This Review is in a thematic series on ***Cardiovascular Imaging,*** which includes the following articles:

T1 Mapping in Characterizing Myocardial Disease: A Comprehensive Review
Fractional Flow Reserve and Coronary Computed Tomographic Angiography: A Review and Critical Analysis
Prognostic Determinants of Coronary Atherosclerosis in Stable Ischemic Heart Disease: Anatomy, Physiology, or Morphology?
Noninvasive Molecular Imaging of Disease Activity in Atherosclerosis
Transcathether Valve Replacement and Valve Repair: Review of Procedures and Intraprocedural Echocardiographic Imaging
Advances in Echocardiographic Imaging in Heart Failure With Reduced and Preserved Ejection Fraction
Viability: Is it Still Attractive?

Guest Editors: Jagat Narula and Y. Chandrashekhar

Transcathether Valve Replacement and Valve Repair

Review of Procedures and Intraprocedural Echocardiographic Imaging

Rebecca T. Hahn

Abstract: **Transcatheter aortic valve replacement for treatment of aortic stenosis has now become an accepted alternative to surgical valve replacement for some patients. In addition, transcatheter mitral valve repair is also routinely used in high surgical risk patients with mitral regurgitation. Other transcatheter procedures are in rapid development. The current review attempts to summarize the procedures and echocardiographic imaging used for transcatheter valve replacement or valve repair. (*Circ Res*. 2016;119:341-356. DOI: 10.1161/CIRCRESAHA.116.307972.)**

Key Words: aortic valve ■ echocardiography ■ mitral valve ■ three-dimensional ■ transcatheter ■ transesophageal ■ tricuspid valve

According to the American Heart Association/American College of Cardiology Guidelines for the Management of Patients with Valvular Heart Disease,[1] echocardiography (transthoracic echocardiography [TTE] or transesophageal echocardiography [TEE]) is the imaging modality of choice for the assessment of valvular heart disease in patients. Numerous less invasive therapies such as percutaneous or transcatheter interventions have recently been introduced for the treatment of structural heart disease. Many of these procedures require extensive multimodality imaging guidance. The imaging advancement that has had the most impact on the diagnosis of valvular heart disease is the real-time 3-dimensional (RT3D) echocardiography. The advantages of RT3D imaging compared with 2-dimensional (2D) imaging have been well described in the most recent societal guidelines: "Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults" update[2] and "Recommendations for Image Acquisition and Display Using Three-Dimensional Echocardiography".[3] These guidelines review the significant data supporting the improved accuracy and reproducibility of 3-dimensional (3D) imaging for ventricular volumes and mass, as well as for valvular morphology and function.

Real-Time 3D Echocardiography

The continued improvement of 3D technology has led to its widespread availability and its growing use, particularly for valvular heart disease.[3] The introduction of RT3D transesophageal probes in 2007 was perfectly timed with the initial trials of transcatheter aortic valve replacement (TAVR) for high risk or inoperable patients with severe symptomatic aortic stenosis.[4–7] 3D echocardiography has been shown to improve sizing of the transcatheter valve.[8–10] RT3D TEE is comparable to computed tomography for annular assessment and prediction of paravalvular regurgitation (PVR) because of oversizing[11,12]

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Nonstandard Abbreviations and Acronyms	
2D	two-dimensional
3D	three-dimensional
AV	aortic valve
CS	conscious sedation
GA	general anesthesia
ICE	intracardiac echocardiography
LVOT	left ventricular outflow tract
MR	mitral regurgitation
PVR	paravalvular regurgitation
RT3D	real-time three-dimensional
TAVR	transcatheter aortic valve replacement
THV	transcatheter heart valve
TEE	transesophageal echocardiography
TR	tricuspid regurgitation
TTE	transthoracic echocardiography
VIV	valve-in-valve

and measurement of coronary height.[13] RT3D TEE has been shown to provide superior spatial visualization and anatomic orientation, optimizing procedural performance, and RT3D TTE can be used to assess the severity of PVR after TAVR.[14] RT3D TEE also plays a significant role in the accurate and rapid identification of specific valve pathologies. This imaging modality is an essential imaging tool for the intraoperative evaluation of patients undergoing open[15–18] and catheter-based mitral valve repair.[19–23] New tricuspid valve interventions also rely on RT3D TEE for intraprocedural guidance.[24–26]

3D color Doppler may overcome the limitations of 2D and standard Doppler measurements for quantifying regurgitation.[3,27,28] Studies have shown the feasibility of measuring the 3D vena contracta (narrowest portion of the regurgitant jet) on RT3D echocardiography to assess the severity of regurgitation for native regurgitant valve disease[27,29–31] and after surgical[32] or transcatheter interventions.[33]

Intracardiac Echocardiography

Although TEE imaging is well established and provides exceptional images, particularly for intraprocedural guidance, it most commonly requires general anesthesia and may be associated with intermittent obstruction of fluoroscopic viewing.[34] With the current move toward conscious sedation (CS) for structural heart disease interventions, intracardiac echocardiography (ICE) may be an acceptable alternative in some patients with no other adequate intraprocedural imaging options. Evidence that ICE guidance can improve safety and outcome of interventional procedures is still lacking; however, ICE imaging for paravalvular leak closure has been reported to be feasible and advantageous.[35,36] A reduction in contrast use has also been reported in 2D ICE when used in TAVR (Figure 3).[37] The recently introduced AcuNav V catheter (Siemens, Inc, Mountain View, CA) represents the only commercially available RT3D ICE system. The 10F catheter carries a matrix transducer providing a 22°×90° real-time volume image. Larger field-of-view transducers may increase the use of this imaging modality in catheterization laboratories.

Fusion Imaging

Combining images from ≥2 different imaging techniques, or fusion imaging, has been accomplished most recently with real-time echocardiography and fluoroscopy.[38–40] This technology, which coregisters the TEE probe position with the intervention table and the angulation of the fluoroscopy C-arm, allows for relatively accurate placement of the transesophageal echocardiography image onto the fluoroscopic image. This integration eliminates the need for 2 different image display monitors and the mental integration of 2 different imaging data sets by the operator of structural heart disease interventions, which should improve guidance of structural heart disease interventions. This technology has been shown to be safe and feasible for the transcatheter mitral repair procedure with the MitraClip device (Abbott Vascular Structural Heart, Menlo Park, CA) and shows a trend toward reduction of fluoroscopy and procedure time.[41] The potential benefits of echocardiographic fluoroscopic fusion imaging in structural heart disease interventions require further study.[42]

Intraprocedural Imaging for Specific Valvular Interventions

Transcatheter Aortic Valve Replacement

Although computed tomography is typically used for both preprocedural vascular and aortic measurements, in situations where the scans are not interpretable or cannot be performed, TEE can be used to confirm the annular diameter[43] and evaluate the aortic valve (AV) complex for risk of complications such as acute coronary occlusion, annular rupture, or PVR.[44–46] Reports of improved outcomes with the use of intraprocedural TEE[47] likely stem from the continuous imaging during the procedure and the rapid diagnosis of complications such as PVR[48] or even reduction in nephrotoxic contrast use.[49,50] Initial early TAVR randomized trials mandated the use of general anesthesia (GA) and TEE imaging for intraprocedural guidance[4,5]; however, numerous recent reports of the safety of TAVR under monitored anesthetic care or CS[51,52] have resulted in the increasing use of this management protocol.[53] When monitored anesthetic care or CS is used, TTE is typically used, although some sites report successful intraprocedural imaging using TEE and monitored anesthetic care.[54] Two recent observational studies support the safety of the minimalist anesthetic approach compared with GA. First, the European Society of Cardiologist's Transcatheter Valve Treatment Registry found that survival at 1 year, compared by Kaplan–Meier analysis, was similar between groups (log-rank: P=0.1505), although in the highest tertile logEuroSCORE group, GA patients had higher mortality. Interestingly, GA patients had a higher immediate procedural success rate and a lower rate of periprocedural complications, and CS patients had a strong trend to higher combined (myocardial infarction, major stroke, and in-hospital death rates) adverse event rate (7.0% CS versus 5.3% GA; P=0.053).[55] The most recent report of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy registry (J. Giri, MD, unpublished data, 2016) showed that moderate sedation

use is associated with improved patient outcomes and shorter hospital stays, as compared with traditional GA. When propensity-matched for factors known to predict early TAVR mortality, moderate sedation compared to GA had lower 30-day mortality (2.96% versus 4.01%; $P<0.0001$) and 30-day mortality or stroke (4.80% versus 6.36%; $P<0.0001$). Conversion to GA, known to result in poorer outcomes and previously reported in 10% to 17% of cases,[56,57] occurred in only 5.9% of patients in this report. Further studies should be performed as the field begins to address TAVR in the lower risk patient population who are also at lower risk for GA complications and whose expected outcomes are significantly better than patients treated in these registries.[58,59]

Many of the steps of the procedure are primarily guided by fluoroscopy with TEE as an adjunct or confirmatory tool that could reduce fluoroscopic time. Recommendations for intraprocedural TEE imaging throughout TAVR have been extensively reviewed and are summarized in Table 1.[60] It is important to remember that the imaging planes on TEE and fluoroscopy are different. The optimal imaging plane of fluoroscopy typically cannot be obtained from a TEE imaging position in the esophagus. Because of this, the posterior edge of the transcatheter heart valve (THV) imaged on TEE is typically the edge between the noncoronary and left coronary cusps, whereas the posterior edge of the THV on fluoroscopy is the edge adjacent to the left coronary cusp. Imaging the THV before deployment requires angulating the transducer and reducing gain to identify an echodense, sharp-edged structure (as opposed to the heterogeneous appearance of the underlying deflated balloon; Figure 1).

After THV deployment, TEE or TTE imaging provides rapid and accurate assessment of valve position, valve shape, leaflet motion, and transvalvular gradients. In addition, the causes of hemodynamic compromise can be rapidly assessed: acute valvular dysfunction (aortic or mitral regurgitation [MR]), tamponade physiology (chamber perforation or annular rupture), ventricular dysfunction (acute coronary obstruction or ischemic dysfunction), and aortic root catastrophe (aortic dissection or rupture). The long-axis view is best for determining valve position. The short-axis view is essential in the assessment of valve shape, leaflet motion, coronary artery patency, and presence and severity of paravalvular and central aortic regurgitation (Figure 1C). Determining the circumferential extent of the jet requires integrating the discontinuous small jets between the stent cells and taking care not to include the stent frame in the assessment. Because of significant acoustic shadowing by the THV, as well as the perpendicular nature of the paravalvular regurgitant jets, it is highly recommended to perform imaging that will align the Doppler jets with the insonation beam to confirm the presence of these jets. Deep transgastric views for TEE and apical views for TTE (Figure 1D) are thus highly recommended to identify the jet

Table 1. Recommendations for Intraprocedural Imaging for Transcatheter Aortic Valve Replacement Using TEE

Procedural Step	Imaging Recommendations	Possible Complications
Pacing wire position	1. Confirm position in the right ventricle.	1. RV perforation and pericardial effusion
Stiff wire position	1. Ensure stable position of wire in the apex without entanglement in mitral apparatus	1. Acute severe mitral regurgitation. 2. LV perforation and pericardial effusion
BAV	1. Image during and immediately after BAV for aortic leaflet motion and aortic regurgitation. 2. Image the coronary arteries (particularly the left main). 3. Image the displacement of leaflet and aortic root calcium.	1. Acute aortic valve injury (avulsion/flail) or frozen aortic valve leaflet resulting in acute severe aortic regurgitation 2. Risk of acute coronary occlusion 3. Risk of acute aortic wall injury
Positioning of transcatheter valve	1. Balloon-expandable valve (SAPIEN 3): outflow (also known as distal or aortic) edge of the THV should cover the native leaflets while being below the STJ. Optimal final position covers the native leaflets. 2. Self-expanding valve (Evolut R): higher edge of the stent (posterior typically) should be 3–5 mm below the annulus. Optimal position is <10 mm below the annulus to avoid conduction disturbance.	1. Malpositioning with risk of paravalvular regurgitation, valve embolization, or coronary occlusion
Transapical cannulation	1. Confirm location of the transapical puncture site by imaging the intended apical cannulation site (either from midesophageal views or transgastric views).	1. Right ventricular, interventricular septum or LV papillary muscle injury
Postdeployment	1. Assess stent positioning, shape, and leaflet motion; perform comprehensive hemodynamic measurements including effective orifice area. a. New LVOT diameter can be the outer-to-outer stent diameter at the inflow edge if well-positioned, or inner-to-inner stent diameter at the level of the leaflets if THV is too low. b. Match the velocity time integral for the location of the LVOT diameter measurement. 2. Assess paravalvular regurgitation relying on short-axis images of the LVOT just apical to the inflow edge of the THV (and gastric views for confirmation). 3. Assess coronary artery patency and ventricular function; confirm ventricular size and function are similar to baseline or improved. 4. Assess mitral and tricuspid valve function.	1. Malpositioning of THV 2. Significant central or paravalvular regurgitation 3. Coronary occlusion with acute change in LV function 4. Aortic root or annular injury 5. Worsening of mitral regurgitation 6. Pericardial effusion or tamponade

BAV indicates balloon aortic valvuloplasty; LV, left ventricular; LVOT, left ventricular outflow tract; THV, transcatheter heart valve; RV, right ventricular; and STJ, sinotubular junction.

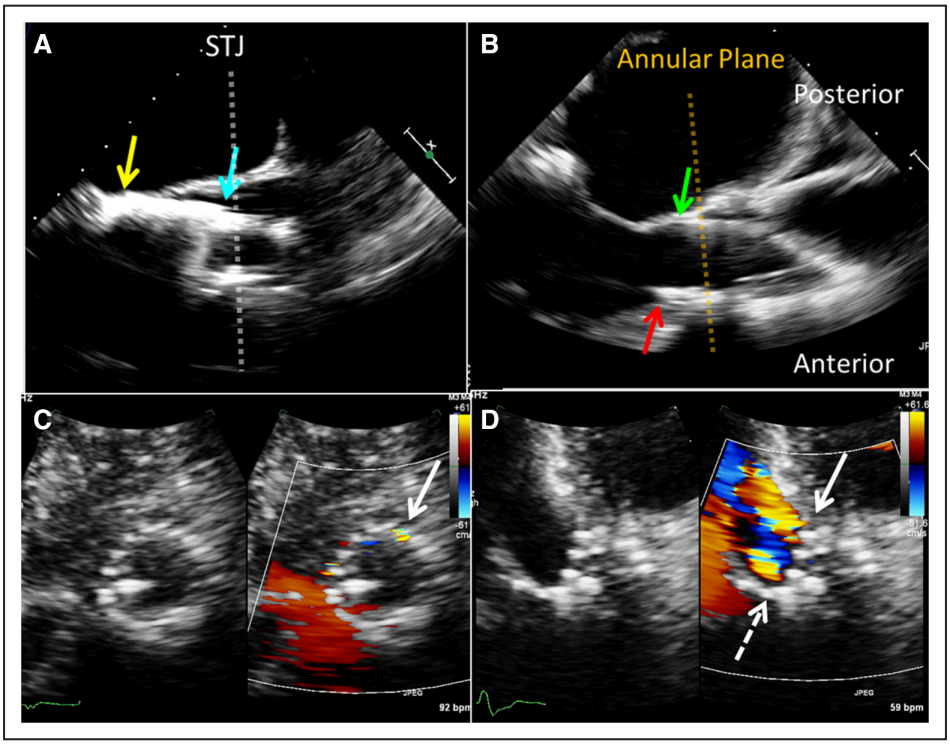

Figure 1. Transesophageal and transthoracic imaging during transcatheter aortic valve replacement. **A**, Positioning of a crimped balloon-expandable valve (aortic end at blue arrow and ventricular end at yellow arrow). **B**, The positioning of a self-expanding valve (posterior edge at green arrow and anterior edge at red arrow). Intraprocedural transthoracic imaging for paravalvular regurgitation should be performed from multiple imaging planes. **C**, Parasternal short-axis views suggest a single small regurgitant jet at 2 o'clock (white arrow); however, (**D**) from and apical 3-chamber view shows a second jet (white dashed arrow).

location and image the vena contracta. Importantly, the jet area and length should not be used to assess severity.[61,62]

Evaluation of Aortic Regurgitation Post TAVR

When making intraprocedural decisions about the severity of PVR immediately after THV deployment, a comprehensive, integrative approach must always be used. Because of multiple grading schemes used for grading aortic regurgitation using both numeric scales[63] and simple categories,[61] a unified grading scheme has recently been proposed and is summarized in Table 2.[62] Of note in this proposed grading scheme is not intended to replace existing guidelines and can be collapsed into the 3-class grading scheme. Although THV shape and position may be clues to PVR severity, color flow Doppler imaging is the primary method of assessment. Color flow Doppler imaging of PVR relies heavily on a multiwindow, multilevel approach, first documenting that the suspected PVR jet actually extends beyond the skirt into the left ventricular outflow tract (LVOT).

Note that reduced compliance of both the ventricle and aorta will influence pressure halftime, making this particular parameter less useful. Similar issues exist for flow reversal in the aorta that can occur in the setting of aortic noncompliance and hypertension,[64,65] although true holodiastolic reversal may still be useful.

Assessing Prosthetic Valve Area

Intraprocedurally, TEE Doppler should be performed in the deep gastric view that optimally aligns the transaortic flow with the insonation beam. Although peak and mean transaortic gradients should always be recorded, these measurements are flow dependent, and use of flow-independent measures of the valve function are preferred. These include the assessment of effective orifice area by the continuity equation, or Doppler velocity index. The Valve Academic Research Consortium update outlines criteria to determine dysfunction for the THV.[66] These criteria may continue to be refined as clinical trial data and registries report normal values for both balloon-expandable and self-expanding valves.[67,68]

An accurate calculation of LVOT stroke volume after TAVR can be performed for both the balloon-expandable valve[69,70] and the self-expanding valve.[71] The LVOT diameter measurement should be performed from the outer-to-outer edge of the most proximal (ventricular) edge of the THV stent. The matching pulsed-wave Doppler sample volume position should be just apical to the proximal THV stent.[70] A cutoff of ≤0.25 would represent significant stenosis. Recent reports of large randomized trials of TAVR suggest that the Doppler index (the ratio of LVOT and transaortic velocities or velocity time integrals) in normal balloon-expandable valve should be >0.45[67] and for the CoreValve Classic the Doppler index post implantation=0.55±0.13.[71] The appropriate method for assessing post-TAVR function for other valve designs may differ and have yet to be fully described.

Transcatheter Valve for Bioprosthetic Valve Failure (Valve-in-Valve)

Echocardiography is the primary imaging modality to assess the cause and severity of bioprosthetic valve failure and associated chamber remodeling and function.[61] Echocardiography

Table 2. Proposed Echocardiographic Doppler Criteria for PVR

Unifying 5-class grading scheme	None/Trace	Mild	Mild-to-Moderate	Moderate	Moderate-to-Severe	Severe
How to collapse into the 3-class grading scheme	None/Trace	Mild		Moderate		Severe
Doppler parameters (qualitative or semi-quantitative)						
Jet features: color Doppler*						
Extensive/wide jet origin	Absent	Absent	Absent	Present	Present	Present
Multiple jets	Possible	Possible	Often present	Often present	Usually present	Usually present
Jet path visible along the stent	Absent	Absent	Possible	Often present	Usually present	Usually present
Proximal flow convergence visible	Absent	Absent	Absent	Possible	Often present	Often present
E/A ratio†‡	<1.0	<1.0	<1.0	≥1.5	≥1.5	≥1.5
Vena contracta width, mm: color Doppler†§	Not quantifiable	<2	2–4	4–5	5–6	>6
Vena contracta area, mm^2: 3D color Doppler†‖	Not quantifiable	<5	5–9	10–19	20–29	>30
Jet width at its origin, %LVOT diameter: color Doppler*§	Narrow (<5)	Narrow (5–15)	Intermediate (16–30)	Intermediate (31–45)	Large (46–60)	Large (>60)
Jet density: CW Doppler†	Incomplete or faint	Incomplete or faint	Variable	Dense	Dense	Dense
Jet deceleration rate (PHT, ms): CW Doppler†¶	Slow (>400)	Slow (>400)	Slow (>400)	Variable (200–400)	Variable (200–400)	Steep (<200)
Diastolic flow reversal in the descending aorta: PW Doppler†¶	Absent	Absent or brief early diastolic	Intermediate	Intermediate	Holodiastolic (end-diastolic velocity >20 cm/s)	Holodiastolic (end-diastolic velocity >25 cm/s)
Circumferential extent of PVR, %: color Doppler*§	Not quantifiable	<5	5–9	10–19	20–29	>30
Echocardiographic						
Regurgitant fraction, %#	<15	<15	15–29	30–39	40–50	>50

2D indicates 2-dimensional; 3D, 3-dimensional; AR, aortic regurgitation; CW, continuous wave; E/A, ratio of mitral pulsed wave Doppler E-wave and A-wave; LV, left ventricular; LVOT, left ventricular outflow tract; PHT, pressure half-time; PVR, paravalvular regurgitation; PW, pulsed wave; and TAVR, transcatheter aortic valve replacement.

*Parameters that are most frequently applicable and used to grade PVR severity by echocardiography.

†Parameters that are less often applicable because of pitfalls in the feasibility/accuracy of the measurements and because of the interaction with other factors.

‡This parameter is highly influenced by concomitant LV diastolic dysfunction: what is useful is the change in E/A flow pattern immediately pre vs post TAVR.

§These parameters are generally assessed visually.

‖The vena contracta area is measured by planimetry of the vena contracta of the jet(s) on 2D or 3D color Doppler images in the short-axis view.

¶Applies to chronic PVR but is less reliable for periprocedural or early postprocedural assessment.

#There are important variability in the cut-point values of regurgitant fraction and volume reported in the literature to grade AR by cardiac magnetic resonance imaging.

should be used to exclude major contraindications to the transcatheter valve within a failed bioprosthetic surgical valve or ring (VIV) procedure such as active endocarditis and significant PVR. Sizing of the THV relies heavily on knowing the type and size of the implanted prosthesis and the use of reported true internal diameters of the prosthesis.[72] If the type and size is known but there is no accessibility to the VIV app, the following general rules can be applied: for porcine valves, the true ID is equal to the stent ID minus 2 mm; for pericardial valves with leaflets sewn on the inside of the stent, the true ID is equal to the stent ID minus 1 mm; for pericardial valves with leaflets sewn outside the stent, the true ID equals the stent ID. Oversizing the transcatheter valve is recommended to ensure secure sealing and anchoring the device,[73] but severe oversizing will result in distortion of the valve leaflets that may affect the longevity of the valve. The prosthetic internal dimensions can also be confirmed on computed tomography or confirmed by TEE although blooming artifacts from the sewing ring should be carefully avoided. Fluoroscopy however remains the primary intraprocedural imaging modality required for the VIV or valve-in-ring procedure.[74,75] Echocardiographic imaging can be an adjunctive imaging modality and has been well described in a recent review.[76] Although mitral prostheses fail more commonly than aortic, most studies in the literature have reported on the aortic VIV procedure. In the Valve-in-Valve International Data Registry with data from 55 participating sites, multivariable determinants of 1-year mortality were as follows: surgical valve ≤21 mm, stenosis as the mode of failure, transapical access, and Society of Thoracic Surgeons score.[77] Both the stent posts and the bioprosthetic leaflets can

obstruct the coronary ostium and thus risk factors include supra-annular valves, low-lying coronary arteries, narrow sinuses and sinotubular junction, bulky prosthetic leaflets, lack of stent frame (ie, homograft or stentless valve), and internal stents.

High transvalvular gradients may be seen particularly if stenosis as the primary mode of failure and in smaller surgical valve sizes (19 or 21 mm). Mean transaortic gradients reported in the Valve-in-Valve International Data Registry registry were 15.9±8.6 mm Hg with >26.8% of patients having mean gradients of ≥20 mm Hg.[77] In vitro evaluation of the balloon-expandable valve performance revealed VIV mean gradients of 9.1±4.1 mm Hg in a 23-mm surgical bioprosthesis, 19.5±5 mm Hg in a 21 mm surgical valve, and 46.5±9.3 mm Hg in a 19-mm surgical valve.[78] If a small surgical heart valve requires a VIV procedure, then theoretically a supra-annular THV device like the self-expanding valve, instead of an intra-annular device might yield larger valve areas.

Transcatheter Mitral Valve Repair With the MitraClip

Transcatheter edge-to-edge mitral valve repair with the MitraClip (Abbott Vascular) is now an established treatment option for patients with severe degenerative MR at prohibitive risk for open repair.[79–82] Delivered to the left atrium by a 24 Fr femoral venous delivery sheath, the cobalt chromium, polyester-covered MitraClip grasps and approximates the edges of opposing mitral leaflet segments. This results in a double orifice similar to the Alfieri stitch.[83] The EVEREST II study (Endovascular Valve Edge-to-Edge Repair) lent support to this treatment option for high-risk patients with functional or degenerative MR, advanced heart failure symptoms, and mitral valve anatomy suitable for percutaneous repair.[84] In this population, transcatheter repair showed improved early safety with no difference in mortality when compared with mitral valve surgery but at the cost of increased MR. The ongoing COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial is currently enrolling patients with moderate-to-severe or severe functional MR in symptomatic heart failure patients who are treated per standard of medical care (ClinicalTrials.gov Identifier: NCT01626079).

One of the primary roles of echocardiographic imaging for transcatheter mitral valve repair is to assess anatomic feasibility. The EVEREST echocardiographic inclusion criteria included: sufficient leaflet tissue for mechanical coaptation, nonrheumatic/endocarditic valve morphology, ≥4 cm^2 mitral valve area, flail gap ≤10 mm, flail width ≤15 mm, coaptation depth ≤11 mm, and coaptation length ≥2 mm. Success rates were highest for regurgitant disease originating from the A2-P2 region.[84] Since the EVEREST trials, however, numerous case reports and observational studies have shown that real-world patients are different and can be successfully treated with this technology.[79,85–87] The 12-month follow-up of consecutive patients who underwent MitraClip implantation in the Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation (GRASP) registry was obtained from an ongoing prospective registry. Two different groups were defined according to baseline echocardiographic criteria (investigational group [$EVEREST_{OFF}$] and control group [$EVEREST_{ON}$]. The primary safety end point at 30 days was comparable between groups (2.6% versus 6.5%, respectively; P=0.204),with similar improvement in New York Heart Association functional class and no difference in Kaplan–Meier freedom from death, surgery for mitral valve dysfunction, or grade ≥3+ MR at 12 months (log-rank P=0.378). Lubos E et al[88] studied 300 patients in whom 10.7% had MitraClip failure, defined as residual MR of >2+ because of either failure to implant a device or inadequate reduction of MR. Although more failures occurred with degenerative MR than function MR, MR pathogenesis was not identified as an independent predictor of procedural failure. Multinomial logistic regression identified an effective regurgitant orifice area >70.8 mm^2 and a

Table 3. Echocardiographic Features Determining Suitability for the MitraClip

	Ideal Echo Features	Challenging Echo Features	Relative Echo Contraindications
Location of pathology	• Segment 2	• Segments 1 or 3	• Body of leaflet (ie, perforation or cleft/deep fold)
Calcification	• None	• Mild, outside grasping zone • Extensive annular calcification	• Severe calcification at site of grasping zone
Mitral valve area/ gradient	• >4 cm^2 • ≤4 mm Hg	• >3.5 cm^2 and <4 cm^2 with small BSA or mobile leaflets • ≥4 mm Hg	• <3.5 cm^2 and ≥4 mm Hg
Grasping zone length	• >10 mm	• 7–10 mm	• <7 mm
Functional MR	• Normal thickness and mobility • Coaptation depth <11 mm	• Carpentier IIIB (restricted) • Coaptation depth >11 mm	• Carpentier IIIA (rheumatic thickening and restriction)
Degenerative MR	• Flail width <15 mm • Flail gap <10 mm	• Flail width <15 mm with large valve area and option for >1 MitraClip • Flail gap >10 mm with possibility of adjunctive measures	• Barlow's disease with significant regurgitation segments 1–3
Other pathology		• Annuloplasty ring with adequate mitral valve area and leaflet length • HOCM with systolic anterior motion • Extreme disease (markedly dilated annulus or EROA ≥70.8 mm^2)	

BSA indicates body surface area; EROA, effective regurgitant orifice area; HOCM, hypertrophic obstructive cardiomyopathy; and MR, mitral regurgitation.

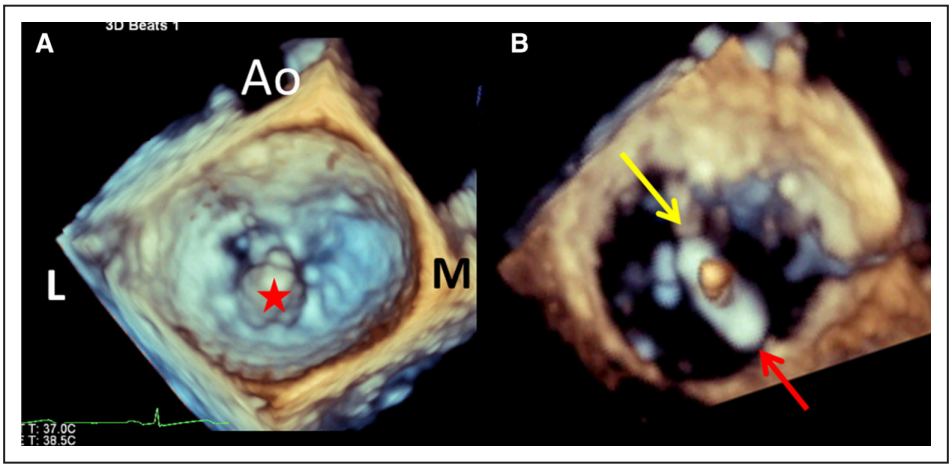

Figure 2. Use of three-dimensional (3D) transesophageal echocardiography (TEE) for MitraClip. **A**, The use of 3D from the surgical view with the aorta (Ao) at the 12 o'clock position, and lateral (L) commissure to the left, medial (M) commissure to the right. The leaflets and location of the flail P2 scallop (star) are imaged using normal gain settings. Imaging of the MitraClip (yellow arrow=anterior arm and red arrow=posterior arm) both above and below the leaflets can be achieved from the midesophageal view by reducing the gain settings (**B**). In this instance, the clip arms should be rotated in a clockwise direction to align perpendicular to the coaptation line.

transmitral mean pressure gradient ≥4 mm Hg as independently predictive of clip failure, and a native mitral valve area ≤3.0 cm^2 and a transmitral mean pressure gradient ≥4 mm Hg as independently predictive of procedure abortion.

Table 3 lists ideal and challenging echocardiographic parameters for the MitraClip. Poor candidates may include those with large effective regurgitant orifice area and small baseline valve area, and also a markedly dilated mitral annulus that would benefit from annular reduction.[89] Many case reports show the feasibility of the procedure in mitral morphology that might be not have been considered feasible before the extensive use of 3D TEE imaging. These include patients with failed mitral annular rings[90–92] and systolic anterior motion of the mitral valve.[93,94] 3D TEE may also improve procedural success and shorten procedure time for the MitraClip device (Abbott Vascular Structural Heart; Figure 1).[19,21,95] Not only is multiplane imaging (a 3D function) essential during all steps of the procedure, but real-time 3D imaging from a fixed position in the midesophagus allows rapid imaging of clip arm orientation above and below the leaflets (Figure 2). The procedural steps with recommended imaging techniques for the MitraClip are listed in Table 4. Altiok et al[19] performed a structured analysis to compare information and guidance capability provided by RT3D TEE compared with 2D TEE and found 3D TEE advantageous in 9 of 11 steps of the percutaneous mitral repair procedure, including optimizing transseptal puncture site, guidance of the clip delivery system, precise positioning of the clip delivery system simultaneously in anterior–posterior and lateral–medial direction, valvular regurgitation jet position, adjustment and visualization of the clip position relative to the valvular orifice, and assessment of remaining regurgitant jets. After MitraClip, assessment of residual regurgitation could also be assessed by 3D color Doppler. A >50% reduction in regurgitant volume using the product of vena contracta areas defined by direct planimetry of RT3D color Doppler and velocity time integral using continuous-wave Doppler was associated with greater left atrial and ventricular remodeling.[33]

Multiple operators have suggested various advanced techniques to aid the leaflet capture of difficult cases with less than ideal coaptation characteristics. These include the following:

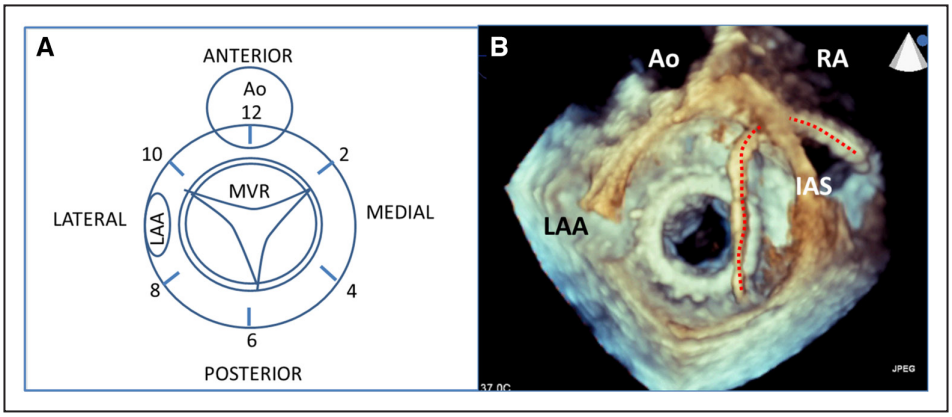

Figure 3. Recommended surgical view for a mitral valve replacement. **A**, A schematic of mitral valve replacement (MVR) in the surgical view. **B**, A bioprosthetic MVR with an Agilis catheter across the interatrial septum and directed toward a paravalvular regurgitant leak at the 5 o'clock position (red dotted line). Ao indicates aorta; IAS, interatrial septum; LAA, left atrial appendage; and RA, right atrium.

Table 4. Procedural Imaging Steps for MitraClip

Procedural Step for MitraClip	Imaging Recommendations	TEE Mode	Probe Position
Transseptal puncture and introduction of catheters	• Locate the position and direction of transseptal catheter puncture 3.5–4 cm above the annular plane in the midposterior fossa with a posterior and superior direction of the catheter	• 2D localization • 3D confirmation if necessary	• Midesophageal bicaval view (transducer angle 90–100°) for superior-inferior position • Midesophageal aortic valve short-axis view (35–60°) for anterior-posterior position
	• Position the MitraClip guiding catheter so that the tip (double-echodensity) is across the interatrial septum	• 2D primarily • 3D if tip is out-of-plane	• Midesophageal bicaval view (rotating transducer counterclockwise as the guide is advanced)
Advancing the clip delivery system	• Follow the entrance of the Clip into the left atrium, ensuring that the clip is clear of adjacent anatomy	• 2D to image the distal end of the clip • 3D confirmation if necessary (simultaneous multiplane 2D and 3D surgical view)	• Midesophageal 4Ch/ Commissural/2Ch views (3D surgical view from any position)
	• Guide the manipulation of the steering mechanisms to position the clip above the A2-P2 scallops	• 2D imaging of grasping region • 3D confirmation (simultaneous multiplane 2D and 3D surgical views)	• Midesophageal commissural view with simultaneous multiplane image of the long-axis view • 3D surgical view from any position
Position the clip and orient the clip arms	• Based on the preprocedural anatomic imaging (TEE) of the mitral valve, the clip is positioned over the regurgitant orifice	• 3D (simultaneous multiplane 2D and 3D surgical views)	• Midesophageal 3D surgical view from any position
	• The clip arms are partially opened to determine orientation	• 3D (surgical view)	• Midesophageal 3D (surgical view)
	• Guide the orientation/rotation of the clip arms to be perpendicular to the leaflets at the site of the regurgitant orifice*	• 3D (surgical view)	• Midesophageal 3D (surgical view)
	• Use color Doppler to confirm positioning above the regurgitant jet	• 2D color Doppler • 3D color Doppler confirmation (simultaneous multiplane 2D)	• Midesophageal commissural view and long-axis view
Positioning below the leaflets	• Check the trajectory of the clip in the medial–lateral plane	• 2D (single plane) • 3D confirmation with simultaneous multiplane 2D • 3D surgical view most helpful	• Midesophageal commissural view is helpful to determine medial–lateral orientation
	• Confirm orientation of the clip arms†	• 3D (simultaneous multiplane 2D) • 3D surgical view most helpful	• Midesophageal views • 3D (surgical view)
Grasping the leaflets	• Assess position of the clip beneath the regurgitant orifice	• 2D color Doppler • 3D color Doppler confirmation (surgical view)	• Midesophageal views (long-axis view of open clip arms most helpful)
	• Continuously image the 2 clip arms as the clip is withdrawn (toward the leaflets) and grasps both anterior and posterior leaflets with the device grippers	• 2D (single plane) • 3D confirmation with simultaneous multiplane 2D (Note: 3D surgical views less helpful)	• Midesophageal long-axis view of open clip arms with assessment of amount of posterior and anterior leaflet grasp
	• Verify capture of both leaflets prior to full closure of the clip arms‡	• 2D (single plane) • 3D confirmation with simultaneous multiplane 2D (Note: 3D surgical views less helpful)	• Midesophageal 2D long-axis view • Midesophageal 3D commissural view
	• Recapture if confirmation of capture cannot be made	• (see above)	• (see above)
	• On initial closure note reduction in MR (may see acute increase in BP)	• 2D color Doppler • 3D color Doppler confirmation (surgical view)	• Midesophageal views
Postdeployment assessment	• Verify mitral regurgitation reduction by multiple methods:	• Color Doppler for MR jet area and vena contracta with 3D planimetry of the vena contracta • PW Doppler for reversal of pulmonary vein flow • CW Doppler for peak and mean transmitral gradients • Planimeter double orifice for total effective orifice area	• Midesophageal views

(*Continued*)

Table 4. Continued

Procedural Step for MitraClip	Imaging Recommendations	TEE Mode	Probe Position
Determine whether second clip is required	• Position second clip if needed: ensure second clip does not dislodge first clip, follow usual grasping protocol	• (see above)	• (see above)
Image the delivery catheter to assure safe withdrawal	• Avoid lateral LA structures	• 2D to image the distal end of the delivery catheter • 3D confirmation if necessary (simultaneous multiplane 2D and 3D surgical view)	• Midesophageal 4Ch/ Commissural/2Ch views (3D view from any position)
	• Document the resulting interatrial defect	• 2D imaging • 3D confirmation if necessary	• Midesophageal bicaval view

*Although typically the clip is perpendicular to the commissures, maximum reduction in regurgitant volume may require an off-axis orientation of the clip.

†Reducing gain to the point where leaflets are no longer seen will allow imaging of the clip arms below the leaflets (Figure 3B).

‡Use of simultaneous multi-plane imaging with the commissural view as the primary view permits imaging of long-axis views on either side of the clip to confirm capture of both leaflets.

2D indicates 2-dimensional; 3D, 3-dimensional; LA, left atrium; PW, pulsed wave; and TEE, transesophageal echocardiography.

1. Attempt an acute angle of approach for extreme flail: aorta hugging in cases of extremely deviated posterior leaflet and posterior approach for dynamic posterior left ventricular motion.
2. Rapid pacing in selected cases where leaflet coaptation is improved in the systolic position (ie, tethered leaflets).
3. Adenosine in selected cases where leaflet coaptation is improved in the diastolic position (ie, flail leaflets).
4. Breath holds to reduce medial–lateral motion.
5. Performing 2 clips: the first grasp may be adjacent to the largest coaptation gap to approximate leaflets and facilitate the second clip grasp.

Final assessment of the post-MitraClip procedure should always include measurement of the peak and mean transmitral gradient, planimetry of the resulting mitral orifices from short-axis views, color Doppler assessment of residual regurgitation (vena contracta diameters and jet area) with use of 3D color Doppler measurement of vena contracta area if possible, pulsed wave Doppler of the pulmonary veins, and at least a visual assessment of the residual interatrial shunt (significant shunts have a color Doppler diameter typically of at least 1 cm). Data from the Society of Thoracic Surgeons/ American College of Cardiology Transcatheter Valve Therapy Registry on patients commercially treated with the MitraClip have recently been reported.[96] Although the success rate of the MitraClip (defined as a composite of postimplantation MR of grade ≤2+, without conversion to open cardiac surgery, and without in-hospital mortality) is high (91%), there are complications that can be diagnosed during the procedure by echocardiography including cardiac perforation (with or without tamponade), injury to the mitral leaflets or subvalvular apparatus, and transseptal complications. Device-specific adverse events were defined as occurrence of single leaflet device attachment, complete detachment of leaflet clip, device thrombosis, or device or delivery system component embolization. MitraClip detachment can be avoided by careful systematic assessment of leaflet insertion before complete clip closure and final assessment of adequacy of MR reduction.[97] In addition, entrapment of chordal apparatus can be detected by leaflet tethering in excess of that expected with the MitraClip and may contribute to excessive reduction in mitral valve area and increase in mean gradients. The expected reduction in mitral valve area compared with the patient's baseline is ≈40% but was greater for function MR patients compared with degenerative MR patients. There was no significant difference in reduction for 1 compared with 2 clip procedures. The mean mitral valve gradient increased after clip placement from 1.7±0.9 to 4.1±2.2 mm Hg (P<0.05).[98]

Transcatheter Mitral Valve Replacement

The use of balloon-expandable TAVR devices in the mitral position has been discussed in the setting of the VIV procedure; however, numerous reports have also shown the feasibility of implanting these devices within native mitral stenosis secondary to severe mitral annular calcification.[99–103] Initial results showed a significant rate of embolization and LVOT obstruction; however, the current investigator-initiated multicenter Mitral Implantation of TRAnscatheter vaLves (MITRAL) trial currently underway (ClinicalTrials.gov Identifier: NCT02370511) has focused on preprocedural imaging with multi-slice computed tomography (MSCT) to help define the population at risk for these complications. Although current American Heart Association/American College of Cardiology guidelines recognize the clinical importance of significant functional MR, there are currently no studies that show that intervention in these patients improves outcomes. Nonetheless, transcatheter mitral valve replacement may be a future option in patients with advanced mitral valve disease deemed high or prohibitive risk for surgery.[99,101–106] The mitral valve has numerous anatomic considerations that make transcatheter valve design more complicated than the AV: a complex and dynamic mitral annular geometry, an asymmetrical bileaflet anatomy, left ventricular interaction through papillary muscles and attached chordae, and continuity between the mitral inflow and aortic outflow. In addition, unlike for valve-in-mitral annular calcification, there is no calcified anchoring structure, and the closing forces on the mitral valve (ie, ventricular systolic pressure) are greater than the systolic or diastolic force on the AV. Numerous valve designs are currently in various stages of clinical application; however, similar to valve-in-mitral annular calcification, procedural planning relies on preprocedural

imaging with TEE and MSCT, and intraprocedural imaging with TEE. LVOT obstruction remains a primary concern for most valve designs, as is direct interaction with the AV. The imaging protocols for each device vary depending on the access site (transfemoral vein, direct transatrial, or transapical), the anchoring mechanism (leaflets, annulus, or apical tether), and the height and intended position of the valve (annular or supra-annular). Protocols for imaging will likely be developed during this early investigational period.

Surgical Prosthetic Valve PVR

Many studies have shown that percutaneous closure of PVR is not only possible using many different devices[107–111] but also successful in treating both heart failure and hemolysis.[112–115] Thus, percutaneous repair is an attractive alternative to repeat valve replacement given the high procedural success rate.[112,113]The current class IIa indication for percutaneous intervention includes patients with prosthetic heart valves and intractable hemolysis or New York Heart Association class III/IV heart failure who are at high risk for surgery with anatomic features suitable for catheter-based therapy and when performed in centers with expertise in the procedure (level of evidence B). Improvement in heart failure symptoms is typically limited to patients with no or mild residual regurgitation after closure.[114] Early studies suggested that improvement in hemolysis, however, was variable, with ≤33% of patients experiencing worsening of hemolysis and 10% developing new hemolysis.[116] Persistent or worsening hemolysis was likely because of the use of devices with a large-caliber nitinol mesh that fail to conform to the irregular shapes of the paravalvular defects. More recently, the Amplatzer vascular plug (AVP II and IV) devices have been used that have a smaller profile and conform to the shape of the defect allowing them to fit into the small, irregular paravalvular defects resulting in reduced paradevice leak and hemolysis.

Standard TEE imaging views for the aortic and mitral valves should be used throughout the preinterventional imaging and procedural guidance.[117] Much of the preprocedural assessment of paravalvular leaks are performed by 3D imaging.[3] The surgical or anatomic view of the mitral valve is suggested by the American Society of Echocardiography guidelines places the AV anterior (or at 12 o'clock) with the left atrial appendage identifying the medial sewing ring (9 o'clock), and the interatrial septum the medial sewing ring (3 o'clock; Figure 3).

Echocardiographic imaging for aortic prostheses may require multiple imaging planes (deep esophageal or transgastric views) because of acoustic shadowing of the anterior sewing ring. Alternatively ICE can be used, but the experience with this imaging modality during paravalvular leak closure is more limited. Periaortic leaks can typically be approached via a retrograde aortic approach. Transcatheter closure of mitral PVR can be approached from a retrograde or antegrade approach. The transapical approach for mitral PVR closure has been shown to reduce procedural and fluoroscopy time[118]; however, use of a steerable guide catheter (ie, Agilis) has made the antegrade approach highly feasible for any paramitral paravalvular defect (Figure 3B).

Preprocedural planning for transcatheter closure of PVR requires a determination of (1) the number and location of defects; (2) the shape and exact size of the each defect; (3) the distance and orientation of the defect to the sewing ring or

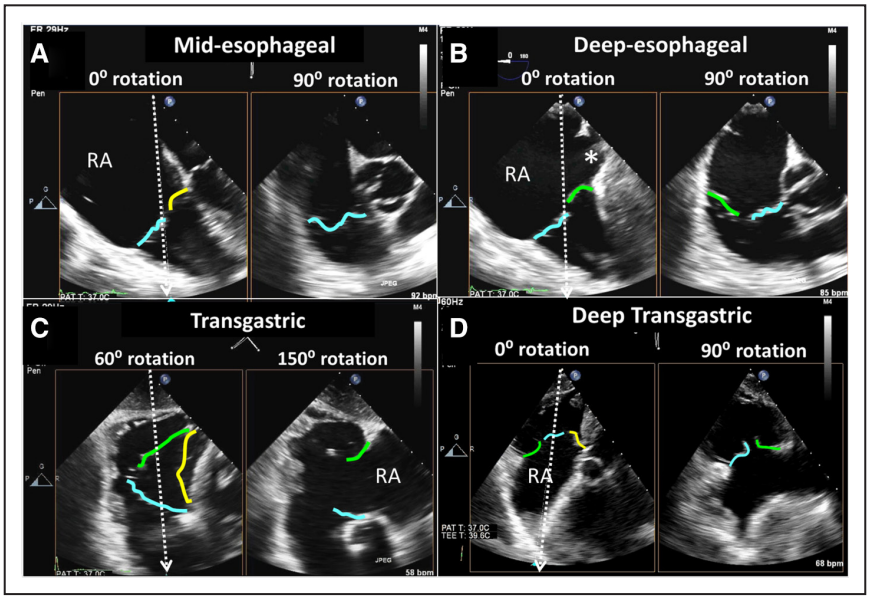

Figure 4. Multilevel imaging of the tricuspid valve (TV). **A**, An example of simultaneous multiplane imaging at the midesophageal depth. The 4-chamber view permits visualization of the septal and typically the anterior leaflet; simultaneous biplane imaging may help clarify which leaflet is imaged because the anterior leaflet is typically seen adjacent to the aorta. Low esophageal views (**B**) at the level of the coronary sinus (*) typically image the posterior and anterior leaflets. Advancing the TEE probe into the stomach and rotating ≈20–60° produces the transgastric basal short-axis view (**C**), which is the only 2-dimensional (2D) view that usually provides simultaneous visualization of all 3 TV leaflets. Using the simultaneous multiplane imaging mode, all the leaflet coaptation points can be imaged. Advancing the transesophageal echocardiography probe along with rightward anterior flexion and returning the multiplane angle to 0–20° produces a deep transgastric view of the TV (**D**).

prosthesis. This assessment requires extensive 2D and well as 3D transesophageal imaging.[113,119,120] The shape and size of the defect determines the choice of device. Long, crescent-shaped leaks often require multiple closure devices. Para-aortic leaks tend to be smaller than para-mitral leaks, and simultaneous or sequential closure devices are infrequently necessary.

Intraprocedural TEE can help recognize many complications including malpositioning of the closure device[35] and obstruction or impingement of prosthetic occluders, device embolization, and coronary artery obstruction secondary to device protrusion over the ostia of the coronary arteries. After device deployment, a full assessment of prosthetic valve function should be performed. This includes (but is not limited to) 2D and 3D imaging of the prosthesis to assess function, continuous-wave Doppler across the prosthetic orifice for the assessment of peak/mean gradients, 2D and 3D color Doppler assessment of residual PVR, effect of device placement on flow in the pulmonary veins and pulmonary artery pressures, and residual transseptal defect.

Transcatheter Approaches to Tricuspid Regurgitation

The rapidly increasing interest in functional tricuspid regurgitation (TR) has been generated by poor outcomes associated with severe secondary disease.[121–124] The most recent post hoc analysis of the PARTNER IIB study (Placement of Aortic Transcatheter Valves) confirms that in the setting of TAVR, baseline severe TR may adversely influence outcomes.[125] Baseline significant TR also predicted mortality after transcatheter mitral valve repair.[126] Current American Heart Association/American College of Cardiology guidelines recommend optimal medical therapy for patients with severe primary TR with class I indication for surgical intervention on the tricuspid valve during their initial left heart valve surgery.[127] In patients who develop severe TR late after left heart valve surgery, operative mortality may be as high as 35%.[128–132] In addition, because high-risk surgical patients undergo transcatheter repair or replacement of their mitral valve disease, less invasive therapeutic options for the tricuspid valve are needed.

Similar to mitral valve interventions, echocardiographic imaging of the tricuspid valve will play an essential intraprocedural role. The American Society of Echocardiography guidelines for a comprehensive TEE examination includes 8 additional imaging views, many of which focus on the right heart and tricuspid valve.[60] Although from the midesophageal views the tricuspid valve is in the far-field, the tricuspid valve becomes near-field in both deep esophageal (gastroesophageal junction) and deep transgastric views, allowing for optimal imaging of this valve for procedures (Figure 4). The following discussion of some of the tricuspid valve devices in development or early trials relies on TEE intraprocedural imaging guidance, and protocols for each device are currently being developed.

Patients with severe TR experience symptoms of chronic right heart failure (peripheral edema, ascites, and orthopnea) with congestive hepatopathy. Treatment of the upstream effect of severe TR by placing valved stents within the venae cavae has been performed by Lauten et al[133] by placing 2 custom-made transcatheter valves into the superior vena cava and inferior vena cava. The inferior vena cava valve was designed to protrude into the right atrium and prevent backflow into the hepatic veins without causing obstruction. The funnel-shaped superior vena cava valve was designed with a skirt covering the entire base of the valve to prevent paravalvular leakage. In the first-in-human report of this technique, there was immediate fall in vena caval pressures with increase in cardiac output. During the 12-month follow-up of this patient, there was continued improvement in mean caval pressures, improvement in symptoms, and normalization of liver function. Current trials testing the hypothesis of treating congestive hepatopathy are underway. The single-center HOVER (Heterotopic Implantation Of the Edwards-Sapien XT Transcatheter Valve in the Inferior VEna Cava for the Treatment of Severe Tricuspid Regurgitation) trial (ClinicalTrials.gov Identifier: NCT02339974)[134] is testing the short-term safety (<30 days) and mid- and long-term efficacy (6 months and >1 year) of the heterotopic implantation of the Edwards-Sapien XT valve in the inferior vena cava for the treatment of severe TR in patients who are inoperable or at a high surgical risk for tricuspid valve replacement.

With the increasing global use of mitral valve repair devices such as the MitraClip (Abbott Vascular, Abbott Park, IL), attempts have been made to translate these devices to the tricuspid valve. The only published used of the MitraClip for TR has been in a patient with congenitally corrected transposition of the great arteries[135]; however, multiple unpublished cases of this technique (personal communication) have been successfully performed in noncongenitally abnormal tricuspid valves.

The Mitralign system (Mitralign, Inc, Tewksbury, MA) received Conformité Européene (CE) mark in Europe for use in patients with severe MR and recently reported the first-in-human implantation of their device on the tricuspid annulus.[25] The Trialign device places pledgeted sutures within the tricuspid valve annulus by means of a transjugular venous approach. A dedicated plication lock device is used to bring the 2 pledgeted sutures together, plicating the annulus and effectively bicuspidizing the tricuspid valve. Initial compassionate use cases in Europe and Canada show significant reductions of regurgitant orifice and annular area. The SCOUT (Early Feasibility of the Mitralign Percutaneous Tricuspid Valve Annuloplasty System) trial (ClinicalTrials.gov Identifier: NCT02574650) is currently enrolling in the United States.

Numerous studies have shown that in function TR, the tricuspid annulus dilates in the septolateral direction. Thus, investigators of The TriCinch System (4TECH Cardio, Galway, Ireland) have developed a tethering device that cinches the anteroposterior dimension of the annulus to improve coaptation. The delivery system allows transfemoral fixation of a stainless-steel corkscrew anchor into the anteroposterior tricuspid valve annulus, which is connected through a Dacron band to a self-expanding nitinol stent placed in the hepatic region of the inferior vena cava. It has been implanted in a limited number of patients with isolated functional TR; however, no published results are available. The PREVENT (Percutaneous Treatment of tricuspid valve Regurgitation With the TriCinch

System) trial (ClinicalTrials.gov Identifier: NCT02098200) is currently enrolling.

A simpler approach to a large regurgitant orifice would be to place a device in the center of the regurgitant orifice, reducing the orifice and forming a surface against which the leaflet tips coapt. The initial experience with the Forma Spacer (Edwards Life Sciences, Irvine, CA) device showed successful device implantation without procedural complications in all 7 patients, with significant reductions in TR severity (moderate in 3 patients and mild in 4 patients).[24] This device is implanted from a left subclavian vein approach, introducing an anchor, attached to a foam-filled spacer device. The anchor is positioned within the right ventricular wall, and the spacer is positioned within the central coaptation of the leaflets using echocardiographic guidance. Because leaflets close on the device, malcoaptation and regurgitation are reduced. The early feasibility trial for this device (ClinicalTrials.gov Identifier:NCT02471807) is currently enrolling.

Disclosures

Dr Hahn reports consulting agreements with Abbott Vascular and St. Jude Medical. She is a speaker for Abbott Vascular and GE Healthcare. She is the nonpaid Principle Investigator for the SCOUT Trial. She is the Cardiovascular Research Foundation Echo Core Laboratory Director for a number of trials for which she receives no direct compensation.

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