




# Tricuspid regurgitation: recent advances in understanding pathophysiology, severity grading and outcome

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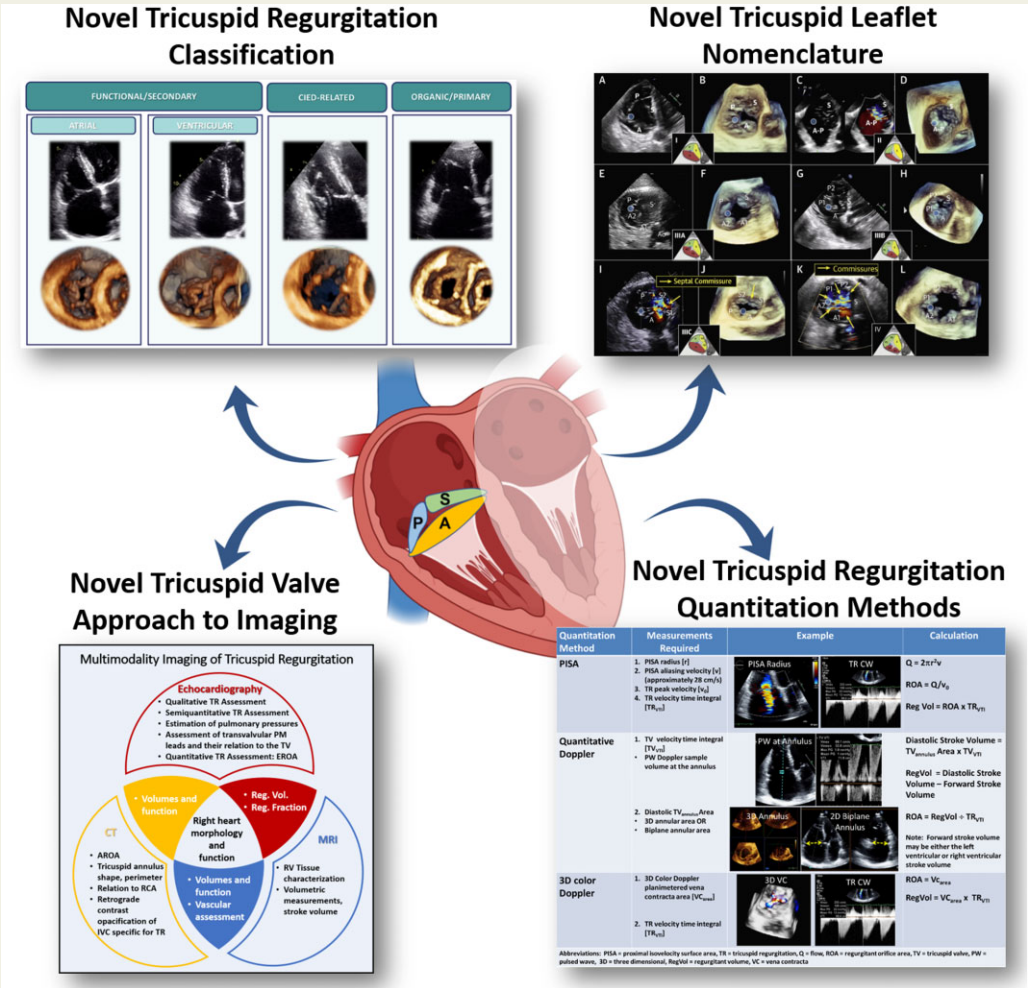
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Heightened interest in tricuspid regurgitation (TR) stems from the consistent association of mortality with greater severity of TR, and a low use of surgical solutions in the setting of high in-hospital mortality attributed to the late presentation of the disease. The delay in intervention is likely related to a limited understanding of the valvular/ventricular anatomy and disease pathophysiology, along with an underestimation of TR severity by standard imaging modalities. With the rapid development of transcatheter solutions which have shown early safety and efficacy, there is a growing need to understand and accurately diagnose the valvular disease process in order to determine appropriate management solutions. The current review will describe both normal and pathologic tricuspid valvular anatomy, the classification of these anatomic substrates of TR, the strengths and limitations of the current guidelines-recommended multi-parametric echocardiographic approach and the role of multi-modality imaging, as well as the role of transcatheter device therapy in the management of the disease.

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Graphical Abstract



Heightened interest in tricuspid regurgitation (TR) has led to a novel classification of the aetiology of TR, novel leaflet nomenclature, novel ways of quantifying TR, and novel methods for imaging the tricuspid valve complex.

**Keywords** tricuspid valve • tricuspid regurgitation • transcatheter

Introduction

Heightened interest in tricuspid regurgitation (TR), the previously ‘forgotten valve’, may be related to consistent findings in three main areas. First, multiple studies show an independent association of mortality with higher grades of TR severity.<sup>1,2</sup> Second, isolated surgical intervention for TR is infrequently performed<sup>3</sup> and associated with ~8–10% in-hospital mortality.<sup>4,5</sup> Third, the early success of transcatheter repair<sup>6</sup> and replacement<sup>7</sup> techniques has increase access to relatively low-risk treatments.

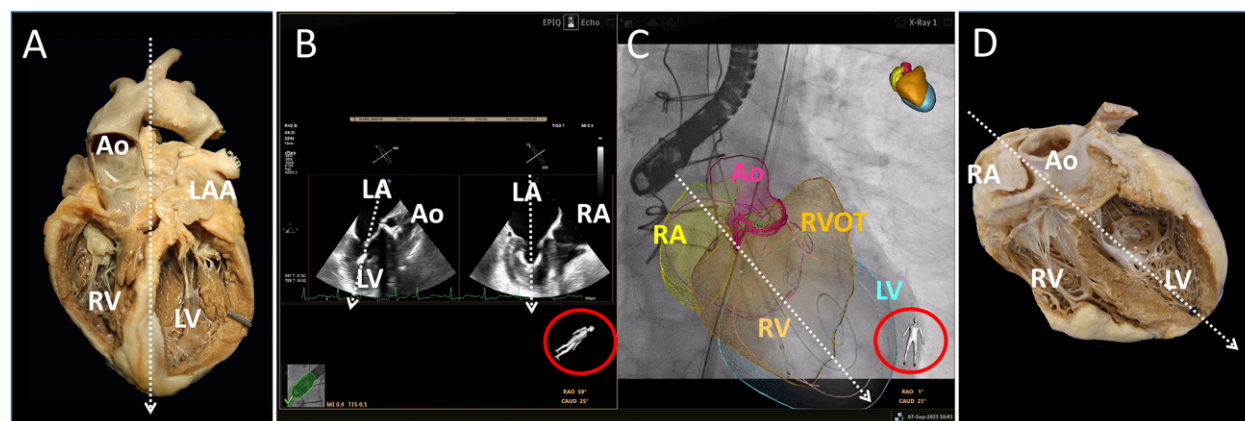
The current review will describe both normal and pathologic tricuspid valvular (TV) anatomy, the classification of the anatomic substrates of TR, and the strengths and limitations of the current guidelines-recommended multi-parametric echocardiographic

approach as well as new methods and algorithms to determining TR severity.<sup>8–12</sup> The role of transcatheter device therapy will also be discussed.

Tricuspid valve anatomy

Tricuspid valve leaflets

The TV is typically composed of three leaflets of unequal size which by convention are named the anterior, posterior, and septal leaflets. However, this convention is based on a vertical position of the long axis of the heart. Whereas by positioning the TV in the anatomic or ‘attitudinal’ position, with the long axis rotated counterclockwise from vertical, the anterior leaflet is anterior–superior, the posterior



**Figure 1** Vertical versus anatomic imaging of the heart. (A) A gross anatomic specimen in the vertical or “valentine” position which is typically obtained with the transoesophageal (TOE) probe behind the dome of the left atrium (panel B) and with the apex of the heart in the far field of imaging. The human model (B, red circle) is oriented to the on-screen TOE image, confirming the valentine position. (C) The fluoroscopic view of the patient with fusion of the segmented 3D TOE volume. The imaging plane of the TOE (white dashed arrow) is along the long-axis of heart generating the valentine view, however the fluoroscopic view is an anterior-posterior projection as shown human model (C, red circle) which generates an antitidinal view (Panel D). The conventional naming system of anterior, posterior and septal leaflets, would become in the antitidinal view, the anterior-superior, inferior and posterior leaflet. Ao = aorta, LAA = left atrial appendage, LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle, RVOT = right ventricular outflow tract.

leaflet is inferior, and the septal leaflet is posterior (Figure 1).<sup>13</sup> The antitidinal position will determine the direction of intra-cardiac catheters during transcatheter procedures.<sup>14</sup> However, there are multiple reasons to maintain the original nomenclature of anterior, posterior and septal leaflets. This nomenclature is derived from the traditional “surgical view” approach used for many years to enhance communication between imagers and surgeons. Similarly, transcatheter interventions will be performed using echocardiographic guidance and clear communication between imager and interventionalist is essential. By naming the TV leaflets based on consistent intra-cardiac anatomy (interventricular septum for the septal leaflet, anterior to the aorta for the anterior leaflet, and posterior to the anterolateral papillary muscle for the posterior leaflet) one maintains a common language that can be used with all imaging modalities, and improves consistent communication within procedures, irrespective of individual antitidinal variability. In the classic three leaflet valve, the anterior and septal leaflets are usually the largest circumferentially, thus the anteroseptal commissure is the longest.<sup>15</sup> There are typically two distinct papillary muscles (anterior, posterior), and a third variable septal papillary muscle. The anterior papillary muscle is the largest and provides chordae to the anterior and posterior leaflets. It arises from the anterior/lateral wall of the right ventricle (RV), near the trabeculations which incorporate the moderator band.<sup>16</sup>

Pathology studies have long recognized that there are a variable number of leaflets in healthy subjects<sup>17,18</sup> but use varying terminology to describe these supernumerary leaflets.<sup>19,20</sup> Recently a simplified nomenclature has been proposed<sup>21</sup> which may be relevant to pre-procedural planning and execution of transcatheter devices<sup>22</sup> as well as determine device success.<sup>22,23</sup> Given the proximity of the TV to the anterior chest wall and diaphragm, identification of the leaflet morphologies can be

performed on either 2D transthoracic echocardiography (TTE) from modified views or 2D transoesophageal echocardiographic (TOE) transgastric short-axis view, or the 3D volume-rendered equivalent using either modality. In this nomenclature proposal, deep indentations and true commissures were considered anatomically equivalent and were used to identify supernumerary leaflets. This convention can be justified by the observation that both folds in the leaflets or true commissures are accompanied by greater numbers of chordae along the leaflet edges and create potential sites for malcoaptation of the leaflet edges. A separate leaflet was then defined by: (i) independent motion from the adjacent leaflet, and (ii) colour Doppler flow in systole extending into the region around the leaflet. Four major classes of leaflet morphologies are shown in Figure 2: Type I is the classic 3-leaflet morphology; Type II is the 2-leaflet morphology with fusion of the anterior and posterior leaflets; Type III is the 4-leaflet configuration with subcategories based on the location of the fourth leaflet; and Type IV has >4 leaflets.

Leaflet structure and function can be used to categorize TR: (i) pathologic changes to the leaflets resulting in leaflet defects or malcoaptation, referred to as primary TR; (ii) insufficient leaflet coverage of a dilated tricuspid annulus (TA), referred to as atrial secondary TR, and (iii) insufficient leaflet coaptation in the setting of apical displacement with leaflet tethering, referred to as ventricular secondary TR (Table 1, Figure 3). Atrial secondary TR has been associated with marked right atrial (RA) and TA dilatation, typically less tethering or tenting of the tricuspid leaflets, and with normal or mildly dilated RV showing more triangular shape and preserved function.<sup>24–26</sup> Although cardiac implantable electronic device (CIED) leads have been traditionally categorized as primary because of the direct effect on the leaflets or subvalvular apparatus, there is nonetheless a



**Table 1** Classification of tricuspid regurgitation (TR).

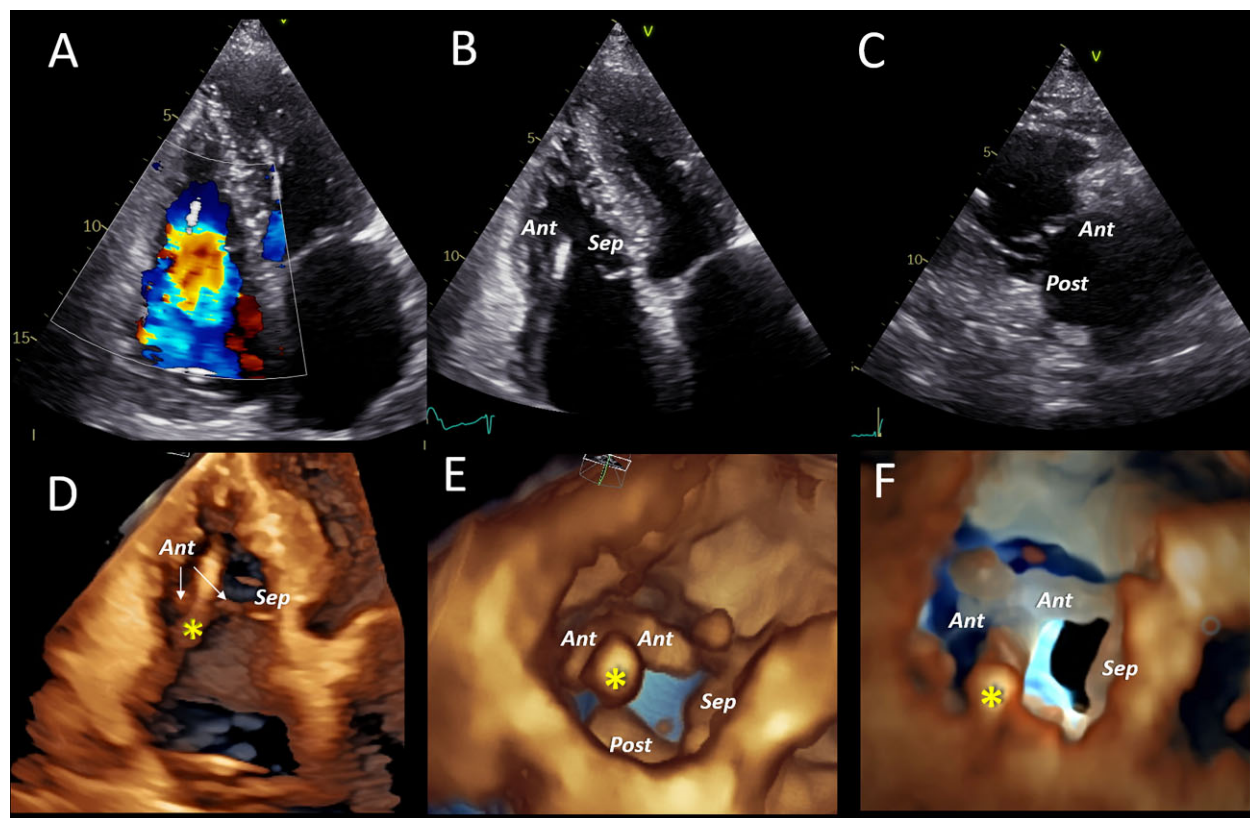
Classification	Etiologies
<b>Structural abnormality of the tricuspid valve apparatus</b>	
<b>Primary TR: ~10-15% of patients</b>	
<b>Degenerative Disease</b>	<ul style="list-style-type: none"> <li>• Prolapse</li> <li>• Flail</li> </ul>
<b>Congenital</b>	<ul style="list-style-type: none"> <li>• Ebstein's Anomaly</li> <li>• Leaflet clefts</li> </ul>
<b>Acquired</b>	<ul style="list-style-type: none"> <li>• Rheumatic disease (usually with left-side disease)</li> <li>• Infective endocarditis</li> <li>• Endomyocardial fibrosis</li> <li>• Carcinoid disease, serotonin active drugs</li> <li>• Traumatic (blunt chest injury, laceration)</li> <li>• Iatrogenic               <ul style="list-style-type: none"> <li>• Right ventricular biopsy</li> <li>• Drugs (e.g. exposure to fenfluramine-phentermine, or methysergide)</li> </ul> </li> </ul>
<b>Morphological normal leaflets with annular dilatation and/or leaflet tethering</b>	
<b>Functional TR: ~ 80% of patients</b>	
<b>Ventricular secondary TR</b>	<ul style="list-style-type: none"> <li>• Left heart diseases (left ventricular dysfunction or left heart valve diseases) resulting in pulmonary hypertension</li> <li>• Primary pulmonary hypertension</li> <li>• Secondary pulmonary hypertension (e.g. chronic lung disease, pulmonary thromboembolism, left-to-right shunt)</li> <li>• Right ventricular dysfunction from any cause (e.g. myocardial diseases, ischemic heart disease, chronic right ventricular pacing)</li> </ul>
<b>Atrial secondary TR</b>	<ul style="list-style-type: none"> <li>• Atrial fibrillation</li> <li>• Heart Failure with preserved ejection fraction</li> </ul>
<b>Cardiac tumors (particularly right atrial myxomas)</b>	<ul style="list-style-type: none"> <li>• Right atrial myxomas</li> </ul>
<b>Cardiac implantable electronic device (CIED) induced TR (~ 5% of patients)</b>	
<b>Primary CIED-induced TR</b>	<ul style="list-style-type: none"> <li>• CIED caused by direct interaction of the lead on the valve leaflets)</li> </ul>
<b>Secondary CIED-induced TR</b>	<ul style="list-style-type: none"> <li>• Incidental CIED, with TR due to functional etiologies or pacing related remodeling</li> </ul>

characterized by the structural integrity of the TV leaflets and is caused by RV remodelling following pressure and/or volume overload.<sup>38</sup> Based on its predominant imaging features, secondary TR may also be described in a practical way using Carpentier's functional classification based on leaflet mobility. Accordingly, Carpentier type I corresponds to normal leaflet motion and predominant TA dilation, as seen in atrial secondary TR. Carpentier type IIIb corresponds to leaflet tethering with restricted motion in systole, as typically seen in ventricular secondary TR. All types of Carpentier classification can be

encountered in primary TR and in CIED-induced TR, in which leaflet mobility may be highly variable depending on the aetiology. However, Carpentier classification was originally intended to guide mitral valve surgical repair or replacement and its usefulness for TR is less well-established.<sup>40</sup>

The variable outcomes based on aetiology of secondary TR<sup>41,42</sup> as well as multiple morphologic characteristics of the valve that predict recurrence of TR following surgical TV repair,<sup>43</sup> have driven the need to redefine the classification of secondary TR based on their primary





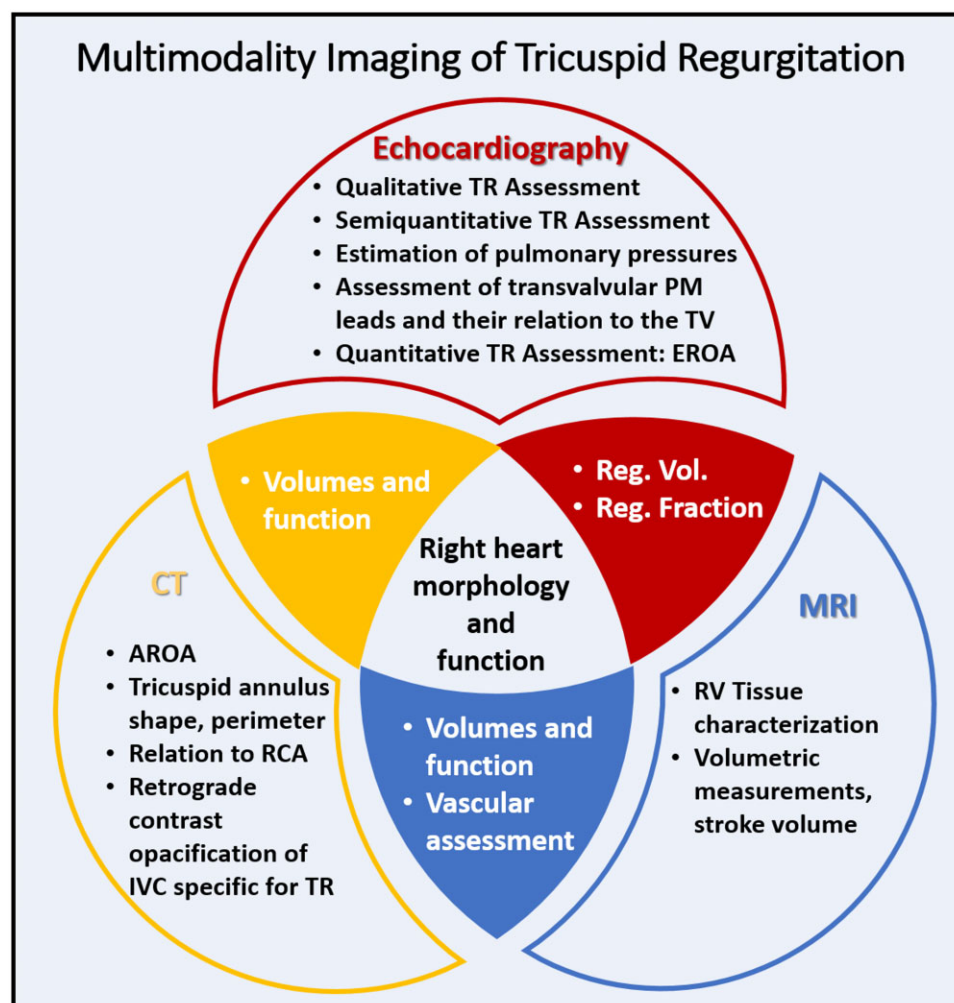
**Figure 4** Examples of cardiac implantable electronic device imaging. (A) A 4-chamber view colour Doppler image showing torrential TR in a patient with pacemaker (PM). (B) A 4-chamber view showing no apparent interference of PM catheter with anterior (Ant) and septal (Sep) leaflet, which are severely tethered and not coapting. (C) A RV inflow view showing the anterior (Ant) and posterior (Post) leaflets. The PM catheter can only be visualized at its most distal part. (D) A RV inflow 3D rendering showing a possible interference of PM catheter (asterisk) with anterior leaflet (Ant). (E) A TV 3D en face views during systole from the ventricular perspective clearly show the PM catheter (asterisk) impinging the anterior leaflet (Ant) in its mid part. (F) The same view as (E), with transillumination slightly tilted to display the close spatial relationship between PM lead (asterisk) and anterior leaflet (Ant).

it has been recently proposed to classify the CIED-related TR as a third distinct category (Figure 3).<sup>14</sup> Finally, as the presence of pacemaker lead is associated with worse outcomes with TR,<sup>56</sup> studies aimed to evaluate the results after interventional or surgical treatment should classify and address these patients as a separate category from the atrial and ventricular forms of TR.

Approximately 25–29% of patients with permanent pacemakers have TR, roughly double the prevalence in comparison groups.<sup>57</sup> However, the pathophysiological link between the presence of the device leads and either the onset of significant TR or the worsening of a pre-existing disease is a relatively recent clinical challenge. Interference of a RV transtricuspid pacing lead with the TV apparatus components might contribute to or cause TR in 7–45% of patients who received a CIED.<sup>54</sup> The large range of the incidence of significant TR after CIED implantation is likely due to the difficulty to identify the association between the presence of the wires/catheters and the dysfunction of the TV using conventional 2DE.<sup>58,59</sup> The clinical implementation of 3DE allows the documentation of this pathophysiological relationships (Figure 4, Supplementary data online, Medias S1 and S2).<sup>60</sup>

Supporting the classification of CIED-induced TR as its own category, patients with TR and a CIED can be divided in primary and secondary disease (Table 1). Primary CIED-induced TR can be defined as an increase of TR severity of ~2 grades during follow-up after CIED implantation in patients with documented interference of the device lead with the TV apparatus. Both echocardiography and post-mortem examinations of hearts with CIED, have shown that the device leads can interfere with the TV apparatus in different ways: impinging upon a leaflet, adhering to a leaflet, interfering with the subvalvular apparatus, perforating/lacerating a leaflet, avulsion of a leaflet (which may happen during lead extraction), and transection of papillary muscles, or chordae tendineae.<sup>54</sup>

Conversely, secondary CIED-induced TR is the consequence of the remodelling of the TV following the RV dilatation due to pacing/heart failure. Seo *et al.*<sup>61</sup> reported that up to 60% of worsened TR after CIED implantation were of secondary origin. However, the two conditions can overlap since untreated primary CIED-induced TR may trigger RV dilatation due to volume overload, and leads to secondary TR. When the latter occurs, lead extraction will be ineffective to reverse TR.<sup>61,62</sup> Permanent AFib and previous open-heart



**Figure 5** Multimodality assessment of tricuspid regurgitation severity. Different imaging methods give complementary information about tricuspid regurgitation aetiology, anatomic and functional substrates as well as TR severity. AROA = anatomic regurgitant orifice, EROA = effective regurgitant orifice area, CT = computed tomography, IVC = inferior vena cava, MRI = magnetic resonance imaging, PM = pacemaker, RCA = right coronary artery, Reg. Fraction = regurgitant fraction, Reg.Vol. = regurgitant volume, RV = right ventricle, TR = tricuspid regurgitation, TV = tricuspid valve.

surgery,<sup>61</sup> as well as a pre-existing RV dilation<sup>63</sup> have been reported among the predictors of secondary CIED-induced TR.

The clinical importance of the diagnosis of CIED-induced TR is further enhanced by the fact that it affects long-term RV function<sup>64</sup> and is associated with poor outcome.<sup>57,61,64–67</sup> Accordingly, in patients in whom clinical, haemodynamic, and echocardiographic assessment provides compelling evidence of CIED-related severe TR, corrective intervention should be indicated in a timely fashion, to avoid the development of severe TA and RV dilation, and severe RV dysfunction.<sup>68</sup>

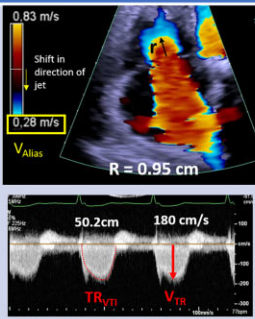
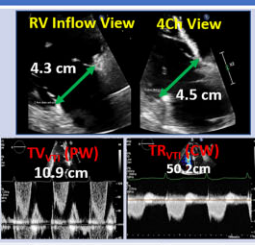
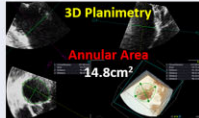
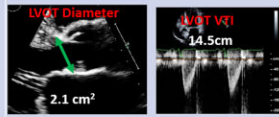
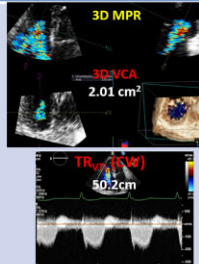
In patients with CIED-related severe TR who are considered for lead extraction, the identification of the type of lead interference by 3DE is important since the procedure can aggravate TR in patients with perforated leaflet, chordae avulsion, or in those with severe adherence or entangled leads. In a series of 200 lead extractions, increase in TR occurred in 5.6% of cases mainly in patients > 75 years, when > 2 leads were extracted and when powered sheaths were

used.<sup>69</sup> However, when the TA is dilated, the lead interference is no longer the primary problem. In a small series of patients undergoing lead extraction to manage significant TR, all patients who had TA dilatation did not benefit from lead extraction.<sup>62</sup> Patients with severe TA and/or RV dilation should be referred to surgery or transcatheter procedures. Taramasso *et al.*<sup>43</sup> analysed 470 patients with severe TR undergoing transcatheter TV repair, and compared patients with and without CIED, and reported similar rates of procedural success, residual TR, symptomatic improvement, and survival.

## Contemporary assessment of TR severity

Regardless of the imaging modality, the foundation of TR severity assessment is a thorough study of its anatomic and functional substrates. Accordingly, a detailed morphological and functional



Proximal Isovelocity Surface Area	Measurements Required	Example	Calculation
Proximal Isovelocity Surface Area (PISA)	Aliasing velocity ( $V_{Alias}$ ) Color Doppler with baseline shift in the direction of regurgitant jet  Radius of PISA ( $r$ )  TR peak velocity ( $V_{TR}$ ) CW of the TR jet  TR velocity time integral ( $TR_{VTI}$ ) CW of the TR jet		<b>PISA EROA:</b> $EROA = 2\pi r^2(V_{Alias}) \div V_{TR}$ <b>TR Regurgitation Volume =</b> $EROA \times TR_{VTI}$  $EROA = (6.282 \times 0.90 \times 28 \text{ cm/s}) \div 180 \text{ cm/s}$ $= 0.88 \text{ cm}^2$ $\text{Reg Vol} = 2.01 \text{ cm}^2 \times 50.2 \text{ cm} = 100.9 \text{ ml}$
Quantitative Doppler	Measurements Required	Example	Calculation
2D Method	2D Diastolic $TV_{Annular}$ Area RV Inflow and 4Ch TV annular diameters in mid diastole  TV velocity time integral ( $TV_{VTI}$ ) PW Doppler sample volume at the annulus  TR velocity time integral ( $TR_{VTI}$ ) CW of the TR jet		<b>TV Diastolic Stroke Volume =</b> $TV_{Annular} \text{ Area} \times TV_{VTI}$ <b>TR Regurgitation Volume =</b> $TV \text{ diastolic volume} - \text{Forward Stroke Volume}$ $EROA = \text{RegVol} \div TR_{VTI}$ <b>Example:</b> <ul style="list-style-type: none"> <li>TV Diastolic SV = <math>(0.785 \times 4.3 \text{ cm} \times 4.5 \text{ cm}) \times 10.9 \text{ cm} = 165.6 \text{ ml}</math></li> <li>TR Reg Vol = 115.6 ml</li> <li>EROA = <math>115.6 \text{ ml} \div 50.2 \text{ cm} = 2.30 \text{ cm}^2</math></li> </ul>
3D Method	Direct planimetry of the 3D Annular Area		<b>Example:</b> $3D \text{ Annular Area} = 14.8 \text{ cm}^2$ $TV \text{ Diastolic Area} = 14.8 \times 10.9 \text{ cm} = 161.3 \text{ ml}$ $TR \text{ Reg Vol} = 111.3 \text{ ml}$ $EROA = 111.3 \div 50.2 \text{ cm} = 2.22 \text{ cm}^2$
Forward Stroke Volume used to quantify RegVol	LVOT Stroke Volume LVOT Diameter LVOT PW  Note: Forward Stroke Volume may be either the LV or RV stroke volume.		<b>Forward Stroke Volume =</b> $LVOT_{Annular} \text{ Area} \times LVOT_{VTI}$ <b>Example:</b> $LV \text{ SV} = (0.785 \times [2.1 \text{ cm}]^2) \times 14.5 \text{ cm} = 50.2 \text{ ml}$
3D Color Doppler	Measurements Required	Example	Calculation
3D Vena Contracta Area (VCA)	3D Color Doppler planimetry of the VCA  TR velocity time integral ( $TR_{VTI}$ )		$EROA \cong VCA$ <b>TR Regurgitation Volume =</b> $VCA \times TR_{VTI}$  <b>Example:</b> $3D \text{ VCA} = 2.01 \text{ cm}^2$ $\text{Reg Vol} = 2.01 \text{ cm}^2 \times 50.2 \text{ cm} = 100.9 \text{ ml}$

**Figure 6** Quantitative echocardiographic methods for tricuspid regurgitation assessment. Summary of the quantitative assessment of tricuspid regurgitation (TR) by Proximal isovelocity surface area (PISA) method, volumetric Doppler quantification using both 2D and 3D methodology, and planimetry of 3D colour Doppler vena contracta area. CW, continuous wave; LV, left ventricle; LVOT, left ventricular outflow tract; PW, pulsed wave;  $r$ , radius; RegVol, regurgitant volume; RV, right ventricle;  $TR_{VTI}$ , continuous wave Doppler TR velocity time integral;  $TV_{Annulus}$ , tricuspid valve annulus;  $TV_{VTI}$ , pulsed wave Doppler annular velocity time integral;  $V_{Alias}$ , aliasing velocity; VCA, vena contracta area;  $V_{TR}$ , peak TR velocity.

area larger than a hemisphere of the same radius resulting in a 30–35% underestimation of EROA.<sup>79,80</sup> Second, similar to functional mitral regurgitation,<sup>81</sup> functional TR is temporally variable (Figure 7C and D, Supplementary data online, Media S3) and depending on the timing of PISA radius measurement, EROA may be under- or overestimated. Integrating PISA radii over the systolic time interval, improves the

estimation of functional mitral ERO,<sup>79</sup> and should be useful for TR assessment. Third, the regurgitant orifice is frequently not positioned within a planar surface (Figure 7E), thus whether the surface is funnel shaped (i.e. primary TR due to flail or marked prolapse) or the opposite wedge-shape (i.e. from marked leaflet tethering), a correction for the leaflet angle may be required. Fourth, in the



setting of marked variability in leaflet morphology, the regurgitant orifice is often stellate or crescent-shape<sup>21</sup> and thus the PISA shell is often hemi-ellipsoid with a larger area than a

Multiple guidelines have suggested that systolic reversal of hepatic vein flow is a sign of severe TR.<sup>8,9</sup> The guidelines also clearly state that this sign is non-specific and is influenced by many other factors (RV diastolic function, atrial fibrillation, RA pressure, or compliance).<sup>83</sup> Moreover, in the original reports systolic flow reversal in the hepatic vein was a sign of moderate or severe TR.<sup>83,84</sup> Hepatic vein systolic flow reversal may be seen in patients with moderate TR, particularly in the setting of high RA or RV pressures for other reasons, and it should not be used as a sole specific criteria for severe TR, but rather as supportive evidence for clinically important disease. In patients with significant TR, RV remodelling due to both dilatation and dysfunction should be assessed. Basal and mid ventricular RV septo-lateral dimensions as well as apex to TA length, are measured from an RV focused view, which typically yields larger dimensions than the apical 4-chamber or RV modified views.<sup>85,86</sup> RV function can be assessed by TA plane systolic excursion, tissue-Doppler systolic velocity, fractional area change, and RV-free wall or global



**Table 3** Possible eligibility criteria for tricuspid transcatheter edge-to-edge repair (TEER) in patients with severe, symptomatic tricuspid regurgitation and high/prohibitive surgical risk.

Feature	Ideal pathoanatomy for optimal tricuspid TEER outcomes	Challenging pathoanatomy for optimal tricuspid TEER outcomes	Relative pathoanatomic contraindications for tricuspid TEER
Leaflet length and mobility	Good leaflet lengths ( $\geq 7$ mm) and primary TR with prolapse only (no flail), or secondary TR with normal appearing leaflet mobility	Primary TR with leaflet prolapse or flail gap $< 10$ mm, or secondary TR with reduced leaflet mobility but tethering height $< 9$ mm,	Severe leaflet thickening (i.e. rheumatic) or shortening (length $< 7$ mm) or destruction (i.e. perforation) or large flail gap ( $\geq 10$ mm), severe leaflet tethering (tethering height $\geq 9$ mm)
Coaptation gap <sup>a</sup>	Significant TR with small coaptation gap ( $< 3$ – $7$ mm)	Moderate coaptation gap ( $> 7$ to $< 8.5$ mm)	Large coaptation gap ( $\geq 8.5$ mm)
TR location and severity	Central TR jet within the anteroposterior commissure with clear grasping zones	Central TR jet extending into multiple commissures (i.e. in patients with $> 3$ leaflets) with possible grasping zone	Non-central or very eccentric jets or jets originating from multiple commissures (i.e. in patients with $> 3$ leaflets) with dense chordae (i.e. no clear grasping zone), with massive or torrential disease (i.e. VC width $\geq 14$ mm, EROA by PISA $> 60$ – $70$ mm <sup>2</sup> )
Intra-procedural imaging	Good TEE windows <sup>b</sup> for leaflet visualization	Sufficient echocardiographic windows <sup>b</sup> for leaflet visualization or availability of alternative imaging (i.e. intra-cardiac echocardiography)	Insufficient echocardiographic windows <sup>†</sup> for leaflet visualizations
Presence of CIED	No CIED	Presence of CIED lead, no significant leaflet interaction and no interaction with clip	CIED-induced TR
Right ventricular remodelling <sup>c</sup>	Normal to mildly reduced RV function, normal to mild RV dilatation	Moderately or severely reduced RV function and/or moderate or severe RV dilatation, attributable to volume overload <sup>d</sup>	Severely reduced RV function or severe RV dilatation not primarily attributable to TR <sup>d</sup>
Pulmonary vascular haemodynamics	Normal peak and mean PAP, transpulmonary gradient and normal TAPSE/PASP ( $> 0.41$ )	PASP $\leq 60$ – $65$ mmHg, pulmonary capillary resistance $\leq 4$ WU, mean PAP $\leq 30$ mmHg, transpulmonary gradient $\leq 17$ mmHg	PASP $> 60$ – $65$ mmHg and/or pulmonary capillary resistance $> 4$ WU, and/or mean PAP $> 30$ mmHg and transpulmonary gradient $> 17$ mmHg, TAPSE/PASP $\leq 0.41$
Concomitant left heart disease	No significant left heart disease	Moderate left heart ventricular or valvular dysfunction which fail to meet criteria for GDMT or intervention	Severe left ventricular or valvular dysfunction amenable to GDMT or intervention

<sup>a</sup>Size of the coaptation defect has to be assessed at the location of the planned clip placement orthogonally to the commissural plane.

<sup>b</sup>Echocardiographic image quality has to be assessed in a 'grasping view' at the location of the planned clip placement.

<sup>c</sup>Stratification of RV size and function (i.e. mild/moderate/severe) is not well-defined at this time.

<sup>d</sup>CMR or 3D TTE RVEF <45% has been associated with adverse outcomes.

3D, three-dimensional; CIED, cardiac implantable electronic device; CMR, cardiac magnetic resonance; EROA, effective regurgitant orifice area; GDMT, guideline-directed medical therapy; LCD, intra-cardiac echocardiography; PAP, pulmonary artery pressure; PASP, pulmonary artery systolic pressure; PISA, proximal isovelocity surface area; RV, right ventricular; RVEF, right ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion; TEE, transoesophageal echocardiography; TR, tricuspid regurgitation, TTE, transthoracic echocardiography; T-TEER, Tricuspid Transcatheter Edge-to-Edge Repair; VC, vena contracta; WU, Woods Units.

points), LV ejection fraction <60% (1 point), and moderate/severe right ventricular dysfunction (1 point). Isolated tricuspid surgery, when performed in patients without comorbidities, preserved RV

function, and no organ failure (i.e. a risk score of  $\leq 3$ ), surgery is associated with an in-hospital mortality of  $\leq 5\%$ .<sup>105</sup> Annuloplasty is the most common treatment, however, it has been associated with

failure in case of leaflet tethering and RV dysfunction/remodelling.<sup>106</sup> In this case, additional leaflet procedures (such as leaflet augmentation or the clover technique) are used to improve short- and long-term durability.<sup>107,108</sup> Repair of complex congenital anomalies (e.g. Ebstein anomaly), or endocarditic TR is only possible with a surgical approach.<sup>109,110</sup> In patients with functional TR and advanced disease undergoing surgery, there is a recent trend for a low threshold to valve replacement as opposed to repair. Given the high-risk profile of reinterventions, a definitive solution is often preferred although the new interventional algorithms may influence the choice in the future.<sup>111</sup> There are no anatomical limits to surgical TV replacement, therefore imaging plays a minimal role in guiding the prosthesis selection and the surgical technique of implantation.

Imaging remains the cornerstone of all decisions related to interventional procedures, particularly in case of repair.<sup>112</sup> In most cases, the intervention targets the culprit lesion with a single device acting on a single dysfunctional element, as compared with surgery in which combined procedures are common. In the last decade, a large number of devices have been introduced to mimic any surgical procedure via a catheter. Most procedures are still investigational, while some interventional approaches are becoming very common. The largest experience is related to the transcatheter edge-to-edge repair (TEER).<sup>113</sup> Most patients can be treated using the TEER approach, however, early data show that there are patient populations whose anatomy or pathophysiology may not result in either optimal reduction to  $\leq 2+$  TR, or improved outcomes (Table 3).<sup>22,23,77,114–118</sup> Procedural success of tricuspid TEER, typically defined as successful clip placement and reduction of TR  $\geq 1$  grade on TTE at 30 days, was the only predictor for freedom from clinical outcomes and independently predicted freedom from the combined endpoint. On multivariate analysis, a smaller TV coaptation gap ( $<7.2$  mm) and a central/anteroseptal TR jet location independently predicted transcatheter TR repair success.<sup>114</sup> Using the newer generation of devices with longer device arms, coaptation gaps of up to 8.4 mm may be achievable.<sup>77</sup> Multiple studies have suggested that patients with massive or torrential disease, also have worse procedural success and outcomes with a VC width  $\geq 14$  mm<sup>42,119</sup> or an effective regurgitation orifice area by PISA method<sup>115,120</sup> of  $>60$ – $70$  mm<sup>2</sup> were associated with lower procedural success. Tricuspid TEER success has also recently been associated with valve morphology; the more complex the morphology, the lower the procedural success<sup>22</sup> which may then affect overall outcomes.<sup>23</sup> Outcomes following tricuspid TEER have been strongly correlated with RV ejection fraction.<sup>117,118</sup> Remodelling of the RV has been seen in patients following tricuspid TEER<sup>120</sup>; however, the extent of remodelling and relationship to baseline measures is currently unknown.

Some annuloplasty devices are available and could be used as stand-alone procedure in patients in whom leaflet tethering is less pronounced. The main factors related to procedural success are the size of the TA, the absence of leaflet restricted motion, and the distance of the TA from the right coronary artery (assessed by CT scan). In theory, annuloplasty and TEER could be used in combination similar to the surgical approach of annuloplasty and clover technique. In patients with more advanced geometrical changes of the TV components and of the RV, valve replacement is an option still in its early phase, with no devices available for commercial use. Patient selection is mainly based on CT scan to assess annular dimensions, anatomy

and size of the RV, and the position of the vena cava. Echocardiography and right heart catheterization are fundamental for patient selection to rule out patients with too advanced right heart disease and significantly increased pulmonary resistance, both of which may be integral to risk stratification.<sup>10,38</sup>

## Conclusion

The independent association of mortality with severity of untreated TR, along with a high mortality associated with isolated TR surgery, has led to intense interest surrounding the improvement in characterization, diagnosis, and treatment of TR. The new classification systems for TR aetiology and severity presented in this review, have anatomic and clinical relevance. The issues surrounding the accurate non-invasive quantitative assessment of TR may be addressed by the use of advanced imaging methods and techniques. Finally, patient-specific transcatheter therapies will undoubtedly require the use of morphologic and TR severity parameters for appropriate device choice.

## Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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## Data availability

No new data were generated or analysed in support of this review.

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