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REVIEW

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Role of 3-dimensional transesophageal echocardiography in guiding transcatheter mitral valve replacement

Nadeen N. Faza MD | **Stephen H. Little MD**

Houston Methodist DeBakey Heart and Vascular Center, Houston Methodist Hospital, Houston, Texas

Correspondence
Stephen H. Little, MD, FRCPC, FACC, FASE, John S. Dunn Chair in Clinical Cardiovascular Research and Education, Department of Cardiology, Weill Cornell Medicine, Houston Methodist Hospital, 6550 Fannin Street, SM-1801, Houston 77030, TX.
Email: shlittle@houstonmethodist.org

Abstract

Background: Transcatheter mitral valve replacement technologies have been developed to treat a wide range of mitral valve pathologies including primary and secondary mitral regurgitation, mitral stenosis, in addition to degenerative bioprosthetic valves and failed annuloplasty rings.

Objective: Transesophageal echocardiography, particularly with use of 3-dimensional imaging is key in successfully guiding these interventions. In this review, we highlight the key role of 3D transesophageal echocardiography in guiding TMVR, including valve-in-native valve, valve-in-prosthetic valve, valve-in-prosthetic ring, and valve-in-mitral annular calcification interventions.

KEYWORDS

structural interventions, transcatheter mitral valve replacement

1 | INTRODUCTION

Transcatheter techniques for repair or replacement of the mitral valve have emerged as viable options for patients deemed at high risk for mitral valve surgery.[1–4] As compared to the transcatheter mitral valve repair using edge-to-edge technique, transcatheter mitral valve replacement (TMVR) has been developed for management of a wider range of mitral valve disorders, including primary and secondary mitral regurgitation, mitral stenosis, in addition to degenerative bioprosthetic valves and failed annuloplasty rings.

Due to lack of direct fluoroscopic visualization of the mitral valve during transcatheter procedures, intraprocedural transesophageal echocardiography (TEE) imaging is invaluable in guiding these interventions. Challenging features of the mitral valve anatomy pertaining to transcatheter interventions include its nonplanar annulus, variability in leaflet morphology and mobility, relationship of the leaflets to the subvalvular apparatus, and the valve's proximity to the left ventricular outflow tract (LVOT).[5]

Echocardiography, particularly with 3-dimensional imaging, plays a pivotal role in assessing the etiology and severity of mitral valve disease, assisting in device selection, guiding device deployment, and identifying immediate postprocedural complications. In this review, we highlight the key role of 3D transesophageal echocardiography in guiding TMVR, including valve-in-native valve, valve-in-prosthetic valve (ViV), valve-in-prosthetic ring (ViR), and valve-in-mitral annular calcification (MAC) interventions.

2 | CHALLENGES OF TMVR AND DEVICE DESIGN

Initial experience with TMVR focused on valve-in-valve replacement which was facilitated by the landing zone provided by the existing prosthetic valve.[6] This was followed by the use of TMVR devices in native mitral valves, a procedure more technically challenging due to the lack of a similar landing zone. Therefore, preprocedural imaging and intraprocedural guidance are instrumental in achieving procedural success. Valve-in-native valve TMVR procedures are currently performed transapically using investigational devices.

Challenges associated with TMVR in native valve include the complex, variable, and dynamic anatomy of the mitral valve in addition to the proximity of the prosthesis to the LVOT.

Ensuring transcatheter heart valve (THV) stability is challenging in TMVR as the valves are implanted in a complex, asymmetric, and dynamic landing zone that often lacks significant calcification. Additionally, the valves must withstand the systolic pressure exerted

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by the left ventricle. Therefore, intraprocedural guidance is of paramount importance in ensuring optimal device deployment and confirming its stability. Current designs of mitral THV include some combination of annular and ventricular anchors, atrial and ventricular flanges, annular docking rings, or systems to create a landing zone, valve stents with radial force, and apical tethers.[7] Additionally, sealing skirts are used to prevent paravalvular regurgitation.[7]

3 | BASELINE IMAGING

Transesophageal echocardiography (TEE) with real time 3D imaging has superior spatial resolution and is the principal imaging modality used for procedural guidance and detection of immediate complications. Intraprocedural guidance plays a fundamental role in improving the accuracy and safety of the procedure, thereby improving patient outcomes. The use of conscious sedation or general anesthesia may significantly alter mitral valve hemodynamics by changing the loading conditions, hence it is important to thoroughly assess the valve function in the preprocedure setting.[8]

A comprehensive TEE exam at the start of the procedure is essential in confirming the findings of the preprocedural imaging in addition to ruling out contraindications to the procedure, which include the presence of an intracardiac thrombus or infective endocarditis.

3.1 | 3D assessment of the mitral valve apparatus

3.1.1 | Mitral valve leaflets

Echocardiographic assessment of the mitral valve leaflets includes evaluation of their thickness, mobility, calcification, and coaptation zone. In patients presenting with mitral regurgitation, 3D TEE is superior in the anatomical assessment of the mitral valve, hence is key in establishing the etiology of mitral regurgitation. Additionally, 3D TEE imaging enables calculation of a 3D-derived mitral valve area.

Detailed assessment of the anterior mitral valve leaflet is particularly important. In contrast to mitral valve surgeries—where the anterior mitral valve leaflet is frequently removed—the anterior leaflet can pose challenges during TMVR procedures. Redundant anterior mitral valve leaflets can lead to neo-LVOT obstruction if it is displaced septally and can result in acute mitral regurgitation if it prolapses within the THV after deployment.[9]

3.1.2 | MV hemodynamics

Mitral valve hemodynamics should be thoroughly assessed before TMVR. This includes measurement of mitral valve gradients in addition to assessment of MR severity. In addition to 2D TEE evaluation, 3D TEE has been increasing used for assessment of mitral valve hemodynamics. Use of 3D color Doppler is a helpful in assessing vena contracta of the regurgitant jet as well as the regurgitant orifice area.[10]

3.1.3 | Mitral valve annulus

While multidetector computed tomography (MDCT) is the primary imaging modality used to determine annular dimensions, the advantage of 3D TEE over MDCT in the assessment of annular size lies in the ability of TEE to evaluate the change in annular dimensions throughout the cardiac cycle. Accurate annular sizing is central in guiding device selection as an undersized valve can lead to paravalvular leak, device migration or embolization.

3.1.4 | Mitral annular calcification

Assessment of mitral annular calcification (MAC) is important as it is a risk factor for the development of LVOT after TMVR. Furthermore, patients with MAC tend to have other predisposing factors for the development of LVOT obstruction, including small, hypertrophied ventricles with a bulging septum, and calcified anterior mitral valve leaflets.[11]

While technical success was achieved in most patients enrolled in TMVR in MAC Global Registry, the serious complication of LVOT obstruction occurred in about 13% of cases.[12] While 3D TEE enables evaluation of the circumferential extent of mitral annular calcification, multidetector computed tomography, is superior in the quantitative assessment of mitral annular calcification and detailed evaluation of its extent. [13,14]

Despite the fact that severe MAC remains as a contraindication to TMVR in multiple studies, THV have been implanted with the compassionate use of balloon-expandable transcatheter aortic valves (Edwards Lifesciences, Irvine, CA) in the mitral position in patients with severe MAC.[15]

3.1.5 | Subvalvular apparatus

The papillary muscles and chordae tendineae play an important role in maintaining normal mitral valve function and should be preserved during TMVR procedures. Therefore, assessing the papillary muscles and chordae tendineae provides information that aids in determining candidacy for TMVR. For instance, anterior displacement of the papillary muscles can increase the risk of LVOT obstruction.[16] The subvalvular apparatus are best evaluated using transgastric TEE views with use of 3D imaging. These views also provide accurate assessment of chordal length.[17] (Figure 1).

3.2 | Assessment of prosthetic valves/rings

The presence of a prosthetic valve or ring may create significant acoustic shadowing. 3D views of a mitral valve bioprosthesis often permit enface visualization of leaflet morphology and mobility, in addition to presence of thrombi or vegetations. 3D color facilitates evaluation of any valvular or paravalvular regurgitation. Zoomed 3D

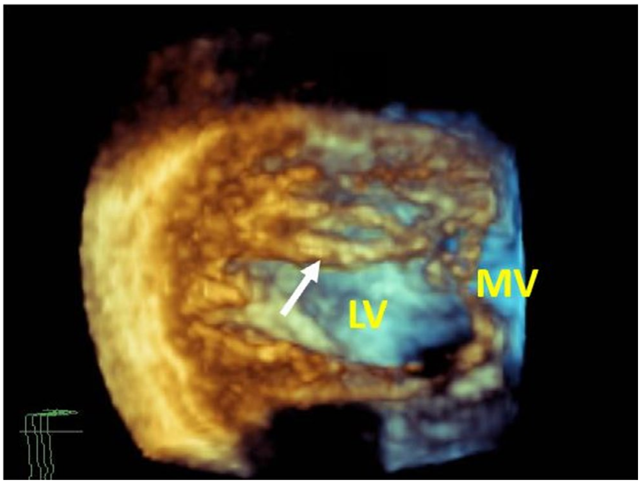


FIGURE 1 3-dimensional deep trangastric view of the mitral valve subvalvular apparatus (arrow). This provides important anatomical data for establishing TMVR candidacy and planning transapical access. MV, mitral valve; LV, left ventricle;

en face views of the mitral valve with application of color Doppler allows for precise localization of any paravalvular regurgitation jets. In the setting of paravalvular regurgitation, paravalvular closure rather than TMVR should be considered.

3.3 | Assessment of the LVOT

A neo-LVOT is created by the interplay between the TMVR device, anterior mitral valve leaflet, and the LVOT.[18] Since the TMVR devices are made of circumferentially covered stents,[19] implantation of these devices can result in LVOT obstruction as the THV frame may project into the LV cavity and the LVOT. Factors that predispose to LVOT obstruction include a long anterior leaflet, hypertrophied interventricular septum, small LV size, and an aorto-mitral angulation of <110°.[20]

LV obstruction can either be fixed or dynamic. Fixed LVOT obstruction occurs when the prosthetic mitral valve pushes the anterior mitral leaflet toward the interventricular septum, thus creating a narrower neo-LVOT. [18] Dynamic LVOT obstruction is caused by Bernoulli forces generated in the neo-LVOT during systole that pull the anterior mitral leaflet toward the interventricular septum. [21]

From the imaging standpoint, MDCT plays a major role in preprocedural LVOT assessment with postprocessing tools that enable determination of neo-LVOT dimensions, hence predicting the risk of LVOT obstruction. [22,23]

The Intentional laceration of the anterior mitral valve leaflet (LAMPOON) procedure has been reported to decrease the risk of LVOT obstruction pre TMVR. This procedure is guided by TEE and fluoroscopy. Two catheters are advanced retrogradely, one of each side of the anterior mitral valve leaflet base. Through the LVOT catheter, an energized wire is passed into the left atrial catheter snare. This is externalized to form a loop around the A2 leaflet. This is subsequently energized and pulled resulting in longitudinal transection of the A2 into 2 halves. This prevents neo-LVOT obstruction by the THV. [24]

3D TEE is central for catheter and wire positioning and confirming leaflet laceration. A THV is then deployed via the transseptal approach. Once the THV is deployed, the two lacerated halves of the anterior mitral valve leaflet are displaced laterally and medially on either side.

In patients at a significant risk for LVOT obstruction, pre-emptive alcohol septal ablation in selected patients has also been reported to result in an increase in neo-LVOT area pre-TMVR thus decreasing the risk of LVOT obstruction.[25]

3.4 | Assessment of the interatrial septum

Evaluation for the presence of an interatrial shunt, aneurysm, surgical patch, or lipomatous hypertrophy of the interatrial septum is imperative prior to the transseptal TMVR procedures.[26] Use of TEE with 3D imaging provides additional views of interatrial septum.

4 | INTRAPROCEDURAL GUIDANCE

4.1 | Transapical approach

This approach is used in valve-in-native valve TMVR procedures.

4.1.1 | Valve-in-native valve

Transapical puncture

The optimal intercostal space and left ventricular apical puncture site for apical TMVR is initially determined by preprocedural MDCT.[20] During the procedure, the “poking finger test” viewed by TEE confirms the ideal site for the ventricular apical incision. This test is performed by having the surgeon manually compress the left ventricle apex while the interventional imager simultaneously confirms the apical site by TEE (Video S1). This serves to ensure a safe transapical puncture that minimizes the risk of delivery system contact with the subvalvular apparatus, septum, and right ventricular apex. This can be monitored with the use of live 3D imaging, which also allows for visualization of the subvalvular apparatus, RV apex, and interventricular septum.

In addition to the potential of causing significant bleeding after sheath removal, use of the transapical approach is associated with the risk of injury to the left anterior descending artery. Continuous monitoring of LV systolic function and wall motion is therefore important when the transapical puncture is performed.

Device positioning and deployment

To facilitate communication between the interventionalist and the structural imager, a standard clock-face view provided by an en face TEE of the mitral valve is utilized. In this view, the aortic valve is located anteriorly, the interatrial septum is located medially, and the left atrial appendage is located laterally.

The wire and delivery catheters can be visualized by 3D TEE as they cross the LV apex. Use of real time 3D imaging enables complete visualization of the delivery system, including the entire length of the catheter, with inclusion of key anatomical landmarks such as the interatrial septum, mitral annulus, and left atrial appendage. This facilitates communication with the interventionist as the delivery system and THV are being positioned in relation to the mitral valve target.

The guidewire is continuously imaged as it passes through the mitral annulus into the right pulmonary vein to ensure that it does not encounter the papillary muscles and chordae tendinae. Likewise, the delivery system is advanced into the left atrium through the mitral valve orifice. Device unsheathing ensues. The delivery system is centered in the mitral valve orifice under TEE guidance. Use of Biplane and 3D imaging is helpful in centering the device within the mitral valve annulus.

The midesophageal commissural (60°–90°) views help in positioning the device in the medial-lateral direction while the midesophageal long axis view (120°–150°) helps in positioning the device in the anterior-posterior direction. This view also aids in assessing for LVOT obstruction. This ensures alignment of the device within the mitral annulus.

TEE further guides the deployment process which occurs under a short run of rapid ventricular pacing. The long axis view is used to monitor the anchoring mechanism (for example, by paddles and flanges) and ensure the apposition of the device to the atrial wall. Unsheathing of the device is also monitored on TEE. Using biplane is particularly helpful in centering the device as it provides 2 simultaneous orthogonal views. The 3D surgical view of the mitral valve guides optimal device rotation.

The procedural steps for implantation of the Medtronic Intrepid™ transcatheter mitral valve are shown in (Figure 2). Videos S2 and S3 demonstrate THV positioning in the left atrium. Videos S4 and S5 demonstrate post deployment evaluation of the THV.

It is worth mentioning that device deployment closer to the atrial side of the annulus can lead to thrombus formation due to the low flow state of the atrium. Deploying it in the other direction, closer to the LV side, can increase the risk of LVOT obstruction. Other complications which are detected by 3D TEE include cuff indentation leading to central MR (Figure 3).

4.2 | Transseptal approach

This approach is currently mainly used for ViV and ViR TMVR in addition to TMVR in MAC. Performing transvenous transseptal

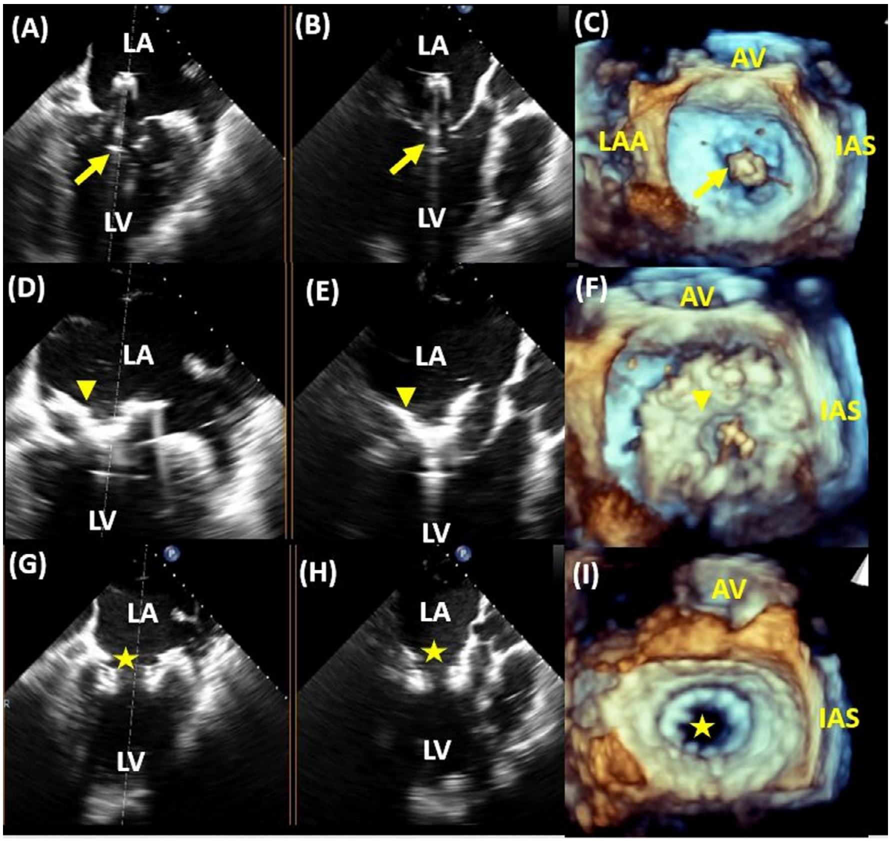


FIGURE 2 Valve-in-native valve TMVR with the Medtronic Intrepid™ valve. Top panel: Biplane 2D TEE images (A and B) and a 3D TEE image (C) of the delivery catheter (arrow) being centered in the left atrium above the mitral annulus. Middle panel: Biplane 2D TEE images (D and E) and a 3D TEE image (F) demonstrating expansion of the atrial brim (arrowhead) and alignment within the mitral annulus. Bottom panel: Biplane 2D TEE (G and H) and a 3D TEE image (I) demonstrating deployment of the valve (asterix) within the mitral annulus. AV, aortic valve; IAS, interatrial septum; LA, left atrium; LAA, left atrial appendage; LV, left ventricle

FIGURE 3 Oversized Medtronic Intrepid™ valve, resulting in outer cuff indentation (arrow) on 2D (A) and 3D imaging (B) with central mitral regurgitation (C). AV, aortic valve; IAS, interatrial septum; LA, left atrium; LAA, left atrial appendage; LV, left ventricle

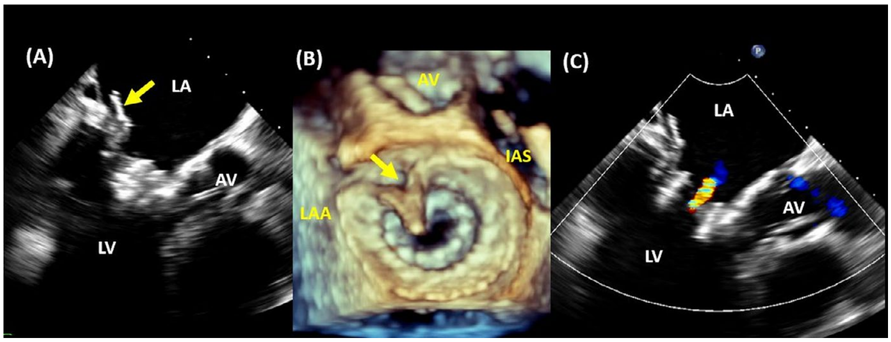
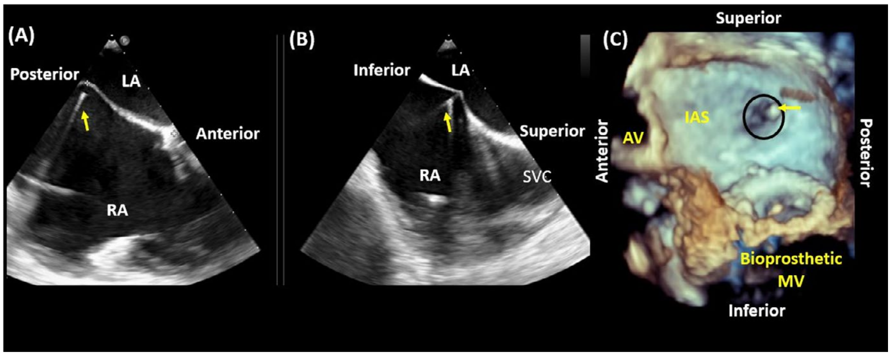


FIGURE 4 Transseptal puncture. Biplane imaging of the interatrial septum (A and B) with 3D imaging demonstrating the posterior site of the transseptal puncture (arrow) in the fossa ovalis (circle). AV, aortic valve; IAS, interatrial septum; LA, left atrium; RA, right atrium; SVC, superior vena cava



valve-in-native valve TMVR remains aspirational, with multiple delivery system being developed. [27,28]

Transseptal puncture

To allow room for manipulation of the delivery system, the optimal location for transseptal puncture lies inferiorly and posteriorly from the midline of the interatrial septum (IAS). Transesophageal echocardiography (TEE) is pivotal in guiding the transseptal puncture. Use of biplane imaging, which allows the simultaneous visualization of 2 orthogonal views, aids in determining the optimal transseptal site. The anterior and posterior aspects of the IAS are best visualized on the midesophageal at 0° and 45°, while the superior and inferior aspects are best visualized on the bicaval view (90°). Three-dimensional imaging of the interatrial septum can provide additional guidance for transseptal puncture. The fossa ovalis can be directly visualized and confirmed by sequential adjustment of 3D gain settings while viewing the IAS from the en face left atrial perspective. Ensuring adequate height of the transseptal puncture facilitates manipulation of the delivery system in the left atrium.

4.2.1 | Valve-in-valve (ViV) and valve-in-ring

Valve-in-Valve and Valve-in-Ring procedures are performed through the transseptal approach primarily using balloon-expandable THVs designed for the aortic position [29] (Figure 4). These procedures are technically less challenging as compared to valve-in-native valve interventions as the landing zone is provided by the prosthetic valve or ring. Additionally, the prosthetic valves and rings are clearly visualized by fluoroscopy, an aspect which facilitates THV positioning and deployment. Challenges associated with ViV and ViR procedure include significant acoustic shadowing caused by the prosthetic mitral valve during imaging. Sizing charts are currently available to determine the best THV based on the size of the prosthetic valve or ring. It is worth mentioning the THV is deployed in an "upside down" with the THV skirt facing the atrial side. Generally, the THV landing zone is targeted at 80% ventricle/20% atria to ensure that the sealing cuff is within the annular sewing ring to effectively prevent paravalvular regurgitation. This 80/20 ratio may be reduced if the risk of neo-LVOT obstruction is high (eg, small LV dimension; thick LV septum; unfavorable aortic-mitral angle).

The transseptal puncture is performed under TEE guidance. A wire is then introduced into the left atrium and guided to a position within the left upper pulmonary vein. A catheter is then advance over the guide wire. After repositioning the catheter, a second guidewire is positioned across the mitral valve target. 3D TEE is critical in this step as it ensure that the wire is crossing the valve rather than a paravalvular defect. A septostomy balloon is then advanced and inflated in the IAS. After the balloon is removed, a balloon-expandable THV delivery system is introduced and advanced across the septum and positioned across the mitral valve prosthetic valve/ring. The position is checked by fluoroscopy and TEE. Once the position is confirmed, the THV is slowly deployed under rapid pacing and breath holding.

The THV valve function is then assessed by TEE. If significant paravalvular regurgitation is detected, then balloon post dilation is attempted. If this fails to resolve the paravalvular regurgitation, then percutaneous closure of the PVL is considered.

The risk of LVOT obstruction is greater in ViR procedures, especially if the anterior mitral valve leaflets is present. For ViV procedures, the absence of a native valve anterior leaflet, and the presence of a prosthetic valve frame generally protects against LVOT obstruction.

The procedural steps for ViV and ViR procedures are demonstrated in Figures 5 and 6, respectively.

4.2.2 | Valve in MAC

Patients with significant MAC are at a higher risk for developing LVOT obstruction given the anterior displacement of the anterior mitral valve leaflet by the calcium. In this patient population, intentional laceration of the anterior mitral valve leaflet can be performed. While feasible, TMVR with balloon-expandable aortic valves has been performed in patients with severe MAC but has been associated with high mortality. [12]

More recently, a novel approach has been described in a few patients whereby balloon-expandable transcatheter valves are delivered through an open transatrial approach in patients with extensive MAC. 30Preprocedural and postprocedural 3D TEE images are demonstrated in Figure 7. If the prosthesis is too large, that poses a risk for mitral annular rupture. Preprocedural imaging, specifically with MDCT, is therefore key in THV sizing. The risk of LVOT obstruction is lower in this type of surgery due to the surgical resection of the anterior mitral valve leaflet.

5 | HEMODYNAMIC ASSESSMENT POST DEVICE DEPLOYMENT

At the end of the procedural, invasive and noninvasive assessments are used to evaluate procedural success. An increase in transgastric LVOT stroke volume is consistent with a reduction in mitral valve regurgitation. Assessment of pulmonary venous systolic waves helps in assessing reduction of LA pressure. Concomitant invasive hemodynamic measurement of LA pressures provides additional confirmatory objective data.

It is worth mentioning that immediately after a TMVR is performed for significant mitral regurgitation, both the LV end-diastolic and LV end-systolic volume indices should decrease. The decrease in LV end-diastolic volume index, however, is greater therefore resulting in an immediate decrease in the left ventricular ejection fraction. Evaluation of pre and post LV volumes and LV function can be achieved by 3D TEE volumetric assessment.

6 | EVALUATION OF COMPLICATIONS

Transesophageal echocardiogram is instrumental in the evaluation of immediate complications post TMVR. Timely detection of such

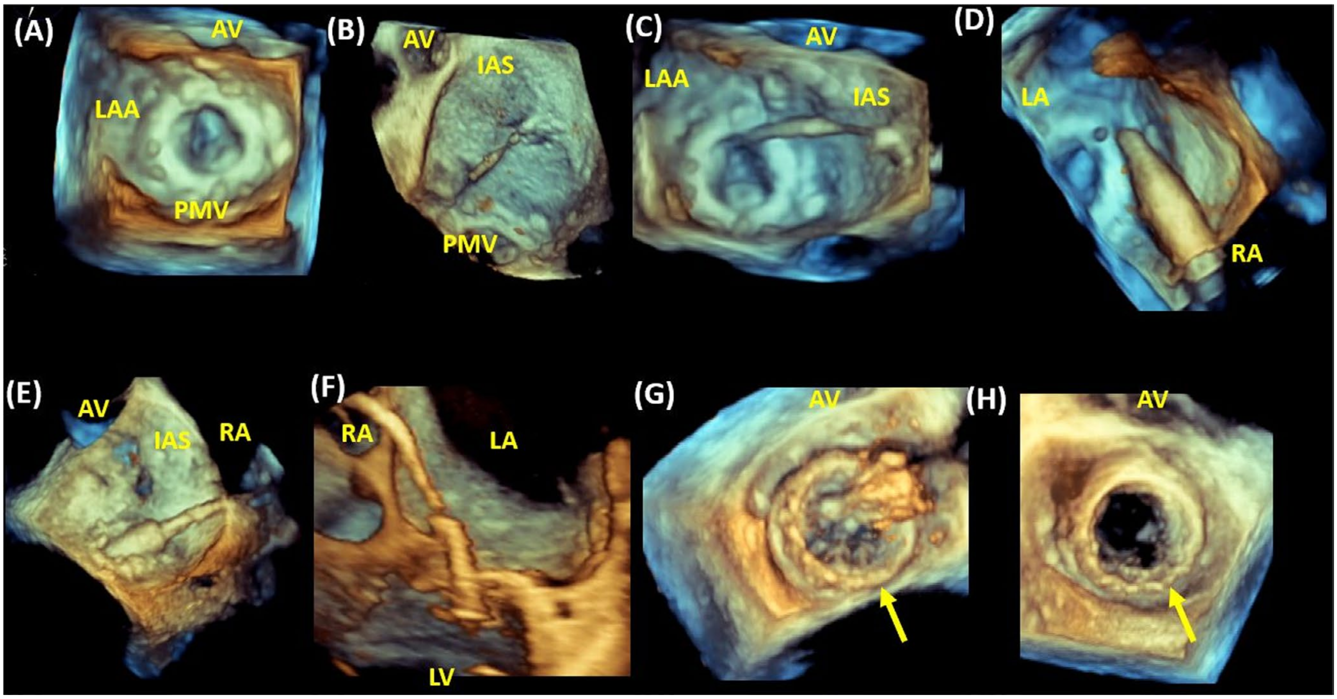


FIGURE 5 Three-dimensional TEE guidance of a valve-in-valve TMVR. Bioprosthetic mitral valve with thickened leaflets (A). Transseptal puncture performed in the posterior aspect of the fossa ovalis (B). This is followed by balloon septostomy (C and D). Positioning of the balloon-expandable transcatheter valve (26 mm SAPIEN 3 valve) (arrow) ensues (E and F), followed by deployment (G), and post deployment assessment (H). AV, aortic valve; IAS, interatrial septum; LA, left atrium; PMV, prosthetic mitral valve; RA, right atrium

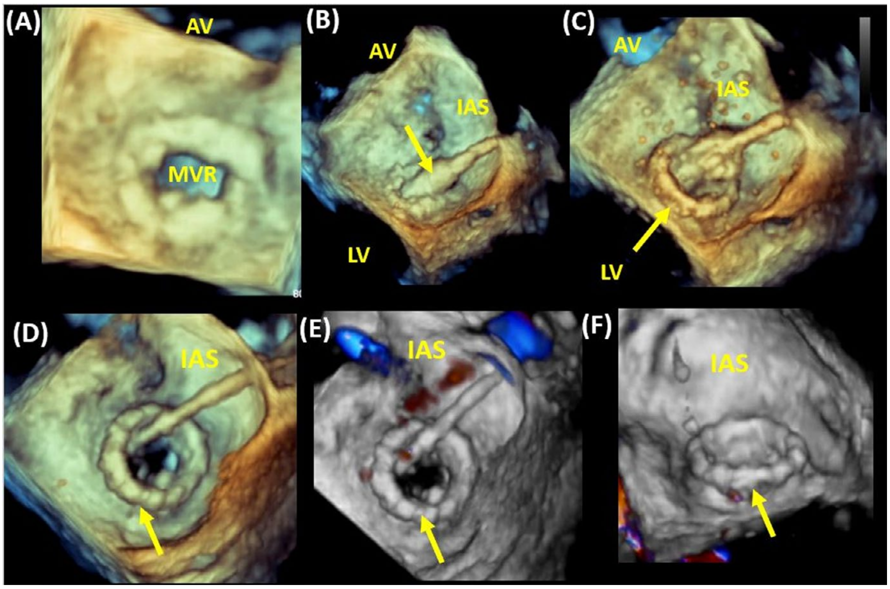


FIGURE 6 Three-dimensional TEE guidance of a valve-in-ring TMVR. Baseline 3D image of a prosthetic mitral rIng with severe obstruction (A). After transseptal access, the balloon-expanded THV (arrow) is positioned within the mitral valve ring (B) and then deployed (C). This is followed by assessment of the final valve position (D) and evaluation for any paravalvular regurgitation (E and F). AV, aortic valve; IAS, interatrial septum; MVR, mitral valve ring

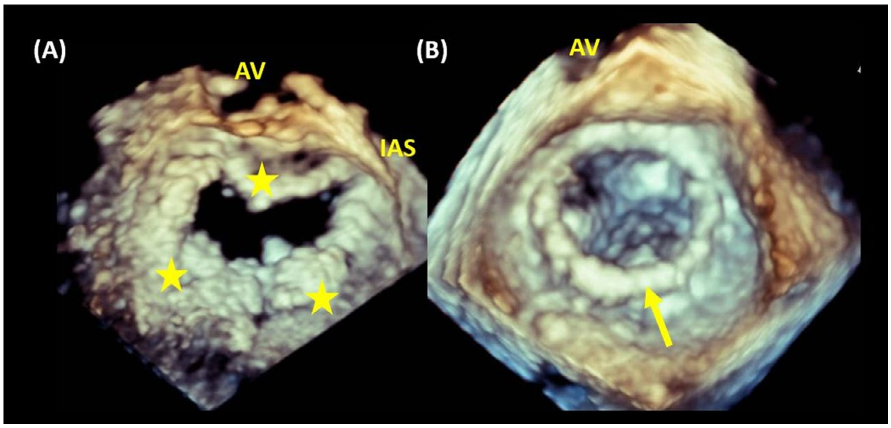


FIGURE 7 Transatrial open mitral valve in MAC using a balloon-expandable transcatheter aortic valve. A, demonstrates the extensive and circumferential nature of the mitral annular calcification by 3D TEE imaging (arrow). B, demonstrates the deployed THV (arrowhead). AV, aortic valve

complications is important as some of these can be potentially life-threatening or require emergent intervention.

Transesophageal echocardiography confirms device location and stability by ensuring that the device is well-seated within the annulus and does not exhibit excessive motion. Device embolization can result from device undersizing or inexact deployment. This complication can be detected by TEE.

TEE is instrumental in identification of the most feared complication of TMVR which is neo-LVOT obstruction. Detailed interrogation of the LVOT is performed before and after valve deployment. Turbulence noted in the LVOT by Color Doppler flow is suggestive of LVOT obstruction but is not a specific finding. Further interrogation with continuous and pulse wave Doppler, ideally in the deep transgastric view, is fundamental in ruling out LVOT obstruction. Direct visualization of the anterior mitral leaflet and its interaction with the LVOT is also important.

Assessment of valvular or paravalvular mitral regurgitation by color Doppler can be challenging due to shadowing from the THV device as well the as the complex geometry of the mitral valve orifice that may give rise to eccentric jets. Incorporating pulmonary venous flow data can aid in the assessment of the severity of the mitral regurgitation jet. The 3D color images of the regurgitant jet additionally allow for the measurement of 3D vena contracta area. [31]

Pericardial effusions can result from wire-related injury during transapical or transseptal puncture, myocardial rupture, or mitral annular rupture. Acute accumulation of pericardial fluid can result in hemodynamic compromise and require immediate drainage.

Left circumflex impingement is one of the potential complications specific to valve-in-native valve and valve in MAC TMVR procedures as the artery courses near the annulus in the atrioventricular groove. As mentioned previously, the left anterior descending artery can be injured at the time of transapical puncture. Any new wall motion abnormalities should raise suspicion for coronary artery compromise.

If a transseptal puncture is performed, careful evaluation of the IAS is performed to evaluate the size and directionality of the interatrial residual shunt, hence the needs for closure. An iatrogenic atrial septal shunt is usually closed if it is predominantly right-to-left in the setting of pulmonary hypertension resulting in hypoxia. Percutaneous closure is also considered in patients with right-to-left shunts in the setting of right-sided ventricular dysfunction. Three dimensional TEE is helpful in accurate sizing of the maximal

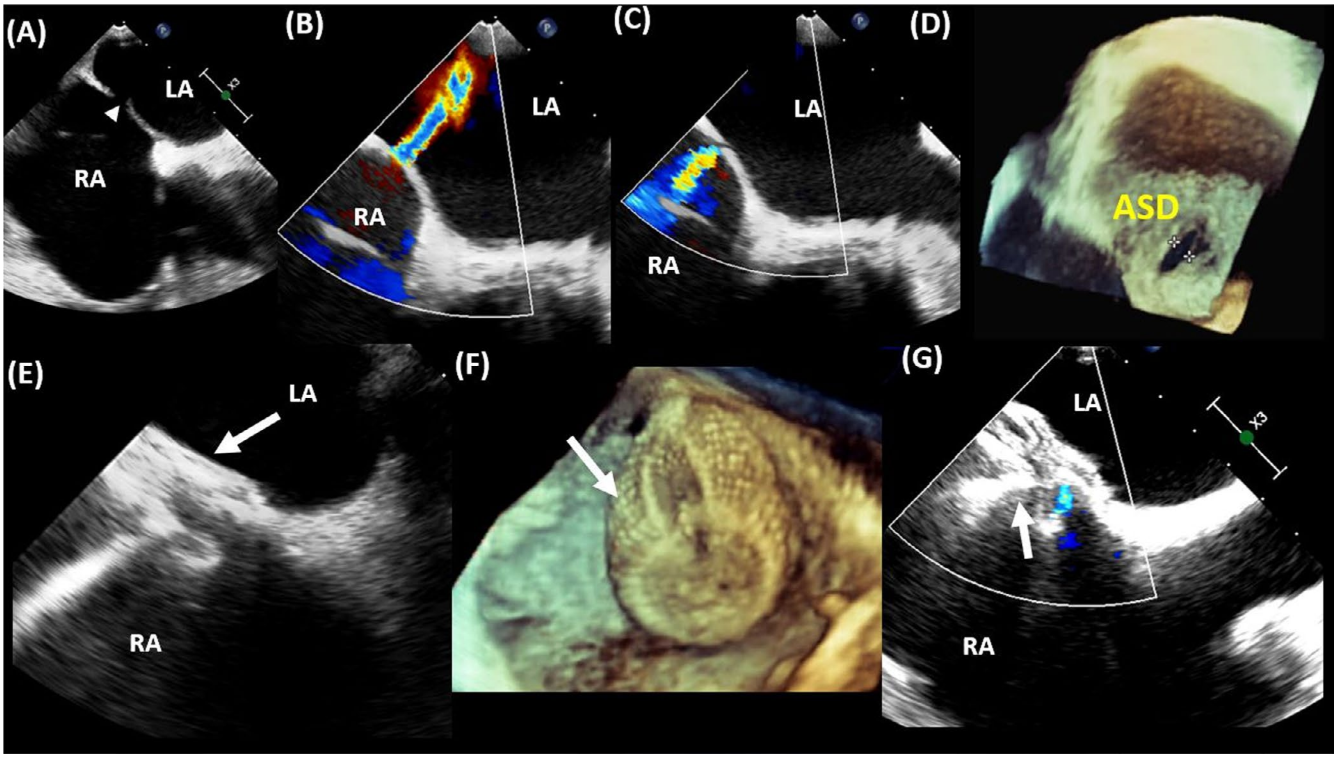


FIGURE 8 Post balloon septostomy iatrogenic atrial septal defect (A, arrowhead) with bidirectional flow (B and C). 3-dimenstional (3D) imaging of the interatrial septum reveals the nonlinear morphology of the defects and aids in its accurate sizing (D). The defect was closed with a 16 mm Amplatzer Septal Occluder (F and E, arrow) with minimal residual shunting (G). LA, left atrium; RA, right atrium

septostomy diameters as it is oftentimes irregular in shape with uneven borders as a result of balloon septostomy (Figure 8). The main challenge associated with percutaneous closure of the septostomy site is that it precludes future transseptal procedures, including redo TMVR or PVL closure, if indicated.

7 | CONCLUSION

Use of 3D TEE imaging is instrumental in the intraprocedural guidance of different types of TMVR and plays a key role in assessing procedural success and the presence of immediate complications.

CONFLICT OF INTEREST

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ORCID

Nadeen N. Faza https://orcid.org/0000-0002-0601-8741

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

Video S1. "Finger poking test" performed to determine ideal transapical puncture site

Video S2. Biplane 2D TEE imaging demonstrating positioning of the mitral THV in the left atrium

Video S3. Three-dimensional visualization of the THV as it is being positioned above the mitral annulus prior to deployment

Video S4. Postdeployment assessment of the THV stability and presence of any central or paravalvular mitral regurgitation

Video S5. Three-dimensional imaging of the deployed THV

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