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REVIEW

Role of 3-Dimensional Echocardiography in the Comprehensive Evaluation of the Tricuspid Valve in Patients With Tricuspid Regurgitation

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Three-dimensional echocardiography is one of the most promising methods for the diagnosis of valvular heart disease, and recently has become an essential clinical tool owing to the continued development of real-time transesophageal echocardiography (TEE) technology. And now an era of renewed interest and enthusiasm surrounding the diagnosis and treatment of valvular heart disease has come, which is driven by emerging trans-catheter procedures. Nonetheless, little or no attention has been given to the treatment of tricuspid regurgitation (TR). The application of 3D-TEE is useful for simultaneous visualization of all 3 leaflets in order to grasp the whole picture of the tricuspid valve (TV; "en face" view). The implications of 3-D assessment of TV annulus, leaflets, and morphology involve an improved understanding of both the mechanics and treatment of TR. This method has been useful for surgical management, including accurate measurement of tricuspid annular diameter and prediction of the post-surgical outcome. Moreover, this method may be indispensable for detailed and comprehensive evaluation of the TV in patients with TR who are candidates for trans-catheter tricuspid procedures. In addition, color Doppler 3D-TEE has been valuable to identify the location of the regurgitant orifice and the severity of the TR. It is now clear that this method will enhance the diagnosis and management of TR patients.

Key Words: 3-D echocardiography; Trans-catheter procedure; Transesophageal echocardiography; Tricuspid valve

Echocardiography has been used to diagnose and assess disease severity in patients with valvular heart disease for many years. Catheter-based treatment of valvular heart disease, such as trans-catheter aortic valve replacement or MitralClip procedure, has been increasingly accepted as a treatment choice for the past several years. Such new treatment options have been highlighting the need for 3-D visualization of cardiac structures with detailed and comprehensive observations of the cause, mechanism, severity, location, associated lesions, and cardiac response in patients with severe valve stenosis and those with severe valve insufficiency.[1] Although there are still limitations to the currently available 3-D ultrasound methods, especially transthoracic echocardiography (TTE), due to its relatively low image quality and time resolution, the use of the high-quality real-time 3-D transesophageal echocardiography (TEE) for such catheter-based treatments is essential for the success of the procedures.[2]

With the recognition of the impact of tricuspid regurgitation (TR) on outcome in a number of disease states, interest in understanding this disease process has grown.[3–6] The prevalence of clinically significant TR is relatively high (0.55%) in community residents diagnosed on Doppler echocardiography, and increases with age.[7] Indeed, TR was also found to be heterogeneous in survival according to its cause[8] and severity.[9] Overall, however, very high mortality has been noted, even in isolated TR stratified by proximal isovelocity surface area (PISA)-derived effective regurgitant orifice area (PISA-EROA), in which the 10-year survival rate was lower in patients with severe TR (PISA-EROA ≥40 mm², 38±7% vs. PISA-EROA <40 mm², 70±6%; P<0.0001), and lower than expected in the general population.[10] Even though TR is prevalent and is associated with poor prognosis, it remains substantially undertreated compared with left-sided valvular disease;[11] therefore clearly more attention is needed, with emphasis on better means of treatment, including newly developed trans-catheter tricuspid valve (TV) devices. The aim of this article is therefore to review recent publications on this issue and present perspectives on the role of 3-D echocardiography in the comprehensive evaluation of the TV in patients with TR.

Real-Time 3D-TEE Data Acquisition and TV Demonstration

Three-dimensional TEE is usually performed under sedation with i.v. injection of midazolam using an EPIQ7 ultrasound system equipped with a fully sampled matrix-array TEE transducer (X8-2t Live 3-D transducer, Philips Medical Systems, Andover, MA, USA), which can display both 2-D and 3-D images at a high volume rate. A learning

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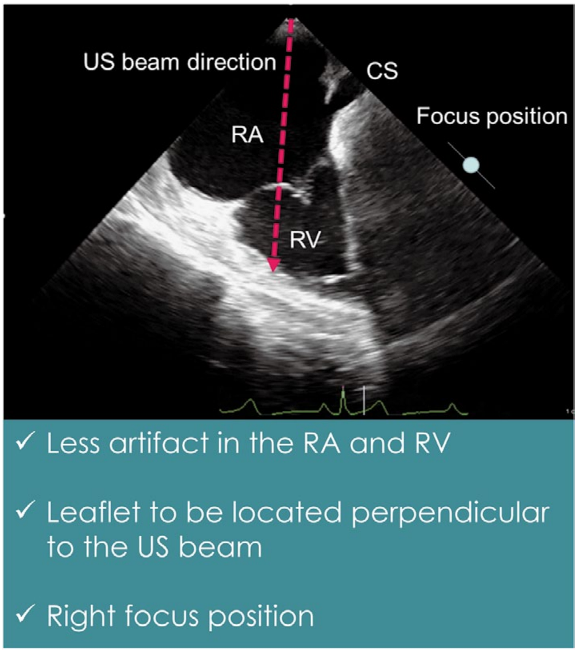

Figure 1. Appropriate 2-D plane for 3-D tricuspid valve data acquisition, in which the tricuspid valve leaflet is located perpendicular to the ultrasound beam. CS, coronary sinus; RA, right atrium; RV, right ventricle.

period may be required to obtain clear 3D-TEE images and make accurate TV measurements. As for 3-D data acquisition, the clearly demonstrated 2-D TV images with less artifact in the right atrium (RA) and right ventricle (RV) are mandatory (**Figure 1**). Appropriate 2-D planes for data acquisition are the mid-esophageal oblique short-axis view, coronary sinus view, or transgastric RV inflow view, in which the TV leaflet can be located perpendicular to the ultrasound beam. The view is optimized for depth and size of area of interest before 3-D acquisition, and close attention is paid to including the entire TV in the sector boundaries. It is of great importance to improve 3-D image quality of the tricuspid leaflets with slight and proper modification of 2-D gain setting, sensitivity time control, dynamic range, and focus distance. From these appropriate 2-D planes, volume data sets focused on the TV are obtained using the live 3-D zoom mode or multibeat full-volume mode. In this way, the live 3-D zoom or full-volume data sets are digitally stored for offline analysis and are imported into the dedicated workstation (QLAB 3-D version 10.7, Philips Medical Systems). The 3-D volume rendering is interrogated to determine the whole picture of the TV ("en face" view), displayed with the interatrial septum (IAS) placed inferiorly in the 6 o'clock position (**Figure 2**).[12] In patients with atrial fibrillation (AF), the live 3-D zoom mode with 1-beat volume acquisition should be chosen to avoid stitch artifacts. Cropping from the RA and RV perspective on both sides is sometimes useful for understanding of leaflet size and the location of the

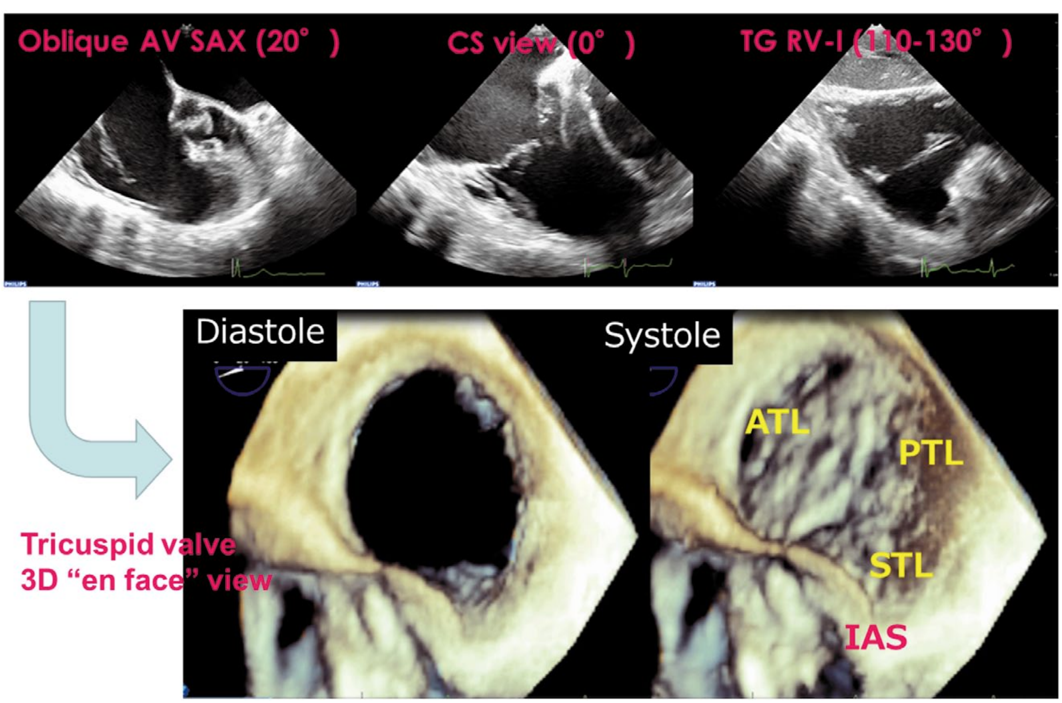

Figure 2. 3-D transesophageal echocardiography data acquisition and tricuspid valve demonstration. From appropriate 2-D planes such as mid-esophageal oblique aortic valve short axis (AV SAX) view, coronary sinus (CS) view, or transgastric right ventricle (RV) inflow view, volume data sets focusing on the tricuspid valve are obtained using the live 3-D zoom mode or 6-beat full-volume mode, and then are imported into the dedicated workstation. 3-D volume rendering is interrogated to grasp the whole picture of the tricuspid valve ("en face" view), displayed with the interatrial septum (IAS) placed inferiorly in the 6 o'clock position. ATL, anterior tricuspid leaflet; PTL, posterior tricuspid leaflet; TG, transgastric; TL, septal tricuspid leaflet.

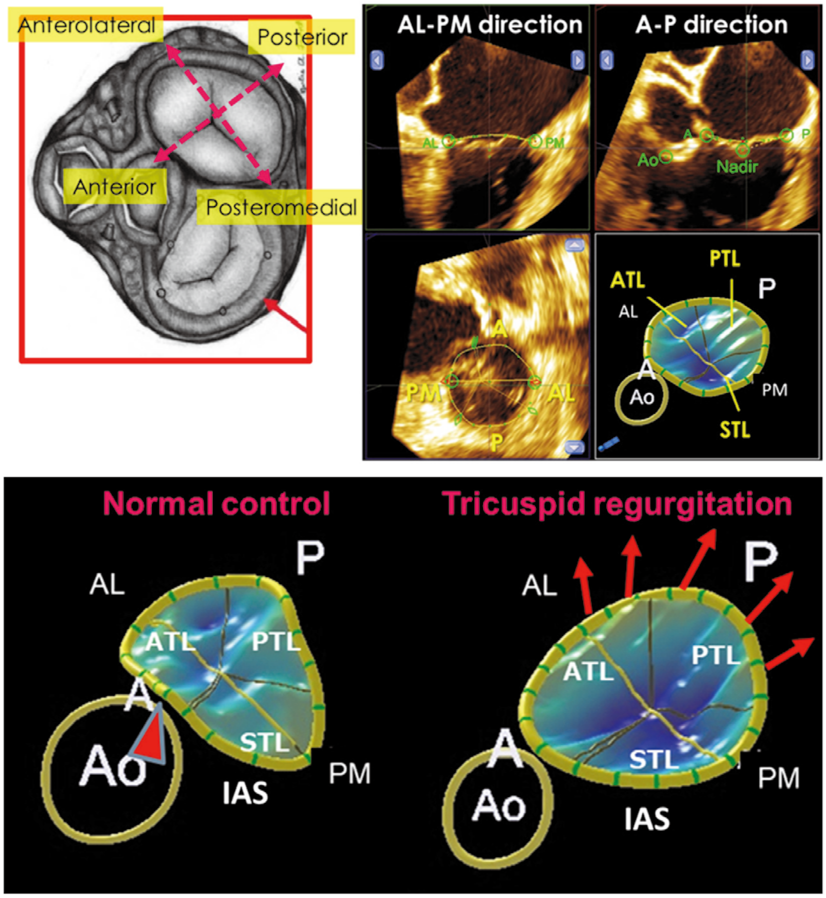

Figure 3. Assessment of tricuspid annulus using 3-D transesophageal echocardiography. Anteroposterior (A-P) and anterolateral-posteromedial (AL-PM) directions are determined using the commissure between the anterior and septal leaflets as the anterior aspect (arrowhead). Patients with functional tricuspid regurgitation caused by longstanding atrial fibrillation have a more dilated, planar, circular, and dysfunctional annulus compared with normal controls. Ao, aorta; ATL, anterior tricuspid leaflet; IAS, interatrial septum; PTL, posterior tricuspid leaflet; STL, septal tricuspid leaflet.

anatomical regurgitant orifice. Additionally, in some cases, color Doppler live 3-D zoom or multibeat full-volume data sets are also acquired with the narrowest possible depth during a breath hold to obtain a higher volume rate, applying the following settings: color Doppler gain, 50%; smoothing, 2; color vision, 2; flow optimization, medium; and color filter, 8.

Assessment of TV Annulus, Leaflets, and Morphology

Annulus Size, Shape, and Orientation

The mitral module of the QLAB mitral valve navigator software can be used in an off-label fashion for semi-automated indirect 3-D measurement of the TV annulus. We use 20 landmarks to delineate the TV annulus and analyzed the leaflets using ≤22 intersections per patient. The anteroposterior and anterolateral-posteromedial directions were determined using the commissure between the anterior and septal leaflets as the anterior aspect to obtain the saddle-shaped 3-D annular model (**Figure 3**).[13] The annular area, annular height, and ellipticity (anterolateral-posteromedial/anteroposterior ratio) can be obtained on mid-systole and mid-diastole frames. In a previous study, patients with functional TR caused by longstanding AF had a more dilated, planar, circular, and dysfunctional annulus compared with normal controls.[13] In that study, compared with normal controls, patients with TR had an 84% increase in the TV annular area in mid-diastole (TR group: median, 1,404 mm^2; IQR, 1,207–1,614 vs. control group: median, 761 mm^2; IQR, 705–821), a 110% increase in the TV annular area in mid-systole (TR group: median, 1,288 mm^2; IQR, 1,085–1,495 vs. control group: median, 613 mm^2; IQR, 555–656), a 48% decrease in annular height (TR group: median, 4.1 mm; IQR, 3.3–4.6 vs. control group: median, 8.0 mm; IQR, 7.5–8.3), and a 60% decrease in TV annular contraction (TR group: median, 8.2%; IQR, 6.2–10.1 vs. control group: median, 20.3%; IQR, 18.2–21.6).[13] As for the orientation of the tricuspid annulus, the angle between the major annular axis and IAS parallel to the vertical axis ($\alpha°$) can be directly measured as an index of annular orientation (**Figure 4**). This angle represents the direction of annular expansion. Most recently, we observed that TR subgroups had a larger α irrespective of TR etiology and cardiac rhythm, with the posteriorly displaced annulus most frequently noted in patients with AF and RA enlargement.[14] This posterior annular expansion might be explained by the fact that the posterior wall is the only region of the RA that is not constrained by other cardiac structures and thus there is less support in this region. The probable interaction between right heart remodeling and the changes in annular morphology, however, remains unclear.

Leaflet Tethering, Length, and Coaptation Status

For the measurement of leaflet length in mid-diastole and tethering angle in mid-systole of the septal, anterior, and

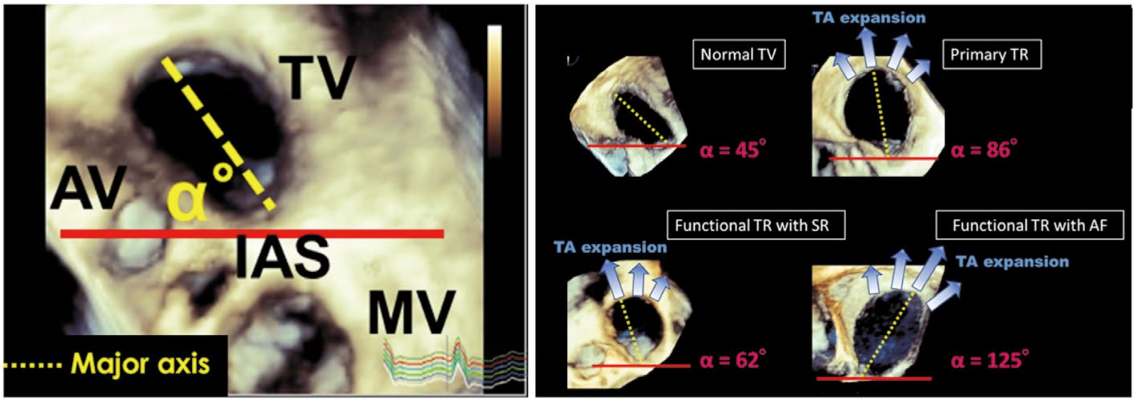

Figure 4. Determination of tricuspid annular orientation and its distribution according to tricuspid regurgitation (TR) etiology and heart rhythm. (**Left**) By means of 3-D annular analysis, the angle between the major annular axis and interatrial septum (IAS) parallel to the vertical axis (*α*°) can be directly measured as an index of tricuspid annular orientation. This angle represents the direction of annular expansion. (**Right**) Note that atrial fibrillation (AF) rhythm, rather than TR etiology, may be associated with more posterior annular expansion. AV, aortic valve; MV, mitral valve; SR, sinus rhythm; TA, tricuspid annulus; TV, tricuspid valve.

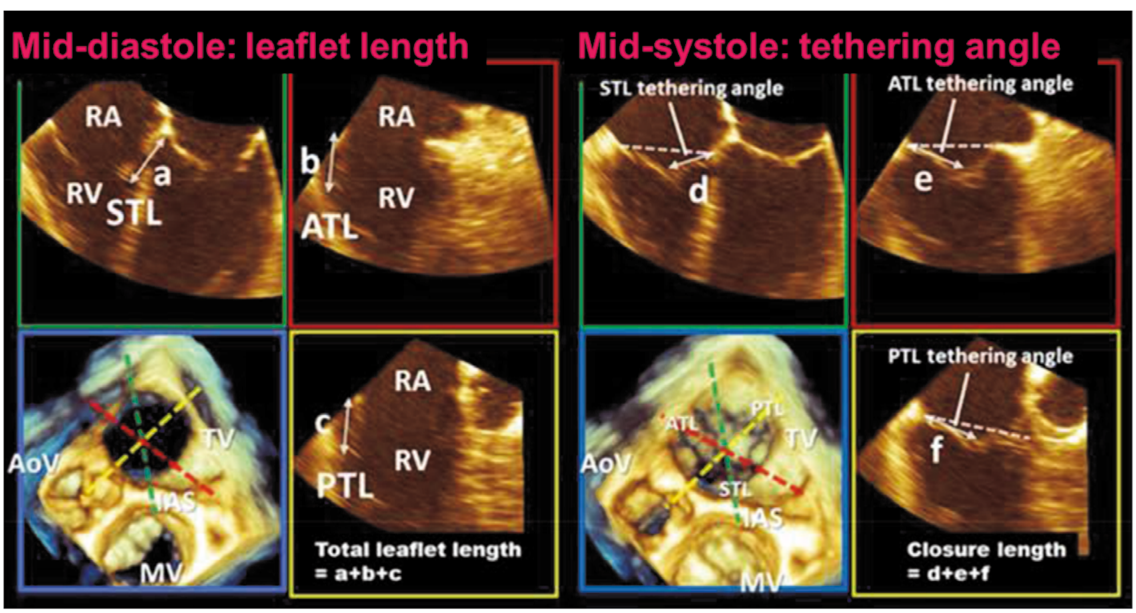

Figure 5. Assessment of tricuspid leaflet using 3-D transesophageal echocardiography. The 3 long-axis planes, which perpendicularly cross the middle of each tricuspid valve (TV) leaflet, are generated carefully using guidance on the short-axis image of the TV. On each of the 3 long-axis planes, the tethering angles of the leaflets are measured on a mid-systole frame. In addition, (a–c) the leaflet lengths are measured on mid-diastole frame, and (d–f) the closure lengths are measured on mid-systole frame. AoV, aortic valve; ATL, anterior tricuspid leaflet; IAS, interatrial septum; MV, mitral valve; PTL, posterior tricuspid leaflet; RA, right atrium; RV, right ventricle; STL, septal tricuspid leaflet.

posterior tricuspid leaflet (STL, ATL, and PTL, respectively), 3-D quantification software is used to interrogate the 2-D planes perpendicularly crossing the middle of each TV leaflet, generated carefully using guidance on the short-axis image of the TV.[13,15] On each of the 3 long-axis planes, the leaflet lengths were measured on a mid-diastole frame; the leaflet tethering angles between the annulus line and the 3 leaflets can be measured on a mid-systole frame (**Figure 5**). With the mitral valve navigator software, the closed TV leaflets are traced in mid-systole on successive contiguous long-axis planes parallel to the anteroposterior direction to obtain the TV 3-D tenting height and volume. Averaged tethering angle or 3-D tenting height represents the degree of global leaflet tethering. In contrast, 3-D tenting volume may be influenced by both annular dilatation and leaflet tethering. The leaflet coaptation status of the TV

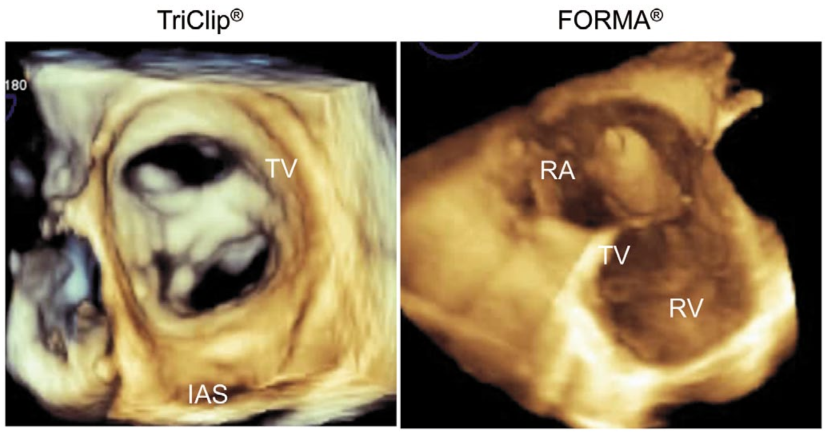

Figure 6. 3-D transesophageal echocardiography of trans-catheter tricuspid valve (TV) coaptation devices. (**Left**) Interventional edge-to-edge repair with the TriClip system; (**Right**) Forma Repair System. IAS, interatrial septum; RA, right atrium; RV, right ventricle.

can be assessed using the ratio of total leaflet length in mid-diastole (*a*+*b*+*c* in **Figure 5**) to total closure length in mid-systole (*d*+*e*+*f* in **Figure 5**) obtained on 3-D analysis.[13,16] Not only annular dilatation and leaflet tethering but also leaflet coaptation status have been proven to be associated with mechanisms of both functional mitral regurgitation and functional TR.[13,17,18]

Leaflet Morphological Abnormalities

Leaflet morphological abnormalities, which include an assessment of restricted leaflet motion, valve thickening, subvalvular fibrosis, and valve calcification, are another important point to be considered. Using guidance on en face views of the TV, the 3 orthogonal long-axis planes are generated to perpendicularly cross the middle of each leaflet, and then they are shifted throughout each TV leaflet to assess the presence of structural abnormalities. The TV morphological score can be derived from this analysis, and is semiquantitatively graded from 0 to 4 according to the modified Wilkins criteria.[15]

TV 3-D Analysis Before Surgical Ring Annuloplasty

Tricuspid annular dilatation appears earlier in the course of the disease; therefore, current recommendations have incorporated enlarged tricuspid annular diameter (TAD) in addition to TR severity as an indication for concomitant TV annuloplasty at the time of left-sided heart surgery to avoid the occurrence of significant late TR and to promote RV reverse remodeling and improvement of RV function.[19] The advent of 3-D echocardiography enables detailed evaluation of the TV apparatus before surgical ring annuloplasty; accurate measurement of TAD; and prediction of post-surgical outcome.

Measurement of TAD

Current guidelines recommend that TAD measurements be made in an apical 4-chamber view on 2-D TTE; and 2D-TTE-TAD ≥40 mm or >21 mm/m^2 is considered as the threshold of annular dilatation.[19] In daily clinical practice, 2D-TTE is the most common modality used to measure TAD, but 2D-TTE measurement of the maximum dimension of the tricuspid annulus will not be as accurate as a 3-D echocardiographic measurement, because the annulus is not optimally oriented for it to be measured from an apical 4-chamber view.[14,20–23] Similar to Dreyfus et al[20] and Addetia et al,[21] our group also found in patients with TR that 2D-TTE-TAD is highly correlated with 3D-TEE-TAD, but that 2D-TTE-TAD was significantly smaller than 3D-TEE-TAD, with a mean bias of 3.9±2.6 mm.[14] These inconsistencies between measured 2D-TTE-TAD and the actual annular diameter are mainly explained through various orientations of the dilated annulus (**Figure 4**). Therefore, in patients with clinically significant TR and annular dilatation, a comprehensive method for the measurement of TAD using both 2-D and 3-D echocardiography needs to be established.

Prognostic Value of 3-D Echocardiography Parameters

In this decade, tricuspid ring annuloplasty has been performed using various rings and bands, such as Carpentier classic ring, a flexible partial annular ring (Carpentier-Edwards Physio Tricuspid Annuloplasty Ring), and a 3-D ring invented by McCarthy et al (Edwards MC3 Tricuspid Annuloplasty Ring).[24] Residual TR, however, occurs in 22–39% of patients early after annuloplasty, and the mechanism and determinants of residual TR have been associated with severe tethering of the TV leaflet.[25,26] Recent studies demonstrate the usefulness of 3-D echocardiographic parameters of the TV to predict residual TR and adverse outcome following tricuspid annuloplasty.[15,16] Utsunomiya et al found that short total leaflet length (<53.5 mm), large tenting volume (>3.5 mL), and high TV morphological score (>18) are associated with residual TR after surgery.[15] It is worthy of note that in some cases diagnosed as "functional" TR, it is difficult to differentiate completely functional vs. organic TR. Accordingly, we obtained detailed information on leaflet morphological abnormalities using 3-D echocardiography and incorporated it into an appropriate scoring system.[15]

Trans-Catheter Procedures for TR

Isolated TV surgery remains infrequent and is associated with the highest mortality of all valve procedures. Most recently, a retrospective cohort study with a propensity-matched sample found that in patients with isolated severe TR, there is no difference in long-term survival for patients who undergo surgical intervention compared with medical

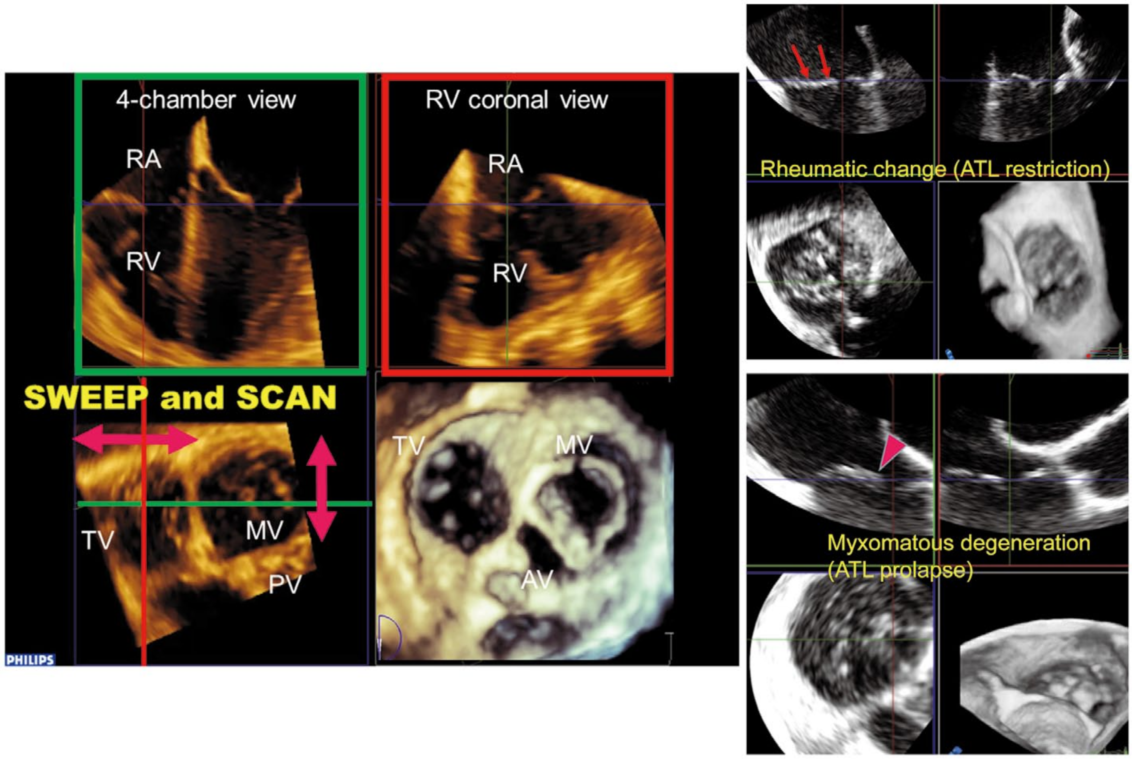

Figure 7. Tricuspid valve (TV) screening for determination of tricuspid regurgitation (TR) cause. (**Left**) 3-D multiplanar reconstruction planes through the TV in mid-systole. On the short-axis plane, the 2 orthogonal long-axis planes are shifted throughout the TV to assess the presence of organic disease. (**Right**) Echocardiographic appearances of rheumatic TR with thickened and restricted motion of the anterior tricuspid leaflet (ATL; arrows) and myxomatous TR with thickened and billowing ATL (arrowhead). AV, aortic valve; MV, mitral valve; PV, pulmonary valve; RA, right atrium; RV, right ventricle.

management alone.[27] Hence, a largely unmet clinical need exists for less invasive therapeutic options in these patients. In recent times, multiple percutaneous therapies have been developed for treating severe TR, including interventional edge-to-edge repair with the TriClip system and Forma Repair System (**Figure 6**).[28] As for the trans-catheter TV leaflet clip procedure, a recent study showed that a central/anteroseptal TR jet location and small coaptation gap size independently predicted procedural success.[29] Therefore, assessing the orientation of the dilated annulus, detecting the exact location of proximal flow convergence, and then first trying to capture the diseased lesion correctly might be of vital importance for this procedure. With anticipation of improvements in trans-catheter TV interventions in the future, this 3-D echocardiography information may be utilized to improve the chances for procedural success.

Comprehensive 3-D Analysis in Patients With TR

Cause/Etiology

Causes of TR are classified into 2 major categories: organic and functional. Organic TR is caused by an anatomic abnormality of the TV itself, such as rheumatic, iatrogenic, carcinoid disease, traumatic, Ebstein anomaly, pacer-related, myxomatous degeneration of the TV, and infective endocarditis.[30] In contrast, functional TR occurs on structurally normal TV leaflets and is caused by abnormalities of the surrounding or supporting structures, which are often secondary to left-sided heart disease from myocardial or valvular causes, pulmonary arterial hypertension, RV dysfunction, and dilatation of right-sided cardiac chambers.[31] Prevalence of organic TR ranges from 9.5% on 2D-TTE[32] to 26% on direct inspection of the TV at the time of TV annuloplasty.[33] These seemingly conflicting results likely reflect differences in the methodology of TR pathogenic stratification in the respective populations. Although 2D-TTE continues to be the standard method in the diagnosis of TV pathology, there are several limitations inherent to 2-D imaging. These include difficulties in accurate leaflet identification,[34] missing occult organic TV disease,[32,35] and misdiagnosing pacer-related TR.[36] Therefore, a new 3-D imaging-based TV pathogenesis stratification may be required. Recently, 3D-TEE was able to detect the underlying causes of TR on thorough screening of the TV (**Figure 7**).[13] The prevalence of primary TR was 31%,[13] which is higher than that determined on 2D-TTE in previous studies.[32] Notably, TR because of regional rheumatic or myxomatous change, and pacer-related TR tended to be overlooked. In this 3D-TEE study, Utsunomiya and colleagues[13] assembled the TR cohort to investigate the prevalence of functional TR caused by long-standing AF (AF-TR), which was 9.2% of the total TR cohort and 13.3% of the functional TR cohort.

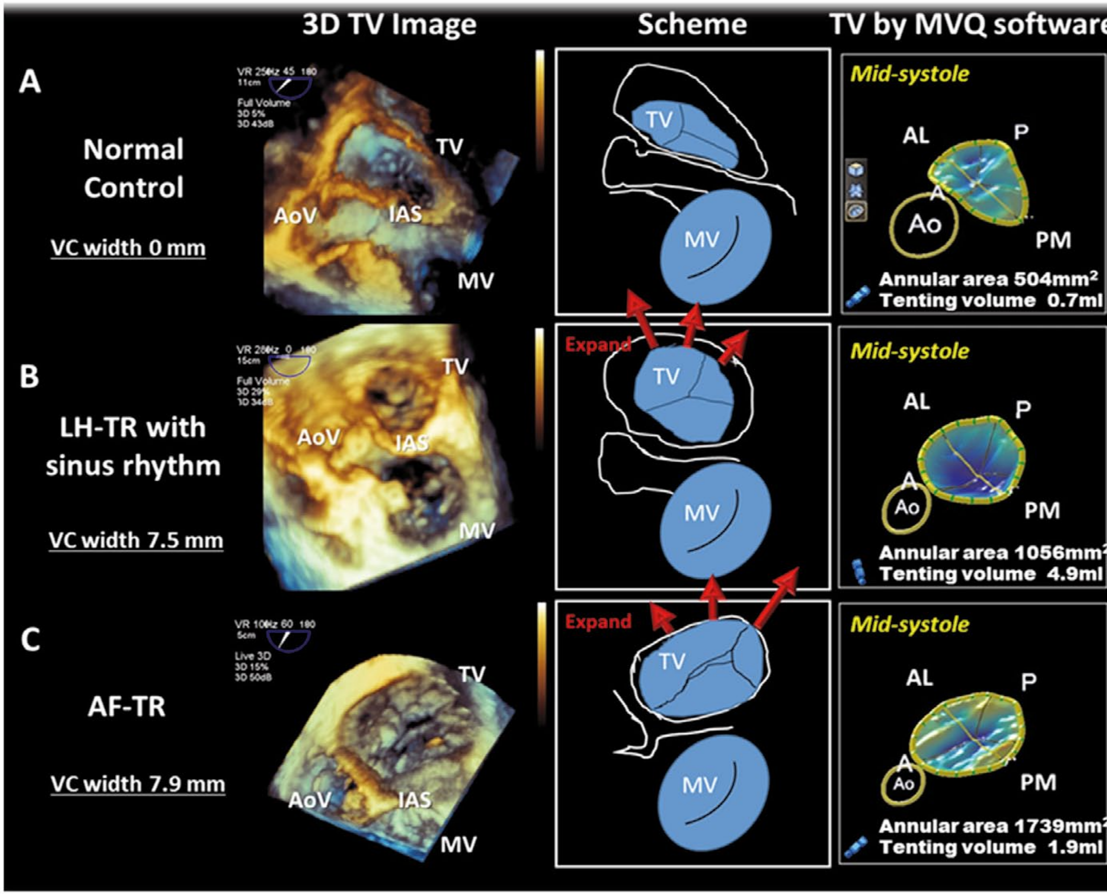

Figure 8. Pathoanatomy and mechanisms of functional tricuspid regurgitation (TR) according to TR subgroup. (**A**) Normal control. Normal size, ellipsoidal, and saddle-shaped tricuspid annulus without leaflet tethering. (**B**) Functional TR caused by left-sided heart disease (LH-TR) with sinus rhythm. TR results from significant leaflet tethering and preferential annular dilatation along the anterolateral border. (**C**) Functional TR caused by long-standing atrial fibrillation (AF-TR). TR results from prominent annular dilatation and right atrial (RA) enlargement expanding mostly along the posterior border. Impact of leaflet tethering is relatively small in this subgroup. Reprinted from Utsunomiya et al.[13] with permission from the publisher. A-P, anteroposterior; Ao, aorta; AL-PM, anterolateral-posteromedial; AoV, aortic valve; IAS, interatrial septum; MV, mitral valve; TV, tricuspid valve; VC, vena contracta.

Mechanism

The pathophysiology of functional TR has been investigated, and critical TV deformations in its development have been proven to be annular dilatation,[13,37] leaflet tethering,[38] and poor coaptation status with insufficient leaflet adaptation.[13,16,17] In most of these previous studies, however, the study population was limited to functional TR because of the pulmonary hypertension. Recent real-time 3D-TEE elucidated different pathoanatomy and mechanisms of functional TR according to TR subgroup.[13] For example, in patients with functional TR caused by left-sided heart disease (LH-TR) with sinus rhythm, a larger annular area (preferential annular dilatation along the anterolateral border), a larger tethering angle, and lower ratio of total leaflet length : closure length were all independently associated with TR severity. Meanwhile, in AF-TR, TR is due to prominent annular dilatation expanding mostly along the posterior border. The impact of leaflet tethering was relatively small in this subgroup (**Figure 8**).[13] That study has therefore demonstrated fundamental differences in TV deformations and possible mechanisms between AF-TR and LH-TR with sinus rhythm, suggesting the need to establish the entity of AF-TR.[1] These results will help in trans-catheter treatment selection for functional TR in the future.

Location

With regard to trans-catheter TV treatment, the practical value of the simultaneous assessment of TR location and severity intraprocedurally would be the ability to optimize detection of the exact jet location, accurate treat of the diseased lesion, and then determination of the immediate TR reduction.[28,29,39] 3-D echocardiography has been used to provide the cross-sectional area of the vena contracta (VC), which is located at the narrowest neck of the TR jet just above and toward the RA side of the flow convergence zone.[40,41] With the use of a 3D-TEE transducer that can display color Doppler 3-D images at an excellent frame rate, the location of the TR jet can be evaluated using the 3-D VC analysis with high feasibility.[42]

Severity

Current recommendations emphasize the necessity of an integrated approach to grade TR severity using qualitative and semiquantitative parameters to identify severe TR (ECHO-integ): (1) dilated annulus with valve malcoaptation or flail leaflet; (2) large central jet with >50% of RA area; (3) averaged VC width ≥0.7 cm; (4) PISA radius >0.9 cm at a Nyquist limit of 30–40 cm/s; (5) dense and triangular continuous-wave Doppler TR jet; (6) systolic reversal of hepatic vein flow; and (7) dilated RV with preserved function.[1] Individual echocardiographic parameters, however, are often discordant when assessing TR severity in clinical practice. Quantification of VC area on color Doppler 3-D echocardiography is a promising technique for more accurate grading of TR severity. The most recent publication by Utsunomiya et al investigated 116 TR patients using color Doppler 3D-TEE and found that a 3-D VC area cut-off of 0.61 cm^2 discriminated severe TR with a sensitivity of 78% and specificity of 97%.[42] 3-D VC area, dilated RV, and hepatic vein systolic reversal were independently associated with regurgitant volume. Because of the very high specificity of the 3-D VC area cut-off >0.61 cm^2 to differentiate between moderate and severe TR, we would like to advocate the 2-step method for diagnosing severe TR: the first step is at least 2 positive ECHO-integ findings, which yield a sensitivity of 100% and specificity of 53%, and the next step is using 3-D VC area.[42]

Cardiac Response (RV Dilatation and Remodeling)

Factors leading to leaflet tethering are associated with RV dilatation and remodeling and papillary muscle displacement.[37] Patterns of RV remodeling such as globular or conical shape and their association with geometric changes in TV complex might differ according to TR subgroups, but the precise mechanism is yet to be defined.

Conclusions

Clinically significant TR cannot be ignored when performing corrective surgical procedures for left-sided valvular heart disease. Because reduction of TR is sometimes insufficient even after successful left-side valve surgery and reoperation for residual or recurrent TR is associated with high event rates,[27] few patients are offered reoperation. Less invasive trans-catheter approaches to TR may allow earlier mechanical treatment of TR than is currently offered. The development of high-quality real-time 3D-TEE enables 3-D visualization of the TV with detailed and comprehensive evaluation of TR including cause, mechanism, location, severity, and cardiac response. Many challenges to emerging minimally invasive trans-catheter approaches will be accomplished with evolving 3-D echocardiography as well as surgical and interventional techniques.

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Disclosures

The authors declare no conflicts of interest.

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