Transcatheter Mitral Valve Repair Using the Edge-to-Edge Clip

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Percutaneous intervention for mitral valve (MV) disease has been established as an alternative to open surgical MV repair in patients with prohibitive surgical risk. Multiple percutaneous approaches have been described and are in various stages of development. Edge-to-edge leaflet plication with the MitraClip (Abbott, Menlo Park, CA) is currently the only Food and Drug Administration-approved device specifically for primary or degenerative lesions. Use of the edge-to-edge clip for secondary mitral regurgitation is currently under investigation and may result in expanded indications. Echocardiography has significantly increased our understanding of the anatomy of the MV and provided us with the ability to classify and quantify the associated mitral regurgitation. For percutaneous interventions of the MV, transesophageal echocardiography imaging is used for patient screening, intraprocedural guidance, and confirmation of the result. Optimal outcomes require the echocardiographer and the proceduralist to have a thorough understanding of intra-atrial septal and MV anatomy, as well as an appreciation for the key points and potential pitfalls of each of the procedural steps. With increasing experience, more complex valvular pathology can be successfully percutaneously treated. In addition to two-dimensional echocardiography, advances in three-dimensional echocardiography and fusion imaging will continue to support the refinement of current technologies, the expansion of clinical applications, and the development of novel devices. (J Am Soc Echocardiogr 2018;31:434-53.)

Keywords: Percutaneous mitral valve repair, MitraClip, 3D echocardiography, Interventional echocardiography

Percutaneous intervention for mitral valve (MV) disease has been established as an alternative to open surgical MV repair, particularly in patients with increased surgical risk.[1,2] Multiple percutaneous approaches have been described and are in various stages of development.[3] Edge-to-edge leaflet plication with the MitraClip (Abbott, Menlo Park, CA) is currently the only Food and Drug Administration-approved device specifically for primary or degenerative lesions. Utilization of the edge-to-edge clip (E-EC) for secondary mitral regurgitation is currently under investigation and may result in expanded indications. During this procedure anterior and the posterior mitral leaflets are percutaneously "clipped" to convert the MV into a double orifice valve analogous to the surgically performed Alfieri stitch.[4] Transesophageal echocardiography (TEE) imaging is integral to the success of the procedure. Its role extends from assessing suitability, procedural guidance, confirming success, and exclusion of complications.

ANATOMICAL PERSPECTIVE

Anatomically, the MV is part of an apparatus that includes leaflets, annulus, chordae tendineae, and the papillary muscles with the underlying myocardium.[5,6] The MV has an anterior and a posterior leaflet, which are continuous with an anterolateral commissure and a posteromedial commissure where the leaflets merge. Centrally, the leaflets overlap by approximately 10 mm (coaptation height), and reduction of this overlap by annular dilatation or tethering of one or both leaflets may result in valvular incompetence. The leaflets are enclosed in a saddle-shaped annulus and attached to the papillary muscles via chordae tendineae.[5] The anterolateral papillary muscle and the posteromedial papillary muscle support both leaflets. The lateral half of the MV including the lateral commissure is supported via chordae tendineae attached to the anterolateral papillary muscle. The medial half of the MV including the medial commissure is supported via chordae tendineae attached to the posteromedial papillary muscle. The central portion of each leaflet is relatively free of chordal insertion, making it an ideal location for E-EC placement. Leaflet attachments to the annulus are continuous with commissures formed where both leaflets merge. Echocardiographically, the MV is examined to assess its function, that is, competence during systole and nonrestriction during diastole. The anterior leaflet is longer than the posterior leaflet that has indentations along its free edge,

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Abbreviations

2D = Two-dimensional

3D = Three-dimensional

AP = Anteroposterior

CDS = Clip delivery system

CFD = Color flow Doppler

E-EC = Edge-to-edge clip

GA = General anesthesia

HOCM = Hypertrophic obstructive cardiomyopathy

iASD = Iatrogenic atrial septal defect

IAS = Intra-atrial septum

LA = Left atrium

LAX = Long axis

LV = Left ventricle

LVOT = Left ventricular outflow tract

MAC = Mitral annular calcification

ME-LAX = Midesophageal long axis

MR = Mitral regurgitation

MV = Mitral valve

MVA = Mitral valve area

PLAX = Parasternal long axis

PSAX = Parasternal short axis

SAM = Systolic anterior motion

SGC = Steerable guide catheter

TEE = Transesophageal echocardiography

TTE = Transthoracic echocardiography

VC = Vena contracta

giving it a scalloped appearance (Figure 1). The degree of coaptation between the two leaflets determines the extent of mitral annular dilation that can be sustained without overt Mitral regurgitation (MR).

The chordae tendineae are attached to the free edge (marginal chords) and ventricular surface (strut chords) of the leaflets and serve to prevent excessive leaflet motion during systole and to maintain the ideal geometry of the left ventricle (LV) during papillary muscle contraction. Leaflet prolapse is defined as the coaptation point moving above the plane of the mitral annulus in the anteroposterior (AP) axis of the annulus. The leaflet is considered flail when there is chordal rupture with the ventricular surface of the leaflet exposed to the left atrium (LA; Figure 2). The Carpentier nomenclature for description of MV anatomy is generally followed both for transthoracic echocardiography (TTE) and TEE.[7,8] It is based on the surgical exposure of the MV through the LA.

PREPROCEDURAL TRANSTHORACIC IMAGING

Patient Selection and Preprocedural Imaging

For percutaneous MV repair, TEE is the primary imaging modality for qualitative and quantitative assessment of the MV apparatus and procedural guidance. However, TTE has value as screening tool.[9,10] Screening TTE is used to classify the severity of MR, including both qualitative and quantitative assessment of MR per the current guidelines,[11] distinguish the etiology as primary (degenerative) or secondary (functional), and establish the initial suitability for an intervention, including possible E-EC based on the EVEREST trial criteria.[12-15]

Transthoracic Views

Of the standardized views, the following views provide the most relevant information that is integral for preprocedural planning and establishing suitability for E-EC (Figure 3).

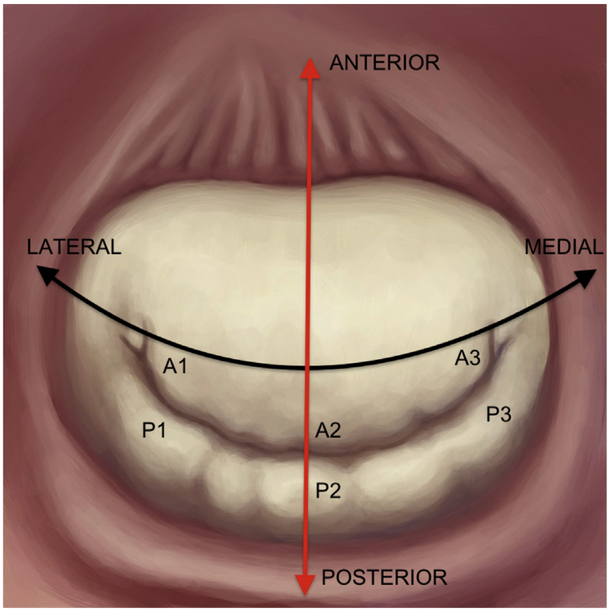

Figure 1 Schematic demonstrating the Carpentier nomenclature of the segments of the MV. The lateral, middle and medial scallops of the posterior leaflet are termed P1, P2, and P3, and the corresponding anterior leaflet A1, A2, and A3, respectively. The central A2/P2 portion of each leaflet is relatively free of chordal insertion, making it an ideal location for clip placement.

Parasternal Long-Axis View

In the parasternal long-axis (PLAX) view, malcoaptation involving the middle scallops of the MV (A2/P2) can be visualized, annular and LV diameter can be measured, and subvalvular apparatus can be evaluated. Visual qualitative estimation of the MR jet and its physical characterization (direction) can help elucidate the etiology. Since the coaptation zone is orthogonally displayed, the vena contracta (VC) can be accurately measured in this view.

Apical Four-Chamber View

Besides structural assessment, the apical four-chamber view enables quantitative assessment of MR through proximal isovelocity surface area derived effective regurgitant orifice area, measurement of trans-valvular gradient and calculation of MV area (MVA). A baseline transvalvular gradient of < 3 mm Hg has been associated with improved outcomes after E-EC[16] Conversely, patients with a large baseline (effective regurgitant orifice area > 70 mm^2), small MVA (<3.0 cm^2), and an elevated baseline gradient (>4 mm Hg) had poorer procedural outcomes.[17] Primary MV pathologies such as thickening, restriction, prolapse, and flail can also be appreciated in this view. Calcification of the leaflet at the potential grasp point should be described.

Two-Chamber View

With the scan plane parallel to the zone of coaptation, the entire width of the MR jet from medial to lateral commissure and the likelihood of deploying multiple clips is evaluated. As the coaptation zone is curved, a sweep from the anterior leaflet through to posterior leaflet will allow visualization of the entire coaptation zone.

Parasternal Short-Axis View

The parasternal short-axis (PSAX) view provides the characteristic "fish mouth" view of the MV. The baseline MVA is crucial in determining patient suitability for E-EC. In addition to determining the origin of the MR jet, the PSAX enables planimetry at the leaflet tips; this allows for direct measurement of the diastolic MVA that is independent of loading conditions, chamber pressure, and compliance.

Three-Dimensional Imaging

Three-dimensional (3D) TTE can be used to assess the MV apparatus and may evaluate chamber size and function. Unlike TEE, high-resolution TTE 3D MV imaging is limited in most patients and not considered a routine screening test.

PREPROCEDURAL AND INTRAPROCEDURAL TEE EXAMINATION

In the EVEREST-II trial, preprocedure TEE was also performed for precise delineation of the MV anatomy and to determine the suitability for the intervention.[15,18] Besides confirmation of TTE findings, TEE is particularly helpful in patients with suboptimal TTE windows and to identify LA or LA appendage thrombus, which would necessitate postponement. As compared to TTE, TEE can generate higher resolution 3D en face views of the MV from the LA perspective (3D LA en face). The echocardiographic views provide a detailed structural assessment of the MV and enable quantification of the severity and mechanism of MR (Figure 4).[19,20] A comprehensive TEE examination consists of a complete qualitative and quantitative examination of the MV using all of the echocardiographic modalities[11,21-23] (Figure 5). Classification of the MV pathology using the expanded Carpentier classification[24] aids in description of the valvular pathology but also distinguishes between primary and secondary MR[6,8,20,25-27] (Table 1; Figure 6). The location of the dominant jet should be identified in the midesophageal long-axis (ME-LAX) view (Video 1, available at www.onlinejase.com), and the leaflet tips inspected in the region of the largest regurgitant jet and the VC should be measured for assessment of MR severity. Additional grasping areas may need to be evaluated if a single wide central jet or multiple jets are present. According to the recent registry data, nearly 40% of patients with functional MR required more than one clip.[28]

Intraoperative TEE examination is performed after induction of general anesthesia (GA). This exam differs from the screening TEE examination in being more procedurally focused and point of care in nature.[29] It is possible to suspend respiration under GA to facilitate high frame rate R-wave gated 3D en face images of MV with and without color flow Doppler (CFD) acquisition for structural and functional analysis and will better define the extent and location of the coaptation defect from both the LA and LV perspective (Figure 7). The LA en face view will also identify additional features such as clefts or prominent scallops.[30] For atypical, eccentric MR and functional MR jets, VC area obtained by 3D CFD is possibly more accurate than two-dimensional (2D) derived area (Figure 8).[31,32] However, a multibeat 3D acquisition may not be feasible in patients with irregular rhythms.[33] In these patients, the volume of the 3D region of interest should be decreased to maximize spatial and temporal resolution.

HIGHLIGHTS

- Echocardiography is key to determining mitral valve pathology and suitability for percutaneous repair.
- Two-dimensional and 3D echocardiography is invaluable for MitraClip procedural guidance, confirming success, and exclusion of complications.
- The role of interventional echocardiography will increase with the development of novel new devices.

A basal transgastric view should be obtained with and without CFD. The transgastric LAX view should be used to evaluate the morphology of the subvalvular apparatus and its interaction with the MV leaflets. In secondary MR, tethering of MV leaflets due to left ventricular dilation can also be appreciated.

If the intraprocedural MR quantification differs significantly from the preoperative MR it is important to consider the impact of GA and positive pressure ventilation on loading conditions, and an attempt should be made to restore physiologic loading conditions.[34,35]

Based on the EVEREST II[15] exclusion criteria, ideal morphologic characteristics for percutaneous repair include a central origin of the MR, absence of calcification in the gasping area, and adequate MVA (>4 cm^2; Figure 9). In primary MR, ideal morphologic characteristics include a small flail gap (<10 mm) and narrow flail width (<15 mm). Currently under investigation for secondary MR, ideal morphologic characteristics include a small tenting height (<11 mm) and adequate (>2 mm) residual coaptation length (Figure 10). Additionally, a posterior leaflet length of greater than 10 mm is considered ideal.[20,25,26,36]

While it has been demonstrated that patients who did not meet EVEREST II criteria can have favorable results both in terms of mortality and residual MR, patients with flail gaps >10 mm and flail widths >15 mm are associated with increased chance of repeat intervention.[37-39] Characteristics of valves less suitable to percutaneous repair (Figure 9) include patients with commissural or broad multisegment pathology, leaflet clefts, and leaflet calcification in the grasping area. Such cases should only be attempted by experienced high-volume centers in the absence of therapeutic alternatives. Contraindications to E-EC include patients with MVAs < 3 cm^2 or elevated gradients at baseline > 5 mm Hg.[20,25,26,36] (Table 2)

PROCEDURAL IMAGE GUIDANCE WITH TEE

Real-time 3D TEE guidance during E-EC provides the depth perception as well as the spatial orientation and constraints of cardiac anatomy that cannot be visualized during fluoroscopic imaging. The fluoroscopic image and the TEE-derived image are simultaneously displayed on a screen during the procedure to facilitate orientation and catheter manipulation by the interventionalist. Clear and effective communication between the echocardiographer and the interventionalist is paramount to facilitate procedural guidance and optimize outcomes.

Procedural Steps and Echocardiographic Guidance

Procedural steps include transseptal puncture, advancement of the steerable guide catheter (SGC) into the LA, insertion of the clip delivery system (CDS) through the SGC into the LA, positioning the

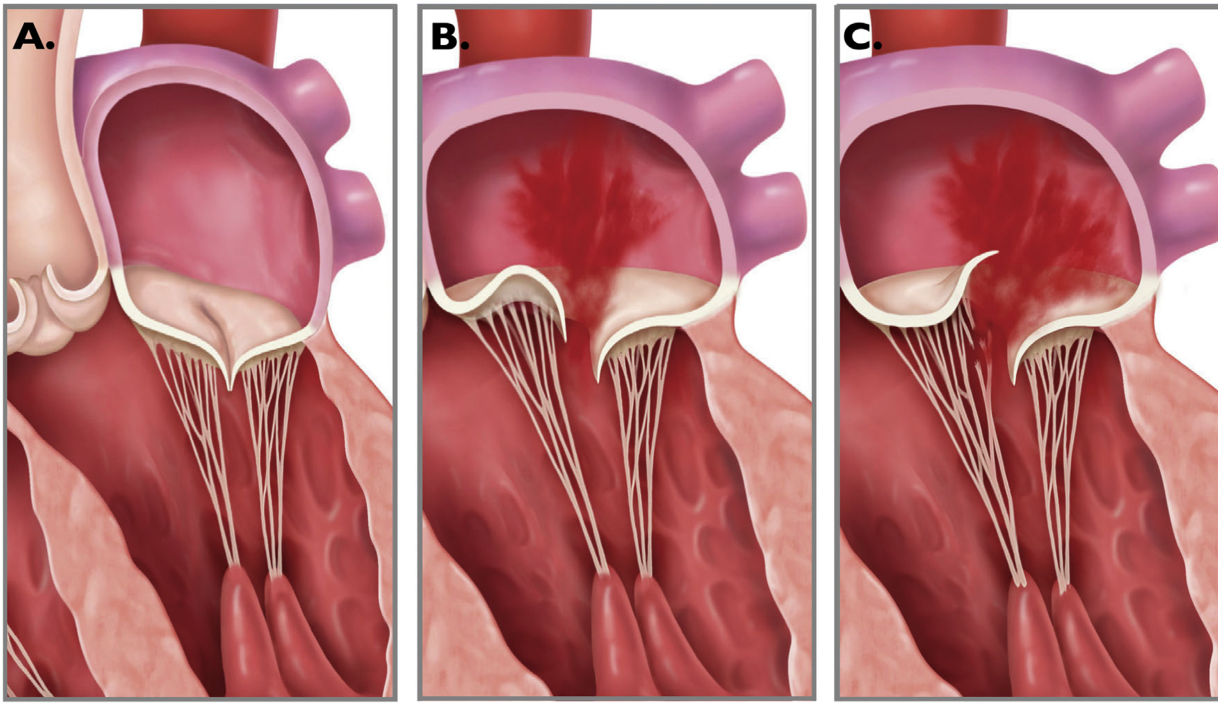

Figure 2 Schematic of **(A)** normal, **(B)** prolapse, and **(C)** flail leaflet coaptation. **(A)** In a normal valve, the leaflets and the point of coaptation are below the AP plane of the annulus. **(B)** In valvular prolapse leaflet, tissue rises above the annular plane, however, the leaflet tips remain directed towards the LV. **(C)** In flail leaflet, due to chordal rupture the leaflet tip is no longer tethered, and the leaflet tips extend into the LA exposing the ventricular surface of the leaflet to the LA.

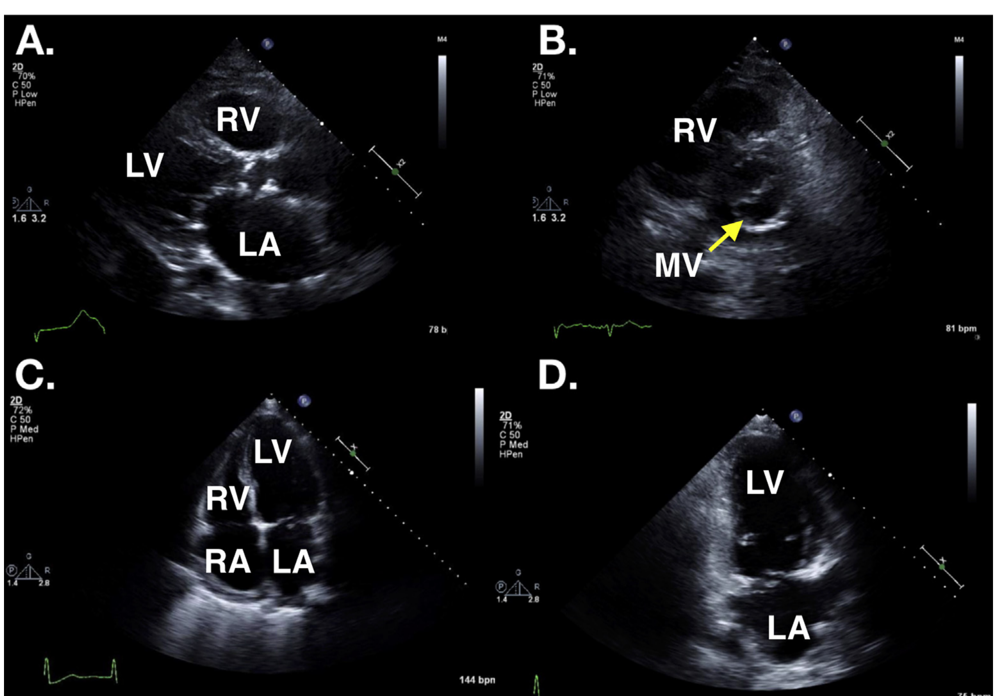

Figure 3 TTE views of the MV. **(A)** PLAX view provides visualization of the central anterior and posterior leaflet (A2/P2); for medial (A3/P3) and lateral (A1/P1) visualization the probe can be tilted toward the tricuspid valve and aortic valves, respectively. **(B)** PSAX view of the MV provides the characteristic "fish mouth" view of the MV and will allow for the origin of the MR jet to be determined and for planimetry of MVA (*yellow arrow*). **(C)** Apical four-chamber view allows for chamber quantification, both qualitative and quantitative assessment, of the MR as well as measurements of transvalvular gradients. **(D)** Apical two-chamber view of the MV allows for interrogation of the line of coaptation. *RA*, Right atrium; *RV*, right ventricle. (See associated Video 1, available at www.onlinejase.com.)

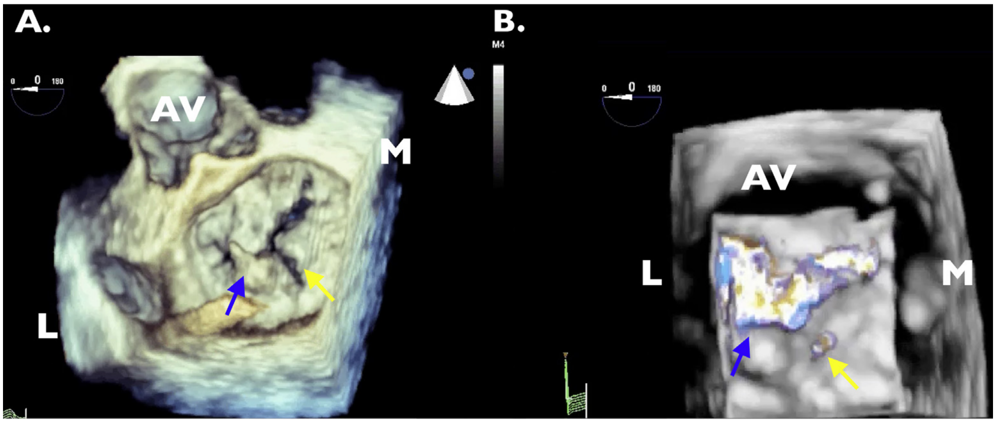

Figure 4 The 3D en face views of the MV from the LA perspective. **(A)** 3D Gated en face view of the MV demonstrating a P1 flail (*blue arrow*) and a central P2 cleft (*yellow arrow*). **(B)** 3D gated color flow Doppler of the MV demonstrating the dominant jet originating from the flail segment (*blue arrow*) and a trivial jet from the central P2 cleft (*yellow arrow*). *AV*, Aortic valve; *L*, lateral; *M*, medial. (See associated Video 2, available at www.onlinejase.com.)

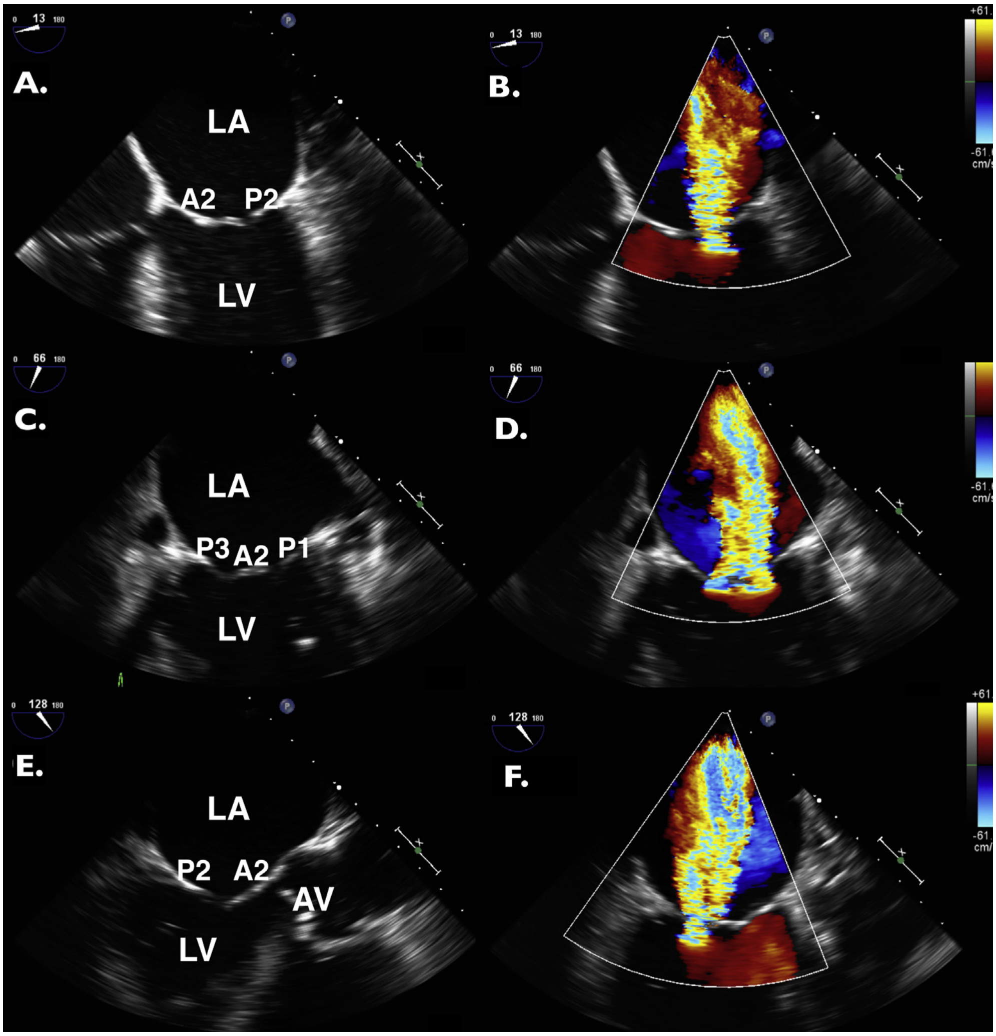

Figure 5 **(A)** TEE of the ME four-chamber view with A2 and P2 scallops visualized. **(B)** Corresponding color flow Doppler. **(C)** TEE of the ME commissural view with P3, A2, and P1 scallops visualized. **(D)** Corresponding color flow Doppler. **(E)** TEE of the ME-LAX view with A2 and P2 scallops visualized. **(F)** Corresponding color flow Doppler. *AV*, Aortic valve.

Table 1 Expanded Carpentier classification of MV pathology

Type I: Normal leaflet motion
(A) Perforation
(B) Cleft valve
(C) Dilated annulus (without leaflet tethering)
Type II: Excessive leaflet motion
(A) Flail leaflet (localized to one segment)
(B) Billowing prolapse
(C) Bileaflet prolapse with flail segment
Type III: Restricted leaflet motion
(A) Systolic and diastolic restriction (e.g., rheumatic)
(B) Symmetric systolic restriction (e.g., dilated or ischemic cardiomyopathy; dilated annulus with leaflet tethering)
(C) Asymmetric systolic restriction (e.g., segmental ischemic dysfunction resulting in focal tethering)
Type IV: SAM of the leaflet(s)
(A) Hypertrophic cardiomyopathy with SAM-related mitral regurgitation
(B) Post-MV repair SAM
(C) Hemodynamic-induced SAM (e.g., hypovolemia, inotropic stimulation, and tachycardia)
Type V: Hybrid conditions: Combined pathologies (e.g., a flail leaflet (Type II A) and cleft valve (Type I B))

Adapted from Shah and Raney.[24]

clip above the grasping area, advancing the clip into the LV, grasping the leaflets, comprehensive valve assessment, and clip release.

Transseptal Puncture. Key Points: Thorough understanding of the anatomy of the intra-atrial septum (IAS) and corresponding TEE views will optimize accurate transseptal puncture, which is key to procedural success. Septal puncture height should be 4-5 cm above the plane of leaflet coaptation.

A thorough understanding of the anatomy of the IAS and its associated structures is necessary for both safe and optimized transseptal puncture. Inappropriate or inaccurate transseptal puncture may add significant time and complexity to the procedure or may result in iatrogenic injury.[20,40,41] In the normal anatomic orientation of the heart, the right atrium is positioned anterior to the LA and the IAS is angled in right-posterior to left-anterior orientation.[42] The aortic valve is positioned at the anterosuperior aspect of the IAS, and the MV is positioned in a plane perpendicular to the septum. The superior and inferior vena cava are attached to the superior and inferior borders of IAS, respectively. For central pathology the ideal puncture site is in the posterosuperior aspect of the IAS in line with the plane of coaptation.[20,36,40] The transseptal sheath and needle are gradually withdrawn from the superior vena cava under TEE guidance until the sheath is seen tenting the IAS. Subsequently, a modified ME aortic SAX view is obtained with the aortic valve serving as an anterior reference point; clockwise rotation of the transseptal sheath/needle will move the needle posteriorly (Figure 11). The TEE probe may need to be withdrawn or rotated further to the right to maintain visualization of the transseptal sheath/needle. Simultaneous orthogonal imaging of the IAS during this procedure can simultaneously display superior, inferior, anterior, and posterior rims of the IAS (Figure 12). The distance from the intended septal puncture point to the annular plane (or the point of leaflet coaptation in the case of functional MR) is imaged using the ME four-chamber view. However, if tenting cannot be seen on the four-chamber view, then an inverted four-chamber view (150°-170°) can often aid in visualization (Figure 13). A straight-line measurement is made from the annular plane or the plane of leaflet coaptation to a plane aligned with the tenting of the IAS. The optimal distance is between 4 cm and 5 cm of the MitraClip NT system is used (3.5-4.5 cm if the original MitraClip system is used).[40] A septal puncture in close proximity to the MV will limit the maneuverability of the clip delivery system and may result in adjustments needing to be made below the leaflets and risk entanglement within the chordae.[42] A septal puncture too high may limit the ability of the clip delivery system to advance below the leaflet tips to facilitate capture. In patients with more lateral pathology, a lower puncture site can be used as the clip delivery system will gain elevation as advanced laterally.[40,42] Fusion imaging allows for the overlaid display of both fluoroscopic and echocardiographic images, as well as the ability to place markers on the desired point of the transseptal puncture site, possibly reducing procedure time and complications (Figure 14).[43-45] Once the ideal puncture site has been identified, the needle is advanced and pressure is applied until the septum is crossed. Some interventionalists may use a radiofrequency transseptal needle to facilitate septal crossing. This may be required in patients with a fibrotic septum or significant lipomatous hypertrophy or simply to reduce the force required. The transseptal puncture should be performed under continuous TEE monitoring, and the interventionalists should be informed immediately if the trajectory of the needle is toward the aortic root or the posterior wall of the LA. Following advancement of the sheath, the needle is removed and a guide wire is advanced into the left upper pulmonary vein under fluoroscopic and TEE guidance.[20]

Advancement of SGC. Key Point: Advancement of SGC under continuous TEE guidance will minimize chance of iatrogenic injury and confirm adequate distance across septum.

The SGC and its associated dilator are advanced over the guide wire into the LA under 2D or 3D TEE and fluoroscopic guidance. The dilator is grooved and creates a characteristic echocardiographic appearance (Figure 15). Additionally, the tip of the SGC is radiopaque and easily seen on fluoroscopy and TEE. The SGC is advanced until approximately 2 cm of the SGC is across the septum. Continuous TEE guidance is provided to avoid LA injury. Wide-sector full-volume

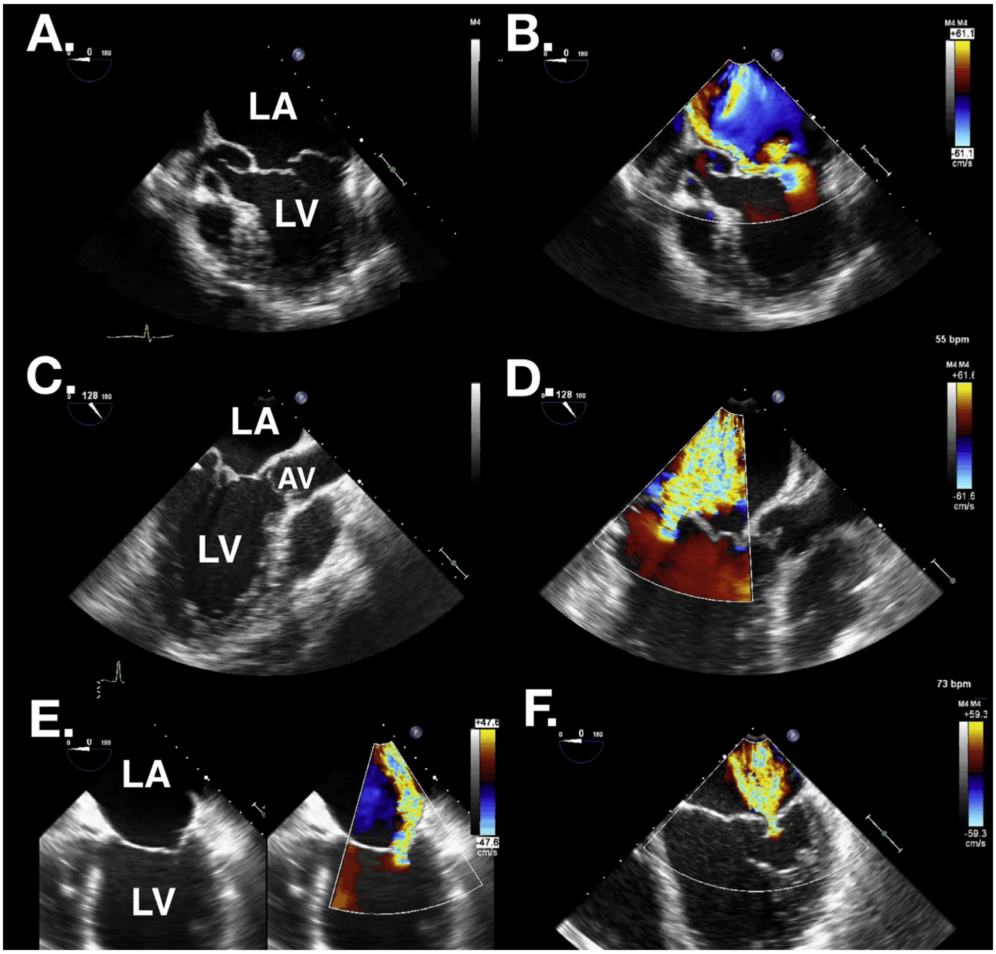

Figure 6 **(A)** 2D TEE four-chamber view of the MV showing posterior leaflet flail, expanded Carpentier classification excessive leaflet motion type IIa. **(B)** Corresponding color flow Doppler of the type IIa jet directed away from the flail segment. **(C)** 2D TEE ME-LAX view of the MV showing billowing prolapse, expanded Carpentier classification excessive leaflet motion type IIb. **(D)** Corresponding color flow Doppler of the type IIb central jet. **(E)** 2D TEE four-chamber and color flow Doppler comparison view of the MV showing asymmetric systolic restriction, expanded Carpentier classification type IIIc; the greater restriction of the posterior leaflet leads to a posteriorly directed jet. **(F)** 2D TEE four-chamber view color flow Doppler of the MV showing symmetric systolic restriction, expanded Carpentier classification type IIIb, and the associated centrally directed jet. *AV*, Aortic valve. (See associated Video 3, available at www.onlinejase.com.)

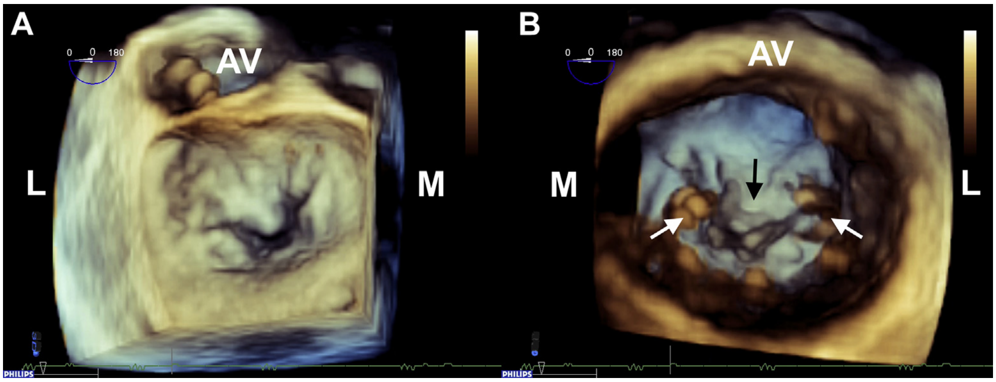

Figure 7 **(A)** 3D en face view of the MV from the left atrial perspective. **(B)** 3D en face view of the MV from the left ventricular perspective. Note the subvalvular apparatus medially and laterally (*white arrows*) and the central area relatively free of chords (*black arrow*). *AV*, Aortic valve; *L*, lateral; *M*, medial. (See associated Video 4, available at www.onlinejase.com.)

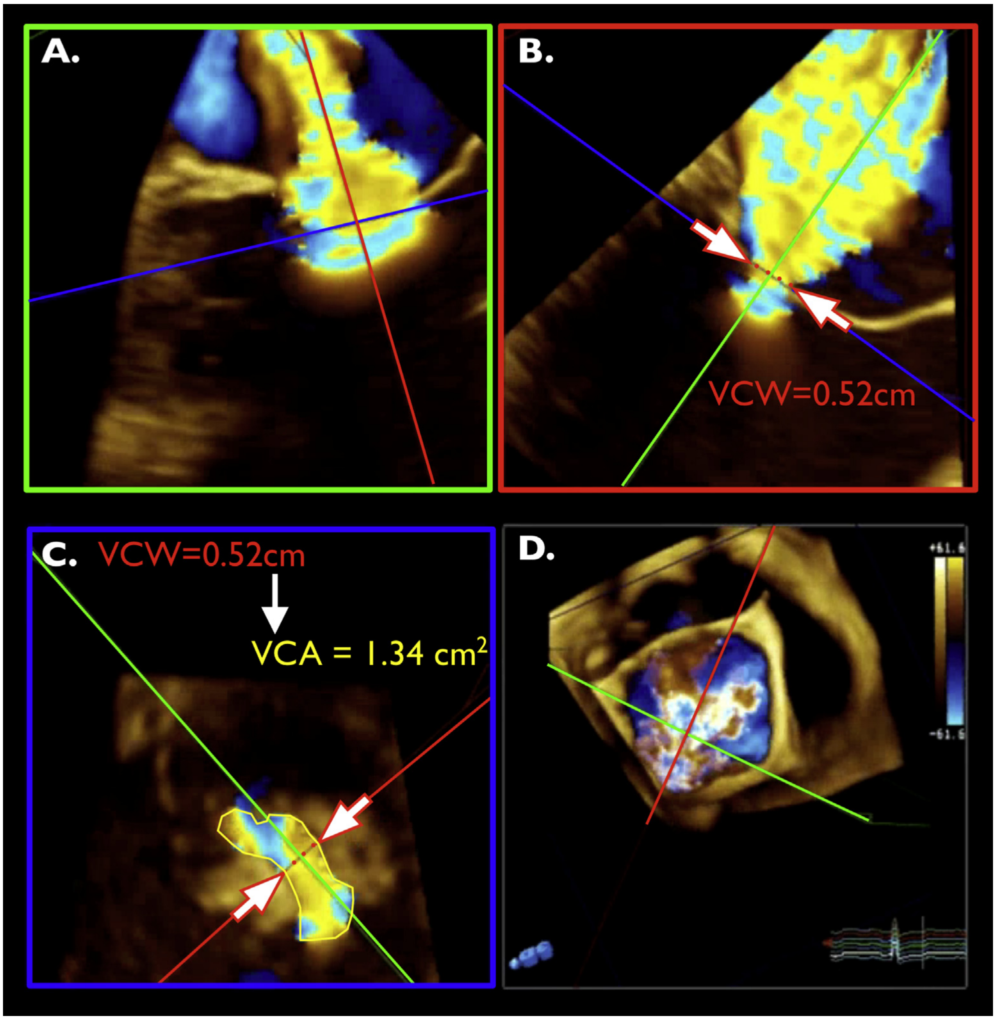

Figure 8 3D TEE multiplanar reconstruction planes in orthogonal orientation to the mitral regurgitant jet with color flow Doppler in a patient with severe functional MR. **(A)** The 3D volume has been cropped along a plane aligned with the width of the jet and is represented by the *green line* in the other views **(B)** The 3D volume has been sliced along a plane similar to a rotated 2D LAX view represented by the *red line* in the other views. **(C)** The 3D volume has been sliced along a plane aligned with the jet VC. The VC area (VCA) can be measured by tracing the jet area in this plane. Note that the VC width (VCW) of 0.52 cm (*white arrows*) would be consistent with moderate MR and significantly underrepresents the severity of the MR. As a surrogate for effective regurgitant orifice area, this patient's VCA (1.34 cm^2) would classify the degree of MR significantly above the cutoff for severe MR. **(D)** A 3D view of the MV and the MR jet. The corresponding planes are represented by the *green and red lines*.

live 3D imaging will allow for continuous visualization of the SGC and its relationship other structures. The dilator is subsequently withdrawn, and TEE is used to confirm distance of the SGC across the septum and the guide wire is then withdrawn (Figure 15).

Insertion of the CDS. Key Point: Wide-sector full-volume view of the LA will allow visualization of the CDS to avoid injury to left atrial wall or left atrial appendage.

The CDS is advanced within the SGC under fluoroscopic guidance. Under continuous TEE guidance the CDS is advanced beyond the SGC into the LA. Wide-sector full-volume live 3D TEE or 2D TEE with careful adjustment of the scan plane angle to elongate the CDS to avoid foreshortening is performed to avoid LA injury.[20,46] In patients with a small LA or if the tip of the CDS makes contact with cardiac structures, the entire system may need to be withdrawn to avoid perforation (Figure 15).

Positioning the Clip above the Grasping Area. Key Point: The 3D TEE en face view of the MV will allow for orientation of the clip graspers in an orthogonal orientation to the line of coaptation.

The CDS is gradually deflected medially until it is directed towards the MV. The SGC can be rotated to move the CDS anteriorly or posteriorly or advanced or withdrawn to move laterally or medially along the valve, respectively, until it is above the target grasping area. Ideally, this is monitored using live 3D TEE guidance using an en face view of the MV. Alternatively, either with individual views or with simultaneous orthogonal biplane, 2D TEE ME commissural view will allow for alignment in a medial and lateral orientation, while the ME-LAX view will allow for visual alignment in the anterior and posterior orientation. A live narrow-sector 3D TEE image can be used to confirm that the 2D TEE imaging plane is aligned with the intercommissural line. The position can be further confirmed using CFD to demonstrate the origin of MR jet at the

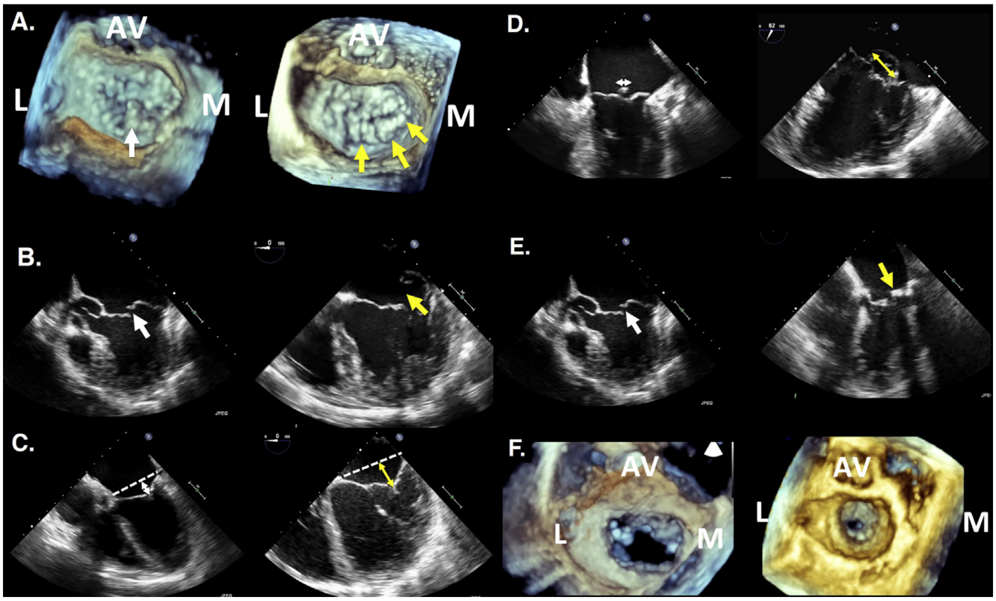

Figure 9 **(A)** 3D TEE en face views of the MV showing an ideal E-EC pathology in the central A2/P2 region (*white arrow*) and a challenging broad-based pathology, extending from the central A2/P2 region including the A3/P3 scallops and the medial commissure (*yellow arrows*). **(B)** 2D TEE four-chamber views demonstrating an optimal posterior flail with a small (<10 mm) flail gap (*white arrow*) and a more challenging large (>10 mm) flail gap (*yellow arrow*). **(C)** 2D TEE four-chamber views demonstrating an ideal (<11 mm) tenting height (*white double arrow*) and a more challenging (>11 mm) tenting height (*yellow double arrow*). **(D)** 2D TEE commissural views demonstrating an ideal (<15 mm) narrow flail width (*white double arrow*) and a more challenging broad (>15 mm) flail segment, often necessitating multiple clips (*yellow double arrow*). **(E)** 2D TEE four-chamber views demonstrating the ideal lack of calcium in the leaflet grasping area (*white arrow*) and unfavorable leaflet calcification in the grasping area and decreased leaflet mobility (*yellow arrow*). **(F)** 3D TEE en face views of the MV showing an ideal (MVA > 4 cm^2) morphology for E-EC and a stenotic MV (<3 cm^2 or mean gradient > 5 mm Hg), which would contraindicate E-EC placement (*yellow arrow*). *AV*, Aortic valve; *L*, lateral; *M*, medial.

desired location. Simultaneous orthogonal imaging (ME commissural and ME-LAX views) in 2D TEE and CFD will expedite positioning.

At this point, the clip arms are opened and positioned perpendicularly to the line of coaptation. Visualization of MV in 3D en face view will allow for visualization of the clip arms in relation to the line of coaptation and may shorten procedural times and obviate the need for transgastric views for clip alignment (Figure 16).[30,46,47] Alignment of the clip with 2D TEE requires transition between the ME commissural and ME-LAX views (or simultaneous orthogonal visualization using a matrix array probe). In the ME commissural view, no clip arms should be seen, and in the ME-LAX view the entire length of both clip arms should be visualized. If clip arms are visualized in the commissural view or the clip arms appear foreshortened in the LAX view, the clip should be rotated. The scan plane angle in both the ME commissural and ME-LAX views would need to be reduced or increased for patients with medial or lateral pathology, respectively (Figure 16).[26,46]

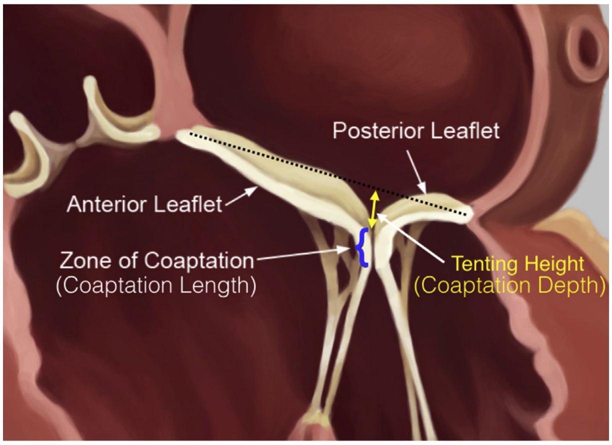

Figure 10 In secondary mitral regurgitation, the leaflets are apically displaced via traction from the subvalvular apparatus, and the tenting height (ideally <11 mm) is defined as the distance from the point of coaptation to the annular plane (*yellow arrow*). Coaptation length (ideally >2 mm) is defined as the length of residual leaflet below the point of coaptation (*blue bracket*).

Advancing the Clip into the LV. Key Point: The clip may deviate and rotate during advancement into the ventricle. Reducing the 3D gain will facilitate visualization of the clip arms below the leaflets.

After the clip is positioned above the desired grasping area, the CDS is advanced into the LV under fluoroscopic and TEE guidance (3D TEE en face view or simultaneous orthogonal 2D TEE views). It is possible for the clip to deviate and rotate during advancement into the LV, and appropriate clip positioning and alignment should be confirmed as described above. In the 3D TEE en face view, the clip arms may not be visualized below the leaflets in the LV without reducing the gain sufficiently to cause leaflet dropout (Figure 17). Significant adjustment in the LV should be avoided, particularly when outside of the central aspect of the valve as damage to or entrapment within the subvalvular apparatus may occur. If necessary, the clip arms can be inverted and the CDS withdrawn into the LA for repositioning.

Table 2 Morphological suitability criteria for the MitraClip intervention based on expansion of EVEREST criteria

Optimal morphology	Challenging morphology	Unsuitable morphology
Central A2/P2	Peripheral A1/P1 or A3/P3	Cleft or perforation
No calcification	Calcification present but not in grasping zone	Calcification in grasping zone
MVA > 4 cm^2	MVA > 3 cm^2	MVA < 3 cm^2 or MG > 5 mm Hg
Posterior leaflet > 10 mm	Posterior leaflet 7-10 mm	Posterior leaflet < 7 mm
Tenting height < 11 mm Coaptation reserve > 2 mm	Tenting height ≥ 11 mm	
Normal leaflets and mobility	Carpentier IIIB	Carpentier IIIA
Flail gap < 10 mm flail width < 15 mm	Flail width > 15 mm (with sufficient valve area to tolerate multiple clips)	Multiple segments, Barlows

MG, Mean gradient.
Optimal morphology is well suited for implantation and initial institutional experience. Challenging morphology should be preferably treated in experienced centers. Unsuitable morphology would not be suited to E-EC placement, and evidence of mitral stenosis (MVA < 3 cm^2 or MG > 5 mm Hg) would be considered a contraindication. Reproduced with permission from *Clinical Research in Cardiology*.[25]

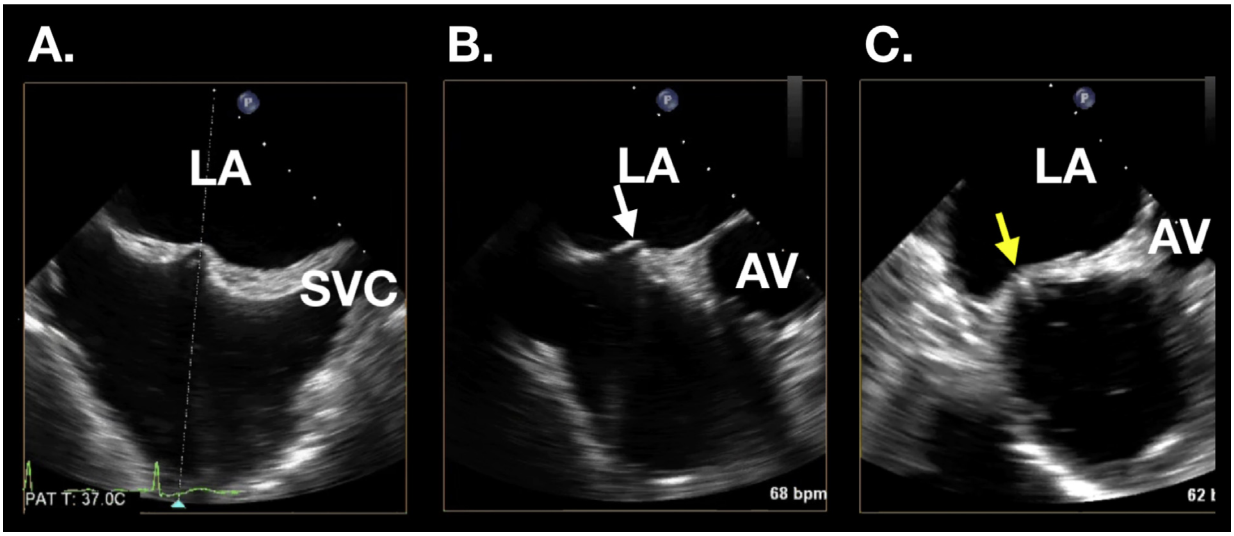

Figure 11 **(A)** 2D TEE bicaval view of the IAS in a superior inferior orientation. **(B)** 2D TEE aortic SAX view with the transseptal needle tenting the IAS more anterior than ideal (*white arrow*). **(C)** 2D TEE aortic SAX view after clockwise rotation of the transseptal needle. The needle is now tenting the IAS more appropriately posteriorly away from the anterior aortic valve (*yellow arrow*). *AV*, Aortic valve; *SVC*, superior vena cava.

Leaflet Grasping. Key Point: Extended loop capture will facilitate subsequent review of the adequacy of leaflet grasping.

Once appropriately positioned in the LV, the CDS is withdrawn slightly until the leaflets are resting on the clip arms. Simultaneous orthogonal biplane or 2D TEE imaging in ME-LAX view is performed to demonstrate the leaflets, clip arms, and grippers. The imaging sector should be reduced in order to optimize spatial and temporal resolution. A longer loop should be acquired as the grippers are lowered and the clip arms are partially closed. This will allow for review of the leaflet grasping (Figure 18) to ensure adequate leaflet length is within the clip, ideally >4 mm (<2 mm may increase the risk of clip detachment).[36,46] Of note, the last time that the leaflet tips can be well visualized is before the grippers come down and the clip arms are closed. The MitraClip NT grippers are able to descend fully onto the clip arms, and this may facilitate leaflet capture in patients with larger flail or coaptation gaps. The clip is then interrogated under 2D TEE and CFD in both commissural and LAX views or biplane to ensure that the clip grasped in the desired location. In the ME-LAX view, the leaflets should be visualized draped over the partially closed clip arms and typically already show decreased mobility if adequately grasped (Figure 18D). Following or during CFD TEE assessment, the clip is fully closed (Figure 18E).

Leaflet capture can be challenging in patients with a significant coaptation defect, for example, in patients with a large flail gap or in functional MR when the posterior leaflet is tethered to a greater degree than the anterior leaflet resulting in a large coaptation gap. Different maneuvers have been described to facilitate leaflet grasping, such as the Valsalva maneuver, rapid ventricular pacing, administration of adenosine, increased positive end-expiratory pressure, reduced tidal volumes, pausing ventilation, and placement of the pigtail catheter under the posterior leaflet.[48-51] Finally, the "zip and clip" technique can be used to reduce the coaptation defect width by placing a first clip lateral or medial to the largest coaptation

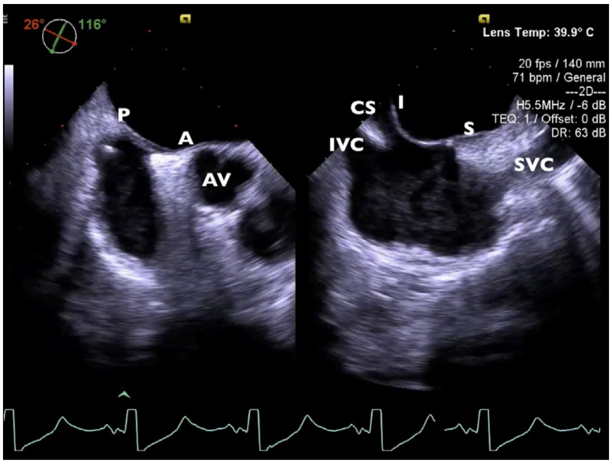

Figure 12 2D TEE Simultaneous orthogonal imaging of the IAS simultaneously displaying the superior, inferior, anterior, and posterior rims of the IAS. *A*, Anterior; *AV*, aortic valve; *CS*, coronary sinus; *I*, inferior; *IVC*, inferior vena cava; *P*, posterior; *S*, superior; *SVC*, superior vena cava.

defect to reduce the coaptation width in the area more challenging to grasp.[48,52] A second or even third clip can then be placed under more favorable grasping conditions as long as the mean mitral diastolic gradient is not significantly elevated (Figure 18).

Pre- and Postdeployment Comprehensive MV Assessment. Key Points: This assessment is based on exclusion of significant residual MR and stenosis. Cumulative vena contractor areas will allow for assessment of multiple jets. Loading conditions and gain settings should be the same as at baseline assessment. Subsequent mean transmitral gradient should be less than 5 mm Hg.

The assessment of MR severity using 2D and 3D TEE CFD should be performed during a period of hemodynamic stability and prior to clip release preferentially using quantitative assessment of MR per the current guidelines[11] (Figure 19). The CDS should be adjusted to reduce traction on the deployed clip, possibly impacting the assessment of the residual MR. Due to significant change in the valve geometry, multiple MR jets, and imaging artifacts, quantitative methods for severity assessment may be challenging and inaccurate and have not been validated in this setting.[20,53,54] Automated volumetrically derived continuous comparison of transaortic and transmitral stroke volume was described as a means to improve accuracy and may have utility in this patient population.[55,56] VC area derived from addition of multiple areas allows for a quantitative assessment of residual MR in the setting of multiple regurgitant jets.[11,32,57] It is important to ensure that periprocedural hemodynamic conditions and instrument settings are similar to preprocedural imaging to avoid inaccurate quantification of any residual MR.[20,46] An additional parameter to aid in the qualitative evaluation of residual MR is pulsed-wave Doppler of pulmonary vein flows. Interval improvement postdeployment of an E-EC is reassuring, however, residual MR should be assessed by quantitative measures where feasible.

Focus should then be shifted to assessment of the transmitral gradients and areas (Figure 19). The diastolic mean gradients should be measured though the residual orifice(s). Although the area and peak velocities may differ between the orifices, the mean gradients should be similar.[58] Ideally, the mean pressure gradient drop should be <5 mm Hg as mean gradients above 5 mm Hg have been shown to be associated with decreased survival.[59] Gradients should be interpreted with caution, taking into account the planimetered MVA, the patient's functional status, and the contribution from the residual MR.[46,59] Cumulative planimetry of the residual orifice(s) using multiplanar reformatting (Figure 19) at the leaflet tips will allow for quantification of the residual MVA. The 2D transgastric basal SAX view may used as an alternative, however, given that the nonplanar orientation of the double orifice 2D planimetry may lead to overestimation of the MVA.[57] MVA greater than 2 cm^2 is considered ideal, whereas areas <1.5 cm^2 may result in clinically significant stenosis. Calculation of MVA via pressure half time is not recommended as it is influenced by loading conditions and chamber compliance. Lastly, a decision needs to be made based on both the residual MR and the MVA as to whether the clip should be adjusted or released with subsequent additional clip placement if residual MR is present.

Spontaneous echo contrast may appear following a clip placement in patients without significant mitral stenosis.[60] While this can be best explained with the reduction of the "washing effects" of the MR jet, the significance of spontaneous echo contrast needs further evaluation as a potential a risk factor for thrombus formation or stroke. Currently, there are no established anticoagulation guidelines for E-EC patients.

Clip Release. Key Point: The degree of residual MR may change post-clip release. Residual MR impacts long-term survival; multiple clips may be required.

Once the clip location, reduction in MR, and residual MVA are considered satisfactory, the clip is released. The CDS holds the clip in a relatively fixed position prior to release, and as a result the MV must be reassessed for any increase in MR, in the same manner as described above, postrelease. Recent evidence suggests that the grade of residual MR is a predictor of long-term survival and that placement of two clips may have superior durability as compared with a single clip.[61-63] The decision to deploy additional clips is based on the severity of residual MR and likelihood of stenosis with further reduction in valve area and its impact on outcome.[59] Additional clips may be positioned but not released and assessed as described above and subsequently removed should an elevated gradient be noted.

COMPLICATIONS

E-EC is an effective and safe procedure with an acceptably low incidence of procedural complications. Potential complications include death (1%-2.2%), cardiac tamponade (0.7%-1.9%), urgent cardiac surgery (2%), stroke (0-1%), bleeding requiring transfusion (7.4%-13%), vascular injury (1.4%), partial leaflet detachment (2%), clip embolization (0.5%), and gastrointestinal injury (1%).[15,28,64] TEE is a vital monitoring tool for both procedural guidance and early detection of intraprocedural complications (Table 3). It is imperative for baseline TEE to note the presence and size of any baseline effusion, and periodic monitoring throughout the procedure should be performed to assess for any interval change in order to diagnose perforation promptly. Following removal of the SGC, TEE can be used to assess the iatrogenic septal defect (iASD). The majority of

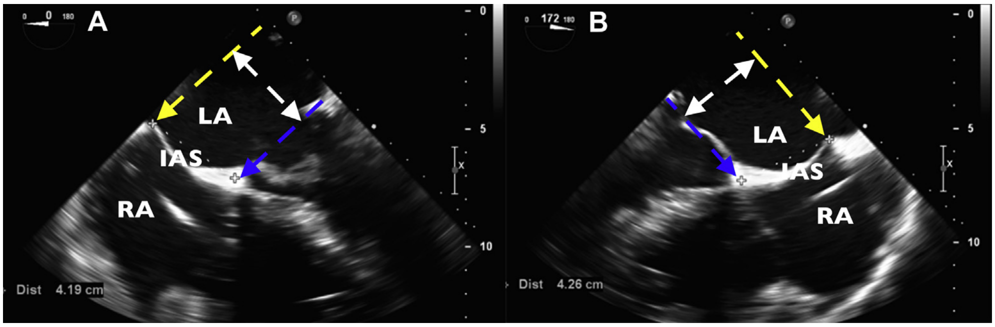

Figure 13 **(A)** 2D TEE four-chamber (0°-20°) view and **(B)** 2D TEE inverted four-chamber (150°-170°) view measuring the transseptal puncture height. The transseptal puncture height (*white double arrow*) is measured from the septal tenting plane (*yellow double arrow*) to the annular plane (*blue double arrow*) or point of leaflet coaptation if there is significant tethering of the leaflets below the annular plane. *RA*, Right atrium.

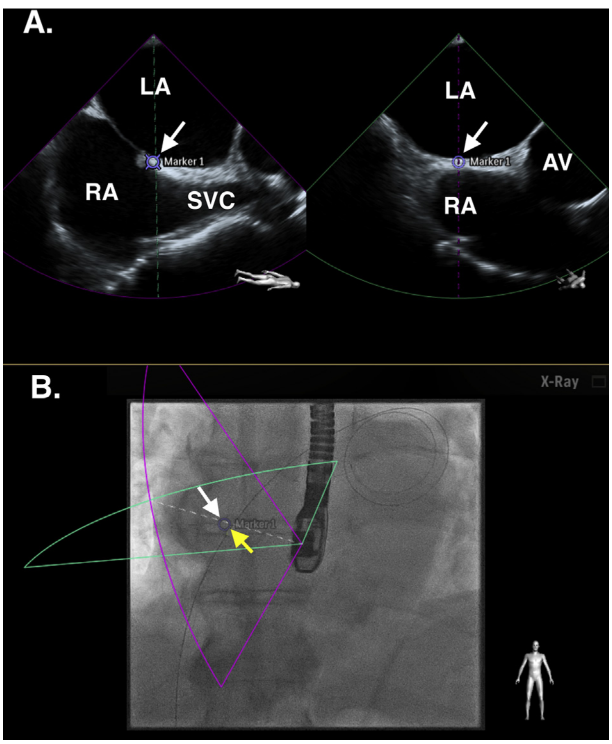

Figure 14 **(A)** Orthogonal 2D TEE views of the IAS. A marker (*white arrow*) is placed on the IAS at the desired point of crossing. **(B)** The TEE probe is coregistered with fluoroscopy, and the marker (*white arrow*) is superimposed on the fluoroscopic image. The guide wire (*yellow arrow*) over which the SGC and its dilator is advanced is seen traversing the septum in close proximity of the location of marker. *AV*, Aortic valve; *RA*, right atrium; *SVC*, superior vena cava.

these defects resolve with time,[65] however, persistence of an iASD was shown to be associated with worse functional outcomes and increased mortality.[66] Whether this is a reflection of persistent elevated left atrial pressures or a direct consequence of the iASD has yet to be determined. Closure of the iASD is only recommended if hypoxia is present in the setting of significant right to left shunt. Further studies are needed to identify which patients may benefit from prophylactic iASD closure.[65]

How Far to Push: TEE for E-EC outside A2/P2

Ever since the safety, feasibility, and efficacy of E-EC were demonstrated for patients with 3 to 4+ MR and optimal MV morphological features,[14,67] there has been growing evidence that even patients that fall outside of the echocardiographic inclusion criteria for the EVEREST trials can be safely and successfully treated with the E-EC (Table 2).[38,68] Taking into account the increased procedural complexity and challenges for patients with pathology outside of the EVEREST criteria, it is the opinion of the authors that such cases only be attempted at experienced centers and in the absence of any therapeutic alternatives.

MV Prolapse of A1/P1 or A3/P3 ± Flail Segment and Commissural Regurgitation

The deployment of the E-EC is more challenging in Carpentier's classification segments 1 and 3, especially when dealing with large prolapsing leaflets and flail segments.[7,24] This is largely due to increased risk of entanglement of the device in the more complex commissural chordal apparatus and difficulty in optimal orientation of the device clip arms. Therefore, important practical issues should be considered with respect to the treatment of noncentral degenerative MR. First, a thorough 3D-TEE assessment of the prolapsing and flail elements and the entire MV apparatus before the procedure is key for successful planning of the percutaneous approach.[69] Second, in noncentral pathology (either lateral A1/P1 or medial A3/P3), periprocedural 3D TEE is essential to optimize the orientation of the clip (Figure 20).[26] During grasping, 2D imaging will often have to rely on either simultaneous orthogonal plane or off-angle multiplane imaging for leaflet grasping. Even in noncentral pathology, the clip has to be positioned perpendicular to the line of coaptation of the MV leaflets and ideally in the center of the regurgitant orifice and MR jet. Since the line of coaptation curves toward the commissures, the ME commissural and ME-LAX no longer remain orthogonal at this location. The probe and scan plane orientation need to be changed. This will result in the addition of approximately 10°-40° to the original LAX grasping view for A1/P1 pathologies or in the subtraction of about 10°-40° for pathologies in the A3/P3 segment. Alternatively, the multiplane angle of the initial ME commissural view can be corrected by either subtracting 10°-40° for A1/P1 pathologies or adding 10°-40° for a prolapse in the A3/P3 segment. This will permit a perpendicular LAX view as the 90° angle between the biplane angles is maintained. Third, procedural changes must be

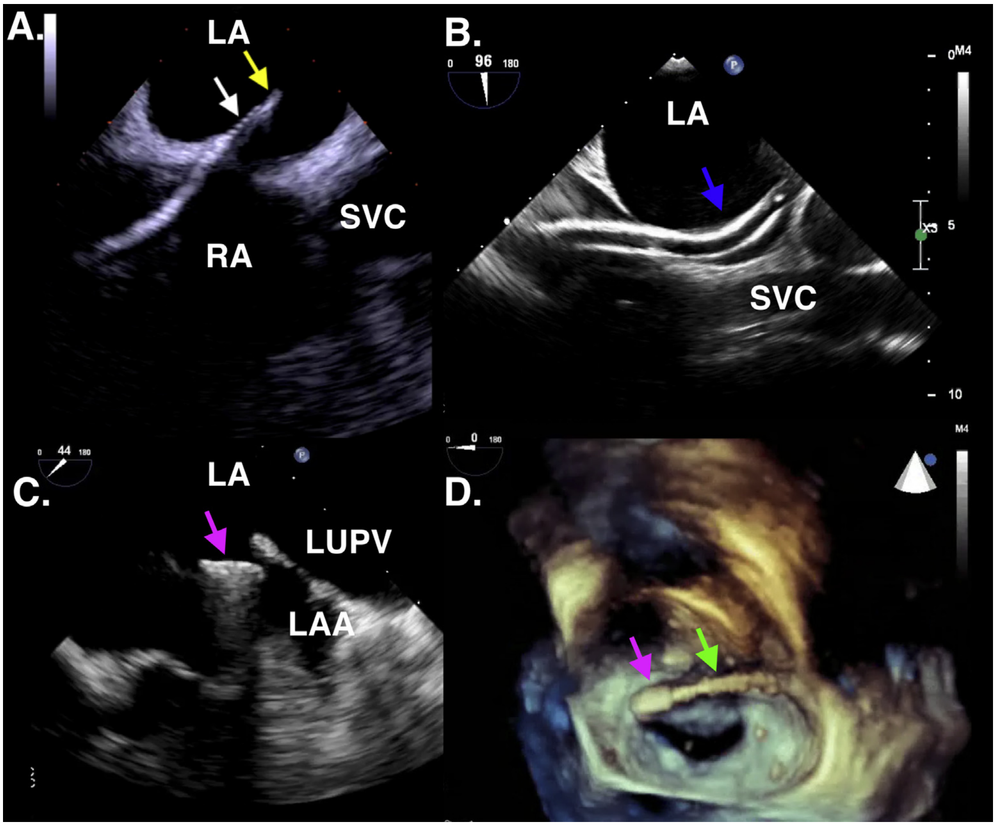

Figure 15 **(A)** 2D TEE bicaval view of the SGC and its associated grooved dilator (*white arrow*) being advanced over the guide wire (*yellow arrow*) into the LA. **(B)** 2D TEE bicaval view of the SGC (*blue arrow*) across the IAS. Following removal of the dilator, the distance across the septum can be measured. **(C)** 2D TEE left atrial appendage view. The clip (*magenta arrow*) can be seen below the Coumadin ridge in close proximity to the left atrial appendage. **(D)** 3D En face view of the MV clip delivery system (*green arrow*) and the attached clip (*magenta arrow*). The clip's relationship to anatomical structures is clearly seen. The entire system has been withdrawn to avoid injury to the atrial appendage. Constant echocardiographic surveillance will minimize the chance of iatrogenic injury. *LAA*, Left atrial appendage; *LUOV*, left upper pulmonary vein; *RA*, right atrium; *SVC*, superior vena cava. (See associated Video 5, available at www.onlinejase.com.)

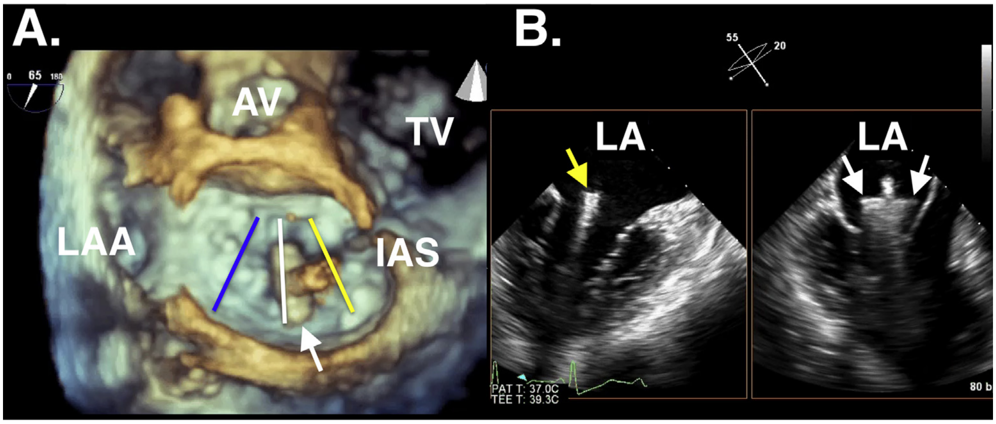

Figure 16 **(A)** 3D TEE en face view of the MV. The clip (*white arrow*) should be aligned above the target grasping area and clip arms aligned perpendicular to the line of coaptation as reflected by the colored lines. Note that the clip should be rotated a few degrees clockwise to be perpendicular with the line of coaptation. **(B)** 2D TEE simultaneous orthogonal ME commissural and ME-LAX can be used to guide positioning. For central pathology (*white line*), the full length of the clip arms (*white arrows*) are seen in the LAX view, and in the midcommissural view, no clip arms (*yellow arrow*) should be seen. The multiplane angle in both the ME commissural and ME-LAX views would need to be decreased or increased for patients with medial (*yellow line*) or lateral (*blue line*) pathology, respectively. *AV*, Aortic valve; *LAA*, left atrial appendage; *TV*, tricuspid valve. (See associated Video 6, available at www.onlinejase.com.)

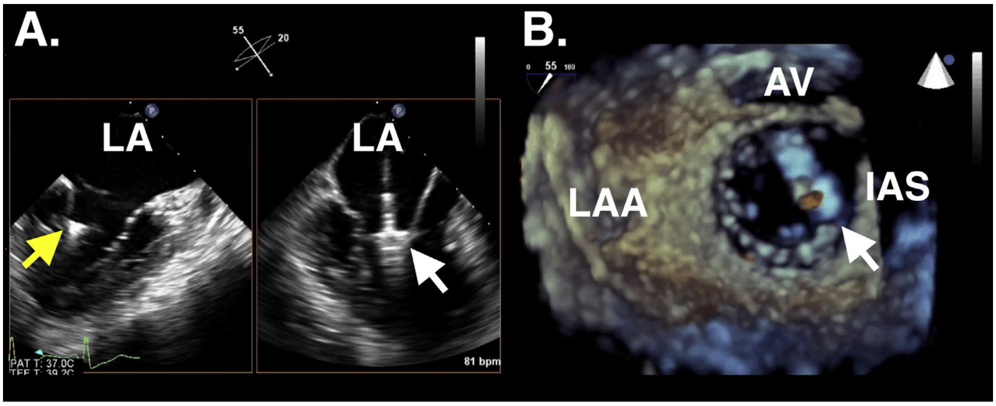

Figure 17 **(A)** 2D TEE simultaneous orthogonal midcommissural and LAX views. The clip has migrated medially on advancement into the LV and is in close proximity with the posteromedial papillary muscle (*yellow arrow*) and risks entanglement within the chordae. In the LAX view, the clip arms (*white arrow*) appear fore shortened, indicating the clip is slightly off axis. **(B)** 3D TEE en face view of the MV with the gain settings reduced to cause leaflet dropout to allow visualization of the clip beneath the MV leaflets in the ventricle. Note, the clip (*white arrow*) has deviated medially and rotated; adjustment within the ventricle could potentially cause injury to the chordae. *AV*, Aortic valve; *LAA*, left atrial appendage. (See associated Video 7, available at www.onlinejase.com.)

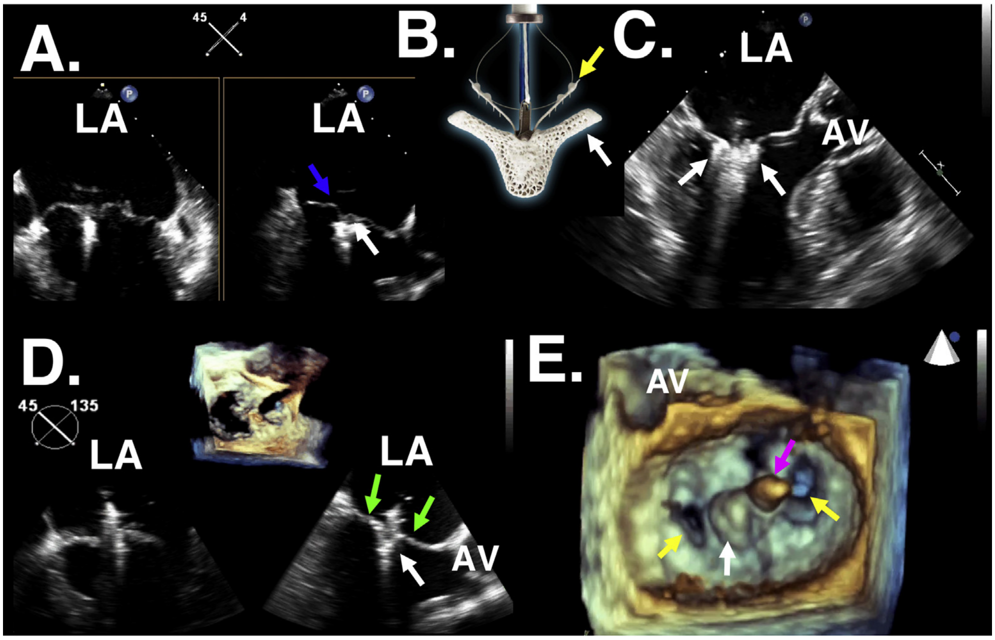

Figure 18 **(A)** 2D TEE orthogonal commissural and LAX views of the MV after dropping the grippers. The anterior leaflet is resting on the clip held by the gripper (*white arrow*), and the posterior leaflet is seen rising above the clip arm and is not grasped by the gripper (*blue arrow*). **(B)** Image of the E-EC showing clip arm (*white arrow*) and gripper (*yellow arrow*). **(C)** 2D LAX view of the MV following regrasping of the leaflets and partial clip closure. Both leaflets are now within the clip arms (*white arrows*), and the leaflet shows decreased mobility. **(D)** 3D TEE en face view of the MV and the associated 2D orthogonal views following complete closure of the clip (*white arrow*). The leaflets are under increased tension and show further decreased mobility (*green arrows*). **(E)** 3D TEE en face view of the MV showing the "zip and clip" technique whereby placement of the first clip (*white arrow*) allowed for leaflet grasping by the second clip (*magenta arrow*) resulting in a double orifice valve (*yellow arrows*). *AV*, Aortic valve. (See associated Video 8, available at www.onlinejase.com.)

considered with regard to the height and position of the transseptal puncture (lower for A1/P1 and higher for A3/P3) and guide catheter positioning above the grasping area as described above. In addition, the first grasp may have to occur close to the largest leaflet gap to approximate the free edges to the MV before a second device can be brought in to effectively reduce MR. Finally, the safe and successful treatment of noncentral MR depends on the experience of both the implanter and the interventional echocardiographer. Undoubtedly, there is a significant learning curve effect and an ability to accept more challenging valve anatomy with growing experience.[68]

Presence of Mitral Annular Calcification (MAC) ± MV Leaflet Calcification

MAC is a degenerative process affecting the fibrous annulus of the MV and is often associated with MR.[70] MAC is routinely identified

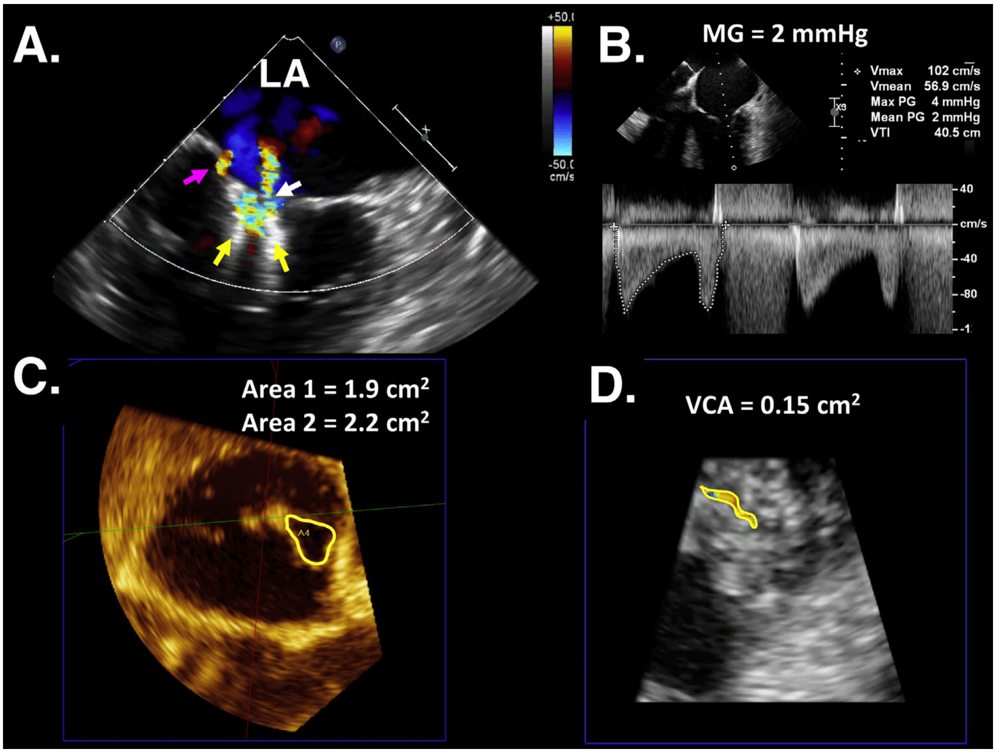

Figure 19 **(A)** 2D TEE color flow Doppler of commissural view postdeployment of two clips (*yellow arrows*) showing a trivial medial jet (*magenta arrow*) and a mild jet (*white arrow*) between the two clips. **(B)** Mean transvalvular gradients can be measured in either orifice, and gradients > 5 mm Hg may result in suboptimal clinical outcomes. **(C)** Using multiplanar reformatting, planimetry of each residual orifice will allow for calculation of cumulative MVA. Each orifice should be measured in separate planes as they are not in the same plane. **(D)** Planimetry of the SAX of the residual regurgitant jet will allow for measurement of VC area (VCA). *MG*, Mean gradient.

by echocardiography, and a number of echocardiographic scoring systems that classify the severity of MAC have been developed.[71,72] Based on the EVEREST trials, moderate to severe MAC and MV leaflet calcification in the grasping zone were considered exclusion criteria. This was due to a number of reasons including the difficulty in grasping nonpliable, thick leaflets and the increased risk of introducing unacceptable inflow gradients in patients with suboptimal MV opening areas (<3-4 cm^2) at baseline. However, a recent study by Cheng *et al.* suggest that the E-EC therapy is safe and feasible and results in comparable midterm durability in the treatment of MR in patients with significant MAC but without severe leaflet calcification or thickening.[73] In that study, patients with moderate or severe MAC had demonstrable improvements in clinical symptoms and decreased left ventricular dimensions.

E-EC Therapy in Patients with Failed Surgical MV Annuloplasty Repair

Although the feasibility of transcatheter MV implantation after failed surgical ring annuloplasty has already been reported, there is limited evidence about the feasibility and efficacy of percutaneous repair with the E-EC. Grasso *et al.* reported their initial experience with the E-EC in six patients with failed surgical MV repair (annuloplasty).[74] Although preliminary in nature, these authors were able to demonstrate the safety and efficacy of the percutaneous repair with E-EC in patients with surgical MV annuloplasty failure. Patients with prior surgical annuloplasty routinely have reduced MVAs due to the previously implanted annuloplasty ring. As a result, caution is required to avoid a secondary increase in the diastolic inflow gradients, especially when more than one clip has to be implanted to effectively reduce MR. Other challenges include the potential entanglement of the clip with artificial or native chords during the approach to and through the valve (Figure 21) and the shadowing effect of the annuloplasty ring, which results in poor visibility of the posterior MV leaflet, especially when assessing the adequacy of posterior leaflet insertion during grasping. Although transgastric views or 3D TEE may at times be helpful, intracardiac echocardiography has been used adjunctively to improve procedural success.[75]

Systolic Anterior Motion (SAM)

Recently, the off label use of the E-EC was described in patients with SAM associated with hypertrophic obstructive cardiomyopathy (HOCM).[76] The goals of intervention include a reduction of the gradient across the left ventricular outflow tract (LVOT) and a reduction of MR, which is frequently associated with SAM. Provided that the LVOT obstruction is predominantly due to SAM-induced anatomical narrowing of the LVOT and not due to profound HOCM causing the majority of the LVOT obstruction, preventing SAM in these patients is likely to result in a mechanical improvement. However, HOCM is often accompanied by abnormalities of the MV and the subvalvular apparatus (abnormal position of the papillary muscles, elongation, and pathological thickening of the MV).[77] During procedural planning, these HOCM-associated features need to be screened

Table 3 Potential complications of the MitraClip procedure

Complication	Etiology	Detectible by TEE	Prevention	Treatment
Pericardial effusion or tamponade	Cardiac perforation during transseptal puncture, or advancement of guidewire, dilator, or CDS	Yes	Appropriate location for transseptal puncture. Continuous TEE monitoring during guidewire, dilator or CDS advancement.	Pericardial drainage
Thrombus formation	Presence of foreign material	Yes	Prompt anticoagulation following transseptal puncture and maintenance of appropriate ACT (250-300 s)	Administration of additional anticoagulation.
Partial clip detachment (complete detachment is rare)	Insufficient leaflet grasping, clip malposition, or device malfunction	Yes	Appropriate clip positioning, TEE assessment of adequate leaflet insertion and grasping	Additional clip placement in close approximation of the partially detached clip, to address the MR and stabilize the clip. (For complete detachment, percutaneous or open surgical retrieval.)
Entrapment of MitraClip in chordae tendineae or chordal injury	Inappropriate movement of the clip within the LV, most common when the clip is moved outside the central aspect of the valve	Yes	Appropriate positioning and clip arm orientation under TEE guidance within the LA. Once in LV, if significant repositioning or movement is required, clip eversion and withdrawal back into LA.	Clip arm eversion and withdrawal into the LA. In circumstance, of chordal entrapment, advancement of CDS further into the LV, below the level of the papillary muscle before closure and subsequent withdrawal may be attempted
IASD	Transseptal puncture and dilatation by the SGC	Yes	Avoid need for repeat transseptal puncture by optimizing position of first septal puncture.	Most resolve spontaneously and require no intervention. In the presence of hypoxia due to right to left shunting closure should be considered.
Major bleeding and vascular injury	Large bore catheter	Often late, TEE or TTE may detect signs of hypovolemia	Placement of vascular closure device. Appropriate management post-sheath removal.	Supportive, vascular injury may require intervention.
Gastrointestinal injury	Prolonged TEE examination	No (may note blood on TEE probe after withdrawal)	Appropriate application of lubricant. Minimize extensive or excessive probe manipulation.	Upper endoscopy. May require surgical intervention.

ACT, Activated clotting time; *IASD*, iatrogenic atrial septal defect.

for echocardiographically as they may not impact only the procedural approach but also the effective mitral orifice area after E-EC implantation.

Other Challenging Pathologies

Additional challenging pathologies include patients with end-stage heart failure in whom the E-EC might be considered as a last resort,[78] patients with mitral clefts or cleft-like deep indentations,[79] or teenage patients with no alternative treatment options.[80]

POSTPROCEDURAL IMAGING AND FOLLOW-UP

Postprocedural TTE should include a complete qualitative and quantitative examination of the MV per current guidelines,[11,22] with particular focus on residual MR if present and transvalvular gradients. The location of residual MR, identification of multiple jets, and quantification of severity will guide in assessment of therapeutic stability and the potential need for further intervention. The 2D PLAX and SAX views of the MV should allow for assessment of the

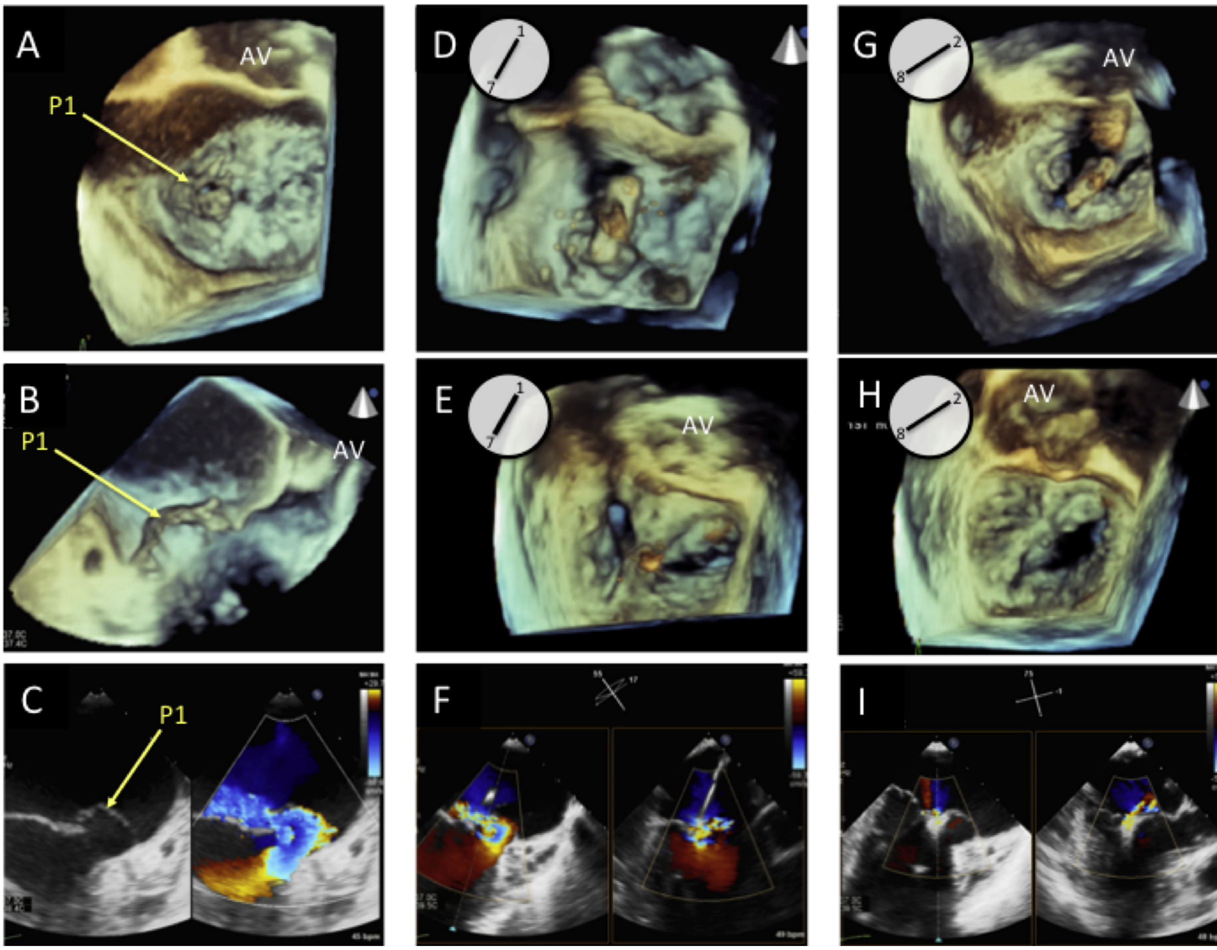

Figure 20 Intraprocedural 3D-TEE is essential to optimize the orientation of the E-EC in noncentral MV pathology. This figure illustrates how a severe P1 prolapse with flail can only be successfully treated with an appropriate orientation of the E-EC. Panels **A**, **B** (3D image cropped from medial), and **C** (biplane color Doppler) illustrate the underlying pathology in 3D and 2D with color Doppler. Note the P1 prolapse with flail close to the anterolateral commissure (*yellow arrow*) resulting in a very large commissural color jet **(C)**. Panels **D**, **E**, and **F** demonstrate that a clip orientation in the 1-7 o'clock position was not sufficient to capture the large prolapse. The 2D biplane color in panel F illustrates a severe remaining commissural MR jet. Thus, the clip was rotated to mimic a 2-8 o'clock position (**G**, **H**, and **I**). Now the P1 prolapse is successfully captured, and the remaining MR is significantly reduced.

clip, the MV scallops, and any associated MR. For central (A2/P2) clips, the 2D PLAX view should allow for visualization of leaflet insertion within the clip. For medial (A3/P3) and lateral (A1/P1) clips, the probe will need to be tilted towards the tricuspid valve and aortic valves, respectively. Significant mobility of the clip should prompt further interrogation to rule out the possibility of leaflet detachment. The 2D apical four-chamber, commissural, three-chamber, and five-chamber views allow for further 2D evaluation and will facilitate Doppler interrogation of both residual MR and transvalvular gradients. The limitations of proximal isovelocity surface area, as well as the frequent eccentricity and presence of multiple jets can make echocardiographic quantification of residual MR post E-EC challenging.[11,53] Regurgitant volume can be calculated by subtracting the LVOT stroke volume from the inflow stroke volume at the mitral annulus, however, there are limitations to this method, for example, in the setting of aortic regurgitation.[11,53] Three-dimensional CFD echocardiography can also be used to measure the VC area of each regurgitant jet.[32] An additional method, which requires further investigation and validation, is real-time 3D CFD echocardiography. The simultaneous calculation of transmitral and aortic stroke volumes avoids the geometric assumptions in calculating regurgitant volume.[32,56]

In addition to quantification of any residual MR, transmitral gradients should be measured using pulsed-wave Doppler at each orifice and the MVA calculated as per the current guidelines. The apical four-chamber view and the subcostal four-chamber view will allow for visualization of the IAS while CFD interrogation will allow for detection of a residual iASD.

The presence of moderate or greater residual MR, a mean transvalvular gradient of $>$ 5 mm Hg, and a residual iASD after 6 months are all features associated with worse clinical outcomes.[59,61,62,66] Further studies are needed to assess whether additional interventions will positively impact this population, for example closure, of the iASD.

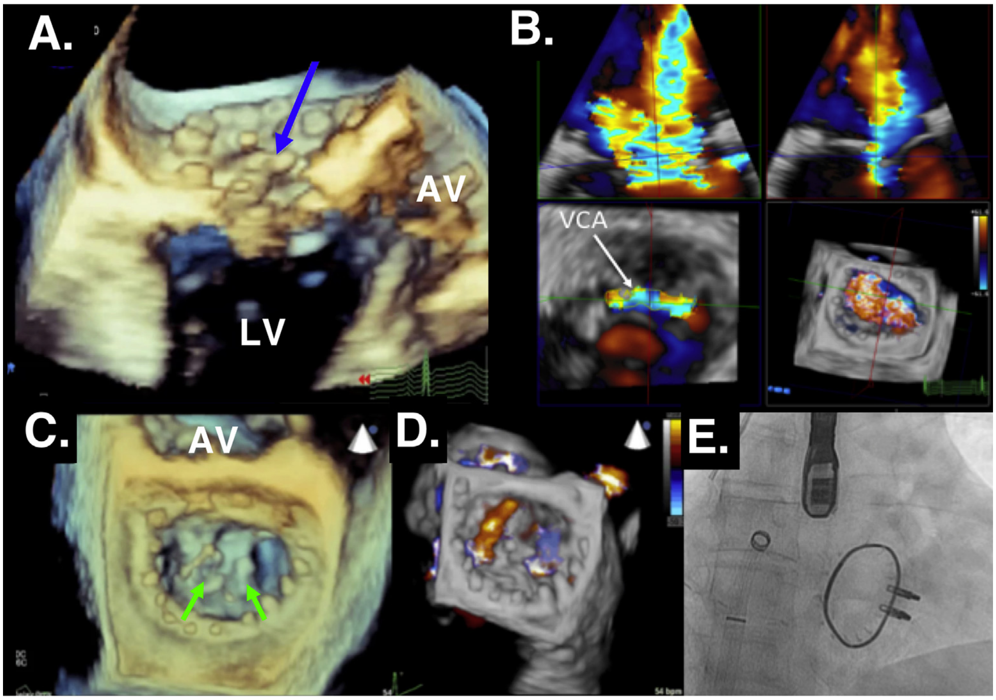

Figure 21 This figure illustrates how the E-EC can be used to reduce MR in patients with failed prior surgical ring annuloplasty. **(A)** In this patient, the posterior MV leaflet is prolapsing along the commissural line and surgically placed neochords (*blue arrow*) can be seen on the atrial side of the leaflet. **(B)** The multiplanar 3D color flow Doppler illustrates the large VC area (VCA). **(C)** Following two centrally placed clips (*green arrows*), the patient is left with the two MV ostia and no more than mild MR **(D)** and an inflow gradient of no more than 3 mm Hg (not shown). **(E)** illustrates the annuloplasty ring and the two clips as seen with fluoroscopy. *AV*, Aortic valve. (See associated Video 9, available at www.onlinejase.com.)

FUTURE PERSPECTIVE

Beyond edge-to-edge leaflet plication, multiple devices using various techniques to address MR are at various stages of development, including direct and indirect transcatheter annuloplasty, chordal replacement, and percutaneous valve replacement.[3,81] These developments in transcatheter MV therapy will offer new opportunities for treatment of MV disease. With improvements in instrument design and operation, percutaneous repair may be offered for more complex lesions with improved results. Advances in real-time coregistration of multiple imaging modalities may make percutaneous MV repair a more precise and efficient procedure.[43-45] Echocardiography both as a screening tool and as a tool for real-time intraprocedural guidance will continue to support the refinement of current technologies and aid the development of novel new devices.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.echo.2018.01.012.

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