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REVIEW

The role of multi-imaging modality in primary mitral regurgitation

Caroline M. Van de Heyning[1,2], Julien Magne[1], Christiaan J. Vrints[2], Luc Piérard[1], and Patrizio Lancellotti[1]*

[1]Department of Cardiology, Heart Valve Clinic, University of Liège, CHU Sart-Tilman, Liège B-4000, Belgium; and [2]Department of Cardiology, University Hospital Antwerp, Edegem, Belgium

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Primary mitral regurgitation (MR) is the first cause of valvular regurgitation in Western countries. Echocardiography is the cornerstone for diagnosing MR and more specifically for establishing its aetiology and mechanism, for quantifying its severity, progression, and repercussion and for assessing the likelihood of successful of valve repair. Two-dimensional/three-dimensional transthoracic and transoesophageal echocardiography are the most widely used methods. Interest is growing for exercise echocardiography particularly in patients in whom symptoms do not correlate well with MR severity and for risk stratification. The experience of multi-slice computed tomography in primary MR is still limited. Conversely, cardiovascular magnetic resonance has gained progressive relevance and represents the alternative method of choice.

Keywords Primary mitral regurgitation • Transthoracic echocardiography • Transoesophageal echocardiography • 3D echocardiography • Multi-slice computed tomography • Cardiovascular magnetic resonance imaging

Introduction

Mitral regurgitation (MR) is the second most frequent valve disease in Europe after aortic valve stenosis. Since the decline in the incidence of rheumatic valve disease over the past decades, its origin is predominantly degenerative (61%), followed by rheumatic (14%), and ischaemic disease (7%).[1] The ESC guidelines advocate surgery in severe primary MR when symptoms, left ventricular (LV) dysfunction, atrial fibrillation or pulmonary hypertension (PHT) at rest occur.[2] Whether asymptomatic patients with severe MR should be operated before LV dysfunction or PHT is established remains the subject of debate. The progress of primary MR is in general insidious due to progressive atrial and ventricular remodelling which compensates for the overload caused by the increased regurgitant volume (RVol). The subsequent late onset of symptoms might lead to late referral for surgery and the outcome of medically treated asymptomatic severe primary MR remains unclear. Enriquez-Sarano *et al.*[3] found a 5-year probability of 62 ± 8% for cardiac-related death, heart failure, or new atrial fibrillation in asymptomatic patients with severe MR while more recently Kang *et al.*[4] reported a 7-year survival free of cardiac death or heart failure of 85 ± 4% in asymptomatic MR with a preserved LV ejection fraction. Conversely, Rosenhek *et al.*[5] showed an excellent outcome in asymptomatic severe MR with the ‘watchful waiting’ strategy in accordance with the ESC guidelines. Recently, numerous studies have provided evidence for the prognostic value of left atrial enlargement,[6,7] exercise capacity,[8,9] and exercise PHT.[10] This underlines the importance of an adequate assessment of the severity and consequences of primary MR. Moreover, accurate valve analysis for predicting repairability is mandatory since it is well established that mitral valve repair yields a better prognosis than mitral valve replacement.[11] Transthoracic (TTE) and transoesophageal (TOE) echocardiography are the classic tools used for evaluating primary MR.[2] Real-time three-dimensional (3D) echocardiography has moved over the past few years from the research arena to general clinical practice in many centres. In experienced hands, 3D echocardiography has become the method of choice for evaluating mitral valve. Evidence has also grown for implementation of stress echocardiography in the imaging armamentarium for assessing asymptomatic patients.[12] Although new imaging modalities such as multi-slice computed tomography (CT) and cardiac magnetic resonance (CMR) might provide supplementary findings in selected cases, their use is still limited in clinical practice. In this

* Corresponding author. Tel: +32 4 366 71 94; fax: +32 4 366 71 95. Email: plancellotti@chu.ulg.ac.be

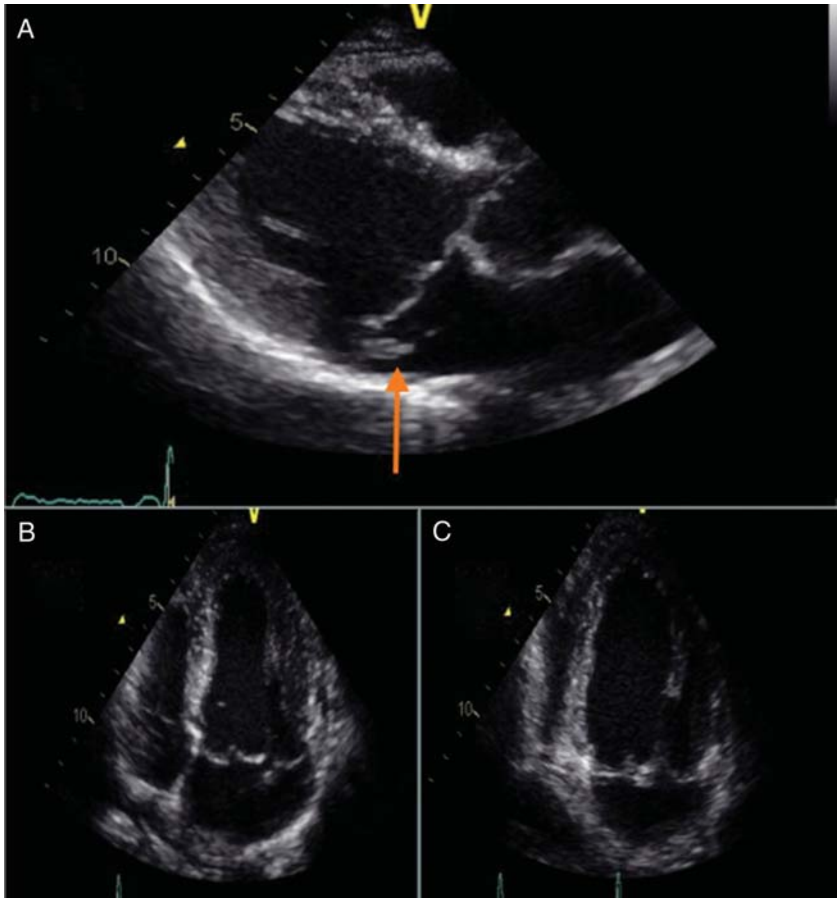


Figure 1 Two-dimensional transthoracic echocardiography images acquired in a 56-year-old male patient with an isolated P2 prolapse and severe mitral regurgitation. (*A*) The parasternal long-axis view shows a prolapse of P2 with a ruptured chordae (arrow). (*B* and *C*) The four-chamber and two-chamber views do not provide evidence for other prolapsing segments.

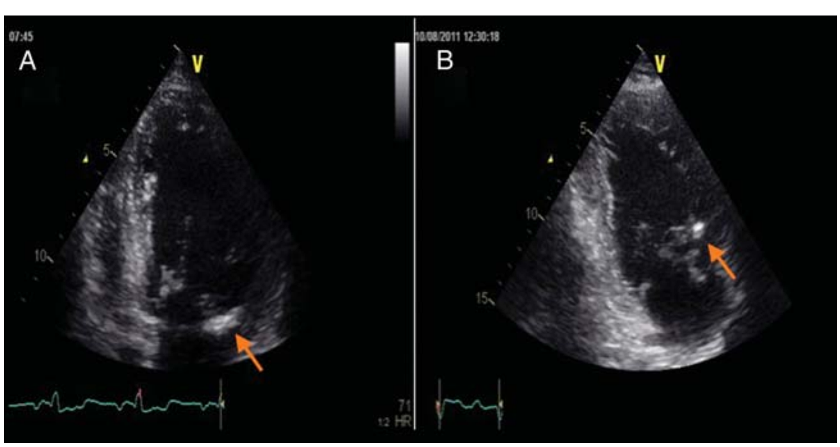


Figure 2 (*A*) Two-dimensional transthoracic echocardiography images. Example of a 71-year-old male patient with a P2 prolapse and a voluminous calcification (arrow) attaining the posterior part of the mitral annulus and the posterior mitral leaflet. (*B*) Example of a 66-year-old male patient with Barlow's disease and a calcification (arrow) at the insertion of the chordae into the anterolateral papillary muscle.

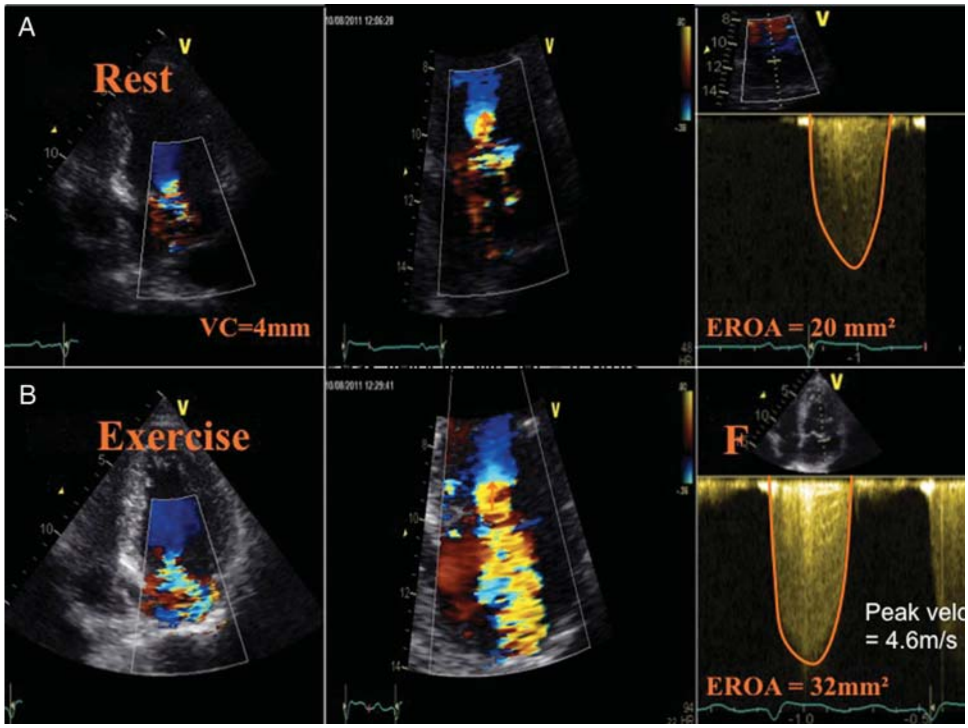


Figure 3 (*A–B*) Assessment of the severity of mitral regurgitation at rest (*A*) and during exercise (*B*) in a 66-year-old male patient with Barlow's disease. During test, the severity of MR increased significantly. VC, vena contracta; EROA, effective regurgitant orifice area.

review, we will examine the cutting-edge knowledge related to the role of non-invasive multi-imaging modalities in patients with primary MR.

Transthoracic echocardiography

The European Association of Echocardiography (EAE) recommends TTE as the first-line examination for primary MR.[13] A complete exam includes careful valve analysis, hereby describing the aetiology, the mechanism and the likelihood of valve repair, as well as the assessment of MR severity.

Mitral valve analysis

The different components of the mitral valve apparatus have to be evaluated in order to understand the mechanism of MR and predict the repairability[13]:

- Leaflets: both anterior and posterior leaflets are classically divided into three scallops, respectively, referred to as A1-A2-A3 and P1-P2-P3. The leaflets come together at the commissures. All these elements can be seen in the parasternal short-axis view. The parasternal long-axis view usually shows A2-P2. The apical four-chamber view depicts A3-A2-P1 and the apical two-chamber view A1-A2-P3. Any anatomical lesion or prolapsing segment should be described (*Figure 1*).
- Annulus: the presence and extent of calcification should be reported (*Figure 2*). Dilatation of the mitral annulus is defined as the ratio of annulus/anterior leaflet >1.3 or when the mitral annulus diameter is >35 mm (parasternal long-axis view).
- Chordae tendinae: classified as marginal (primary), intermediate (secondary), basal (tertiary), and strut chordae. The presence of ruptured chordae, calcification, fusion, or redundancy should be noted.
- Papillary muscles: the posteromedial and the anterolateral papillary muscles adhere, respectively, to the chordae of the medial half and lateral half of both leaflets. The former is usually inserted at the inferior wall and the latter at the lateral and posterior wall, although this distribution can vary significantly. Any rupture, fibrotic elongation, or displacement should be described.

Aetiology and mechanism

MR is generally classified as primary (organic) or secondary (functional) MR. Primary MR is caused by intrinsic valve lesions as in endocarditis, degenerative, or rheumatic disease, whereas secondary MR results from regional and/or global LV remodelling without structural abnormalities of the mitral valve (as in cardiomyopathy or in ischaemic heart disease).

The mechanism is classified according to Carpentier's functional classification. In type I, leaflet mobility is normal and MR is the result of mitral annular dilatation or leaflet perforation. In type II,

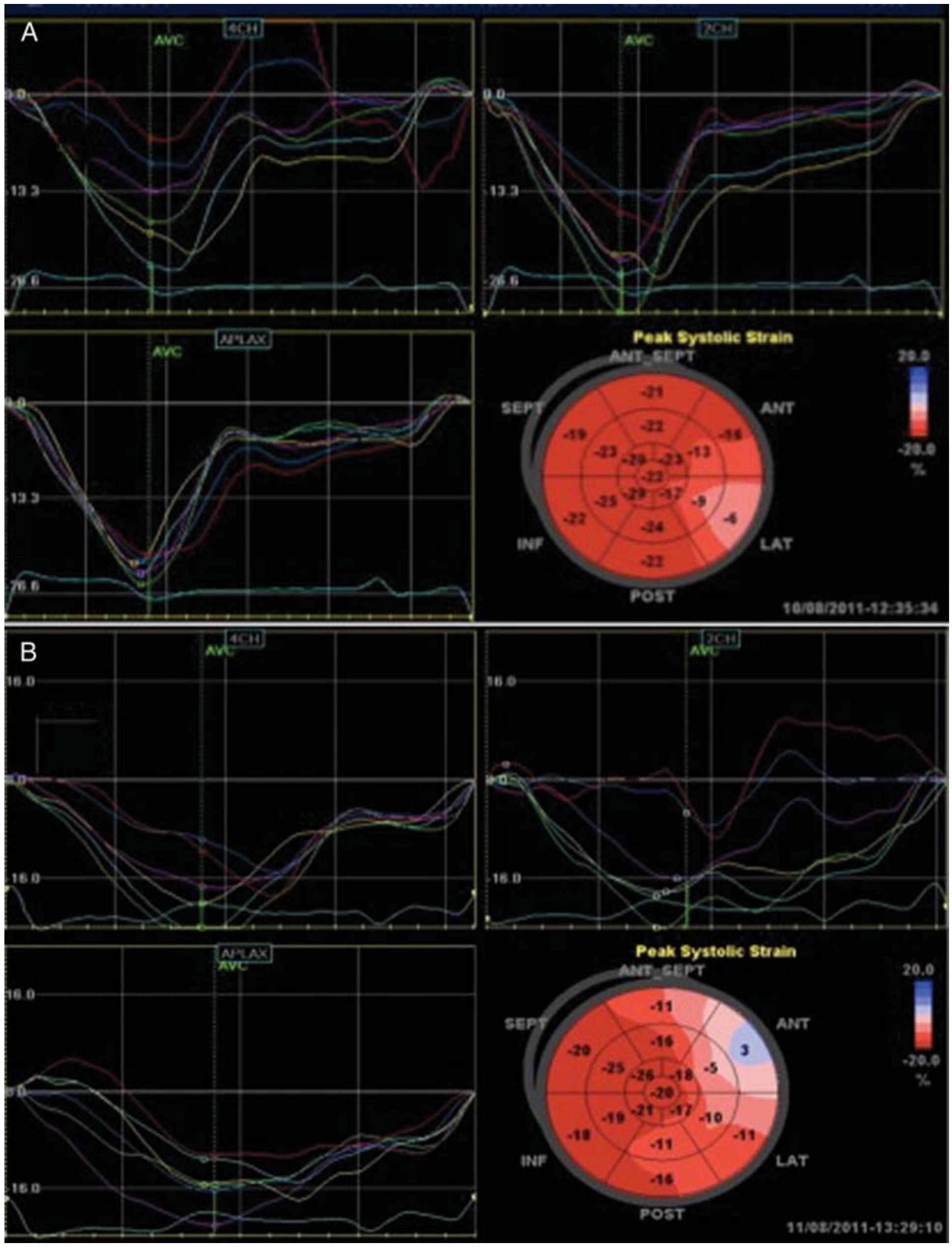


Figure 4 Example of calculation of the global longitudinal strain in two patients with Barlow's disease, severe mitral regurgitation and normal left ventricular ejection fraction (>60%). (*A*) preserved global longitudinal strain (19.8%); (*B*) altered global longitudinal strain (16%).

MR is due to excessive motion of one or both leaflets as in prolapse or flail leaflet. In type III, MR is caused by restriction of leaflet mobility during diastole and systole (type IIIa, rheumatic MR) or only during systole (type IIIb, functional MR).

Repairability

The likelihood of mitral valve repair in degenerative MR is excellent in patients with a P2 prolapse, but is importantly reduced in case of extensive disease (≥3 scallops affected), anterior commissural prolapse, severe mitral annulus dilatation (>50 mm), extensive mitral valve calcification (annulus + leaflets), and large central regurgitant jet. Mitral valve repair in other forms of primary MR (rheumatic, endocarditis, . . .) is unlikely.[13]

Assessment of mitral regurgitation severity

MR can easily be diagnosed with colour flow imaging, but this technique should not be used for grading MR severity. When feasible, measurement of the vena contracta width and the flow convergence method is recommended if more than a small central jet is observed.[13] The vena contracta is the narrowest portion of the MR jet and reflects the regurgitant orifice area. The vena

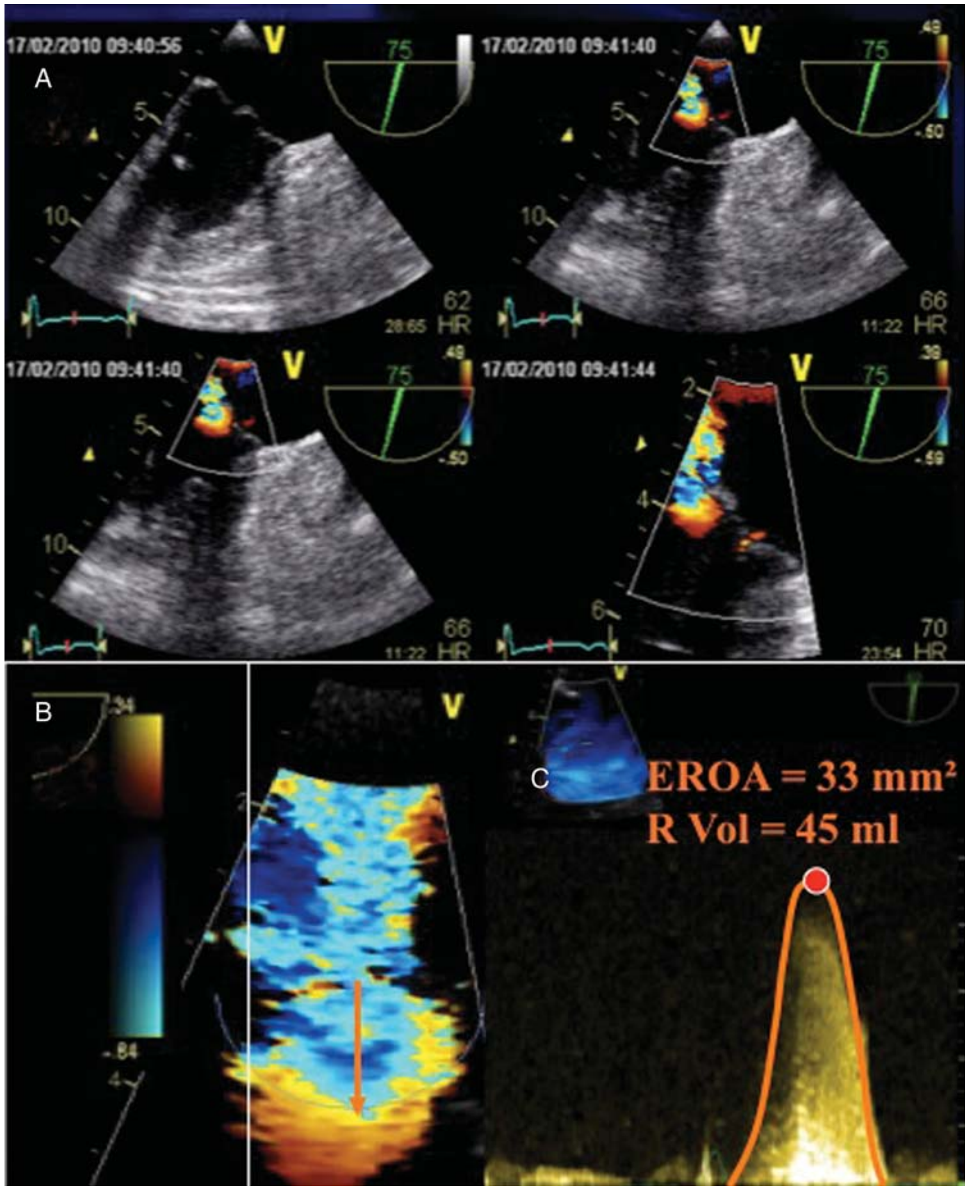


Figure 5 Assessment of the severity of mitral regurgitation by the proximal isovelocity surface area method during two-dimensional transoesophageal echocardiography. Stepwise analysis: (*A*) two-dimensional images at 75° in a patient with primary mitral regurgitation. (*B*) The echo beam focuses on the origin of the mitral regurgitation jet. Contrary to transthoracic echocardiography, the Nyquist limit is augmented in transoesophageal echocardiography until a hemispheric proximal isovelocity surface area is obtained and the proximal isovelocity surface area radius is measured at mid systole (arrow). (*C*) After tracing the time-velocity integral of the MR jet acquired by continuous wave Doppler, the effective regurgitant orifice area is automatically calculated. R Vol, regurgitant volume.

contracta is best imaged in the parasternal long-axis view or in the apical four-chamber view with an adapted Nyquist limit (colour Doppler scale) of 40–70 m/s. A vena contracta width <3 mm is considered as mild MR, whereas a width ≥7 mm indicates severe MR. Intermediate values require confirmation by another approach as with the flow proximal isovelocity surface area (PISA) method (*Figure 3A*).

The PISA is best imaged in the apical four-chamber view (or the parasternal views in anterior mitral valve prolapse) with a reduced Nyquist limit (15–40 m/s) to obtain a hemispheric isovelocity area. The PISA radius is measured at mid-systole using the first aliasing. The use of continuous wave Doppler of the MR jet allows calculation of the effective regurgitant orifice area (EROA) and the RVol. Mild primary MR is defined as an EROA $<20\,mm^2$ or a RVol <30 mL. Severe primary MR is defined as an EROA $\geq 40\,mm^2$ or a RVol ≥60 mL. Intermediate values define moderate MR (*Figure 3A*).

If the PISA method is not feasible, the more time-consuming Doppler volumetric method can alternatively be used in experienced hands to quantify MR. Additional indicators in favour of

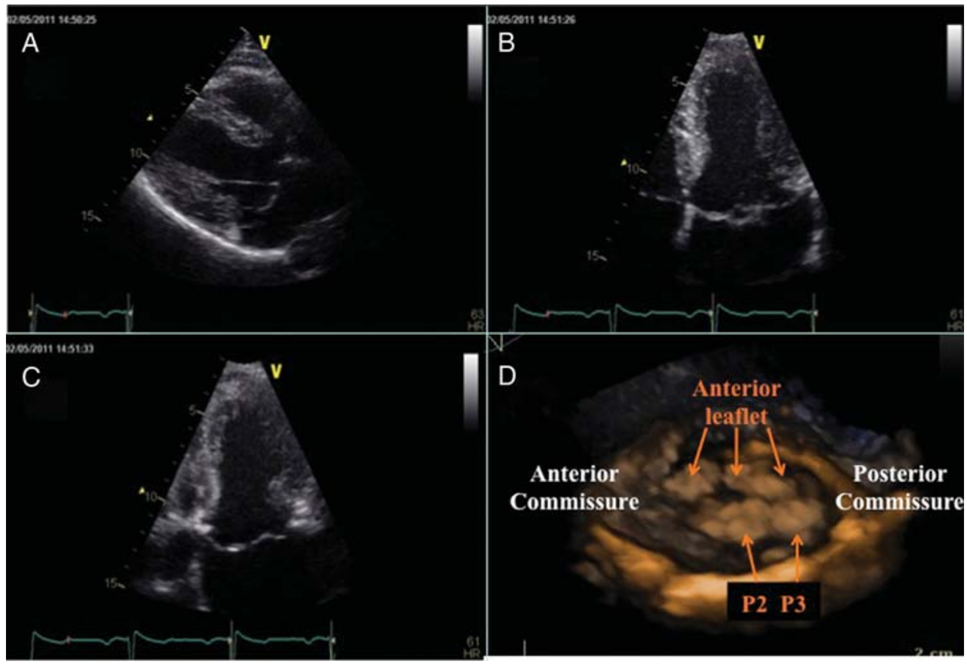


Figure 6 Two-dimensional and three-dimensional transthoracic echocardiography images of the mitral valve in a 46-year-old male patient with a complex Barlow's disease (bivalvular prolapse). (*A*) parasternal long-axis, (*B*) apical four-chamber, (*C*) apical two-chamber, (*D*) The three-dimensional 'en face' view from the left atrium shows more clearly the prolapsing segments (anterior leaflet prolapse + P2–P3 and A3–P3 commissure prolapse.

severe MR are systolic pulmonary flow reversal (depicted by pulsed wave Doppler of the pulmonary veins), a peak mitral E velocity >1.5 m/s in the absence of mitral stenosis, a pulsed wave Doppler mitral to aortic velocity time integral ratio >1.4 and a dense continuous wave Doppler signal of the MR jet.

From a clinical standpoint, the echocardiographic assessment of MR includes integration of data from two-dimensional (2D)/3D imaging of the valve and ventricle as well as Doppler measures of regurgitation severity.[13]

Downstream and upstream repercussions of mitral regurgitation

MR is associated with several haemodynamic changes, which can alter the clinical outcome. The assessment of LV function, left atrial dimensions, and pulmonary artery systolic pressure (PASP) is warranted. The 2007 ESC guidelines advocate surgery when the LV ejection fraction is ≤60% or the LV end-systolic diameter reaches ≥45 mm^2. However, the LV ejection fraction only decreases in an advanced state since it first increases in maintain the forward stroke volume. The LV end-systolic diameter is less load dependent than the LV ejection fraction, making it a more appropriate parameter to assess LV dysfunction. Recently, a large multicentre study provided evidence that elective surgery is a reasonable option in patients with a flail leaflet and a LV end-systolic diameter >40 mm,[14] a value already adopted by the 2008 ACC/AHA guidelines.[15] Moreover, this study confirms previous data[16] that post-operative outcome is better if patients are operated before LV dysfunction is established. These findings imply the necessity to assess LV function by more sensitive means. Reduced systolic tissue Doppler velocity at the mitral lateral annulus might predict post-operative LV dysfunction in patients with asymptomatic primary MR and preserved LV ejection fraction and normal LV end-systolic diameter.[17] Furthermore, tissue Doppler imaging can be used to derive LV strain and strain rate, parameters that appear more accurate to identify subclinical LV dysfunction.[18] Nevertheless, a disadvantage of tissue Doppler imaging is its angle dependency. Longitudinal strain and strain rate obtained by 2D-speckle tracking imaging, a technique which is not angle dependent, seem to be more sensitive parameters to identify subclinical LV dysfunction in primary MR[19] (*Figure 4*). A global longitudinal strain <18.1% has been shown to be associated with post-operative LV dysfunction in patients with normal pre-operative LV ejection fraction.[20] Another application of speckle tracking is the relative easy acquisition of torsional parameters, e.g. twist and torsion (=twist/LV long-axis dimension), which may represent useful markers of ventricular function.[21] Two recent studies showed progressive deterioration of the torsion profile in primary MR,[22,23] making these parameters promising indicators of subclinical LV dysfunction. Practically, the incremental value of tissue Doppler and strain imaging for identifying latent LV dysfunction remains to be determined.

Several studies have showed that left atrial enlargement in primary MR is independently associated with overall and cardiac

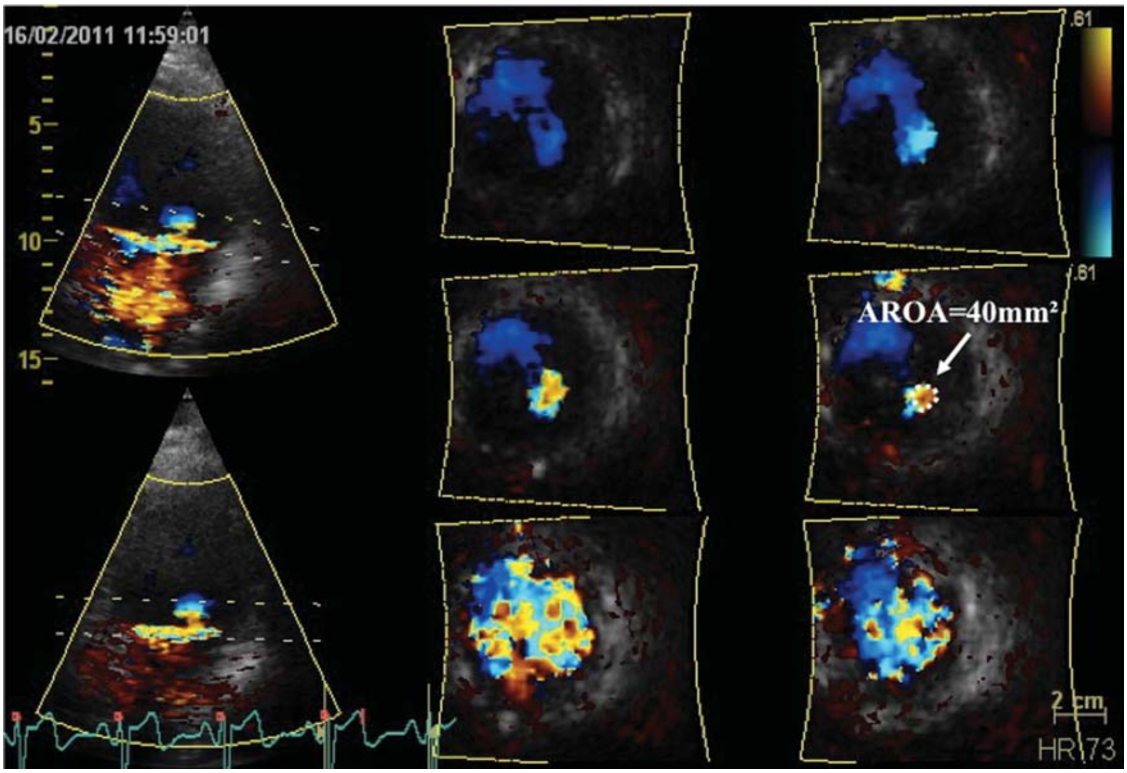


Figure 7 Planimetry of the anatomic regurgitant orifice area by three-dimensional transthoracic echocardiography.

mortality[6,7] (diameter >40–50 mm or LA volume index >60 mL/m^2). In addition, data showed that left atrial remodelling precedes and exceeds LV remodelling[24] and that mitral valve surgery in patients with left atrial enlargement restores life expectancy.[7] These are strong arguments to take this parameter into account for deciding whether or not an asymptomatic patient with severe MR and normal LV ejection fraction should be operated. The indexed left atrial volume has been shown to correlate better with indirect indices of LV filling pressure than the antero-posterior left atrial diameter,[25] and is thus the preferred parameter to assess left atrial enlargement.

Finally, the PASP is classically obtained by summing the transtricuspid pressure gradient and the estimated right atrial pressure. A value >50 mmHg is a Class IIa indication for mitral valve surgery.[2] Recent data have shown that PHT is a predictor of worse outcome after mitral valve surgery,[26] favouring early surgery before PHT is established.

Transoesophageal echocardiography

TOE is recommended in the operating room just before mitral valve surgery and in case of insufficient transthoracic imaging quality.[13] Usually TOE is also performed for further diagnostic refinement in the pre-operative setting, although TTE is highly accurate in experienced hands to predict valve reparability since the introduction of harmonic imaging technology.

According to the 2010 EAE recommendations for TOE, essential views for accurate valve analysis are the following:[27]

- Transgastric basal short-axis view at 0°: allows the visualization of the six scallops and the two commissures. The use of colour Doppler in this view may also indicate the localization of the origin of the regurgitant jet and thus of the prolapse.
- Multiple lower transoesophageal views: for complete appreciation of all scallops, rotation of the image through 180° as well as systematic analysis of parallel planes can be performed. Papillary muscle and chordae integrity have to be evaluated. Any vegetation should be excluded.
- Colour Doppler assessment of the regurgitant jet: the severity of MR is graded by the same criteria as in TTE[13] (*Figure 5*).
- Pulsed wave Doppler of the left upper pulmonary vein (right upper pulmonary vein in case of eccentric jet): systolic flow reversal is suggestive for severe MR.

Systolic blood pressure should be recorded during any echocardiographic grading of the severity of MR, since it can be underestimated in conditions of low pre and afterload.[27]

Three-dimensional echocardiography

Although 2D echocardiography remains the primary tool for the assessment of MR, it is reasonable to perform a 3D TTE/TOE in

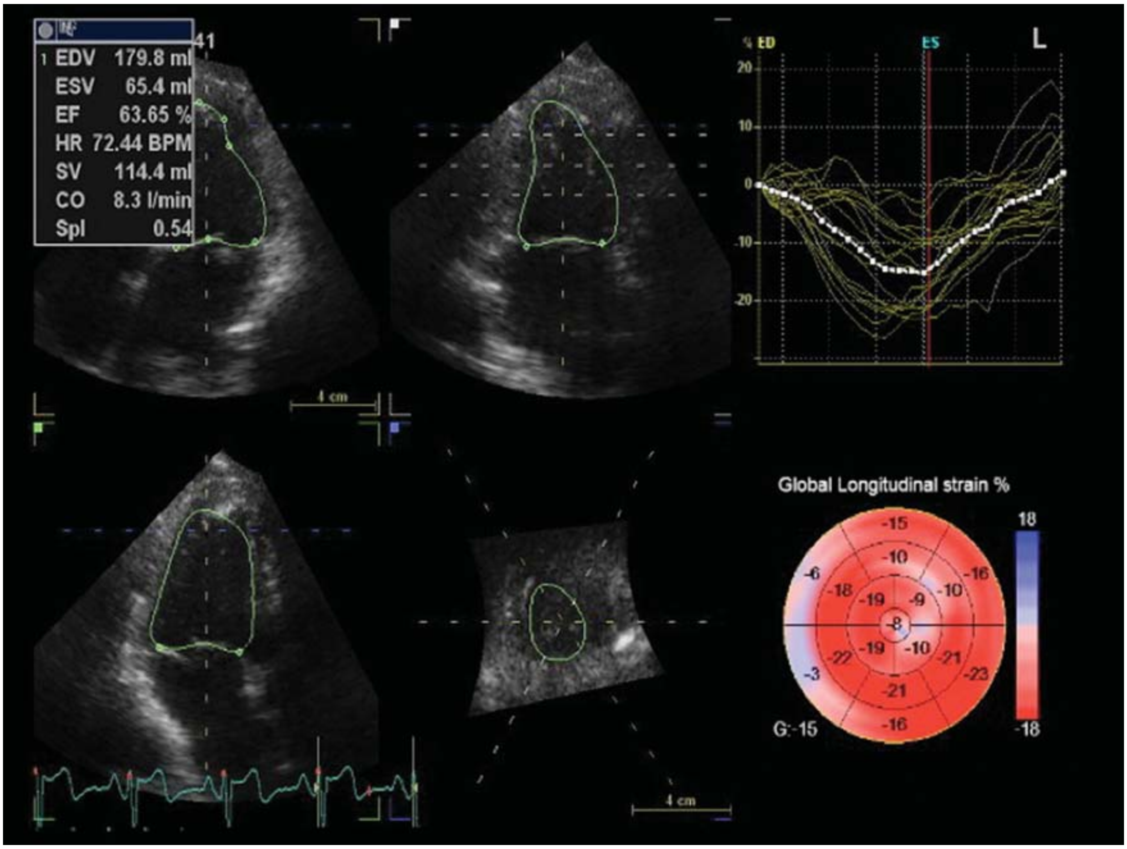


Figure 8 Three-dimensional assessment of left ventricular volumes, ejection fraction, and longitudinal myocardial deformation (speckle tracking) obtained with 3D transthoracic echocardiography.

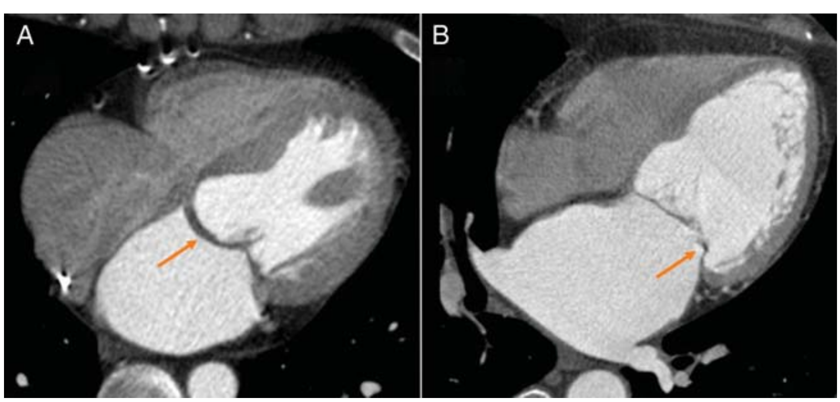


Figure 9 Cardiac multi-slice computed tomography obtained in patients with mitral valve pathology allowing direct visualization of the mitral valve leaflets and the subvalvular apparatus (by courtesy of R.Salgado, University Hospital of Antwerp). (*A*) Four-chamber view showing a prolapse of the thickened anterior leaflet (arrow). (*B*) Four-chamber view in a patient with rheumatic valve disease characterized by the hockey-stick sign of the posterior leaflet (arrow).

complex mitral valve pathology.[13] Three-dimensional echocardiography represents a valuable method for valve analysis when available since several studies have demonstrated its superiority over 2D TTE/TOE for accurate localization of the valve lesion[28,29] (*Figure 6*). To note, the majority of them has used 3D TOE. Despite its lower spatial resolution, 3D imaging has several advantages over 2D imaging in the pre- and intra-operative settings. It is particularly useful in the dialogue between the echocardiographer

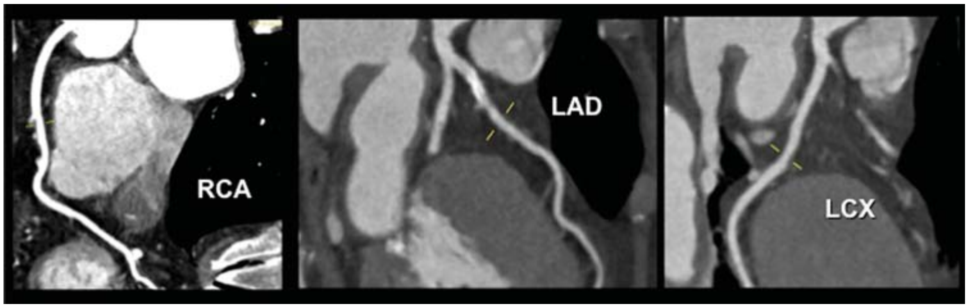


Figure 10 Contrast-enhanced coronary computed angiography. Visualization of normal coronaries in a low-risk patients with mitral valve prolapse. LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery.

and the surgeon. Simultaneous multi-plane imaging permits to precisely determine the localization and the extent of lesions. Colour flow Doppler imaging can be superimposed onto these 2D images, which may make easier the identification of commissural jets. With the use of real-time 3D imaging, the mitral valve is best imaged when obtained in zoom mode to avoid stitch artefacts that may occur in a wide-angled acquisition. With both TEE and TOE, the unique 'en face' view, which is similar to the surgical view after left atriotomy, can be displayed. To simulate the surgeon's view of the valve, the 3D image is reoriented to exhibit the aortic valve at the 11 o'clock position. The subvalvular apparatus is on the opposite best imaged from the LV perspective. To note, the gated full volume modality (wide-angled acquisition of four ECG-gated pyramidal volumes) is the ideal way for imaging the entire mitral valve apparatus (chordae, papillary muscle, LV). Recently, new-dedicated software for advanced 3D analysis of the mitral valve has been developed to be incorporated into clinical practice. It provides a 3D realistic model of the mitral valve and allows the calculation of a range of parameters (annulus, anterior and posterior leaflet, leaflet segmentation, coaptation line and potential coaptation defects, mitral valve spatial relationship with the papillary muscles and aortic valve). The possibility to measure the surface of the anterior leaflet to estimate, in a beating heart, the size of the annular ring ranks among the most interesting features. The added value of these parameters still needs to be defined.

Several studies using 3D TOE for planimetry of the anatomical regurgitant orifice have found a high correlation with the 2D vena contracta and the PISA method.[30,31] A recent study showed its superiority over the PISA method in eccentric jets.[31] This technique was feasible in all patients; however, it remains time consuming and may be challenging in very calcified, perforated, or flail leaflets.

The use of 3D colour flow volumetric imaging allows direct assessment of the size and shape of the regurgitant orifice, preventing the geometric assumptions applied by 2D imaging.[32] With manual cropping of the image plane perpendicularly orientated to the jet direction, the narrowest cross-sectional area of the MR jet can be obtained in an 'en face' view and measured by planimetry in systole (*Figure 7*). In primary MR, the shape of the regurgitant orifice has been shown to be relatively rounder. Three-dimensional colour Doppler imaging for assessing MR severity is, however, not yet daily practice. No method has proved to have a good correlation with reference imaging modalities in large series of patients with varying degrees of MR severity. To note, new 3D/4D ultrasound probe generations will allow automatic visualization of 3D PISA surface and anatomic orifice area, with expected higher accuracy of the subsequent RVol calculation.

Moreover, over the past decade, 3D echocardiography has proved to be more accurate and reproducible than 2D echocardiography regarding measurement of LV volumes and LV ejection fraction when compared with independent reference imaging modalities (radionuclide ventriculography, CMR). Unlike the 3D technique, 2D echocardiography consistently underestimates LV volumes due to foreshortened views and geometrical assumptions. Consequently, 3D echocardiography should be routinely used to assess LV volumes and LV ejection fraction when available.

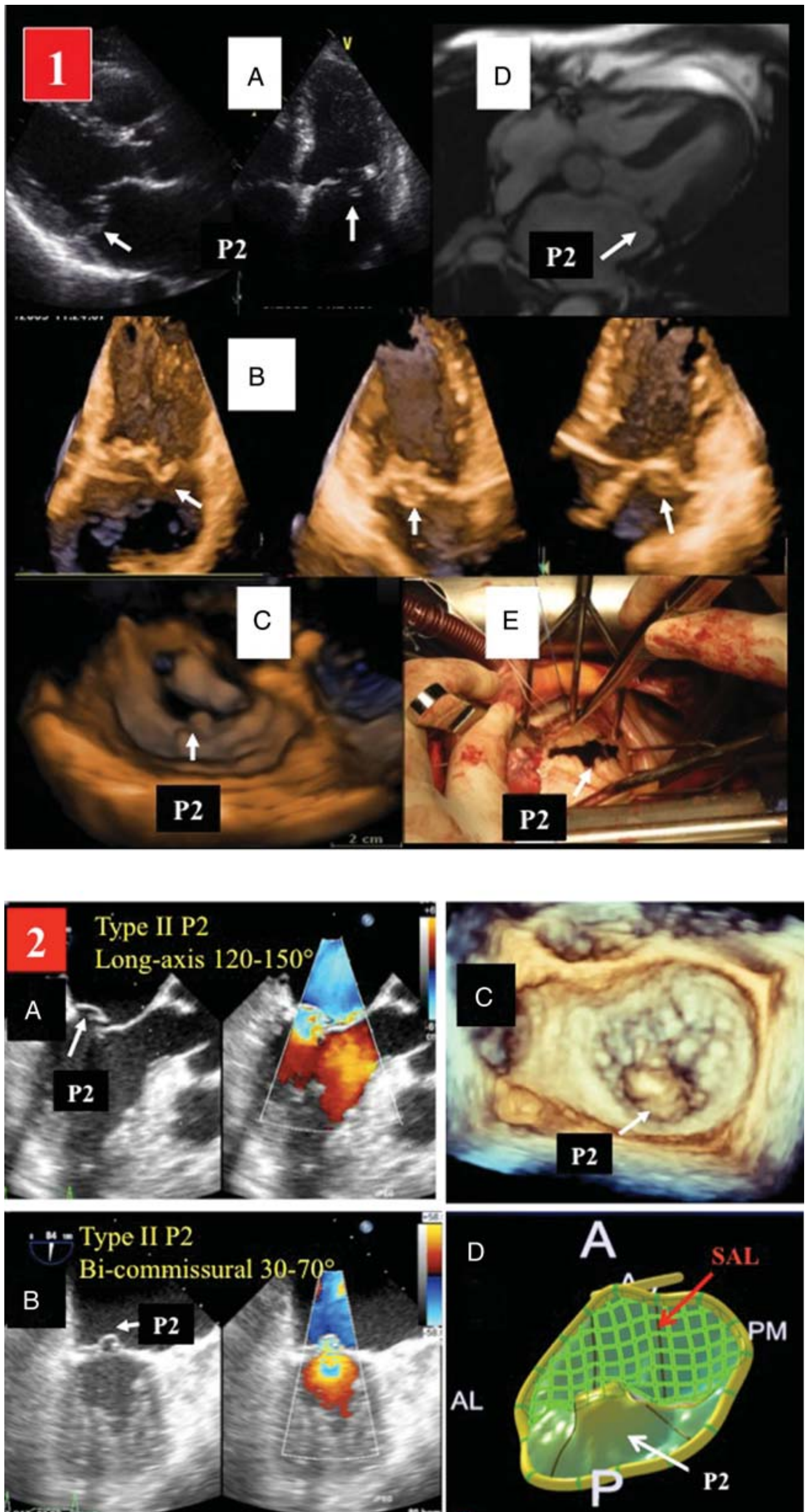
Three-dimensional speckle tracking echocardiography is a new promising method to evaluate regional LV function,[33] but its superiority over standard 2D TTE for the assessment of the LV function has still to be proved (*Figure 8*).

To conclude, 3D echocardiography might provide useful information complementary to the standard 2D echocardiography.

Exercise tests and exercise echocardiography

Recent studies showed that decreased exercise capacity in asymptomatic patients with primary MR, revealed by a reduced peak oxygen consumption during cardiopulmonary exercise testing[9] or a decreased duration at exercise tolerance test,[8] is predictive for cardiac events and mortality. Probably these exercise tests unmask 'asymptomatic' patients who adapted and reduced their daily activities to avoid symptoms.[34] Subsequently, reduced exercise capacity might be considered as an indication for surgery in severe primary MR. The 2008 EAE guidelines for stress echocardiography recommend exercise echocardiography when symptoms are discordant with MR severity at rest.[35] In fact, primary MR can have a dynamic character in up to one-third of patients[36] (*Figure 3*). Exertional dyspnoea in patients with moderate MR at rest might be explained by the development of severe MR with

PHT during exercise.[37] Interestingly, two recent studies showed that either an increased PASP or an increase in EROA was associated with a decreased symptom-free survival.[10,36] Moreover, the absence of contractile reserve—weaker changes in the LV ejection fraction (>4%) or in global longitudinal strain (<2%)—revealed by stress echocardiography identifies patients with subclinical LV dysfunction. These patients are at risk for post-operative LV deterioration and morbidity.[20,38] Consequently, the



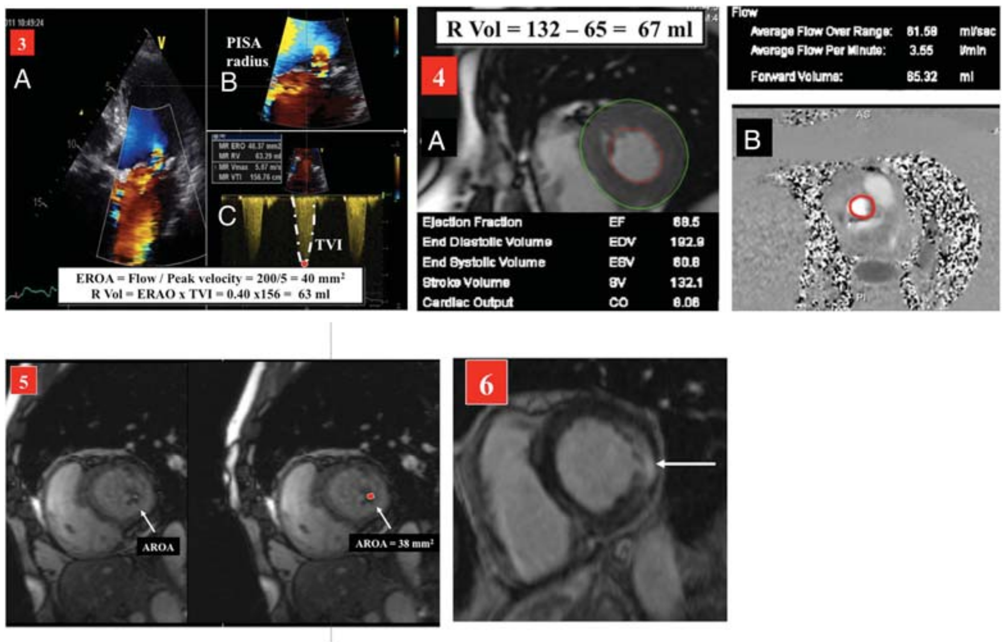


Figure 11 Multi-imaging modality in a patient with posterior mitral leaflet prolapse, preserved left ventricular function and severe mitral regurgitation. (*1A–C*) Two-dimensional and three-dimensional transthoracic echocardiography showing a P2 prolapse. (*1B–C*) Three-dimensional volume rendering of the mitral valve. (*1C*) 'en face view' of the mitral valve. (*1D*) P2 prolapse demonstrated by cardiovascular magnetic resonance. (*1E*) Surgical view of the P2 prolapse. (*2A–D*) Two-dimensional and three-dimensional transoesophageal echocardiography confirming the isolated P2 prolapse. (*2D*) Three-dimensional rendering of the mitral valve allowing the measurement of the surface of the anterior leaflet. (*3*) Quantification of the mitral regurgitation using the proximal isovelocity surface area method. (*A*) Apical four-chamber view with colour flow display, (*B*) zoom of the selected zone + downward shift of zero baseline to obtain an hemispheric proximal isovelocity surface area. (*C*) continuous wave Doppler of mitral regurgitation jet allowing calculation the effective regurgitant orifice area and regurgitant volume. TVI, time-velocity integral. (*4A–B*) Quantification of mitral regurgitation using cardiac magnetic resonance. (*A*) Total stroke volume derived from left ventricular volumes assessment. (*B*) Forward stroke volume derived from velocity-encoded cardiac magnetic resonance flow quantification of aortic flow. (*5*) Planimetry of the anatomical regurgitant orifice area on a slice parallel to the valvular plane obtained by cardiac magnetic resonance. (*6*) Detection of cardiac fibrosis by cardiac magnetic resonance. This delayed contrast enhancement cardiac magnetic resonance image shows an important zone of fibrosis in the free wall of the left ventricle (arrow) (by courtesy of L. Davin, CHU de Liège). Coronary artery disease was excluded by coronary angiography.

2010 EAE recommendations for the assessment of valvular regurgitation[13] support the use of exercise echocardiography to identify high-risk patients who may benefit from early elective surgery. To note, according to the ACC/AHA 2008 Guidelines, exercise Doppler echocardiography is reasonable (class IIa, level of evidence C) in asymptomatic patients with severe MR to assess the effect of exercise on MR severity and on pulmonary artery pressure (significant if $>$60 mmHg).[15] However, exercise PHT in older patients should be interpreted cautiously since one-third of normal subjects older than 60 years may present a PASP $>$60 mmHg at peak exercise.[39] However, exercise PHT during a low level of exercise should be regarded as a pathological finding. Practically, instead of straightforward risk stratification, exercise echocardiography may thus be helpful for guiding the optimal timing of intervention, especially in patients in whom the risk to benefit ratio of surgery is uncertain (doubt about reparability, comorbidity, advanced age).

Multi-slice cardiac computed tomography

Multi-slice cardiac CT, from thin-section reconstructions, allows direct visualization of the thickening and calcification of the leaflets, mitral annulus, chordae, and papillary muscles (*Figure 9*). A recent study showed good correlation with 3D TOE concerning measurements of mitral valve geometry and leaflet lengths and angles.[40] The extent of calcification of the mitral annulus might even be better demonstrated than by echo or CMR.[41]

The inner contour of the regurgitant orifice can manually be outlined on reconstructed cross-sectional images of the mitral valve in oblique short axis. Two studies have demonstrated that cardiac CT-derived anatomical regurgitant orifice area correlates well with EROA measured by echocardiography.[42,43]

Chamber dimensions can be obtained after post-processing of the images with a contour-detection algorithm and manual correction if not satisfactory. The RVol can be generated as the difference between the calculated stroke volume of the left and the right ventricle and has recently be shown to have a good correlation with the RVol obtained by CMR.[44]

Although multi-slice cardiac CT might be particularly useful in the pre-operative setting by providing complementary information on the coronary arteries (high negative predictive value in patients who are at low risk of atherosclerosis), a routine clinical implementation is not yet recommended (*Figure 10*). Radiation exposure and the use of nephrotoxic contrast are the main concerns of this imaging modality at present. Furthermore, this technique is not suitable in patients with arrhythmia because of the ECG-gated acquisition. However, cardiac CT might be an alternative for patients with poor echogenicity when CMR is contra-indicated (pacemaker).

Cardiac magnetic resonance

Practically, in patients with primary MR, CMR should be considered as the first choice alternative, when echocardiography is not conclusive. Indeed, CMR is the most accurate and reproducible non-invasive method for the assessment of LV volumes, LV ejection fraction, and torsional parameters.[45] Basically, the LV dimensions are derived from a series of multi-section perpendicular to the long axis of the LV (10–12 contiguous slices in the short-axis direction).

CMR can also be used for valve analysis using ‘steady-state free precession (SSFP)’ sequences, which precisely discriminate blood from tissue.[46] First, mitral valve function can be assessed with cine imaging. Turbulent flow through MR orifice is easily visible with SSFP (visualization of signal voids due to spin dephasing in moving protons).

Mitral valve anatomy can be imaged by acquisition of standard short-axis, two-, three-, and four-chamber long-axis views in combination with oblique long-axis cines orthogonal to the line of coaptation as described by Chan *et al.*[47] CMR has comparable diagnostic value to echocardiography for the identification of prolapsing scallops,[48,49] but is inferior for imaging the subvalvular apparatus (torn chordae) due to lower spatial and temporal resolution[48] (*Figure 10A* and *B*).

One study has used SSFP CMR for assessing the EROA by planimetry of the regurgitant orifice in a slice parallel to the valvular plane and perpendicular to the regurgitant jet at mid-systole. Quantification of EROA was correlated well with angiographic and echocardiographic data[50] (*Figure 11*). To note, CMR planimetry defines the anatomic regurgitant lesion, whereas the areas of EROA by PISA yield the narrowest flow stream, which tends to be smaller than the anatomic orifice area. It should also be underlined that the regurgitant orifice is frequently inconstant throughout systole in primary MR. This can potentially affect the estimation of the regurgitant severity. Lastly, planimetry of the MR regurgitant orifice is time consuming and remains challenging because appropriate plane alignment and angulation may be more difficult due to the longitudinal movement of the mitral annulus and in case of irregular shapes of regurgitant orifice.

Furthermore, with CMR, blood flow and velocity can be accurately obtained by phase-contrast velocity mapping. Hence, RVol can be measured indirectly as the difference between the total stroke volume and the aortic flow (forward stroke volume), as well as directly as the regurgitant flow across the mitral valve.[46] This latter, however, requires a specialized imaging sequence which tracks the motion of the mitral valve annulus during the cardiac cycle. In the absence of other regurgitant lesions, a rare situation in primary MR, R Vol can also be calculated by substracting the right ventricle stroke volume from the LV stroke volume. However, the calculation of the right ventricle stroke volume is less reproducible due to the extensive trabeculation of the right ventricle.

Late gadolinium enhancement CMR (images obtained 10–20 min after injection of contrast) is widely used to assess cardiac fibrosis in various cardiomyopathies. In contrast, there are practically no studies having investigated cardiac fibrosis by CMR in primary MR (*Figure 11*). Perivalvular ventricular fibrosis and papillary muscle fibrosis have been well described in pathological studies, but not *in vivo*. Recently, Han *et al.*[49] using 3D high-resolution late gadolinium enhancement CMR imaging have shown for the first time the presence of focal myocardial fibrosis in the papillary muscles in several patients with mitral valve prolapse. Such hyperenhancement of papillary muscles was more often associated with the presence of complex ventricular arrhythmias. In addition, the blood-to-leaflet contrast ratio was also increased in these patients, which may reflect the significantly expanded spongia layer with proteoglycans in the myxomatous valve.

In practice, the routine use of CMR is limited because of more difficult access to CMR than to echocardiography, and the need for specific expertise of radiologists and/or cardiologists in imaging. Other disadvantages of CMR are related to its potential incompatibility with pacemakers and the ECG-gated acquisition, which provokes problems in patients with arrhythmia. Lastly, limitations may come from the technique itself as the low spatial resolution of 2D CMR compared with 3D high-resolution late gadolinium enhancement CMR imaging.

Conclusion

TTE and TOE remain the first-line imaging modalities for the assessment of primary MR. Recent techniques as tissue Doppler imaging and speckle tracking echocardiography appear to be promising tools in detecting subclinical LV dysfunction. If available, 3D echocardiography may provide superior evaluation of LV function and valve analysis in experienced centres. Exercise echocardiography is an excellent tool for the assessment of the functional repercussions of primary MR and for the identification of high-risk patients who might benefit from early elective surgery. In patients with poor echogenicity, CMR is the alternative imaging modality of choice for evaluating MR. Routine assessment with cardiac CT is not yet recommended, but its role might increase as radiation and contrast doses further regress in the future.

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