VALVULAR HEART DISEASE

How to measure severity of mitral regurgitation

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The recently revised American College of Cardiology/American Heart Association guidelines for valvular heart disease emphasise that surgery is now indicated for severe mitral regurgitation (MR), even in asymptomatic patients, provided that the valve anatomy is suitable for repair, and that surgery is performed in an experienced centre with at least a 90% chance of successful repair.[1] A corollary to this recommendation is that it is important to determine accurately the severity of MR, since surgery is only indicated for severe MR. In 2003, the American Society of Echocardiography and the European Society of Echocardiography published recommendations for quantification of valvular regurgitation.[2] This paper summarises those recommendations, as they pertain to MR. First, a theoretical framework for understanding the determinants of MR severity and how they relate to echocardiography will be presented. Then, the practical application of various echocardiographic techniques for assessing MR severity will be discussed. In accordance with the above guidelines, an emphasis will be made on integrating multiple parameters into the final determination of MR severity.[2]

HAEMODYNAMIC DETERMINANTS OF MITRAL REGURGITATION

The Gorlin hydraulic orifice equation, commonly used to evaluate aortic stenosis, can also be used to derive the haemodynamic determinants of regurgitant volume in MR.[3] Thus, regurgitant volume in MR is determined by the regurgitant orifice area (ROA), a constant known as the discharge coefficient (C_d), the mean systolic pressure gradient (MPG) between the left ventricle (LV) and left atrium (LA), and the duration of MR during systole (T).

$$RgV = ROA \cdot C_d \cdot \sqrt{MPG} \cdot T$$

When assessing severity of MR, one should give careful consideration to each aspect of this equation. First, the ROA in MR is often dynamic and load dependent.[4] In rheumatic MR, the valve is generally fibrotic, calcified and immobile, and therefore the ROA is fixed. However, in patients with dilated cardiomyopathy or myxomatous degeneration, ROA can vary during the cardiac cycle and can change significantly with alterations in loading conditions. Because ROA is a fundamental determinant of MR severity, its measurement or calculation by echocardiographic techniques is of paramount importance.[2]

The constant C in the hydraulic orifice equation accounts for contraction of the flow stream as it passes through the anatomic orifice. This discharge coefficient is dependent on orifice geometry, flow, and fluid viscosity. It is not likely to be significantly affected by clinical variation in loading conditions, and does not significantly impact measurement of MR severity by echocardiography.

The mean systolic pressure gradient between the LV and LA is a primary determinant of MR severity, but its effect on echocardiographic variables is mitigated by two factors. First, haemodynamic changes tend to move the LV and LA pressures in the same direction such that the net effect on gradient is blunted. Second, the effect of mean systolic gradient on regurgitant volume is a function of its square root. For example, a 144 mm Hg mean systolic gradient has a square root of 12 mm Hg, whereas a 100 mm Hg mean systolic gradient has a square root of 10 mm Hg. Regurgitant volume is only affected by 20%, despite a 44% difference in gradient. Nevertheless, it is prudent to consider extremes of blood pressure when evaluating MR severity by echocardiography. Blood pressure should be measured at the time of echocardiography and recorded on the echocardiography report.

Finally, the duration of MR may be very important, particularly in myxomatous degeneration, where late systolic MR may lead to overestimation of MR severity by techniques that rely on single frame measurements. For example, fig 1 shows a large colour flow jet with a prominent proximal flow convergence region. Continuous wave Doppler indicated only late systolic MR. Frame-by-frame analysis of the colour flow images reveal no MR at all during the first five systolic frames, followed by two late systolic frames showing the large MR jet. The patient is asymptomatic, has normal functional capacity, normal LA and LV size, and an unimpressive late systolic murmur.

MITRAL VALVE ANATOMY

Careful evaluation of the mitral valve anatomy is an integral part of echocardiographic assessment of MR severity. The mitral valve apparatus includes the leaflets, annulus, chordae, papillary muscles, and left ventricle. Severe MR seldom occurs when the mitral valve and left ventricle are anatomically

Heart 2008;94:376–383. doi:10.1136/hrt.2005.086462

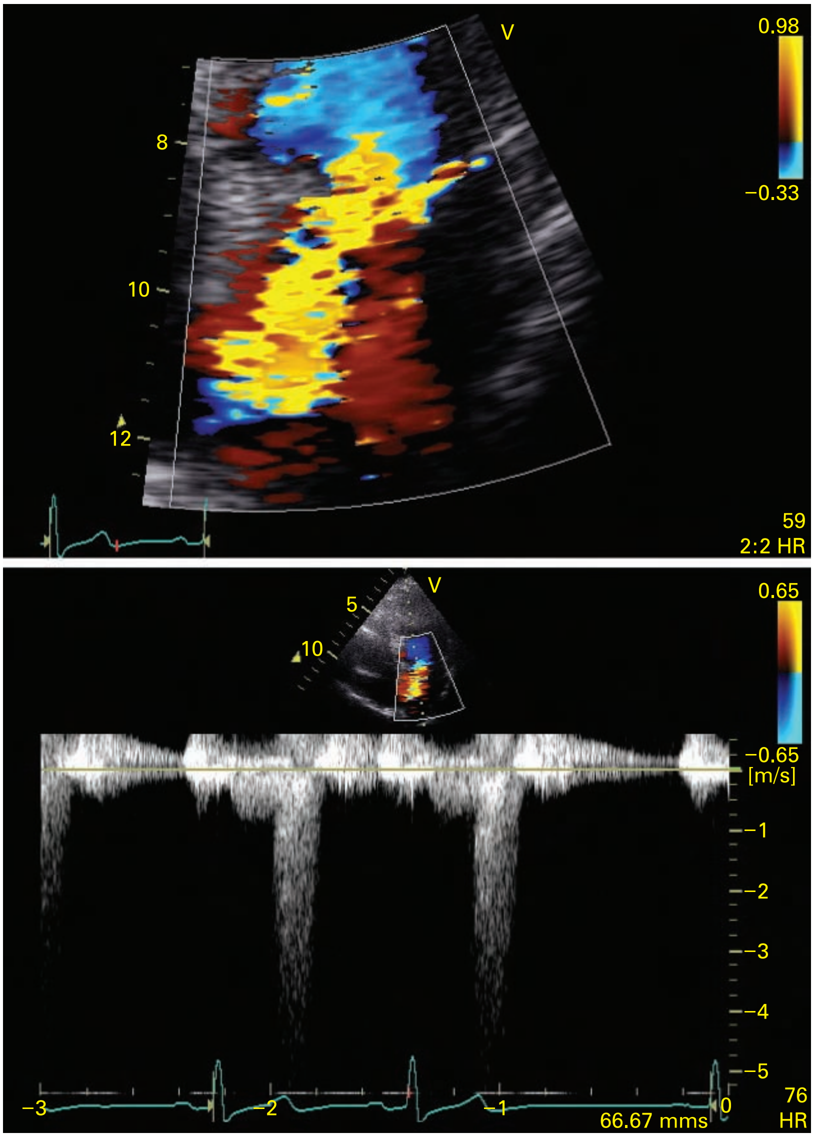

Figure 1 Upper panel. Colour Doppler image from an apical long axis view showing a large mitral regurgitation (MR) jet extending deep into the left atrium in late systole. The jet is large, eccentric, and has a large proximal flow convergence region and wide vena contracta. Lower panel. Continuous wave Doppler of the same MR jet shows that it is present only during late systole. Using a single frame measurement, such as proximal isovelocity surface area (PISA) or vena contracta, may lead to overestimation of MR severity when the MR occurs only in late systole. Thus, the timing and duration of MR, as elucidated in the Gorlin hydraulic orifice equation, affect the clinical assessment of MR severity.

normal. Evaluation of left atrial size and LV function provide clues to the severity and chronicity of MR. Moreover, LV size and function are important determinants of the necessity and timing of surgery.[1]

Distinction should be made as to whether MR is primary (that is, due to an abnormal mitral valve apparatus) or secondary to LV dilation and dysfunction (functional MR). The most common cause of primary MR is myxomatous degeneration. In functional MR, the leaflets are normal with restricted motion due to outward displacement of the LV walls and papillary muscles, with or without annular dilation.[5] Echocardiographic determination of the mechanism of MR, either by transthoracic and/or transoesophageal technique, is the reference standard for determining feasibility of mitral valve repair.[1]

DOPPLER COLOUR FLOW MAPPING

Colour Doppler flow mapping is widely used to screen for the presence of mitral regurgitation. Unfortunately, little attention is generally given to what the colour flow image actually represents. In fact, a colour flow jet is an image of the spatial distribution of velocities within the imaging plane and can be profoundly affected by instrument settings and haemodynamic variables. Since the spatial distribution of velocities is not a primary determinant of MR severity according to the hydraulic orifice equation, it should not be heavily relied upon to grade MR severity. Nevertheless, colour flow mapping does offer several potential ways to assess MR severity.

COLOUR FLOW JET AREA

Generally, large jets extending deep into the LA represent more MR than small thin jets that appear just superior to the mitral leaflets. Measurement of jet area, either alone or indexed for LA area, was originally proposed as a means of grading MR severity. However, the correlation between jet area and MR severity is quite poor due to a variety of technical and haemodynamic limitations.[6] Patients with acute severe MR, in whom blood pressure is low and LA pressure is elevated, may have a small eccentric colour flow jet area, whereas hypertensive patients with mild MR may have a large jet area. Colour flow jets that are directed centrally into the LA generally appear larger because they entrain red blood cells on all sides of the jet. In contrast, eccentric jets that hug the LA wall cannot entrain blood on all sides and tend to appear smaller than central jets of similar or lesser severity (fig 2).[7 8] Therefore, one should avoid grading MR by "eyeballing" the colour flow jet area. A notable exception is a small central jet with an area $<4.0\ cm^2$ or $<10\%$ of LA area, which is almost always mild MR (table 1).[2] Large jets that penetrate into the pulmonary veins are more likely to be haemodynamically significant. Eccentric, wall-impinging jets should prompt the use or quantitative methods described subsequently. Because the mitral orifice is often slit-like in shape, the jets can appear quite large due to a "spray" effect, such as occurs when placing one's thumb over a water hose to create a high velocity jet.

VENA CONTRACTA WIDTH

The vena contracta is the smallest, highest velocity region of a flow jet and is typically located at or just downstream from the regurgitant orifice.[9] It should be measured in a plane perpendicular to mitral leaflet closure (such as the parasternal long axis view), whenever possible (fig 3). If the regurgitant orifice is circular, vena contracta width should be an excellent marker of the ROA.

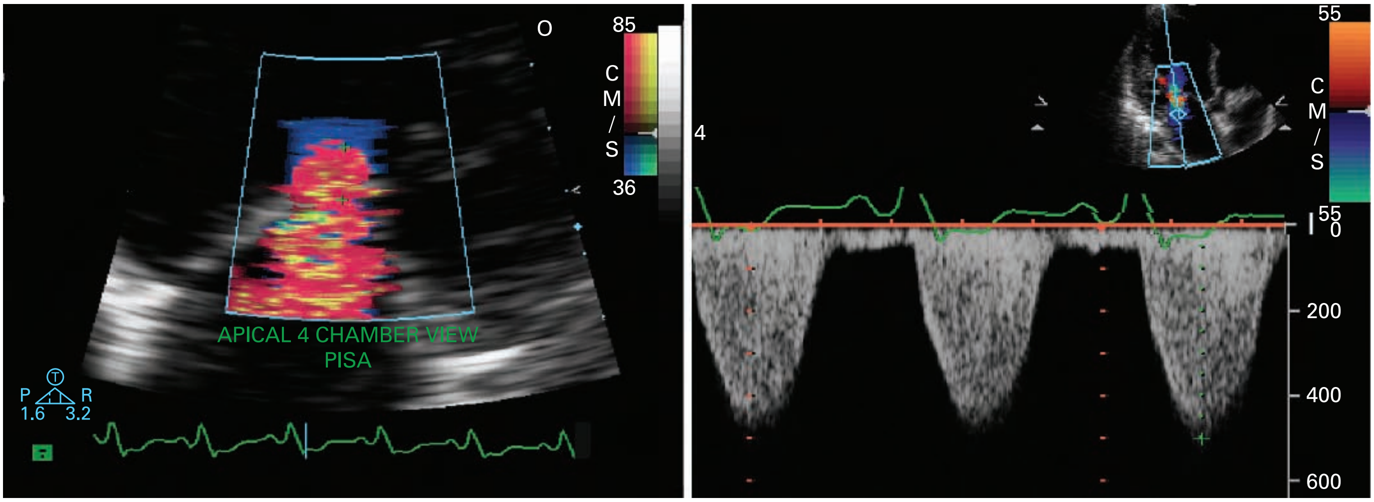

Figure 2 Example of the proximal isovelocity surface area (PISA) method. The left panel shows a large proximal flow convergence region in the apical four chamber view. The colour baseline is shifted downward (in the direction of the mitral regurgitation (MR) jet) to an aliasing velocity of 36 cm/s, which optimises the size and hemispheric shape of the proximal flow convergence region (red colour). The two green plus signs illustrate the measurement of the PISA radius (0.8 cm), and the equation below indicates peak flow rate as $2\pi\ (0.8)^2\ (36\ \text{cm/s}) = 145$ ml/s. The right panel shows a continuous wave Doppler signal from the MR jet which has a peak velocity of 480 cm/s. Effective regurgitant orifice area (EROA) is given as peak flow rate (145 ml/s) divided by peak velocity (480 cm/s) $= 0.30\ \text{cm}^2$. Note that this formula assumes that peak flow rate from the PISA radius occurs at the same time as peak velocity.

Unfortunately, the regurgitant orifice in MR is often elongated along the mitral coaptation line, like a "smiley face". The two chamber view, which is oriented parallel to the line of leaflet coaptation, may show a wide vena contracta even in mild MR, so it should not be used to measure vena contracta width. In the setting of a fixed orifice, vena contracta width is independent of flow rate and driving pressure.[9] However, the regurgitant orifice in MR is often dynamic, such that vena contracta width may vary during systole or with changes in haemodynamic conditions.[10]

Vena contracta width has been shown to be accurate in assessing the severity of MR by transthoracic or transoesophageal echocardiography.[11 12] According to guidelines published by the American and European Societies of Echocardiography, a vena contracta width <0.3 cm denotes mild MR and a vena contracta width ⩾0.7 cm is specific for severe MR.[2] Intermediate values roughly correlate with moderate MR, but there is enough overlap that another quantitative method should be used for confirmation. A particular strength of the vena contracta

Table 1 Application of specific and supportive signs, and quantitative parameters in the grading of mitral regurgitation severity

	Mild	Moderate		Severe
Specific signs of severity	► Small central jet <4 cm² or <10% of LA‡ ► Vena contracta width <0.3 cm ► No or minimal flow convergence¶	Signs of MR >mild present, but no criteria for severe MR		► Vena contracta width ⩾0.7 cm *with* large central MR jet (area >40% of LA) or *with* a wall-impinging jet of any size, swirling in LA‡ ► Large flow convergence¶ ► Systolic reversal in pulmonary veins ► Prominent flail MV leaflet or ruptured papillary muscle
Supportive signs	► Systolic dominant flow in pulmonary veins ► A-wave dominant mitral inflow§ ► Soft density, parabolic CW Doppler MR signal ► Normal LV size*	Intermediate signs/findings		► Dense, triangular CW Doppler MR jet ► E-wave dominant mitral inflow (E >1.2 m/s)§ ► Enlarged LV and LA size† (particularly when normal LV function is present)
Quantitative parameters**				
RVol (ml/beat)	<30	30–44	45–59	⩾60
RF (%)	<30	30–39	40–49	⩾50
EROA (cm²)	<0.20	0.20–0.29	0.30–0.39	⩾0.40

CW, continuous wave; EROA, effective regurgitant orifice area; LA, left atrium; LV, left ventricle; MV, mitral valve; MR, mitral regurgitation; Rvol, regurgitant volume; RF, regurgitant fraction.
*LV size applied only to chronic lesions.
†In the absence of other aetiologies of LV and LA dilatation and acute MR.
‡At a Nyquist of 50–60 cm/s.
§Usually above 50 years of age or in conditions of impaired relaxation, in the absence of mitral stenosis or other causes of elevated LA pressure.
¶Minimal and large flow convergence defined as a flow convergence radius <0.4 cm and ⩾0.9 cm for central jets, respectively, with a baseline shift at a Nyquist of 40 cm/s; cut-offs for eccentric jets are higher, and should be angle corrected (see text).
**Quantitative parameters can help sub-classify the moderate regurgitation group into mild-to-moderate and moderate-to-severe as shown.
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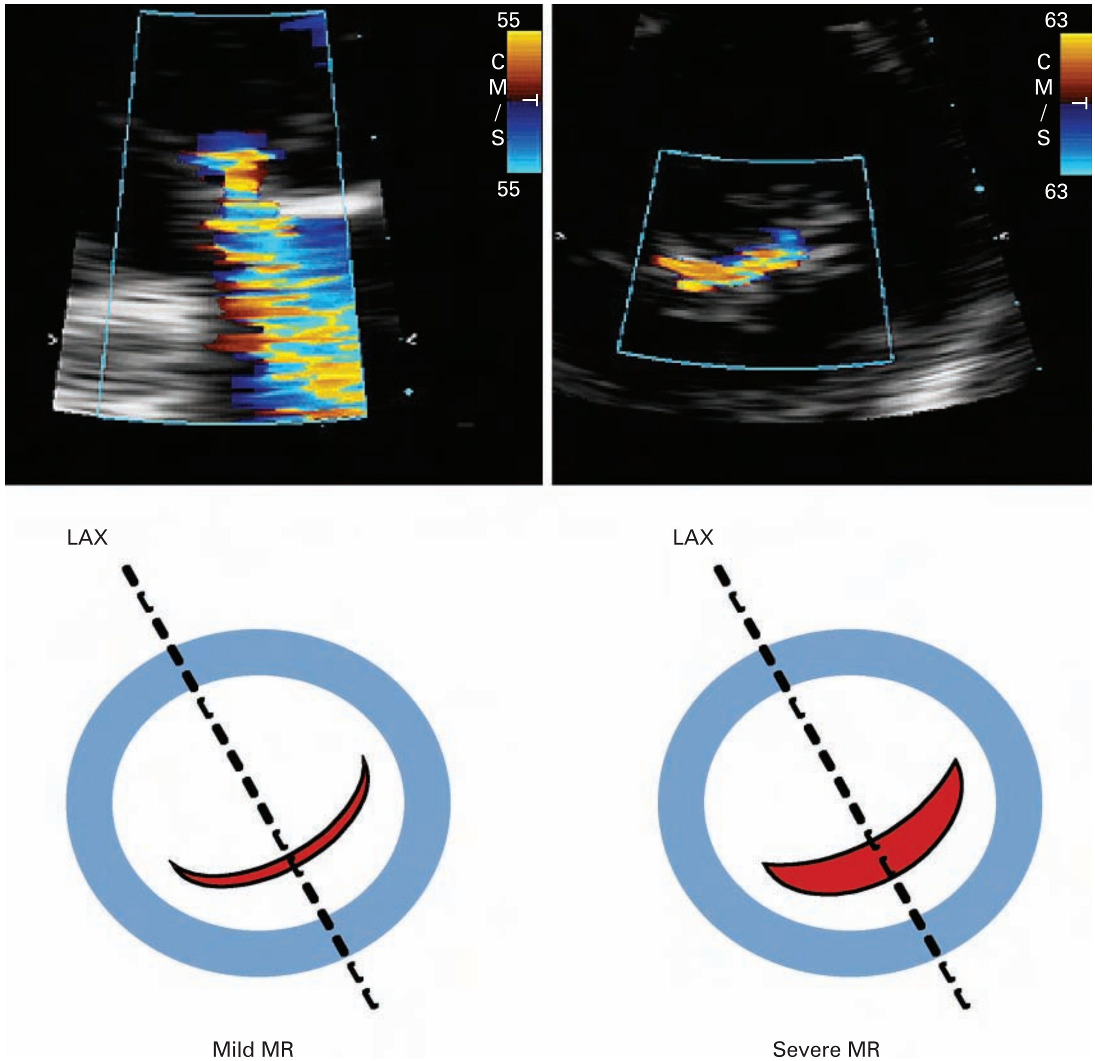

Figure 3 Upper panels. Colour flow images of mitral regurgitation in long axis (left) and short axis (right) views. The vena contracta is clearly seen as a narrow cylindrical region just downstream from the orifice in a long axis view. In the short axis view, it is not possible to tell whether the image is at the vena contracta, above it, or below it. However, it is clear that the orifice is not circular, but extends along the entire leaflet coaptation line. This is common and means that in the long axis view, the vena contracta is narrow in mild MR and wide in severe MR. The two chamber view, which is roughly parallel to mitral closure, can show a wide vena contracta, even in mild MR, and therefore should not be used for vena contracta imaging.

method is that it works equally well for central and eccentric jets.[11] It is not clear how to handle multiple MR jets by the vena contracta method. In the future, three dimensional imaging of the vena contracta should improve the accuracy of measuring MR severity by this technique.

FLOW CONVERGENCE OR PROXIMAL ISOVELOCITY SURFACE AREA (PISA)

The proximal isovelocity surface area (PISA) method is based on the hydrodynamic principle that the flow profile of blood approaching a circular orifice forms concentric, hemispheric shells of increasing velocity and decreasing surface area.[13] In MR, colour flow mapping is usually able to image one of these hemispheres that corresponds to the aliasing velocity of the instrument. The aliasing velocity should be adjusted to identify a flow convergence region with a hemispheric shape. The radius of this hemisphere is then measured, and flow rate (ml/s) is calculated as the product of the surface area of the hemisphere ($2\pi r^2$) and the aliasing velocity (Va) (fig 2). Assuming that the maximal PISA radius occurs at the time of peak regurgitant velocity, the maximal EROA is derived as:

- EROA = $(6.28\, r^2 * Va)/PkVreg$

where PkVreg is the peak velocity of the regurgitant jet by continuous wave (CW) Doppler. If one assumes a constant ROA throughout systole, regurgitant volume can be estimated as EROA multiplied by the velocity time integral of the regurgitant jet. Since the PISA calculation provides an instantaneous peak flow rate, EROA by this approach is the maximal EROA and may be larger than EROA calculated by other methods.

Measurement of PISA by colour flow mapping requires adjustment of the aliasing velocity such that a well defined hemisphere is shown. This is generally done by shifting the baseline toward the direction of flow, or by lowering the Nyquist aliasing velocity, or both (the latter reduces the wall filter, whereas the former does not).[14] If the base of the hemisphere is not a flat surface (180°), then correction for wall constraint should be performed, multiplying by the ratio of the angle formed by the walls adjacent to the regurgitant orifice and 180°. This has been shown to improve the reliability of the measurement.[15]

The limitations of PISA have been reviewed in detail.[16] It is more accurate for central jets than for eccentric jets. In MR, the orifice shape is often elliptical rather than circular, and this can affect accuracy of PISA calculations, which assume hemispheric flow convergence. It is usually easy to identify the aliasing line of the hemisphere. However, it can be difficult to judge the precise location of the orifice. Any error introduced is then squared. If the true PISA radius is 1.0 cm, a 1 mm error in either direction would change the calculated EROA by roughly 20%. At a PISA radius of 0.6, a 1 mm error can change calculated EROA by roughly 40%. Therefore, PISA is more accurate if one can adjust the aliasing velocity to obtain a radius of ⩾1 cm.

Qualitatively, the presence of a large proximal flow convergence region on colour flow mapping (at Nyquist of 50–60 cm/s) suggests the presence of significant MR. Several clinical studies have validated PISA measurements of regurgitant flow rate and EROA.[17,18] Combining data from two views through the major and minor axes of a non-circular orifice (apical two chamber and four chamber views) provides greater accuracy, but adds more complexity. Furthermore, for determination of EROA, it is essential that the CW Doppler signal be well aligned with the regurgitant jet. Poor alignment with an eccentric jet will lead to an underestimation of velocity and an overestimation of the EROA. Generally, an EROA ⩾0.4 cm^2 is considered to be severe MR, 0.16–0.39 cm^2 is moderate MR, and <0.20 cm^2 is mild MR.[2]

QUANTITATIVE DOPPLER VOLUMETRIC MEASUREMENTS

Pulsed Doppler recordings of velocity time integral can be combined with two dimensional measurements to derive flow rate and stroke volume (SV) at any valve annulus, using the formula:

- SV = CSA × VTI

where CSA is the cross-sectional area of the annulus and VTI is the velocity time integral of flow measured at the annulus.[2] In the absence of regurgitation, stroke volume should be equal at different sites, typically the aortic and mitral annulus. In the presence of regurgitation of one valve, without any intracardiac shunt, the flow through the affected valve is larger than through other competent valves. For MR, regurgitant volume is the mitral annular stroke volume minus the aortic annular stroke volume.[2] In MR, regurgitant fraction is then derived as the regurgitant volume divided by the forward stroke volume through the regurgitant valve. Thus:

- Regurgitant volume = SVmitral annulus − SVaortic annulus
- Regurgitant fraction = Regurgitant volume/SVmitral annulus

As with the PISA methods, EROA can be calculated as regurgitant volume divided by the velocity time integral of the regurgitant jet velocity (VTIRegJet) recorded by CW Doppler:

- EROA = Regurgitant volume/VTIRegJet

The most common errors encountered in determining these parameters are: (1) failure to measure the valve annulus properly (error is squared in the formula); (2) failure to trace the modal velocity (brightest signal representing laminar flow) of the pulsed Doppler tracing; and (3) failure to position the sample volume correctly, at the level of the annulus.

In left sided regurgitant lesions, LV stroke volume can also be measured using LV stroke volume calculations by two dimensional echocardiography as end-diastolic volume minus end-systolic volume. Unfortunately, measurement of LV stroke volume by echocardiography can be underestimated due to foreshortening of the apex. Recently, the use of intravenous contrast agents and the advent of three dimensional echocardiography have improved the ability of echocardiography to calculate LV stroke volume accurately.[19] In the future, three dimensional assessment of LV stroke volume could potentially replace mitral annular stroke volume for calculation of regurgitant volume and fraction in MR.

Several studies have shown the validity and clinical utility of quantitative Doppler measurements of MR severity.[20–22] Values for regurgitant volume, regurgitant fraction and EROA by quantitative Doppler are shown in table 1. It should be remembered, however, that in individual patients, these values might vary. For example, a patient with severe MR and a small LV may have a low regurgitant volume but a high regurgitant fraction and EROA. Quantitative Doppler measurements are not accurate if the patient has MR and significant aortic regurgitation. Quantitative pulsed wave (PW) Doppler method offers an advantage in the case of eccentric or multiple regurgitant MR jets, where PISA is less accurate. In addition, quantitative Doppler assesses MR severity over all of systole, whereas PISA or vena contracta methods are typically single frame measurements that can overestimate MR severity in mitral valve prolapse with only late systolic MR.

ADJUNCTIVE FINDINGS

Continuous wave Doppler

The density of the CW Doppler signal is a useful qualitative index of MR severity.[2] A dense signal that approaches the density of antegrade flow suggests significant MR, whereas a faint signal or an incomplete envelope is typical of mild or trace MR, presuming adequate alignment of the Doppler beam and the jet. In eccentric MR, it may be difficult to record the full envelope of the jet due to alignment issues. In most patients, maximum MR velocity is 4–6 m/s due to the high systolic pressure gradient between the LV and LA. An unusually low

Heart 2008;94:376–383. doi:10.1136/hrt.2005.086462

Table 2 Advantages and limitations of echocardiographic and Doppler parameters used in the evaluation of mitral regurgitation severity

Parameter	Utility/advantages	Limitations
Structural		
LA and LV size	Enlargement sensitive for chronic significant MR, important for outcomes. Normal size virtually excludes significant chronic MR	Enlargement seen in other conditions. May be normal in acute significant MR
MV leaflet/support apparatus	Flail valve and ruptured papillary muscle specific for significant MR	Other abnormalities do not imply significant MR
Doppler parameters		
Jet area—colour flow	Simple, quick screen for mild or severe central MR; evaluates spatial orientation of jet	Subject to technical, haemodynamic variation; significantly underestimates severity in eccentric jets
Vena contracta width	Simple, quantitative, good at identifying mild or severe MR	Not useful for multiple MR jets; intermediate values require confirmation. Small values; thus small error leads to large % error
PISA method	Quantitative; presence of flow convergence at Nyquist of 50–60 cm/s alerts to significant MR. Provides both lesion severity (EROA) and volume overload (RVol)	Cumbersome; less accurate in eccentric jets; not valid in multiple jets. Provides peak flow and maximal EROA
Flow quantitation—PW	Quantitative, valid in multiple jets and eccentric jets. Provides both lesion severity (EROA, RF) and volume overload (RVol)	Cumbersome. Measurement of flow at MV annulus less reliable in calcific MV and/or annulus. Not valid with concomitant significant AR unless pulmonic site is used
Jet profile—CW	Simple, readily available	Qualitative; complementary data
Peak mitral E velocity	Simple, readily available. A-wave dominance excludes severe MR	Influenced by LA pressure, LV relaxation, MV area, and atrial fibrillation. Complementary data only, does not quantify MR severity
Pulmonary vein flow	Simple. Systolic flow reversal is specific for severe MR	Influenced by LA pressure, atrial fibrillation. Not accurate if MR jet directed into the sampled vein

CW, continuous wave Doppler; EROA, effective orifice regurgitant area; LA, left atrium; LV, left ventricle; PISA, proximal isovelocity surface area; PW, pulsed wave Doppler; MV, mitral valve; MR, mitral regurgitation; RVol, regurgitant volume.
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velocity (assuming adequate alignment) may indicate haemodynamic compromise due to a high LA pressure and low LV systolic pressure. A truncated, triangular jet contour with early peaking of the maximal velocity indicates elevated LA pressure or a prominent regurgitant pressure wave in the LA.

CW Doppler is also used to assess pulmonary artery systolic pressure from the tricuspid regurgitation jet velocity. The presence of pulmonary hypertension provides another indirect clue as to MR severity and compensation to the volume overload.

Pulsed Doppler

Pulsed Doppler tracings at the mitral leaflet tips are commonly used to evaluate LV diastolic function. Patients with severe MR usually exhibit dominant early filling (E velocity >1.2 m/s) because forward flow across the mitral valve during diastole includes the forward stroke volume and the regurgitant volume.[23] Conversely, an A-wave dominant mitral inflow pattern virtually excludes severe MR.

Pulmonary vein flow

Normal pulmonary venous flow exhibits higher velocity during ventricular systole than during ventricular diastole. With increasing severity of MR, systolic velocity in the pulmonary veins progressively decreases and even reverses in severe MR. However, an increased LA pressure due to any cause can result in blunted pulmonary venous systolic flow. Therefore, the pulmonary venous flow pattern should be used adjunctively with other parameters. Nevertheless, systolic flow reversal in more than one pulmonary vein is usually a sign of severe MR.[2]

CLINICAL INTEGRATION

In evaluating severity of MR, it is important to integrate multiple parameters rather than depend on a single measurement. This helps minimise the effects of technical or measurement errors inherent to each method previously discussed. It is also important to distinguish between the severity of MR and its haemodynamic consequences. For example, moderate MR occurring acutely into a small, non-compliant LA may cause severe pulmonary congestion. Conversely, chronic severe MR with a compliant, dilated LA may be asymptomatic. Thus, the haemodynamic consequences of

How to measure severity of mitral regurgitation: key points

- Evaluation of mitral regurgitation (MR) severity is complex and requires careful attention to multiple parameters.
- Colour flow jet area is often inaccurate due to dependence on technical and haemodynamic variables.
- Vena contracta width in a long axis view can separate mild (<0.3 cm) from severe MR (>0.7 cm) in most cases.
- Quantitation of regurgitant orifice area (ROA) by proximal isovelocity surface area (PISA) or volumetric methods should be used in daily practice.
- Integration of multiple parameters, including valve anatomy, left atrial and left ventricular size, vena contracta width, quantitation of regurgitant volume, fraction, ROA, and adjunctive signs, are important for accurate assessment of MR severity.

MR are reflected in several parameters including LA and LV volumes, the contour of the CW Doppler profile, and pulmonary venous flow pattern. Such parameters should be considered in addition to quantitative measures of MR severity. Advantages and limitations of the various echo/Doppler parameters used in assessing severity of MR are detailed in table 2. An MR index has been devised that assigns different weights to six different indicators of MR, using a score of 0–3 for jet penetration into the LA, PISA radius, CW jet intensity, pulmonary artery pressure, pulmonary venous flow pattern, and LA size.[24] A score of 1.7 or less reliably separated mild MR from severe MR; a considerable overlap, however, was observed between moderate and severe MR. Although it has not been well validated against an independent gold standard, this scoring system emphasises the need to evaluate multiple echocardiographic parameters. Importantly, recent prospective data show that MR severity assessed according to this integrated approach, including quantitation, predicts outcome.[25]

SUMMARY

Echocardiographic evaluation of the severity of MR is complex, and all methods have inherent strengths and weaknesses. It is important to evaluate carefully valve morphology and the size and function of the LA and LV. Simple "eyeball" grading of MR colour flow jets is prone to error and should be discouraged. Quantitative measurements, such as vena contracta width, regurgitant volume and ROA, are valuable and should be used more often than in current clinical practice. Integration of the various echocardiographic measures of MR severity along with clinical data generally leads to accurate assessment of MR severity.

Competing interests: In compliance with EBAC/EACCME guidelines, all authors participating in Education in *Heart* have disclosed potential conflicts of interest that might cause a bias in the article.

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