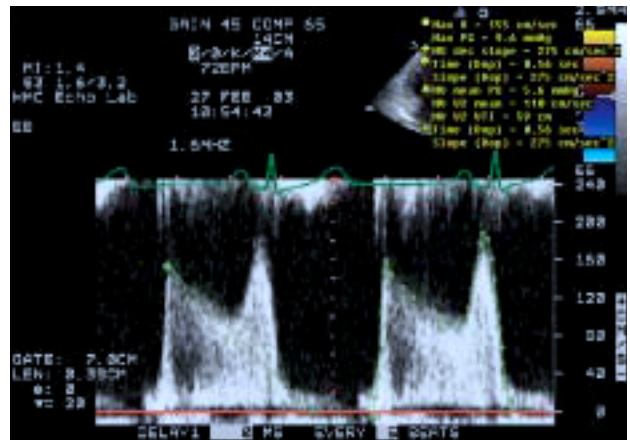


Fig. 5. Continuous wave spectral Doppler of the flow across a stenotic mitral valve shows how tracing the entire spectrum yields the mean gradient.

(3D) echocardiography is in theory much more precise for measuring the mitral valve area by direct planimetry since the technology allows direct visualization of the valve orifice in multiple planes. More specifically, the cut plane through the mitral valve orifice can be adjusted with 3D guidance to ensure that the smallest valve orifice at the very tip of the mitral leaflets and perpendicular to the valve orifice

is being measured by planimetry. In fact, three publications have recently confirmed the lower interobserver variability of 3D echo and claimed better accuracy than 2D echo, although their gold standard in these studies was Doppler pressure half-time, a measure with its own limitations.¹⁰⁻¹² Our own experience with 3D echo measurement of the mitral valve orifice is that planimetry measurement taken from the ventricular side of the valve orifice tends to be more accurate than measurements taken from the atrial side (Figure 7).¹³

Mitral valve area (MVA) also can be estimated from

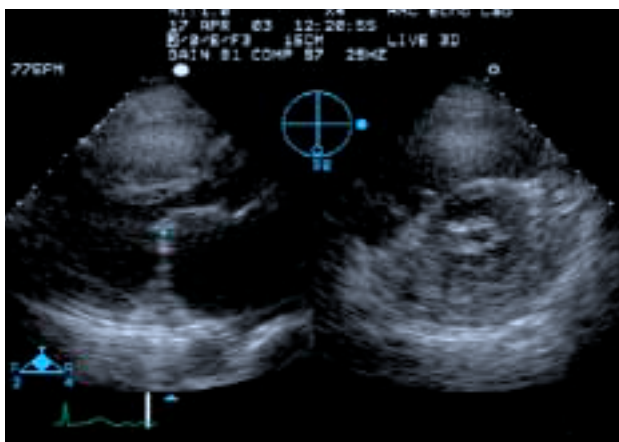


Fig. 6. Biplane view of a stenotic mitral valve allows positioning the cursor at the tips of the mitral leaflets in the parasternal view. The simultaneous orthogonal view allows tracing of the mitral orifice with confidence that is at the leaflet tips. The parasternal long axis view is shown on the left and the short axis view is on the right.

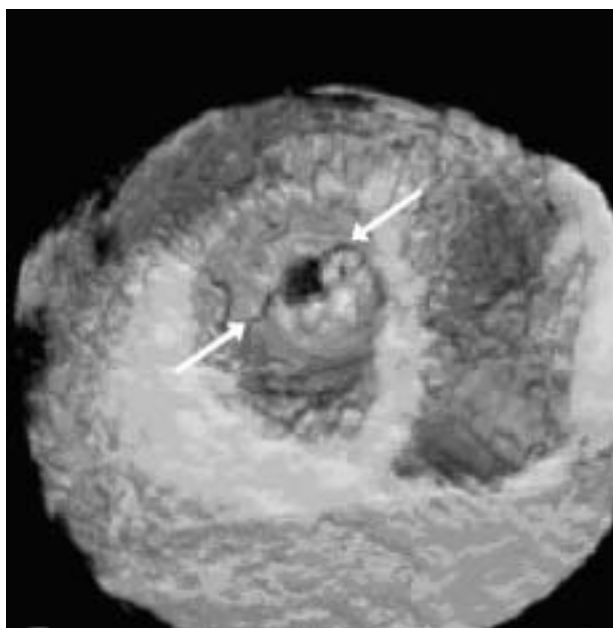


Fig. 7. The mitral orifice is viewed by 3D echo from the ventricular side. Note the fused commissures that are visualized (arrows), suggesting that this valve would be an optimal candidate for percutaneous mitral valvotomy.

the Doppler pressure half-time (PHT) or the time it takes for the gradient across the mitral valve to be reduced to one half the initial gradient. This concept was originally used for valve area using catheterization techniques by Libanoff in 1968 and then developed for Doppler echocardiography by Hatle in 1983.^{14,15} MVA is then calculated using an empiric constant of 220 as:

$$MVA=220/PHT$$

Thus, the valve area is 1 cm² when the PHT is 220 ms. In theory, significant aortic regurgitation may result in overestimation of the mitral valve area with the pressure half-time method but this is usually not clinically significant when rheumatic mitral stenosis is present. Concerns have been raised regarding the accuracy of pressure halftime early post-valvuloplasty because of the changing dynamics between the left atrium and the left ventricle.¹⁶ Others have challenged this limitation. Ultimately two studies confirmed that the pressure halftime is accurate in this setting and the previous questions, raised by alleged underestimation of the valve area by PHT, most likely were due to overestimation by the Gorlin equation caused by the iatrogenic atrial septal defect created by trans-atrial septal puncture during the procedure.^{17,18}

Mitral valve area also can be calculated using the continuity equation:

$$MVA=(A_1 \times VTI_1)/VTI_2$$

where A₁ is left ventricular outflow tract area, VTI₁ is the time velocity integral of the left ventricular outflow tract, and VTI₂ is the time velocity across the

mitral valve. However, this calculation is practically limited as it requires several measurements and is accurate only in the absence of both aortic and mitral regurgitation. When coexisting valve regurgitation is present, transmitral volume flow rate can be calculated from the proximal acceleration region on the left atrial side of the valve and used in the continuity equation.

Accompanying mitral regurgitation is assessed using color Doppler flow mapping. The presence of more than mild mitral regurgitation prohibits percutaneous mitral valvotomy as treatment.

Pulmonary hypertension can be assessed based upon the velocity of the tricuspid regurgitation jet because the velocity (V) of the tricuspid regurgitant (TR) jet reflects the right ventricular to right atrial systolic pressure difference. Right atrial pressure (RAP) can be estimated from the size and respiratory variation of the inferior vena cava as seen on a subcostal view. In the absence of pulmonic stenosis, which is uncommon in adults, right ventricular and pulmonary systolic pressures are equal. Thus,

$$PAP=4 (V_{TR})^2+RAP$$

Evaluation of the mitral leaflets and subvalvular apparatus for the presence of thickening, mobility, and calcification by 2D echo is particularly important as the morphology of the valve apparatus predicts the immediate and long-term hemodynamic results of percutaneous valvotomy. The features evaluated

TABLE 1. The French three-group grading of mitral valve anatomy

Echocardiographic group	Mitral valve anatomy	% with inadequate results following valvotomy
Group 1	Pliable noncalcified anterior mitral leaflet and mild subvalvular disease, i.e., thin chordae ≥ 10 mm long	2.2
Group 2	Pliable noncalcified anterior mitral leaflet and severe subvalvular disease, i.e., thickened chordae < 10 mm long	7.4
Group 3	Calcification of mitral valve of any extent, as assessed by fluoroscopy, whatever the state of the subvalvular apparatus	22.3

include the degree of mitral leaflet thickening, the mobility of the valve, degree of leaflet calcification, and the degree of thickening and shortening of the subvalvular apparatus. Other important features are the presence of commissural calcification and an asymmetric pattern of leaflet calcification. The French 3-group grading system, which is based on the presence of mitral valve calcification and thickening of the subvalvular apparatus, correlates well with hemodynamic outcomes (Table 1).

Timing of intervention

There is some heterogeneity in the literature with regard to what is considered mild, moderate, and severe mitral stenosis. In general, mild mitral stenosis is associated with a valve area greater than 1.5 cm² and a mean gradient less than 5 mm Hg. In moderate mitral stenosis the valve area is 1.0 to 1.5 cm² and the mean gradient is 5 to 10 mm Hg. In severe mitral stenosis the valve area is less than 1.0 cm² and the mean gradient is greater than 10 mm Hg. A well-established indication for intervention with valvotomy or surgery is symptomatic mitral stenosis of at least moderate severity.

When valve morphology is favorable, percutaneous mitral valvotomy rather than mitral valve replacement is the procedure of choice for rheumatic mitral stenosis. Prior to mitral valvotomy, atrial thrombi, and particularly left atrial appendage thrombi must be ruled out using transesophageal echocardiography. Finally, the presence of mitral regurgitation that is more than mild or other reasons for cardiac surgery such as accompanying disease of other valves requiring surgical intervention, or the presence of left main coronary artery disease or equivalent make mitral valve replacement preferable.

It is known that splitting of the commissures at the time of mitral valvotomy is the mechanism for procedure efficacy; hence an accurate method for determining whether the commissures are fused is useful for the interventionalist. In this regard, 3D echo is particularly advantageous for viewing the commissures because of the depth perspective

provided by this technology (Figure 7). Further, 3D echo is useful in showing commissural splitting after the valvotomy.¹⁹ The recent advent of real-time 3D echo allows evaluation of mitral commissural splitting during the mitral valvuloplasty procedure. Documentation of splitting is important because without it, the apparent improvement in hemodynamics is only transient (Figure 8).

Stress Doppler echocardiography

When a patient's symptoms are out of proportion to the resting valve area and gradient or there are coexisting medical conditions that could explain symptoms, stress Doppler echocardiography may benefit management decisions. In a subset of patients with resting hemodynamics consistent with mild or moderate mitral stenosis, stress causes marked increases in left sided pressures and decreases in stroke volume.²⁰⁻²² Symptomatic patients with mild to moderate mitral stenosis tend to have more exaggerated hemodynamic changes and benefit the most from intervention.²³⁻²⁵

Doppler echocardiography may be used to measure pulmonary arterial pressure and mitral valve gradient during rest and with exercise or pharmacologic stress. The American College of Cardiology guidelines recommend consideration for mitral valve interventions when post-exercise pulmonary pressure is greater than 60 mm Hg, or mean transvalvular gradient is greater than 15 mm Hg⁶ regardless of resting hemodynamics. Conversely, if pulmonary arterial pressures and transmitral gradient do not increase to near these levels, these patients are unlikely to benefit from interventions on the mitral valve.

VALVULAR REGURGITATION

Aortic regurgitation

In the adult population, the important causes of chronic aortic regurgitation are degenerative or

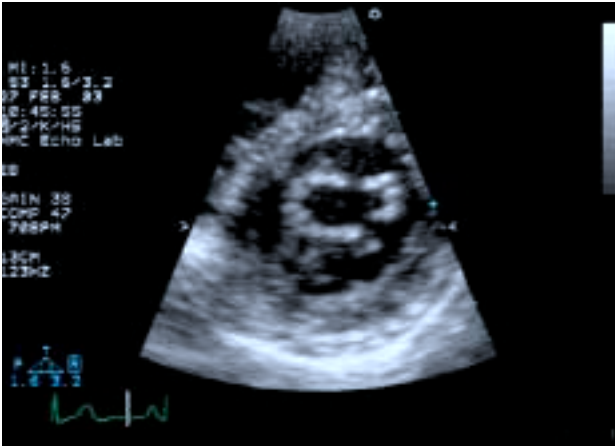


Fig. 8. Short axis view of a patient with mitral stenosis shows the mitral orifice well, but does not show fusion of the mitral commissures as shown in the preceding view by 3D echo.

calcific disease of the aortic valve (accompanying predominant aortic stenosis), bicuspid aortic valve, endocarditis, and rheumatic disease. In addition, chronic aortic regurgitation also may be due to a dilated aortic root in patients with hypertension, cystic medial necrosis, or Marfan syndrome. Acute aortic

regurgitation may result from aortic dissection or endocarditis.

Evaluation of cause and disease severity

Echocardiography. Echocardiography is used to delineate the cause and severity of aortic regurgitation as well as the sequelae of this valve lesion: most importantly left ventricular chamber dilation. Echocardiography allows evaluation of aortic valve structure including the number and orientation of cusps, presence of vegetations, and degree of aortic root enlargement. Echocardiography provides an accurate diagnosis in patients with acute aortic regurgitation, although when transthoracic image quality is suboptimal or when aortic dissection is suspected, transesophageal imaging may be needed to more closely visualize the aortic cusps, and the ascending and descending thoracic aorta. Transesophageal echocardiography is the procedure of choice when the diagnosis of endocarditis is in question with a markedly increased sensitivity compared to transthoracic echocardiography.²⁶ Three-dimensional echocardiography is a promising approach as it allows improved visualization of the

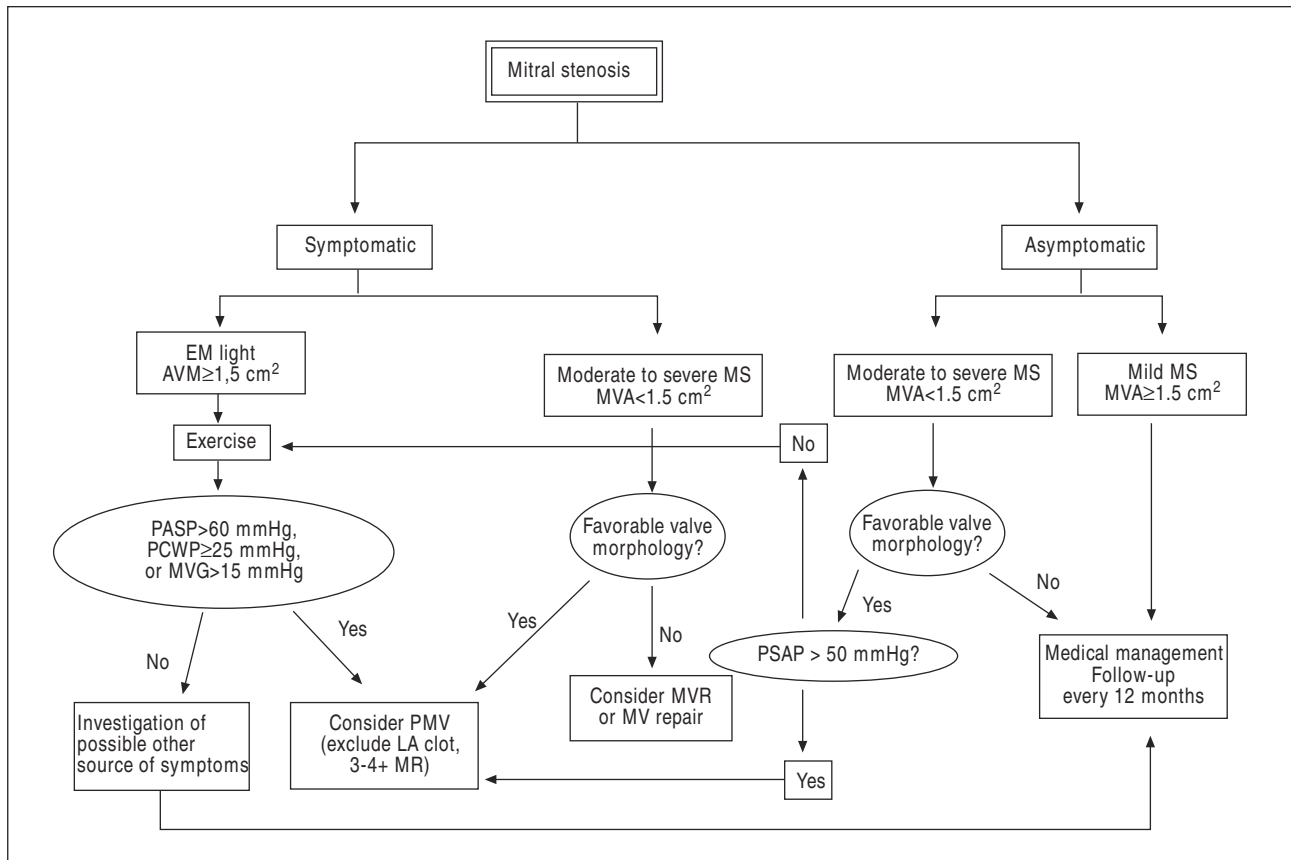


Fig. 9. Algorithm for management of mitral stenosis. MVA indicates mitral valve area; MS, mitral stenosis; MR, mitral regurgitation; PMV, percutaneous mitral valvulotomy; LA, left atrium; MV, mitral valve; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; MVG, mean mitral gradient.

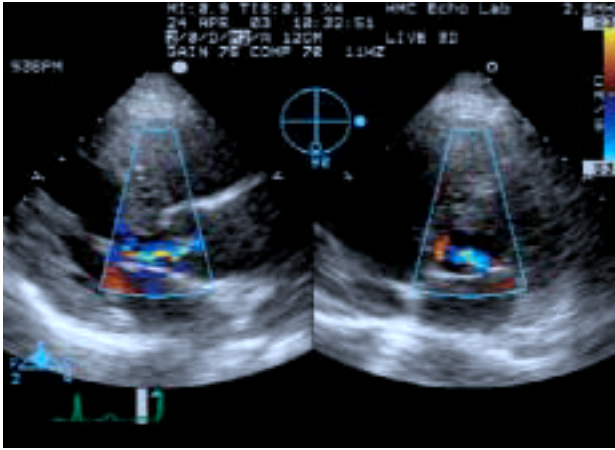


Fig. 10. A biplane view of aortic regurgitation by color. Note that the parasternal long view is used to assess where the origin of the jet is. This allows movement of the cursor to this point. Therefore, the simultaneous orthogonal view shows the jet height also at the origin. This allows simultaneous measurement of the jet height relative to the LVOT width in two orthogonal planes.

body of the valve cusps, views that are suboptimal by two-dimensional echocardiography.

Color Doppler flow mapping provides a practical approach for semi-quantitative grading of aortic regurgitation in the clinical setting.^{27,28} The width of the aortic regurgitation jet at its origin provides the most reliable color flow estimate of regurgitant severity.^{29,30} A rough guideline for approximating severity is the width of the aortic regurgitation jet compared to the width of the left ventricular outflow tract. If this ratio is $<1/3$, regurgitation is usually mild, $1/3$ to $2/3$ moderate and greater than $2/3$ is severe. The width of the jet should be evaluated in at least 2 orthogonal views, typically the parasternal long axis and short axis views (Figure 10). The length that the aortic regurgitation jet travels into the left ventricle is less reliable because jet length is dependent on many factors independent of the actual regurgitant orifice size including jet direction, entrainment of flow by the jet, and the aortic to left ventricular pressure difference.

The density of the aortic regurgitation jet by continuous wave Doppler, compared to the forward jet density is another very qualitative measure of severity of regurgitation.

The half Doppler PHT has also been suggested as a method to quantify aortic regurgitation.^{31,32} The Doppler pressure half time represents the time for the peak gradient between the aorta and left ventricle to decay to $1/2$ its initial value (Figure 11) A very short PHT (<200 ms) indicates severe aortic regurgitation whereas a long PHT (>600 ms) is consistent with mild aortic regurgitation. The major limitation of PHT is that most measurements are between 300 and 600 and hence to not discriminate mid range aortic

regurgitation well. In addition, pressure half-time reflects disease duration with a steep diastolic slope (short half-time) in acute regurgitation as aortic pressure approaches left ventricular pressure at end-diastole and a flat slope (PHT) with chronic compensated regurgitation, regardless of severity.

Another simple approach to evaluation of aortic regurgitant severity is the extent of diastolic flow reversal in the aorta. Holo-diastolic flow reversal (i.e. for the entire duration of diastole) in the proximal abdominal aorta is specific for severe aortic regurgitation. In the descending thoracic aorta, holodiastolic flow reversal is seen with moderate-severe regurgitation with the relative areas under the Doppler spectral curve of antegrade versus retrograde flow reflecting regurgitant severity.³³

However, the most important parameters on echocardiography in patients with aortic regurgitation are left ventricular size and systolic function. The extent of left ventricular dilation is a function of the severity and duration of the pressure/volume overload imposed by the regurgitant aortic valve. Timing of surgical intervention is based on measurements of end-systolic dimension and ejection fraction.

Angiography. Aortic root angiography is rarely needed for evaluation of aortic regurgitation but may be done when cardiac catheterization is being performed for other indications. The severity of aortic regurgitation is defined based on the density of opacification of the left ventricle compared to the density of the aortic root. Typically four degrees of severity are described (1-4+). Mild or 1+ aortic regurgitation is characterized by a jet of aortic regurgitation seen throughout diastole but not impacting the density of the left ventricular volume. Severe or 4+ aortic regurgitation implies immediate complete opacification of the left ventricle to the same degree as the aortic root with the first diastolic frame. Grade 4+ aortic regurgitation also implies that many cardiac cycles are required for the opacification of the left ventricle to clear. Grade 2 and 3+ describe densities in between the extremes of 1 and 4+.

Magnetic resonance imaging. Magnetic resonance imaging (MRI) is an accurate method for evaluation of aortic dissection with the advantage, compared to echocardiography, of a wide field of view with visualization of the entire thoracic and abdominal aorta. The ability to perform contrast-enhanced cine-MRI also allows angiographic assessment of the severity of aortic regurgitation in a similar fashion to aortic root angiography. However, this approach is not widely used due to lack of general availability, inability to perform examinations at the patient's bedside, and cost.

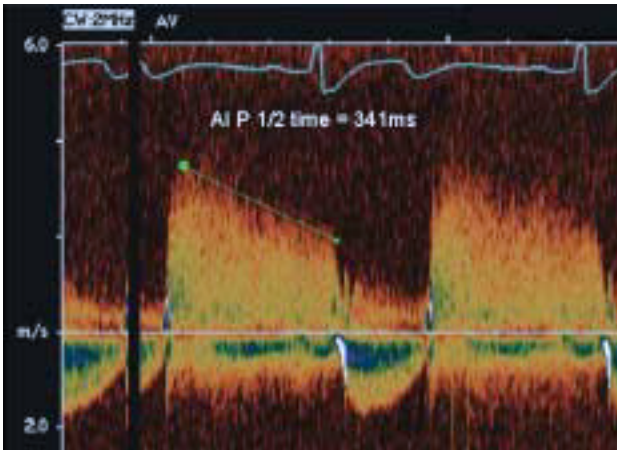


Fig. 11. An example of continuous wave spectral Doppler of an aortic regurgitation jet. Note the PHT of 341 ms consistent with moderate aortic regurgitation (AI).

Timing of intervention

Aortic valve replacement is indicated in adults with symptomatic chronic or acute severe aortic regurgitation (Figure 12). In some patients, irreversible left ventricular dysfunction develops in the absence of symptoms. Periodic echocardiographic

evaluation, typically yearly, allows measurement of ventricular size and ejection fraction for early detection of left ventricular dysfunction. The empiric parameters that are recommended as indicators of early ventricular dysfunction include an end-systolic dimension >55 mm and an ejection fraction <50%.⁶

Surgical intervention may be prevented or delayed in some patients with aortic regurgitation by the use of chronic vasodilator therapy. Vasodilator therapy should be considered in all patients with severe regurgitation and left ventricular dilation. In patients with mild or moderate regurgitation, surgical intervention may never be needed. In these patients, management focuses on prevention of endocarditis and serial studies to evaluate for any change in valve disease.

Mitral regurgitation

The mitral valve apparatus is complex and consists of the valve leaflets, the mitral annulus, the subvalvular apparatus divided into the chordae tendinae and papillary muscles, and the underlying left ventricular wall. The mitral annulus is a heterogeneous structure as well with the anterior portion sharing tissue with and gaining support from the annulus of

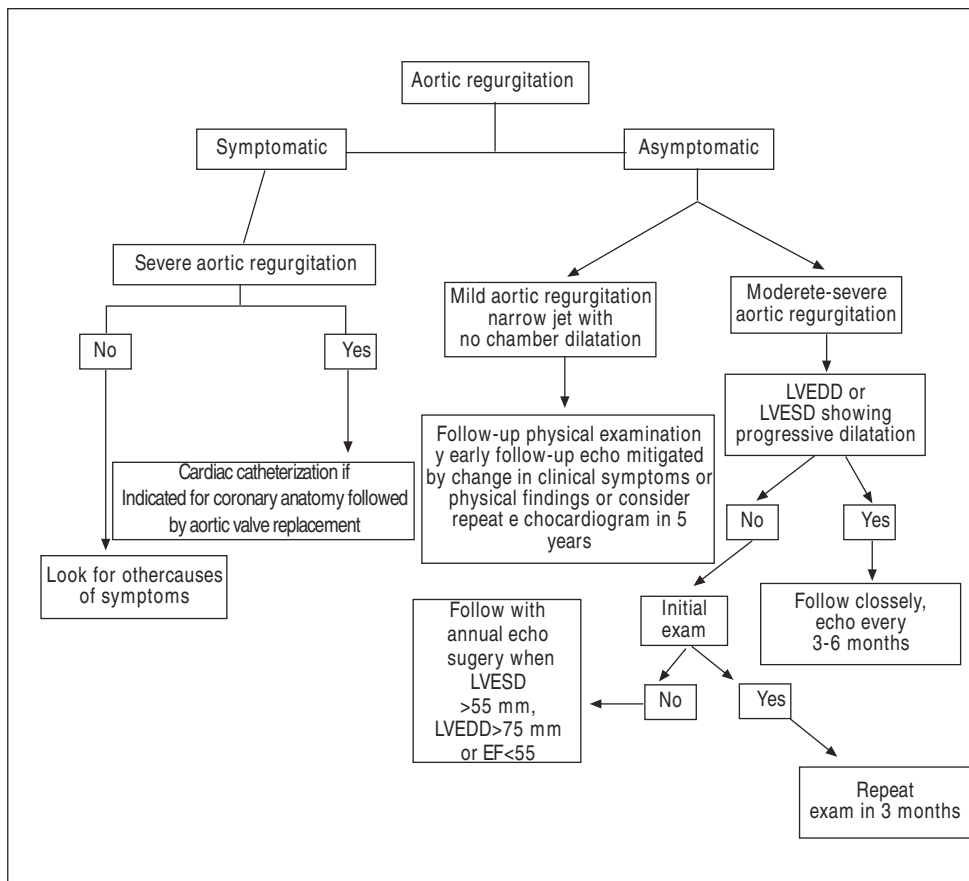


Fig. 12. Algorithm for management of aortic regurgitation. LVEED: left ventricular end-diastolic diameter. LVESD indicates left ventricular end-systolic diameter; EF, ejection fraction.

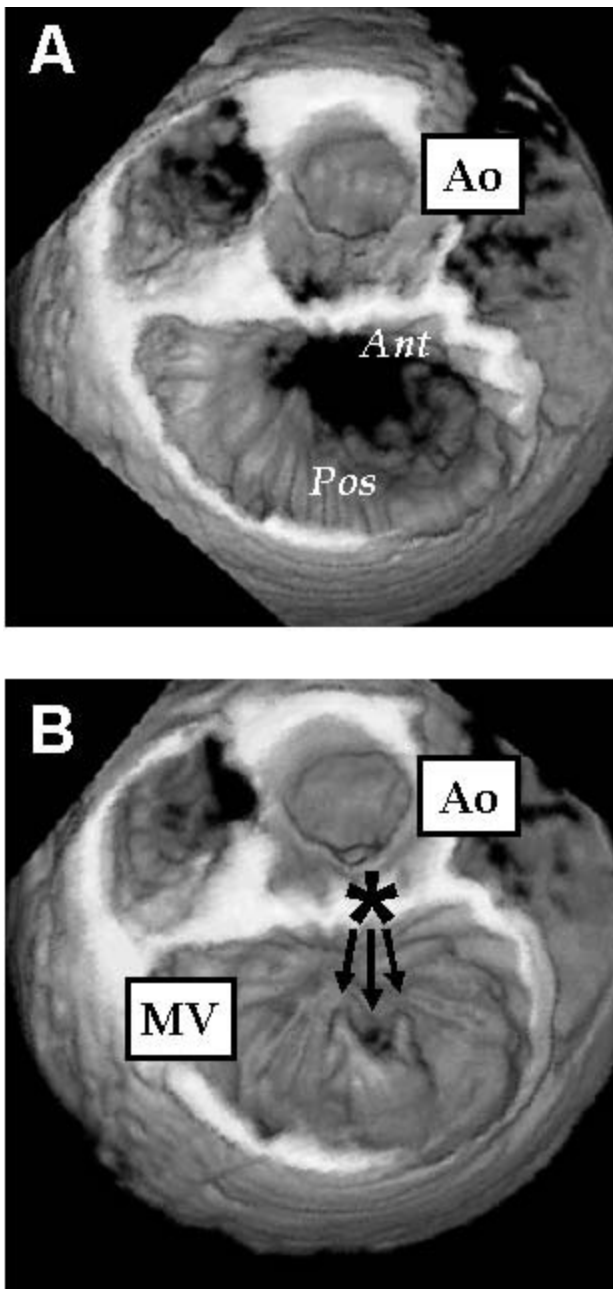


Fig. 13. This 3D echo viewing the mitral valve from the atrial side shows a flail middle scallop of the posterior leaflet. The ruptured chordae tendinea is also visible. Diastolic frame (above) and systolic frame (below) are shown. The arrows point to ruptured chords. Ao indicates aortic valve; MV, mitral valve.

the aortic valve while the posterior structure has a less firm anchor. Mitral regurgitation can be primary, that is due to the valve or valve apparatus directly, or secondary to dilation of the left ventricle.

Examples of primary mitral regurgitation include rupture of the chordae tendinae due to myxomatous disease, rheumatic disease that causes reduction of the valve leaflets and commissural fusion, and

endocarditis resulting in leaflet deformation and destruction. Secondary causes of mitral regurgitation include ischemia of the papillary muscle as well as actual rupture of the papillary muscle caused by acute myocardial infarction. Finally dilated cardiomyopathy results in annular dilation and alters the angle between the papillary muscles and the mitral annulus.³⁴

Evaluation of cause and disease severity

The chest x-ray and ECG are non-specific in mitral regurgitation, although left ventricular enlargement and left atrial enlargement should be sought by both modalities. On chest radiography, a double density may be seen overlying the left ventricular silhouette consistent with left atrial enlargement.

In patients with adequate acoustic windows, transthoracic echocardiography remains the mainstay for the diagnosis of mitral regurgitation, including the cause and severity. However, mitral regurgitation is the valve disease process where transesophageal echocardiography (TEE) plays the most significant role. TEE is used to more accurately define the anatomy leading to regurgitation, especially when valve repair is being considered. This is because transesophageal echocardiography is superior to TTE for defining exact cause and structures involved in a flail leaflet, especially when combined with three-dimensional echocardiography. More specifically, 3D echocardiography can identify with certainty which scallop of the mitral valve is involved when a leaflet becomes flail as well as the degree of prolapse and presence of ruptured chords. (Figure 13).

Myxomatous valve disease of the mitral valve can be identified by the typical combination of mild valve thickening, redundancy to the mitral chordae, and in more advanced cases, prolapse of the mitral valve. Rupture of the mitral chordae and resultant severe mitral regurgitation is also easily diagnosed by the combination of the 2D and color Doppler echocardiography.

The presence of wall motion abnormalities in the inferior/posterior myocardial distribution is a clue to the most common cause of papillary muscle dysfunction, inferior myocardial infarction. The posterior-medial papillary muscle is more prone to ischemic disease than is the anterior-lateral papillary muscle because of dual blood supply to the latter. Mitral annular dilatation is readily visualized in the typical setting of dilated cardiomyopathy, another common cause of mitral regurgitation. Mitral annular calcification often coexists with degenerative disease of the aortic valve and is another important cause of mitral regurgitation, especially in the elderly population.

Quantification of mitral regurgitation is accomplished by many methods using

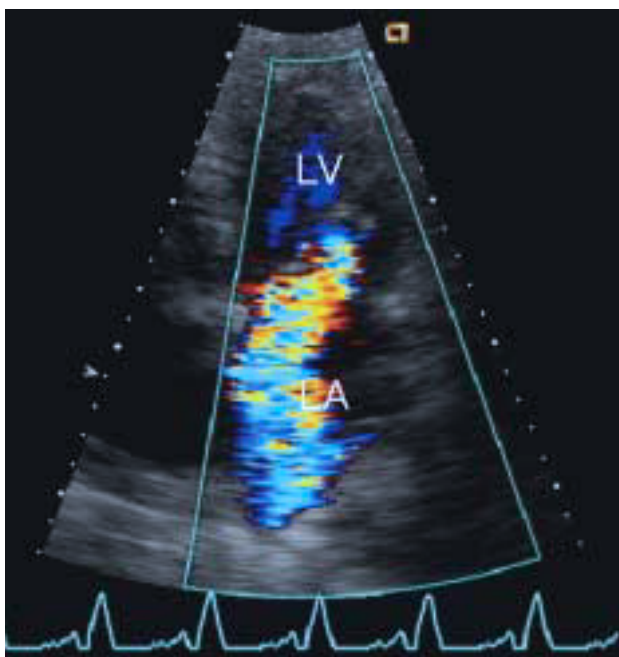


Fig. 14. Color Doppler of severe mitral regurgitation. Note that the regurgitation jet reaches the back of the left atrium and occupies greater than 40% of the left atrial area. LV indicates left ventricle; LA, left atrium.

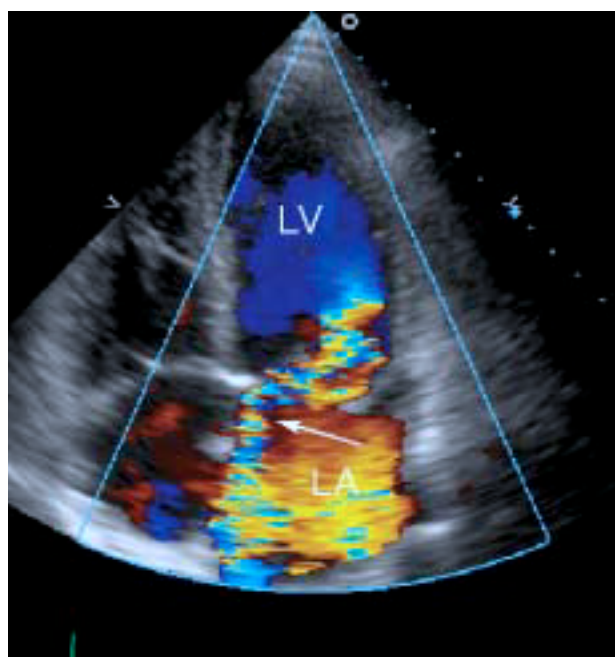


Fig. 15. The mitral regurgitation jet hitting the wall of the left atrium demonstrates an example of the Coanda effect. The result is a regurgitation jet that is smaller than it would be without the atrial wall interference. Qualitative assessment of the regurgitation jet size typically must take into account the Coanda effect, and often means upgrading the severity one level. LV indicates left ventricle; LA, left atrium.

echocardiography, the most clinically useful being Doppler color flow mapping (Figure 14).³⁵ In general, quantification using this methodology takes advantage of visualizing the mitral regurgitation jet using color Doppler. For instance, the color Doppler jet can be measured in terms of its width, length, and area, either by actually measuring these parameters or by semi-quantitatively estimating their size just by visual assessment. Normalizing the regurgitant jet size to the left atrial size also aids this semi quantitative method. However, independent of the degree of mitral regurgitation, the size of the color Doppler jet is affected by the gradient between the left ventricle and the left atrium, the compliance of the left atrium, the direction of the jet and whether it hits an atrial wall, and the color gain of the ultrasound system (Figure 15).

Because of the limitations of color flow mapping, most echocardiography laboratories either use quantitation of regurgitant severity or integration of several types of qualitative data. Although not exhaustive, a fairly complete list would include assessment of regurgitant fraction, measurement of regurgitant orifice area using the proximal isovelocity surface area (PISA) methodology, measurement of vena contracta with, examination of the continuous wave Doppler signal and assessment of systolic flow reversal in the pulmonary veins. The differentiation

between moderate and severe can be aided by the lack of flow reversal in the pulmonary veins with moderate regurgitation. Frequently moderate mitral regurgitation is associated with «blunting» of the systolic pulmonary vein flow signal. In mild mitral regurgitation, pulmonary vein flow in systole typically is normal. Atrial fibrillation limits the ability to assess systolic flow of the pulmonary veins and can cause reversal of flow independent of mitral regurgitation.^{36,37}

Regurgitant fraction can be calculated by comparing the forward stroke volume across the mitral valve to that across the aortic valve, based on the cross-sectional area of flow and velocity time integral of flow across each valve. However, in the presence of aortic regurgitation, the cardiac output across the mitral valve should be compared to one of the right-sided heart valves. Our experience with these types of calculation has not been strong however, especially when forced to resort to comparison of a right-sided heart valve.

The PISA method is based on measurement of the area of flow convergence on the left ventricular side of the mitral valve for the purpose of determining the regurgitant orifice.³⁸ It takes advantage of the area of proximal flow convergence developing a hemispherical shape. The technique requires lowering the blue color Nyquist limit of the color Doppler to a

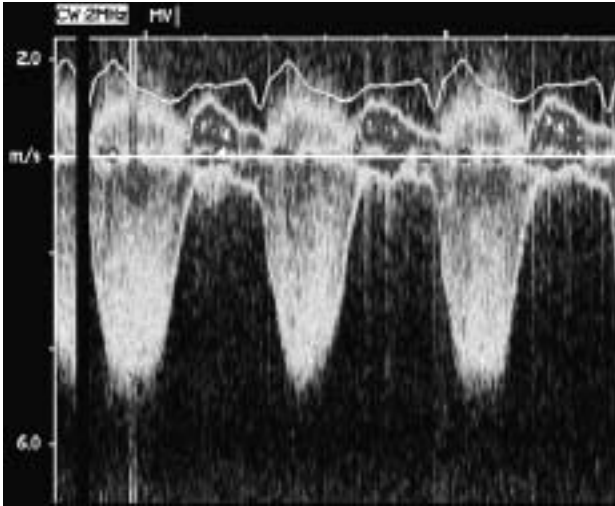


Fig. 16. Example of a very dense mitral regurgitation jet by continuous wave Doppler, suggestive of severe mitral regurgitation.

blue aliasing velocity of 20-40 cm/s in order to enhance the visualization of the largely red colored hemisphere of PISA. This done, the diameter of the PISA can be measured and used to calculate the orifice area (ERO) using the formula:

$$\text{ERO} = 2\pi r^2 \times \text{alias velocity} / \text{MR velocity}$$

Or $6.28r^2 \times \text{alias velocity} / \text{MR velocity}$

r=radius of PISA; alias velocity=color Doppler alias velocity and MR velocity is the continuous wave velocity of mitral regurgitation.

Alternatively, the diameter of the PISA alone can be used as another semi-quantitative method for assessment of mitral regurgitation severity with a diameter of the PISA >10 mm when the aliasing velocity is set at 30 cm/s +/-5cm/s being consistent with severe mitral regurgitation.

Measurement of the vena contracta, strictly defined as the narrowest portion of the mitral regurgitation jet downstream from the orifice,³⁹ has been shown by several studies to accurately assess severe mitral regurgitation.³⁹⁻⁴³ Mild mitral regurgitation is defined as a vena contracta <0.3cm and moderate has variably ranged from 0.6 to 0.8 cm. A particular strength of this method is that it is said to work equally well for eccentric versus central jets.

A final note with regard to quantification of mitral regurgitation is evaluation of atrial and ventricular chamber sizes and quantitation of pulmonary hypertension. Severe mitral regurgitation, unless acute, should be accompanied by significantly elevated left ventricular volumes and particularly left

atrial enlargement as well as elevation of pulmonary pressures.

Hence general guidelines for definite severe mitral regurgitation would include the following:

1. Regurgitant orifice >0.40 cm².
2. PISA diameter >10 mm if aliasing velocity is 30 cm/s +/-5 cm/s.
3. Mitral regurgitation volume >60 mL.
4. Regurgitant fraction >50%.
5. Pulmonary vein systolic flow reversal (specific, but not sensitive).
6. Mitral regurgitation color flow jet reaching the posterior wall of the LA (with a high aliasing velocity of color map).
7. Color flow map consistent with severe mitral regurgitation (10 cm² or >40% of the LA area) the presence of LA size >5.5 cm, LV size >7 cm and significant pulmonary hypertension (PA systolic pressure >50 mm Hg).
8. Vena contracta width >0.7 cm².
9. Dense continuous wave jet (Figure 16).

Angiography

Angiography is rarely needed for evaluation of mitral regurgitation. When transthoracic imaging is suboptimal, the most useful next diagnostic test is transesophageal echocardiography. Angiography may be still indicated when there is discrepancy between the clinical symptoms and the non-invasive evaluation.

Timing of surgery

The timing of surgery for mitral regurgitation depends primarily on two factors: clinical symptoms and development of left ventricular dilation in response to volume overload (Figure 17). Therefore, the main indications for surgery in mitral regurgitation are the presence of severe mitral regurgitation and symptoms that are consistent with this. The surgery should be mitral valve repair when possible and mitral valve replacement when not.

In patients who are asymptomatic, evidence of early left ventricular systolic dysfunction include an ejection fraction <60% and an end-systolic dimension >45mm. The empiric parameters are accepted as an indication for surgical intervention with mitral valve repair again preferred over mitral valve replacement.

The marked improvement of surgical techniques for mitral valve repair in the last decade has led some experts to at least consider surgical intervention when mitral valve repair appears feasible even in asymptomatic patients with preserved left ventricular

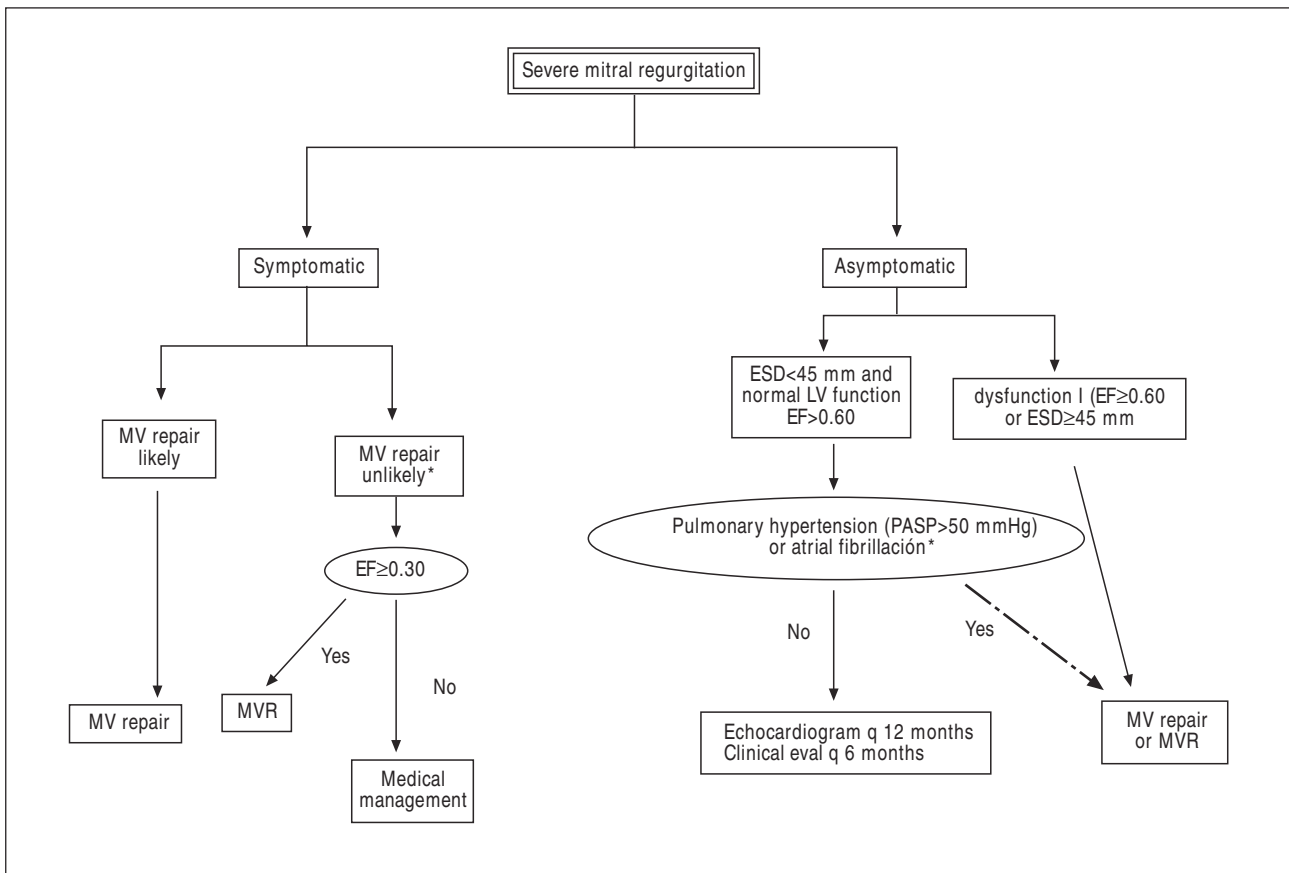


Fig. 17. Algorithm for management of severe mitral regurgitation. *Surgery for asymptomatic patients with atrial fibrillation or pulmonary hypertension and normal left ventricular function is controversial. **Mitral valve repair is more technically demanding and is less likely to be successful with anterior leaflet involvement, calcification, and rheumatic involvement. MV indicates mitral valve; MVR, mitral valve replacement; ESD, end-systolic diameter; LV, left ventricle; EF, ejection fraction.

function. This movement is reinforced by the now available data that mitral valve repair has excellent longevity with a low rate of re-operation ranging from 10%-20% at 5-10 years (David, 1993). However, operative intervention always entails a risk, albeit low, of operative mortality and morbidity and there remains no data to show better long term outcomes with surgical intervention at this point compared to watchful waiting and serial echocardiography and surgery per the current ACC/AHA guidelines.^{6,44}

To summarize, ACC/AHA guidelines for mitral valve surgery indicate that surgical intervention (mitral valve replacement or preferably repair) is indicated in symptomatic patients with severe mitral regurgitation when the ejection fraction is >30%. In addition, surgical intervention is recommended for asymptomatic patients with an:

1. Left ventricular end systolic dimension greater than 45 mm.
2. Left ventricular ejection fraction <60%.

Surgery in the setting of severe mitral regurgitation and severe left ventricular dysfunction (ejection fraction <30%) is always a topic of great debate and controversy. In these patients, mitral regurgitation may be the cause of left ventricular dilation and systolic dysfunction. More often, left ventricular dilation and systolic dysfunction have resulted in severe mitral regurgitation. Some centers advocate mitral valve repair in both these situations. Other centers advocate medical therapy and coronary revascularization, when ischemic but viable myocardium is present. Some patients may be heart transplantation candidates depending on the etiology of ventricular dysfunction and associated clinical factors. At this point, further studies are needed to define the optimal treatment approach for severe mitral regurgitation and left ventricular dysfunction.

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