

CASE REPORT

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EDUCATIONAL CLINICAL CASE SERIES

An Integrative, Multiparametric Approach to Mitral Regurgitation Evaluation



A Case-Based Illustration

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ABSTRACT

Echocardiography is the first-line modality for assessing mitral regurgitation (MR). In addition to evaluation of the MR jet characteristics, echocardiography can provide quantitative parameters of MR severity. This case series illustrates the importance of integrating multiple parameters in the evaluation of MR and the role of multimodality imaging. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:1231-1241) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

The mitral valve (MV) apparatus consists of the MV annulus, leaflets, chordae tendineae, papillary muscles, and underlying left ventricular (LV) myocardium. A dysfunction in any of these components can lead to malcoaptation of the leaflets and various degrees of mitral regurgitation (MR). Therefore, a thorough examination of these different components is imperative in MR evaluation.

A multiparametric integrative approach is underscored by the joint American Society of Echocardiography and Society of Cardiovascular Magnetic Resonance guidelines for noninvasive evaluation of

native valvular regurgitation (Figure 1).¹ When evaluating MR, emphasis should be placed on evaluating its mechanism, severity, and hemodynamic consequences. Although transthoracic echocardiography (TTE) is the first-line imaging modality used in the evaluation of MR, transesophageal echocardiography (TEE) and cardiac magnetic resonance (CMR) are particularly helpful when TTE image quality is suboptimal, MR mechanism and/or severity cannot be accurately determined, and in the setting of discrepancies with clinical findings.

CASE 1

An 83-year-old man with a history of dermatomyositis and pancytopenia presented with progressive dyspnea on exertion. TTE revealed moderate LV dilation with an LVEF of 61% (volume overload pattern), severe left atrial (LA) dilation (60 cc/m²), and a posterior MV flail with an eccentric, anteriorly directed MR jet (Figure 2, Video 1). It was difficult to determine the severity of MR accurately by color Doppler imaging alone given the eccentricity of the

LEARNING OBJECTIVES

- To emphasize the significance of an integrative approach when assessing patients with primary or secondary MR, thus underscoring the strength and limitations of different parameters and imaging modalities.
- To illustrate the role of TEE and CMR imaging in evaluating MR.
- To review residual MR evaluation post TEER.

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

CW = continuous wave

EROA = effective regurgitant orifice area

LA = left atrial

LV = left ventricular

LVEF = left ventricular ejection fraction

LVOT = left ventricular outflow tract

MR = mitral regurgitation

MRF = mitral regurgitant fraction

MRV = mitral regurgitant volume

MV = mitral valve

MVP = mitral valve prolapse

PISA = proximal isovelocity surface area

SLDA = single leaflet device attachment

TEE = transesophageal echocardiography

TEER = transcatheter edge-to-edge repair

TTE = transthoracic echocardiography

VC = vena contracta

VCA = vena contracta area

VTI = velocity time integral

3D = 3-dimensional

MR and the difficulty in ascertaining and measuring the area of flow convergence and vena contracta (VC). Despite the less impressive color Doppler jet, MR was suspected to be significant in the setting of the nearly horizontal angle of the MR jet in relation to the mitral axial plane (color Doppler splay sign or wrap-around effect) (Figure 2).² Clues to suggest significant MR in this case included the presence of a flail leaflet, in addition to LV and LA dilation with preserved LV function and lower left ventricular outflow tract (LVOT) velocity time integral (VTI) values in the presence of a normal left ventricular ejection fraction (LVEF) and an enlarged left ventricle.

EXPERT TIP: MR EVALUATION BY TTE.

Assessment of MR severity by color Doppler imaging relies on evaluation of the 3 components of the MR jet: flow convergence, VC, and jet area.¹ Very eccentric MR jets are more difficult to evaluate. Color Doppler imaging can underestimate MR severity if one relies solely on MR jet area in patients with highly eccentric, wall-hugging jets. In these situations, evaluation of the VC and flow convergence (which can sometimes be appreciated without adjusting the aliasing velocity in significant MR) can help assess whether the MR is significant and needs further quantitation.³ In such situations, as demonstrated in this case (Figure 3), quantification of MR by using volumetric methods is important in determining MR severity.¹ Additionally, hemodynamic consequences of severe MR, which include LA dilation, LV dilation, and pulmonary hypertension, provide important clues and corroboration. Although proximal isovelocity surface area (PISA) provides accurate assessment of primary central jets, it is less accurate in eccentric jets given the ambiguity of PISA diameter measurement and the overestimation of MR when PISA is close to the LV wall.^{3,4}

Table 1 demonstrates the limitations of selected echocardiographic parameters used in MR evaluation. CMR was performed for MR quantification given the known flail MV anatomy and mechanism of MR seen on TTE, the eccentricity of the jet, and the given risk of respiratory decompensation during TEE with the patient's dyspnea. CMR confirmed the presence of a flail P3 segment with severe MR (Figure 4).

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EXPERT TIP: ROLE OF CMR IN MR EVALUATION.

CMR is helpful in quantitation of MR and other relevant parameters in the following situations¹:

- Cases with discrepancy with clinical findings or internal inconsistency among echocardiographic findings
- Multiple MR jets
- Eccentric jets that are difficult to assess and quantitate
- Calculation of cardiac chamber size and function
- Concomitant LV scar or viability assessment in ischemic MR for prognostication⁵
- Multivalvular disease (when echocardiographic quantification methods cannot be used)

Patient-related factors that limit the utility of CMR include the presence of non-CMR-compatible implantable devices, irregular heart rhythm, renal failure, respiratory distress precluding breath-holding, claustrophobia, and morbid obesity.

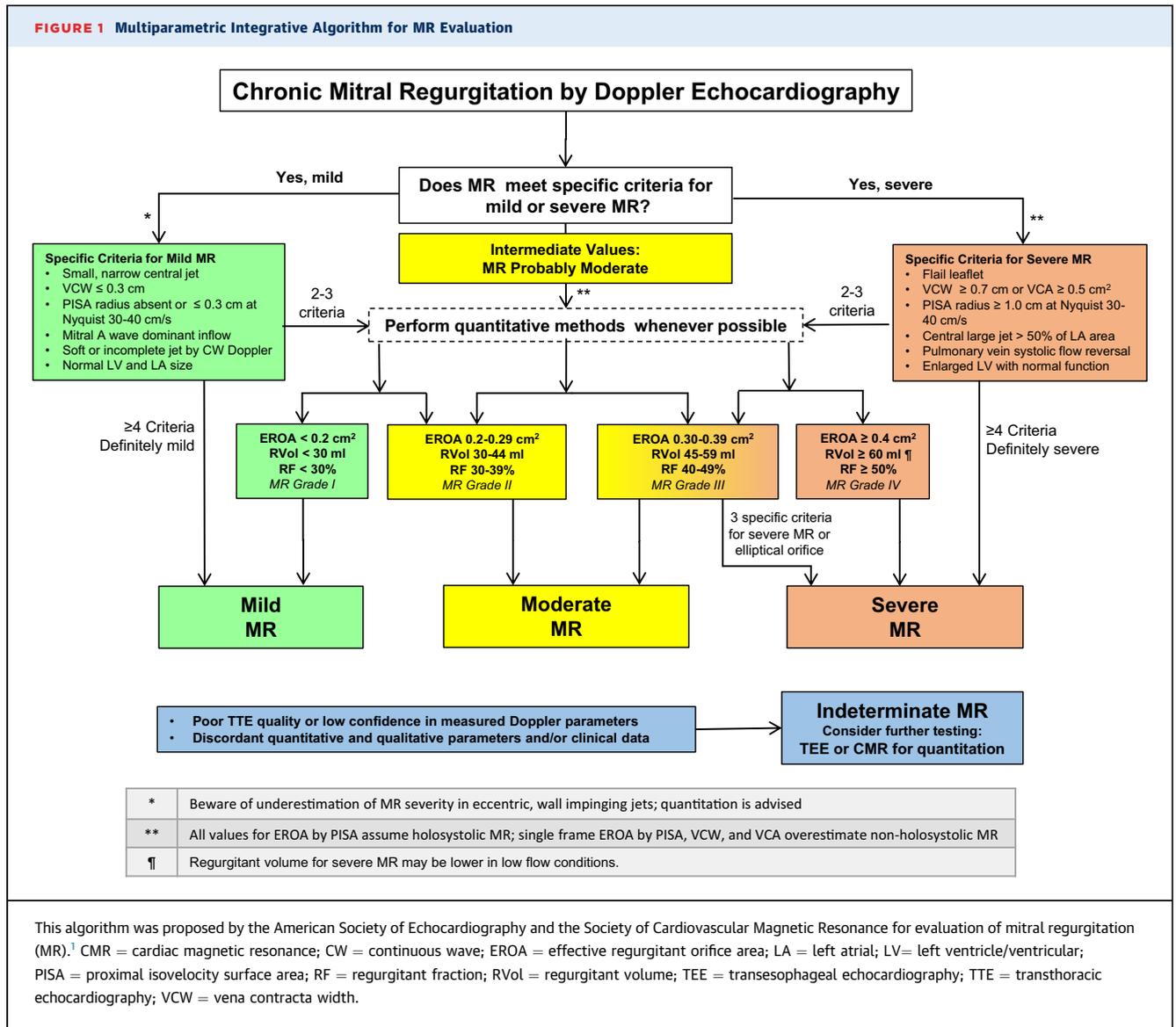
The patient was deemed to be at a high surgical risk and underwent TEE for evaluation for transcatheter edge-to-edge repair (TEER). The study was notable for severe MR secondary to P3 flail. PISA was not used for quantification because of the constraints of the flow convergence in this case. The patient subsequently underwent TEER, with significant reduction of MR (Figure 5).

EXPERT TIP: INTRAPROCEDURAL EVALUATION OF RESIDUAL MR POST TEER.

Intraprocedural parameters suggestive of mild residual MR after TEER include significant reduction in color Doppler jet size, reduction in vena contracta area (VCA) by 3-dimensional (3D) color Doppler imaging, improvement or normalization of systolic pulmonary venous flow, improvement in the LVOT stroke volume, and the appearance of spontaneous echocardiographic contrast within the left atrium or LA appendage.⁶

CASE 2

A 20-year-old man with Barlow disease presented for evaluation of dyspnea at rest. TTE was notable for normal LVEF (60%-64%), normal LV size (LV end-diastolic dimension, 5.3 cm), normal LA size (28 cc/m²), and bileaflet MV prolapse (MVP) with midsystolic to late systolic MR (Figure 6). Using the PISA method without taking timing of the MR into consideration, his effective regurgitant orifice area (EROA) was calculated to be 0.33 cm², suggestive of moderate to severe MR. However, this method overestimated the MR severity because the regurgitation was midsystolic to late systolic rather than holosystolic.¹ By volumetric assessment, the MR severity was mild. CMR, rather than TEE, was performed to provide another independent quantitation given the discrepancy between echocardiographic



findings and the patient’s symptoms; CMR further confirmed the presence of mild MR (mitral regurgitant volume [MRV], 29 mL; mitral regurgitant fraction [MRF], 24%).

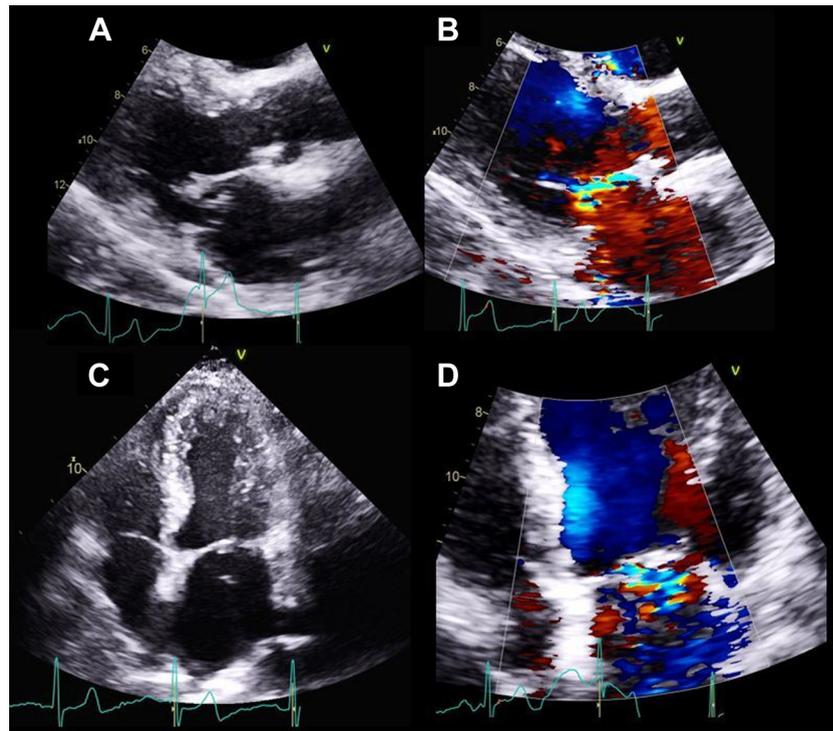
EXPERT TIP: EVALUATION OF NONHOLOSYSTOLIC MR. Determining the timing of MR is key in assessing its severity. In cases of MVP, MR is frequently non-holosystolic, starting in midsystole to late systole. Thus, single-frame color Doppler parameters (qualitative or quantitative) such as PISA-derived EROA, VC, VCA, or jet area will overestimate MR severity because they inherently assume holosystolic MR. Conventional EROA should not be reported in such cases. One measure that can be used is the MRV calculated by multiplying the PISA EROA by the

nonholosystolic VTI of the MR jet by continuous wave (CW) Doppler (midsystolic to late systolic in this case). Alternatively, other volumetric methods can be used to provide a more accurate assessment of MRV and MRF and circumvent the limitations of single-frame quantification. Studies have demonstrated that nonholosystolic MR results in lower MRV and more favorable outcomes as compared with holosystolic MR.⁷

CASE 3

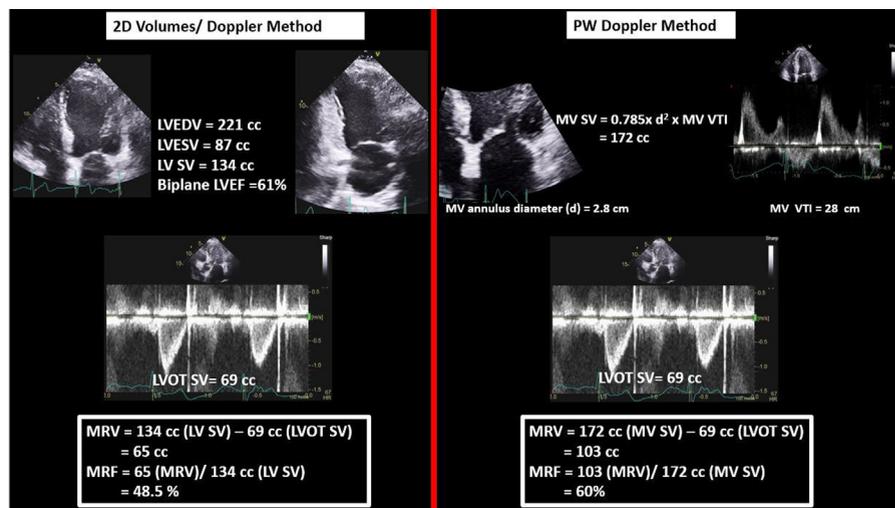
A 65-year-old man who had undergone TEER of the MV with 3 MitraClip (Abbott) devices presented for evaluation of shortness of breath. Immediate

FIGURE 2 Case 1: Transthoracic Echocardiography



(A, B) Parasternal and (C, D) apical views of a posterior mitral valve leaflet flail resulting in an eccentric, anteriorly directed mitral regurgitation jet.

FIGURE 3 Case 1: Quantification of Mitral Regurgitation Severity by Using 2 Methods



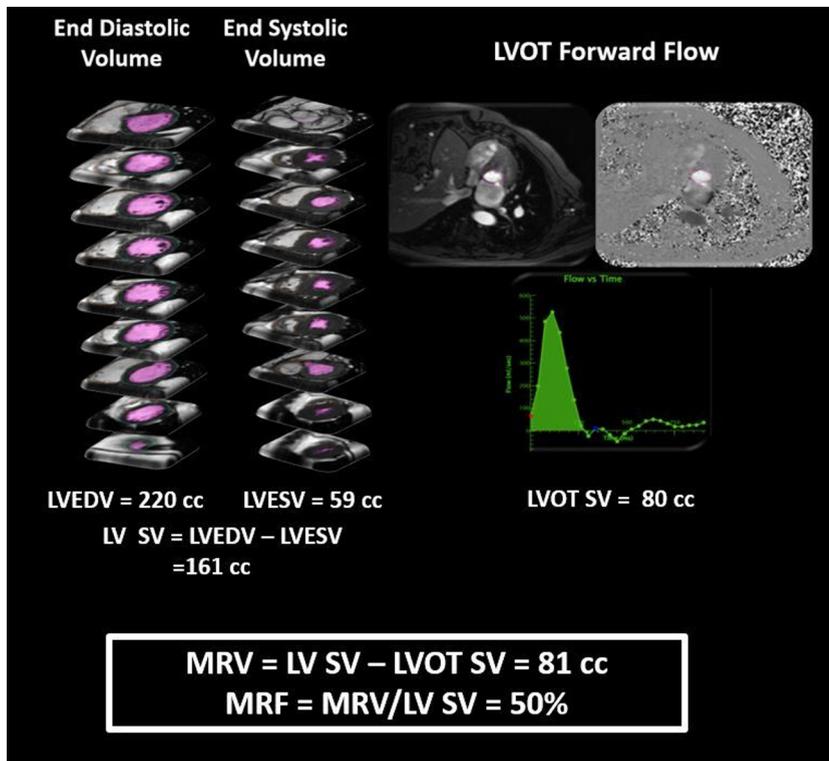
Both methods demonstrate hemodynamically significant mitral regurgitation. LV = left ventricular; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; LVOT = left ventricular outflow tract; MRF = mitral regurgitant fraction; MRV = mitral regurgitant volume; MV = mitral valve; PW = pulsed wave; SV = stroke volume; VTI = velocity time integral; 2D = 2-dimensional.

TABLE 1 Select Echocardiographic Quantification Methods of MR Severity and Their Limitations

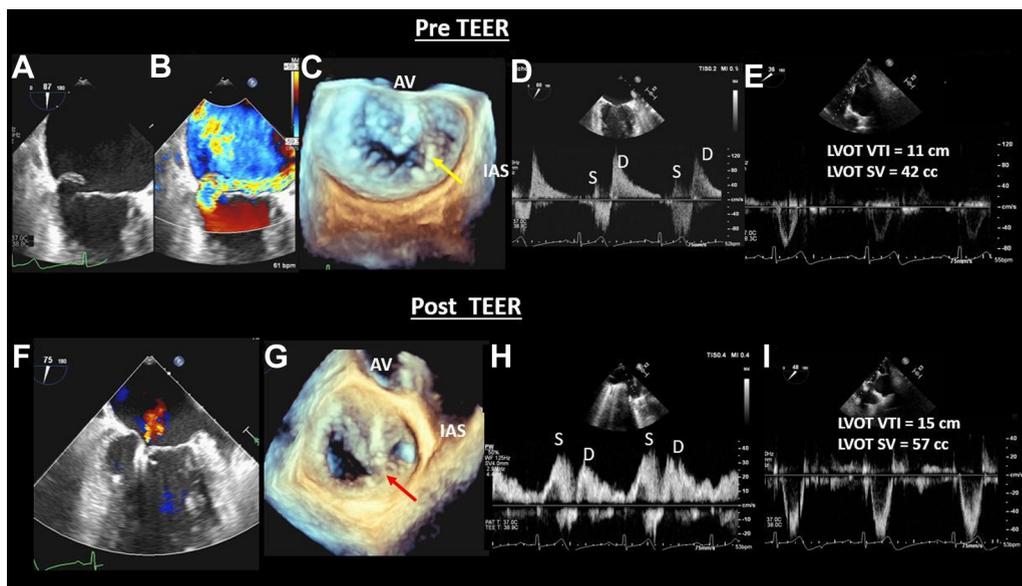
Method	Limitations
Vena contracta	Not valid in multiple jets Needs accurate visualization of the convergence zone Overestimates MR severity when MR is not holosystolic
PISA-flow convergence method	Small errors in PISA radius measurement can lead to substantial errors in EROA (squaring of error) EROA overestimates severity of non-holosystolic MR Regurgitant orifice is not always hemispheric; it can be crescent shaped in functional MR Maximal PISA may not always coincide with MR V_{max} , especially if MR is not holosystolic Not applicable in multiple jets More accurate in central jets; less reliable in eccentric and constrained jets
PW Doppler method	Involves multiple meticulous steps, including appropriate acquisition (accurate spectral Doppler gain and capture) Small errors at each level of measurement can lead to substantial errors Involves assumption that the MV annulus is circular Not valid in combined MR and AR cases
2D and 3D volumes combined Doppler method	LV foreshortening could preclude use of this method More accurate when performed using echocardiographic contrast images, which may not be readily available Use of 3D volumes is preferred but not always readily available Not valid in combined MR and AR

AR = aortic regurgitation; EROA = effective regurgitant orifice area; LV = left ventricular; MR = mitral regurgitation; PISA = proximal isovelocity surface area; PW = pulsed wave; V_{max} = maximal velocity; VTI = velocity time integral; 2D = 2-dimensional; 3D = 3-dimensional.

FIGURE 4 Case 1: Cardiac Magnetic Resonance Quantification of Mitral Regurgitation Severity



Sequential short-axis slices are acquired from the mitral valve annulus to the left ventricular (LV) apex. Left ventricular end-diastolic volume (LVEDV) is calculated by adding the volume (area × thickness) of each short-axis slice during diastole. Left ventricular end-systolic volume (LVESV) is calculated by adding the volume of each short-axis slice during systole. Subtracting left ventricular end-systolic volume from left ventricular end-diastolic volume yields left ventricular LV stroke volume (SV). Subsequently, left ventricular outflow tract (LVOT) stroke volume obtained by phase contrast imaging is subtracted from the left ventricular stroke volume to yield the mitral regurgitant volume (MRV). MRF = mitral regurgitant fraction.

FIGURE 5 Case 1: Baseline and Postprocedural Images

(A) A P3 flail resulting in (B) a severe laterally directed mitral regurgitation jet. (C) The 3-dimensional imaging of the valve shows the P3 flail with a ruptured chord in the left atrium. (D) Baseline systolic flow reversal in the left upper pulmonary vein. (E) Deep transgastric views reveal a left ventricular outflow tract (LVOT) stroke volume (SV) of 42 mL. (F, G) Post-transcatheter edge-to-edge repair (TEER) images show successful implantation of a MitraClip device (Abbott) at A3 to P3 resulting in mild residual mitral regurgitation. (H, I) Follow-up interrogation reveals a forward pulmonary vein systolic wave and an increase in left ventricular outflow tract stroke volume, both suggestive of significant mitral regurgitation reduction. AV = aortic valve; D = diastolic wave; IAS = interatrial septum; S = systolic wave; VTI = velocity time integral.

postprocedural TTE showed mild residual MR. TTE on presentation revealed significant MR with a large area of flow convergence (Figure 7). By volumetric assessment, the degree of MR was significant (MRV, 54 mL; MRF, 60%).

The patient underwent further evaluation with TEE, which revealed single leaflet device attachment (SLDA) of the most lateral MitraClip device resulting in severe MR (Figure 8).

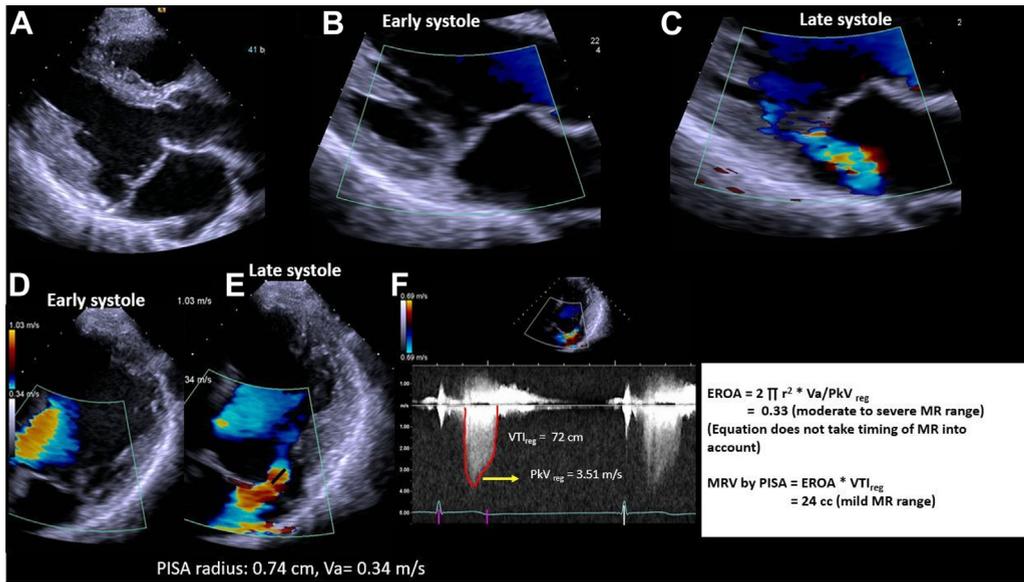
EXPERT TIP: EVALUATION OF RESIDUAL MR POST TEER. Evaluation of residual MR after TEER can be challenging and requires a comprehensive and integrative approach.⁶ The challenges are secondary to the frequent presence of multiple jets, the eccentricity of residual jets, and the limitations from acoustic shadowing caused by the device. Parameters suggestive of significant MR include the presence of SLDA, a large area of flow convergence, a dense and triangular CW Doppler jet, and systolic flow reversal in the pulmonary veins. Additionally, 3D VCA is a reliable parameter for quantification of residual MR

post TEER.⁸ Calculation of EROA by PISA is not recommended after TEER because of the inability to account well for the angulation of flow convergence in the presence of the device.⁶ Further imaging with TEE or CMR is recommended if either the mechanism or the severity of MR is unclear.⁶

CASE 4

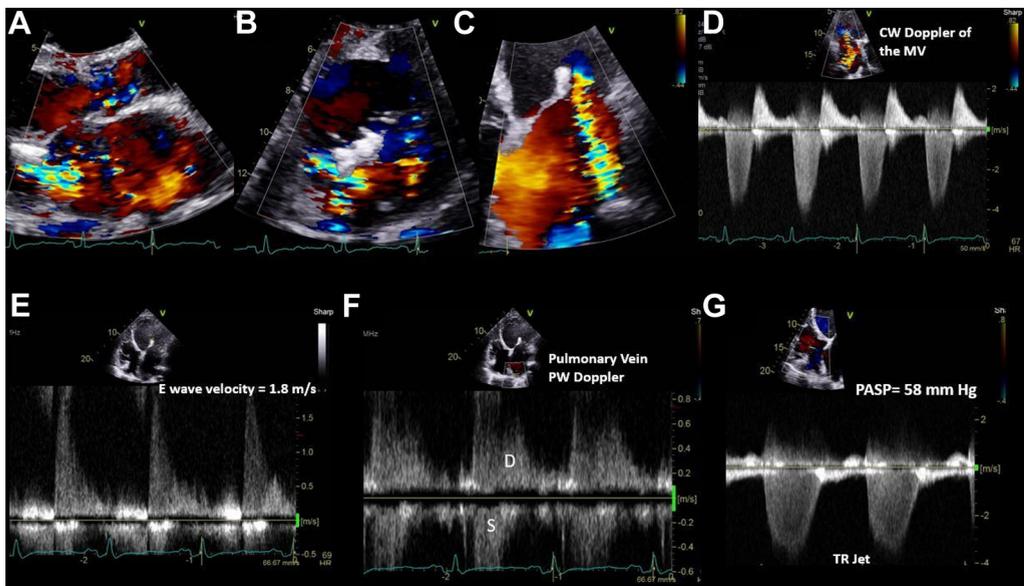
An 89-year-old patient with severe chronic obstructive lung disease and atrial fibrillation complicated by severe atrial MR was admitted with progressive dyspnea. He underwent TEE for evaluation of possible TEER of the MV. The 2-dimensional TEE imaging revealed a central malcoaptation gap resulting in significant MR; 3D TEE revealed the presence of multiple expanded bileaflet indentations (Figure 9, Video 2). These findings had procedural planning implications for TEER because the indentations interfere with the device landing zone. Such indentations can also complicate surgical repair. The patient was referred for transcatheter

FIGURE 6 Case 2: Mitral Valve Prolapse With MR

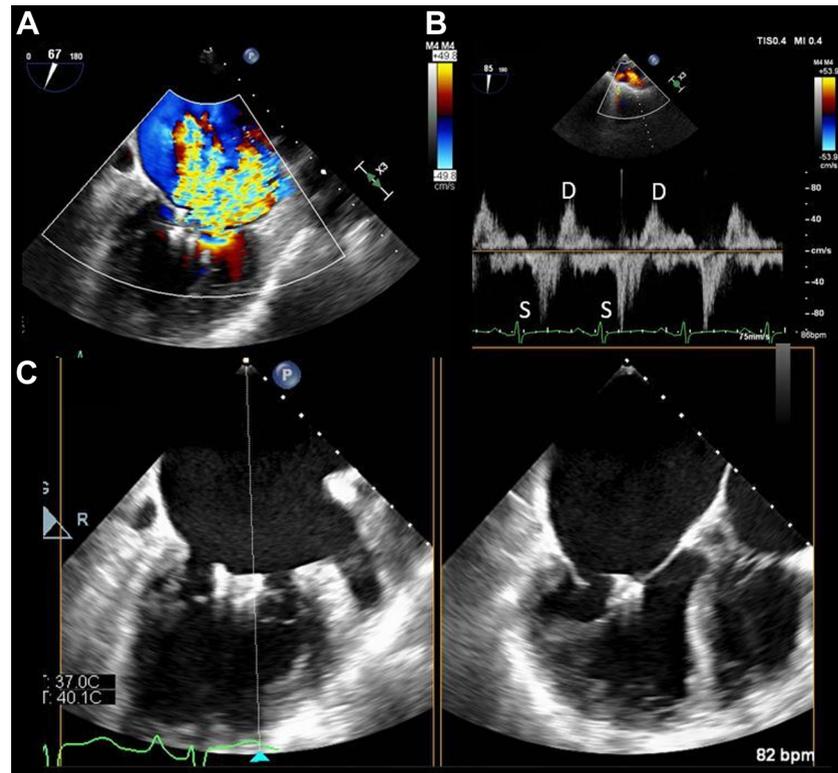


(A to C) Parasternal views of bileaflet mitral valve prolapse resulting in late systolic mitral regurgitation (MR). (D, E) Apical views demonstrating the presence of late systolic mitral regurgitation. (F) Note the discrepancy in mitral regurgitation severity between the proximal isovelocity surface area (PISA)-derived effective regurgitant orifice area (EROA) method and the volumetric method given the timing of the mitral regurgitation jet. MRV = mitral regurgitant volume; PkV_{reg} = peak regurgitation velocity; V_a = aliasing velocity; VTI_{reg} = velocity time integral of the regurgitant mitral regurgitation jet.

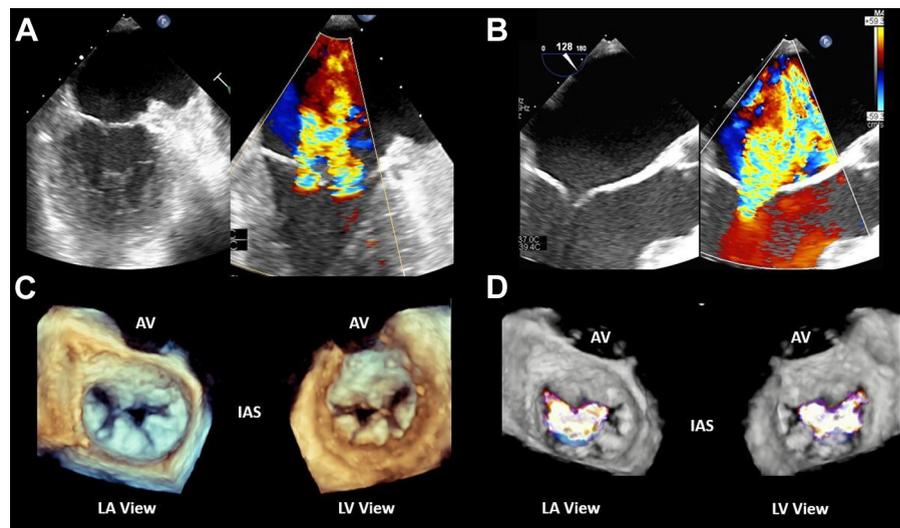
FIGURE 7 Case 3: Transthoracic Echocardiography and Doppler Imaging on Presentation



(A to C) Transthoracic echocardiography demonstrating significant residual mitral regurgitation post transcatheter edge-to-edge repair. (D) Continuous wave (CW) Doppler tracings demonstrating a complete mitral regurgitation jet. Other markers of significant mitral regurgitation include (E) a high E-wave velocity, (F) systolic flow reversal in the pulmonary vein, and (G) pulmonary hypertension. PASP = pulmonary artery systolic pressure; other abbreviations as in Figure 3.

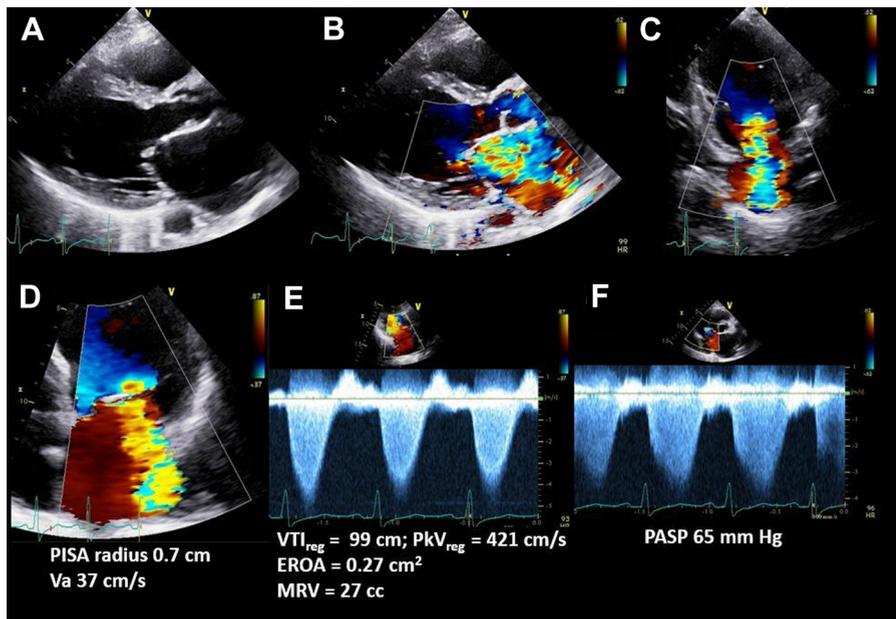
FIGURE 8 Case 3: Transesophageal Echocardiography

(A) Severe mitral regurgitation with (B) systolic flow reversal in the pulmonary vein. (C) Biplane imaging of the lattermost clip reveals single leaflet device attachment with the clip attached to the anterior leaflet. Abbreviations as in Figure 5.

FIGURE 9 Case 4: Transesophageal Echocardiography

(A, B) 2-Dimensional transesophageal echocardiography images demonstrating left atrial (LA) dilation with mitral annular dilation resulting in significant central mitral regurgitation. (C, D) 3-Dimensional and 3-dimensional color transesophageal echocardiography images revealing the presence of multiple mitral valve indentations resulting in significant mitral regurgitation. LV = left ventricular; other abbreviations as in Figure 5.

FIGURE 10 Case 5: Transthoracic Echocardiography



Parasternal long-axis views demonstrating mitral annular dilation and apical leaflet tethering resulting in (A) a central malcoaptation gap with (B) significant mitral regurgitation. (C) This is also demonstrated by apical views. (D, E) In cases of functional mitral regurgitation, effective regurgitant orifice area (EROA) estimation by proximal isovelocity surface area (PISA) may underestimate mitral regurgitation severity because the effective regurgitant orifice area may be elliptical rather than hemispheric in shape. (F) The patient additionally had severe pulmonary hypertension. Abbreviations as in Figures 6 and 7.

MV replacement evaluation given his elevated surgical risk.

EXPERT TIP: ROLE OF 3D TEE IMAGING IN MR ASSESSMENT AND MANAGEMENT. Using 3D imaging of the MV provides a detailed anatomical assessment of the MV in 3 dimensions, thereby deeming it an important modality in delineating MR origin and planning structural interventions.⁹

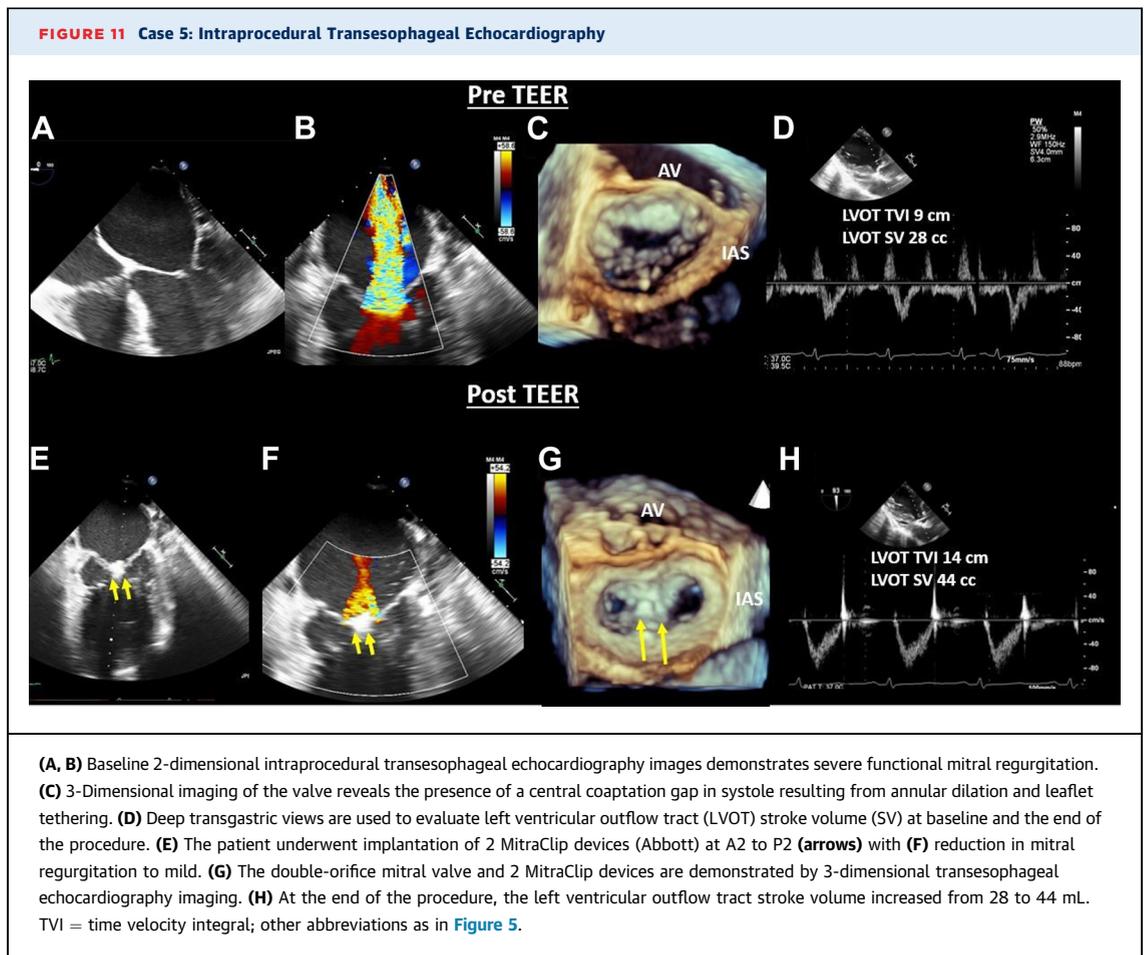
CASE 5

A 68-year-old woman with a history of ischemic cardiomyopathy presented for evaluation of worsening shortness of breath despite optimal guideline-directed medical therapy. TTE showed a severely dilated left ventricle (LV end-diastolic diameter, 6.2 cm), a moderately depressed LVEF (35%-39%), severe LA dilation (57 cc/m²), and moderate to severe functional MR (Figure 10).

EXPERT TIP: SPECIAL CONSIDERATIONS IN FUNCTIONAL MR. Functional MR results from apical tethering of the valve leaflets and annular dilatation leading to

leaflet malcoaptation. Special considerations for evaluation of functional MR include the following:

- The MRV is frequently lower in patients with functional MR compared with primary MR because of the low-flow state.
- The EROA in functional MR is frequently elliptical or crescent shaped rather than hemispheric; this shape can result in MR underestimation when using the PISA method, as demonstrated in Figure 10.¹⁰ However, PISA-derived EROA remains an important diagnostic and prognostic parameter, with studies demonstrating that EROAs >0.2 cm² are associated with worse outcomes.^{11,12}
- Functional MR has a biphasic pattern in systole where it peaks in early and late systole in response to dynamic changes in transmitral pressure.¹³
- Parameters such as LV size and function, LA size, mitral E- and A-wave Doppler velocities, and pulmonary artery systolic pressure are affected by the underlying cardiomyopathy and filling pressures and are therefore less specific for severity of functional MR.



The patient subsequently underwent TEER according to current joint American College of Cardiology and American Heart Association guidelines, with significant MR reduction and symptom improvement ([Figure 11](#)).¹⁴

CONCLUSIONS

Determining the etiology, mechanism, severity, and hemodynamic consequence of MR is key to appropriate evaluation and treatment. A comprehensive and integrative approach allows for thorough MR evaluation, by taking into consideration the strength and limitations of various parameters. Although color Doppler imaging is essential in evaluating MR severity, it is limited in nonholosystolic MR and in patients with very eccentric jets. Volumetric quantitation with echocardiography and Doppler imaging is

needed in these situations, particularly when significant regurgitation is suspected. Imaging with TEE or CMR is additionally beneficial when TTE image quality is suboptimal, when MR severity cannot be accurately determined, and in the presence of discrepancies with clinical findings.

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KEY WORDS cardiac magnetic resonance imaging, mitral regurgitation, transcatheter edge-to-edge repair, transesophageal echocardiography, transthoracic echocardiography, 3-dimensional echocardiography

APPENDIX For supplemental videos, please see the online version of this article.