

Imaging Considerations for Percutaneous Tricuspid Intervention

A review of imaging options relevant to treating functional tricuspid regurgitation with transcatheter techniques.

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Functional or secondary tricuspid regurgitation (TR) is the most common etiology of severe TR,¹ which is progressive^{2,3} and affects patient mortality.⁴⁻⁷ The high prevalence of secondary TR with mitral valve disease,^{8,9} as well as the association with pulmonary hypertension^{6,10,11} and right ventricular dilatation and dysfunction,¹¹ point to the complexity of the disease. The only treatment for functional TR that has a class I indication is use of a diuretic,¹² and once annular dilatation occurs, tricuspid repair and replacement may be needed to prevent disease progression and to improve outcomes.¹³⁻¹⁶ However, this algorithm fails to recognize the frequent comorbidities associated with or resulting in TR.

Trend analysis of the Society of Thoracic Surgeons database between 2000 and 2010 confirmed that, over that time span, patients who underwent surgery for TR in the United States increased in age, comorbidity burden, and proportion of emergency presentations.¹⁷ As a result, surgical mortality for isolated tricuspid valve interventions remains higher than for any other single valve surgery.^{17,18} This evidence has supported early prophylactic interventions (combined tricuspid repair for less severe TR at the time of the left-sided disease treatment); however, concomitant valve surgery for TR remains underutilized.¹⁹⁻²¹

Finally, as more left-sided valve disease is treated with transcatheter therapies,²²⁻²⁵ the negative impact of TR on survival in these patients²⁶⁻²⁸ has underscored the importance of developing transcatheter solutions for this disease. Numerous lessons should be learned from the high recurrence rate after surgical repair for TR.²⁹ One such lesson is that imaging is key to understanding the pathoanatomy, predictors of recurrent or progressive

disease, and appropriateness of transcatheter treatment. Therefore, appropriate imaging is essential for preprocedural, intra-procedural, and postprocedural assessment of transcatheter therapies.

RIGHT HEART ANATOMY WITH FUNCTIONAL TR

Echocardiography remains the primary imaging modality for assessment of right heart size,³⁰ and a number of measurements can be used to describe tricuspid annular and right ventricular changes with functional TR. When functional dilatation occurs, the septal portion of the annulus, which is supported by attachment to the muscular septum, is typically spared, and so the annulus primarily dilates along the anterior and posterior leaflet attachments, causing the annulus to become more circular and planar.³¹ Greater degrees of TR are associated with larger annular areas, larger right and left atrial volumes, a more circular annular shape, and right ventricular (RV) dilatation.³² Animal models of TR have suggested that greater degrees of TR may not be related to a loss of the three-dimensional (3D) annular shape but rather are associated with (1) greater “stretch” of the posterior leaflet (as compared to the anterior or septal leaflets), (2) greater annular or RV dilatation, and/or (3) displacement of the papillary muscles.³³

Recent studies, however, have also shown that significant anatomic differences in the RV, valve, and annular anatomy may occur based on the etiology of functional TR.¹¹ With idiopathic TR, there was marked basal RV dilatation associated with annular dilatation in the absence of leaflet tethering, with relatively normal RV length (RV conical deformation). With functional TR

associated with pulmonary hypertension, there was significant lengthening of the RV with less basal dilatation (and low basal:midventricular diameter ratios) but more midventricular dilatation, resulting in both increased tenting as well as elliptical/spherical RV deformation.^{11,34} The RV morphologic changes associated with pulmonary hypertension may, in part, be related to ventricular interdependence and the interventricular septal shape and dyssynchrony, which is evident on echocardiography as flattening of the interventricular septum.³⁵

RV function is another important contributor to functional TR. Echocardiographic measurements of RV function include tricuspid annular plane systolic excursion, fractional area change, 3D ejection fraction, tissue Doppler for peak systolic annular velocity, and longitudinal strain.³⁰ RV dysfunction is commonly associated with significant TR in the setting of left heart valvular disease^{20,36-38} and likely reflects a longer duration of severe TR.³⁷ After tricuspid annuloplasty, RV function typically improves.²⁰ At what point the right heart fails to improve, however, is unknown. Measures of RV function remain unclear determinants of outcome, with some studies suggesting no significant impact of reduced function on outcomes.^{39,40}

ECHOCARDIOGRAPHIC PREDICTORS OF PROGRESSION OR PERSISTENT DISEASE AFTER LEFT HEART SURGERY

After isolated mitral valve repair, significant residual TR is observed in up to 40% of patients.⁴¹ In patients undergoing concomitant TR repair at the time of mitral surgery, persistent severe TR is still present in 11% at 3 months and in 17% at 5 years.²⁹ Clinical predictors for residual regurgitation after surgical repair have been identified and include higher preoperative TR severity, higher pulmonary artery pressures, mitral replacement rather than repair, worse left ventricular dysfunction, and the presence of pacemaker leads through the valve.⁴²

Echocardiographic predictors of recurrent or progressive disease have also been identified. Significant tricuspid annular dilatation, as measured by transthoracic echocardiography (TTE), may be a better predictor of severe late TR after mitral valve surgery than those previously mentioned.^{14,43,44} Because of the linear relationship between annular diameter and TR volume, the annular diameter criterion has been used as a surrogate for regurgitation volume. Significant annular dilatation is defined by a diastolic diameter ≥ 40 mm or > 21 mm/m² in the four-chamber transthoracic view^{44,45} and is the main imaging criteria used to indicate severe TR in the current American Heart Association/American College of Cardiology guidelines.⁴⁵ Severe TR (stages C and D) is

associated with poor prognosis independent of age, left and right systolic function, and RV size.^{10,46}

Other authors⁴⁷ suggest that the cutoff for severe TR should be > 42 mm or 23 mm/m², which is supported by other studies.⁴⁸ Dreyfus et al⁴⁴ studied intraoperative predictors of worsening TR and found that 48% of patients with a tricuspid annular dimension > 70 mm (septolateral dimension) had worsening TR over time if not repaired at the time of surgery (compared to only 2% with a concomitant repair). Recent studies, however, have called into question the appropriateness of this measurement.⁴⁷ The complex 3D shape of the RV and the multiple apical imaging windows suggested by the recent echocardiographic guidelines³⁰ make for low reproducibility of this single-dimension measurement.

Numerous authors have explored the relationship between tenting of the leaflets and severity of TR, with tenting areas and volumes correlating with TR severity and with recurrence and outcomes after surgical repair.^{42,49-52} A TTE tethering distance > 0.76 cm or tethering area > 1.63 cm predicted recurrent TR after surgery.^{42,53} Tethering has been associated with RV dilatation, and an RV end-systolic area ≥ 20 cm², as determined by TTE, predicted worse event-free survival rates.³⁹

GRADING THE SEVERITY OF TR

Grading of TR severity has been reviewed in the recently updated American Society of Echocardiography (ASE) guidelines,⁵⁴ as well as the European Association of Echocardiography guidelines.⁵⁵ The parameters include structural variables (tricuspid valve morphology, right atrial and RV size, and inferior vena caval diameter) as well as qualitative parameters (color jet parameters, including jet area and flow convergence, and continuous wave Doppler), semiquantitative parameters (color jet area, vena contracta width, proximal isovelocity surface area [PISA] radius, hepatic vein flow, and tricuspid inflow pattern), and quantitative parameters (effective regurgitant orifice area [EROA] and regurgitant volume). Importantly, many of the studies validating the use of various echocardiographic parameters, particularly quantitative measures, have significant limitations and lack of a "gold standard" for comparison or support from outcomes data.

As transcatheter devices are being developed and tested, it is becoming increasingly important that accurate methods of assessing TR severity be validated. Although the PISA method is simple and easy to perform,⁵⁶ the complex relationship of the isovelocity shell to the often elliptical shape^{57,58} and large size of the TR EROA results in a significant underestimation of the true EROA.⁵⁹ More recently, 3D PISA has been used to

quantify TR.⁶⁰ This method uses a vendor-specific software package to analyze the largest convergence zone. Three-dimensional PISA-derived EROA correlated well with 3D planimeted vena contracta area ($r = 0.97$) and may overcome the underestimation of two-dimensional (2D) methods.

Quantification of TR by relative stroke volumes has shown high correlation with catheterization-derived data^{56,61,62} but is underused and not currently advocated by the guidelines. The recently published early feasibility trial of a pledgeted suture annuloplasty device suggested methods for quantifying TR using quantitative Doppler.⁶³ In this study, tricuspid diastolic stroke volume was calculated as the product of the tricuspid annular area and pulsed-wave Doppler annular velocity-time integral (VTI). Tricuspid annular area was calculated with the elliptical formula, using diameters obtained from the orthogonal plane (inflow and the four-chamber views) in early diastole (one frame after initial valve opening) to more accurately calculate annular area. Tricuspid annular area was then multiplied by the tricuspid annular VTI to obtain diastolic stroke volume. The regurgitant volume was calculated as tricuspid valve diastolic stroke volume minus forward stroke volume. The EROA was calculated as the regurgitant volume divided by the TR VTI.

In this study, 2D PISA underestimated quantitative EROA in all patients by up to twofold. The two measurements were nonetheless highly correlative, and a reduction in both PISA EROA and quantitative EROA after transcatheter suture annuloplasty was associated with an increase in left ventricular stroke volume. These echocardiographic improvements in valvular and ventricular hemodynamics were associated with significant improvements in 6-minute walk test, New York Heart Association class, and Minnesota Living With Heart Failure Questionnaire, which helps validate the feasibility of the method for quantification.

A number of studies have shown the utility of 3D color Doppler to quantify TR by planimetry of the vena contracta area.^{57,60,64,65} Velayudhan et al was one of the first to correlate standard Doppler methods of quantifying TR with planimetry of the 3D vena contracta area. Using the validated measure of regurgitant jet area/right atrial area $> 34\%$ ⁶⁶ and regurgitant jet area $> 10 \text{ cm}^2$ to define severe TR,⁶⁷ a 3D TTE planimeted vena contracta area of $> 0.75 \text{ cm}^2$ was the most sensitive cutoff (sensitivity, 85.2%; specificity, 82.1%). This higher cutoff has also been demonstrated by Chen et al, with severe TR (as defined by 2D criteria) associated with a 3D vena contracta area of $> 0.6 \pm 0.4 \text{ cm}^2$ and nonsevere TR (as defined by 2D methods) associated with a 3D vena contracta area of

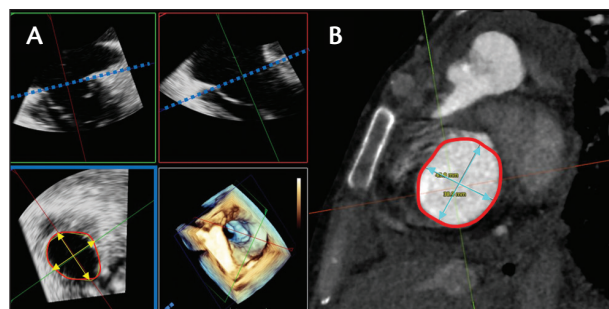


Figure 1. Three-dimensional TEE and CT measurements of the tricuspid annulus. Multiplanar reconstruction of the tricuspid annulus on 3D TEE taken from the deep esophageal view (A). The blue-framed panel shows the annular area and dimension measurements of the tricuspid annulus. Plane of the tricuspid annulus on CT with similar measurements (B).

$\leq 0.3 \pm 0.1 \text{ cm}^2$. However, the receiver-operator curve demonstrated that a 3D vena contracta area of 0.36 cm^2 was the best cutoff value for severe TR, with a sensitivity of 89% and a specificity of 84% in predicting severe TR as defined by 2D echocardiographic integrative criteria.

However, current devices under investigation serve an unusual population of patients. In the SCOUT trial,⁶³ a quantitative EROA of $\leq 1.2 \text{ cm}^2$ was used for inclusion in the trial, and numerous patients were excluded who had an EROA that exceeded this cutoff. Because this patient population has largely been neglected until now, they often present with symptoms late in the disease process with regurgitant orifices that are two- to threefold more severe than what qualifies as severe TR.

Thus, a new grading scheme has been proposed that extends the current ASE categories (mild, moderate, and severe) to include massive (also suggested by the European Association of Echocardiography), as well as torrential.⁶⁸ In this proposal, the additional grades are generated using the ranges defined by the mild, moderate, and severe categories. Thus, *massive* is defined as an average (from two orthogonal planes) vena contracta diameter of 14 to 20 mm, an EROA (by PISA) of 60 to 79 mm^2 , and a 3D vena contracta area or quantitative EROA of 95 to 114 mm^2 . *Torrential* is defined as a vena contracta diameter $\geq 21 \text{ mm}$, an EROA (PISA) of $\geq 80 \text{ mm}^2$, and a 3D vena contracta area or quantitative EROA of $\geq 115 \text{ mm}^2$. Using the old grading scheme, the reduction of mean quantitative EROA from $0.85 \pm 0.22 \text{ mm}^2$ to $0.63 \pm 0.29 \text{ mm}^2$ in the SCOUT trial would not represent a change in severity; however, using the new grading scheme, there is a one-grade reduction that more accurately reflects the changes in TR associated with clinical benefit.

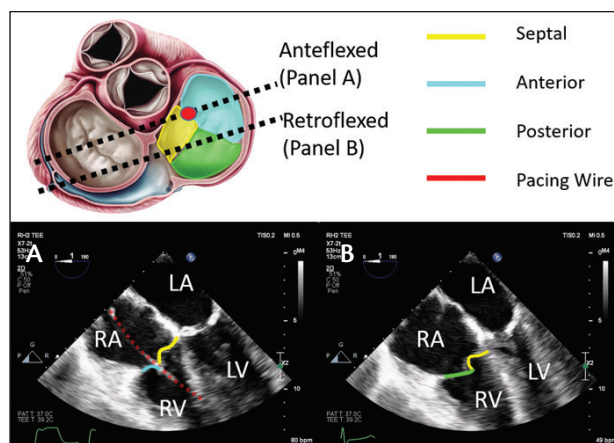


Figure 2. Mid-esophageal four-chamber view of the tricuspid valve. In this example, a temporary pacing wire (red circle or dashed line) has been placed in the septal-anterior commissure to help identify the anatomy. The mid-esophageal four-chamber view, obtained by clockwise rotation of the probe to center the tricuspid valve, will typically image the septal and anterior leaflet (A); however, with retroflexion of the probe, the septal-posterior coaptation is imaged (B). Abbreviations: LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

OTHER IMAGING MODALITIES FOR ASSESSING THE TRICUSPID VALVE

Given the complex, 3D anatomy of both the tricuspid annulus and right ventricle, it is likely that 3D imaging modalities such as 3D echocardiography, CT scanning (Figure 1), and cardiovascular MRI will replace current measurements, which primarily rely on 2D imaging.⁶⁹⁻⁷¹ There are some challenges to imaging the right heart. Homogeneous enhancement of the structures around the tricuspid valve annulus may be difficult, with streak artifact arising from high-attenuation superior vena cava contrast enhancement mixing with unenhanced blood of the inferior vena cava. These artifacts may be reduced by a femoral vein injection of contrast or, ideally, simultaneous injections.^{69,72} Assessing the end-systolic tenting distance and tricuspid annular dimensions, as well as right ventricular volumes and function, is feasible by CT in patients with functional TR.^{70,73}

Kabasawa et al⁷³ showed that preoperative leaflet tenting angles correlated with TR severity, and a tenting distance of > 7.2 mm predicted recurrent TR $\geq 2+$ after surgical annuloplasty. Furthermore, van Rosendaal et al⁷⁰ showed that patients with TR < 3+ have significantly smaller CT annular measurements (anteroposterior diameter; septal-lateral diameter, perimeter, and area) and lower ventricular volumes. Patients with TR $\geq 3+$ had significantly larger tenting angles of the septal

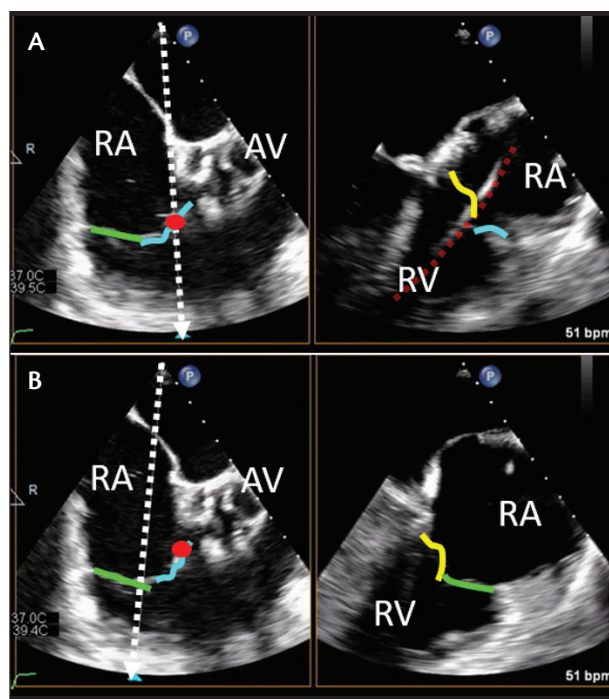


Figure 3. Mid-esophageal biplane imaging of the tricuspid valve. The 60° to 90° view typically allows imaging of the anterior (adjacent to the aorta) and posterior leaflets. Using simultaneous multiplane imaging from this primary view will then permit imaging of anterior-septal coaptation (A), as well as posterior-septal coaptation (B). Note: the color code for tricuspid leaflets is the same as in Figure 2. Abbreviations: AV, aortic valve; RA, right atrium; RV, right ventricle.

and anterior leaflets but not of the posterior leaflet. Significant predictors of TR included pulmonary artery systolic pressure, RV end-systolic volume, and anteroposterior tricuspid annular diameter.

Other studies have shown that CT-defined annulus area correlated strongly with right and left atrial volume, and the annulus shape changed from elliptical to circular in moderate/severe TR.³² Atrial enlargement occurs before right ventricular dilation, which occurs late, when TR is severe. Atrial volume and tricuspid annular dilation may be early and sensitive indicators of significant TR.

Cardiac MRI can be useful for assessing the tricuspid valve annulus size and shape changes associated with the cardiac cycle.^{74,75} Both real-time 3D echocardiography and cardiac MRI are accurate in measuring the tricuspid annular area throughout the cardiac cycle with changes in annular dimensions correlating to right ventricular size (volume) and function.⁷⁵ In addition to dynamic information about the annulus and right ventricle, cardiac MRI can also assess the flow across

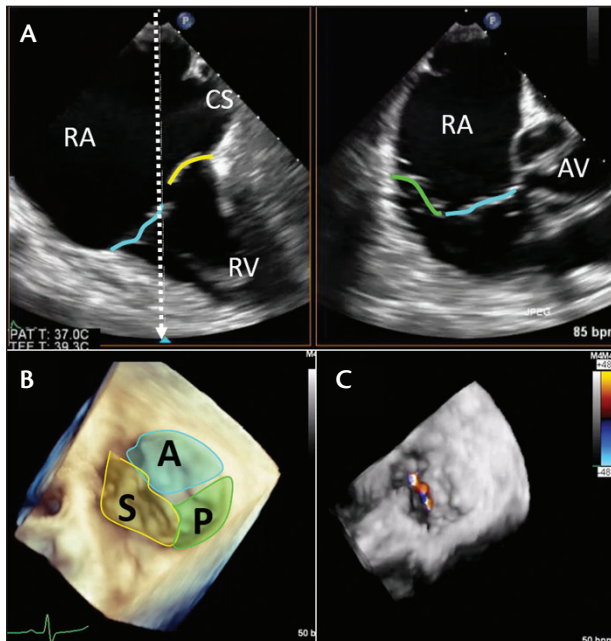


Figure 4. Deep esophageal views of the tricuspid valve. Simultaneous multiplane image (A) shows the tricuspid leaflets at 0° rotation with the orthogonal inflow-outflow image. From this view, the tricuspid leaflets are well-imaged, and 3D volumes (B) or color Doppler volumes (C) can be obtained. Note: the color code for tricuspid leaflets is the same as in Figure 2. Abbreviations: A, anterior leaflet; AV, aortic valve; CS, coronary sinus; P, posterior leaflet; RA, right atrium; RV, right ventricle; S, septal leaflet.

the tricuspid valve. Similar to echocardiographic assessment, a vena contracta of > 7 mm correlates with severe TR.⁷⁶ Regurgitant volumes can be derived by subtracting forward flow (assessed by pulmonary artery phase contrast assessment) from RV stroke volume (assessed by steady-state free precession); however, major limitations include irregular rhythms and concomitant valvular disease (ie, pulmonic regurgitation).^{77,78}

Thus, the recurrence of TR with surgical annular repair is related to RV dilatation and marked tenting, as well as severe pulmonary hypertension with related septal shift. These caveats may be important for deciding which patients should be candidates for treatment with transcatheter annular fixation devices, as these devices may not be ideal in those with predictors of surgical annuloplasty recurrence.

ECHOCARDIOGRAPHIC IMAGING OF THE TRICUSPID VALVE FOR TRANSCATHETER INTERVENTIONS

The current ASE guidelines⁷⁹ for performing a comprehensive examination by transesophageal echocardiography

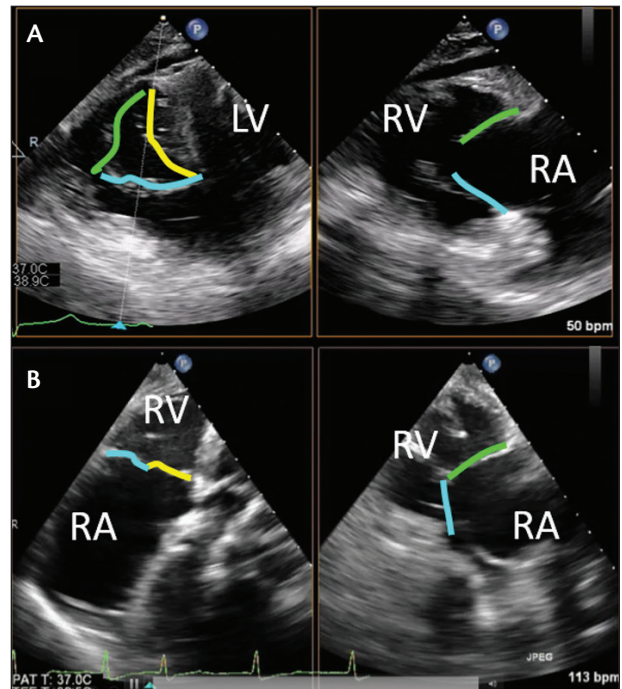


Figure 5. Transgastric views of the tricuspid valve. Advancing the TEE probe into the stomach results in the shallow (A) and deep (B) transgastric views. From the shallow transgastric level, a short-axis view of all three tricuspid valve leaflets is possible, which helps identify catheter positions relative to the leaflets/annulus. Advancing the TEE probe further into the stomach, along with rightward anterior flexion, produces a deep transgastric view of the tricuspid valve and aligns flow across the valve for Doppler assessment of regurgitant severity, as well as spectral Doppler evaluation of the TR jets. Note: the color code for tricuspid leaflets is the same as in Figure 2. Abbreviations: LV, left ventricle; RA, right atrium; RV, right ventricle.

(TEE) include additional imaging views, many of which are intended to improve imaging of the tricuspid valve. Given the position of the heart in relation to the esophagus and stomach, midesophageal, distal esophageal, shallow transgastric, and deep transgastric views may bring the probe close enough to the tricuspid valve for both 2D and 3D imaging. Many imaging planes may be similar to TTE imaging, and therefore, the same anatomic caveats are worth noting.

First, the commissure between the anterior and septal leaflets is adjacent to the noncoronary cusp of the aortic valve; the right coronary cusp is adjacent to only the anterior leaflet. Second, although a small (anterior) portion of the septal leaflet may be seen if the aortic valve is in view, most of the septal leaflet is attached to the interventricular septum. Third, the coronary sinus enters the right atrium at the commissure between the septal

and posterior leaflets. Finally, the right atrial appendage is directly superior to the anterior leaflet. Any two-chamber imaging plane of the RV will tend to image the anterior and posterior leaflets as long as the anterior (curved, right atrial appendage in view) and posterior (flat, on the diaphragm) walls of the RV are imaged.⁸⁰

A comprehensive TEE examination of the TV should include imaging from several depths and multiplane angles. Multilevel imaging begins at the midesophageal depth. The four-chamber view permits visualization of the septal and anterior leaflets, particularly if the probe is slightly anteflexed (Figure 2A). If retroflexed (Figure 2B), the septal-posterior leaflet coaptation is imaged.

The midesophageal inflow-outflow view at approximately 60° images the anterior leaflet (adjacent to the aorta) and the opposing posterior leaflet (Figure 3). From this imaging plane, the septal leaflet is typically only imaged using simultaneous biplane views. An orthogonal imaging plane adjacent to the aorta (Figure 3A) will image septal-anterior coaptation. Moving the orthogonal image away from the aorta (Figure 3B) will image the septal-posterior coaptation. Because the lower right heart border is close to the diaphragm, slow insertion brings the TEE probe to the distal esophagus just proximal to the gastroesophageal junction; there may be no view of the left atrium proximal to the tricuspid valve in this imaging plane, only the right atrium and coronary sinus (Figure 4A). As this view of the tricuspid valve is unobstructed by left heart structures, it is ideal for performing a comprehensive evaluation of tricuspid valve function and for acquiring 3D volumes of the tricuspid valve (Figure 4B and 4C).

Advancing the TEE probe into the stomach results in transgastric views (Figure 5). At 0°, rightward anterior flexion will result in the inflow-outflow view, again with imaging of the anterior (adjacent to the aorta) and posterior (adjacent to the diaphragm) leaflets. Rotating the multi-angle probe to 60° to 90° results in the only 2D view that provides simultaneous visualization of all three tricuspid valve leaflets with the posterior leaflet in the near field, the anterior leaflet in far field, and the septal leaflet adjacent to the septum (Figure 5A). Advancing the TEE probe further into the stomach along with rightward anterior flexion produces a deep transgastric view of the tricuspid valve (Figure 5B), which also permits optimal color flow and spectral Doppler evaluation of TR jets.

THREE-DIMENSIONAL ECHOCARDIOGRAPHY

Because of the variability of imaging planes, as well as individual anatomy, leaflet identification should always be confirmed using 3D echocardiography. Three-dimensional echocardiography obviates the need for mental reconstruction of multiple 2D planes.⁸¹ Lang et

al⁸² have suggested a standardized imaging display for the en face view of the tricuspid valve, with the interatrial septum placed inferiorly (at the 6 o'clock position), regardless of the atrial or ventricular orientation (Figure 4B). Because of the anterior position of the right heart, 3D TTE images may be equal or sometimes better in quality compared to 3D TEE images.

CONCLUSION

Interest in the tricuspid valve has increased due to the evidence that functional TR affects patients' morbidity and mortality. Disease severity may be determined by the multiple comorbidities and right ventricular anatomy that can be identified by various imaging modalities. Transcatheter solutions for functional TR continue to be developed and will rely on optimal imaging techniques for procedural success. ■

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Disclosures: Principal Investigator for the SCOUT trial, but receives no compensation; speaker for Abbott Vascular, GE Medical, and St. Jude Medical.