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Tricuspid Valve Disease

A Comprehensive Guide to Evaluation and Management

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Contemporary Cardiology

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Tricuspid Valve Disease

A Comprehensive Guide to Evaluation and Management

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Part I
Tricuspid Valve Basics

Chapter 1
Anatomy of the Tricuspid Valve

Neel M. Butala and Sammy Elmariah

Introduction

The anatomy of the tricuspid valve is complex and often variable. Gaining a thorough understanding of the development of the tricuspid valve, its distinct components, and its adjacent structures is crucial to understanding both the pathophysiology of tricuspid valve disorders and possible clinical management strategies. This chapter will review the embryology of the tricuspid valve and consider in detail the key components of the tricuspid valve itself: the tricuspid valve leaflets, the tricuspid valve annulus, and the tricuspid tensor apparatus. It will then review clinically relevant adjacent structures and implications of anatomy for tricuspid valvular intervention.

Embryology of the Tricuspid Valve

The heart begins as a primitive coiled tube that develops into a common atrioventricular (AV) canal. Initially, the right AV canal has no direct connection with the right ventricle, but expansion and remolding of the right ventricular myocardium brings it into continuity through a muscular conduit termed the "tricuspid gully," which is immediately downstream of the AV canal [1]. A ring of specialized AV myocardium surrounds the AV canal, which forms protrusions deemed endocardial

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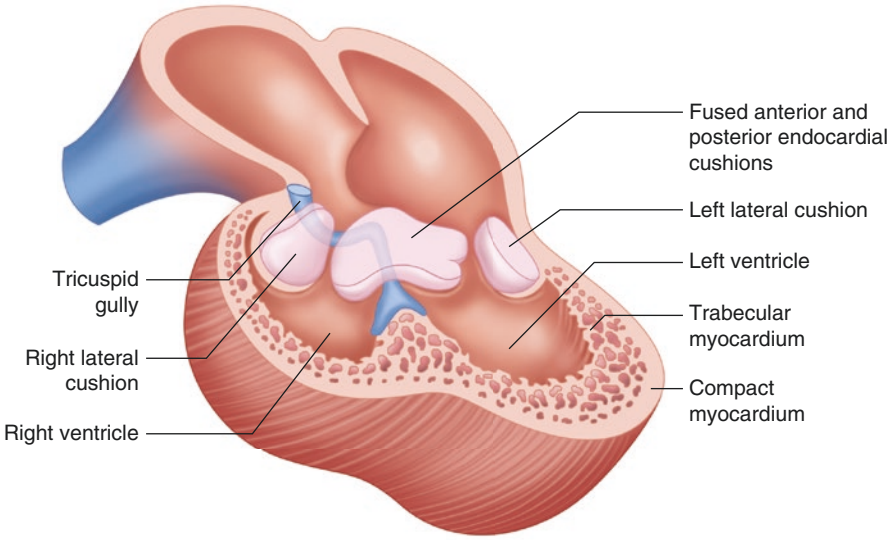

Fig. 1.1 Formation of right ventricular inlet. Right ventricular myocardium remolds and turns into the tricuspid gully, which forms the right ventricular inlet. At the same time, the AV canal cushions fuse to form the inferior septum and split the canal into two separate orifices

cushions. Endocardial cushions are loosely reticulated fibroblastic tissue masses composed of mesenchymal subendothelial tissue [2]. Myocardial protrusions form on the lateral sides of the canal, forming right and left lateral cushions, as well as on the anterior (ventral) and posterior (dorsal) walls of the AV canal, forming the anterior and posterior endocardial cushions. As the AV canal grows and straightens, the anterior and posterior cushions grow inward to begin to divide the common AV orifice into separate mitral and tricuspid orifices (Fig. 1.1).

The primitive tricuspid gully is bordered by the right lateral, posterior, and anterior cushions as well as ventricular myocardium in its inferolateral aspect [1]. The right lateral cushion forms the posterior tricuspid leaflet, and the right half of the posterior cushion forms the septal leaflet of the tricuspid valve [3]. The anterior tricuspid leaflet forms from both the right half of the anterior cushion and the right lateral cushion [1]. Tricuspid valve tissue is ultimately composed equally of endocardial cushion tissue and adjacent ventricular myocardium, with endocardial cushion tissue along the atrial aspect and myocardial tissue along the ventricular aspect, ensuring continuity with the sub-valvular tensor apparatus.

Formation of valve leaflets occurs through proliferation, extension, condensation, and delamination (Fig. 1.2) [3]. Myocardial cells immediately subendocardial to the AV cushions proliferate, which expand and extend the cushions inward. These cushions and adjacent myocardial tissue then differentiate into fibroblasts and condense into a thinner fibrous tissue. Fenestrations develop and coalesce, resulting in delamination of AV myocardial tissue from the myocardial wall in the midportion of the cushion, with attachments only in the cranial and caudal aspects. Further

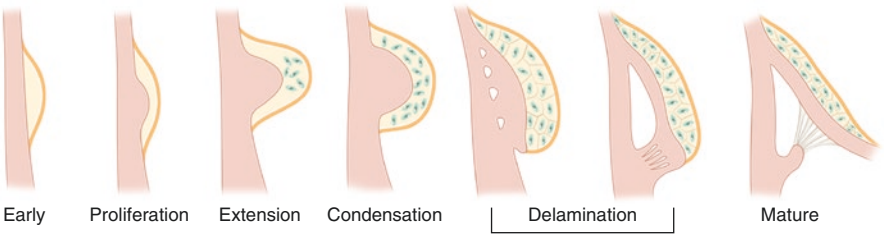

Fig. 1.2 Formation of tricuspid valve leaflets. General stages of tricuspid valve leaflet formation. Tissue in pink represents ventricular myocardium. Tissue in yellow represents endocardial cushions

fenestrations develop between structures on the caudal aspect of the cushion, creating separate papillary muscles and tendinous chordae.

The unique hemodynamics and coalescence of spaces in the ventricular trabeculated tissue during delamination in each individual may result in the creation of unique arrangements of cusps in the tricuspid valve [4], as well as pathology. For instance, Ebstein's malformation occurs from a failure of lamination of the inferior and septal leaflets from the right ventricular inlet wall [5].

A well-delineated AV junction can be seen at approximately 51 days of gestation, and by 56 days, separate AV valves are seen from the fusion of the endocardial cushions [6]. Initially, the valve leaflets are thick, but by 64 days, the leaflets become thinner and more mature in appearance.

Tricuspid Valve Leaflets

The tricuspid valve is composed of three leaflets in the majority of patients. A significant proportion of patients may have a different number of leaflets [4], though differences among studies may be confounded by the lack of a unified definition of commissures and the extent of leaflets [7]. Irrespective of the number, valve leaflets are oriented circumferentially in a curtain-like formation that separates the right atrium from the right ventricle.

The traditional three leaflets of the tricuspid valve are referred to as the anterior, posterior, and septal leaflets and are unequal in size (Fig. 1.3). The anterior leaflet is the largest in size and is oriented in an anterior-superior dimension. The anterior leaflet is the longest leaflet in a radial dimension and also has a large circumferential length along the anterior and lateral aspects of the annulus. It can occasionally contain notches that can seemingly subdivide this leaflet, though these notches do not contain the depth or fan-shaped chordal attachments characteristic of commissures between separate leaflets [7].

The posterior leaflet has a shorter radial length than the anterior leaflet and has the shortest circumferential length of all three leaflets along the posterolateral aspect of the annulus. The posterior leaflet can have multiple scallops and may not be

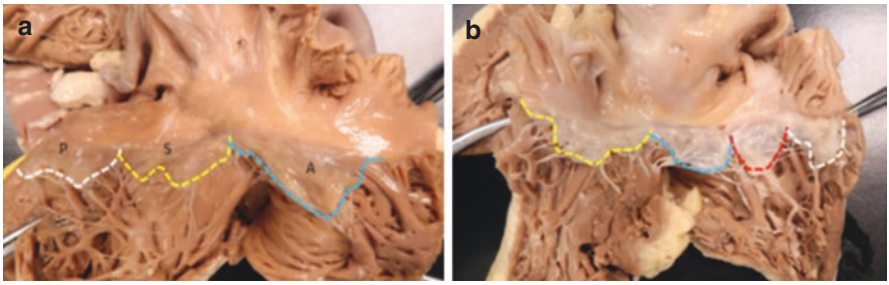

Fig. 1.3 Tricuspid valve leaflets. The number of tricuspid leaflets is highly variable. The most common configuration is a three-leaflet valve (**a**). In this figure, the white line indicates the posterior leaflet, the yellow line indicates the septal leaflet, and the blue line indicates the anterior leaflet. Frequently, more than three leaflets are seen (**b**). The orange line (**b**) represents the fourth leaflet in this quadricuspid valve. A anterior leaflet, P posterior leaflet, S septal leaflet. (Reprinted from Dahou et al. [10], Copyright (2019), with permission from Elsevier)

clearly separated from the anterior leaflet in all patients, calling for some to advocate for the classification of the anterior and posterior leaflets together as a single "mural leaflet," with multiple scallops [8], albeit with multiple zones of apposition during coaptation [9]. The commissure between the anterior and posterior leaflets is typically delineated by the insertion of a fan-shaped chorda near the acute margin of the right ventricle [7].

The septal leaflet is the shortest in the radial dimension and has the largest circumferential length along the straight portion of the annulus, immediately superior to the interventricular septum. These characteristics make it the least mobile among the three leaflets. The septal leaflet does not have any scallops, though it can have notches. The commissure between the anterior and septal leaflets is typically adjacent to the noncoronary sinus of Valsalva in the aortic root, and the commissure between the posterior and septal leaflets is adjacent to the orifice of the coronary sinus in the right atrium [10]. The insertion point of the septal tricuspid leaflet along the right ventricular aspect of the interventricular septum is displaced apically relative to the insertion point of anterior mitral leaflet along the left ventricular aspect of the interventricular septum.

Each tricuspid valve leaflet has a basal zone, rough zone, and clear zone, similar to the mitral valve [7]. The basal zone of the tricuspid leaflet extends 2–3 mm into the leaflet from the annulus and extends onto the commissural areas. The rough zone of the tricuspid leaflets is rough, thick, and semi-opaque and is the location of insertion of most chordae tendinae. The clear zone falls between the rough and basal zones.

The coaptation of the tricuspid valve is complex, with multiple coaptation zones between pairs of leaflets. There is excess coaptation length that can serve as a reserve to accommodate some annular dilation prior to malcoaptation [10]. Because the anterior and septal leaflets have the longest circumferential dimensions, they have the longest coaptation zone. It is along this zone that the majority of tricuspid regurgitation occurs.

Tricuspid Valve Annulus

The tricuspid valve annulus is the largest among the four heart valves, with an orifice area between 7 and 9 cm^2 on average [11]. The tricuspid annulus can change in size dramatically during the cardiac cycle, with the ability to increase its area by 30% [12]. The tricuspid annular area follows a biphasic pattern during the cardiac cycle, with the largest size in late diastole and an additional peak in size in early diastole, though this latter peak often disappears in patients with tricuspid regurgitation.

The tricuspid valve annulus is D-shaped with a straight portion along the interventricular septum and a curved portion along the anterior, posterior, and lateral aspects (Fig. 1.4). As the right ventricle becomes more dilated in secondary tricuspid regurgitation, the annulus dilates toward the free wall since the septal aspect of the annulus is bound by the fibrous skeleton of the heart. It is because of this property that the septal dimension can be used for annuloplasty sizing [13].

The tricuspid annular plane is oriented vertically at approximately a 45° angle from the coronal and sagittal planes, though it is typically not planar. The anteroseptal and posterolateral aspects of the annulus are more atrial, whereas the posteroseptal and anterolateral aspects of the annulus are more ventricular (Fig. 1.5) [12]. However, as tricuspid regurgitation increases in severity, the annular shape becomes more planar in the vertical dimension.

The tricuspid annulus itself is essentially a confluence of tricuspid valve leaflet hinge lines composed of fibro-adipose tissue that electrically insulates the right atrium from the right ventricle [14]. The annulus does not contain much fibrous tissue and there is no fibrous continuity with the corresponding sided semilunar valve [15]; these factors make this distinct from the mitral valve annulus. Histologically, connective tissue in a leaflet joins the subendocardial tissue or unites with a small mass of connective tissue in the ventricle [7]. On the septal aspect, leaflet connective tissue merges directly with a membranous interventricular septum.

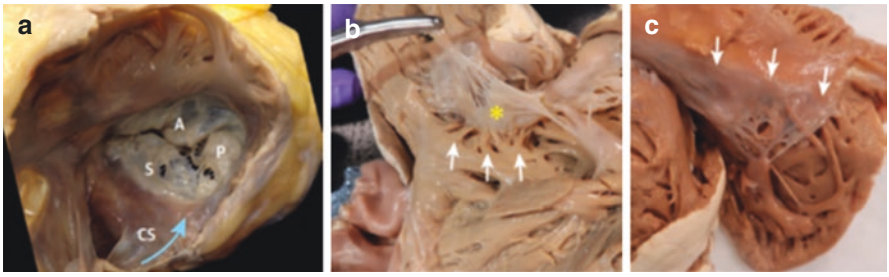

Fig. 1.4 Tricuspid valve annulus. (**a**) The tricuspid valve is seen from the atrial side with the typically D-shaped annulus composed of a flat septal region and curved anterior and posterior regions. (**b**) The ventricular surface of the anterior leaflet (asterisk) with multiple crisscrossing muscle attachments (arrows) directly to the base of the leaflet. (**c**) The atrial surface of the anterior leaflet annulus (white arrows), which is not fibrous and has a smooth transition from atrium to ventricle. CS coronary sinus (curved blue arrow), A anterior leaflet, P posterior leaflet, S septal leaflet. (Reprinted from Dahou et al. [10], Copyright (2019), with permission from Elsevier)

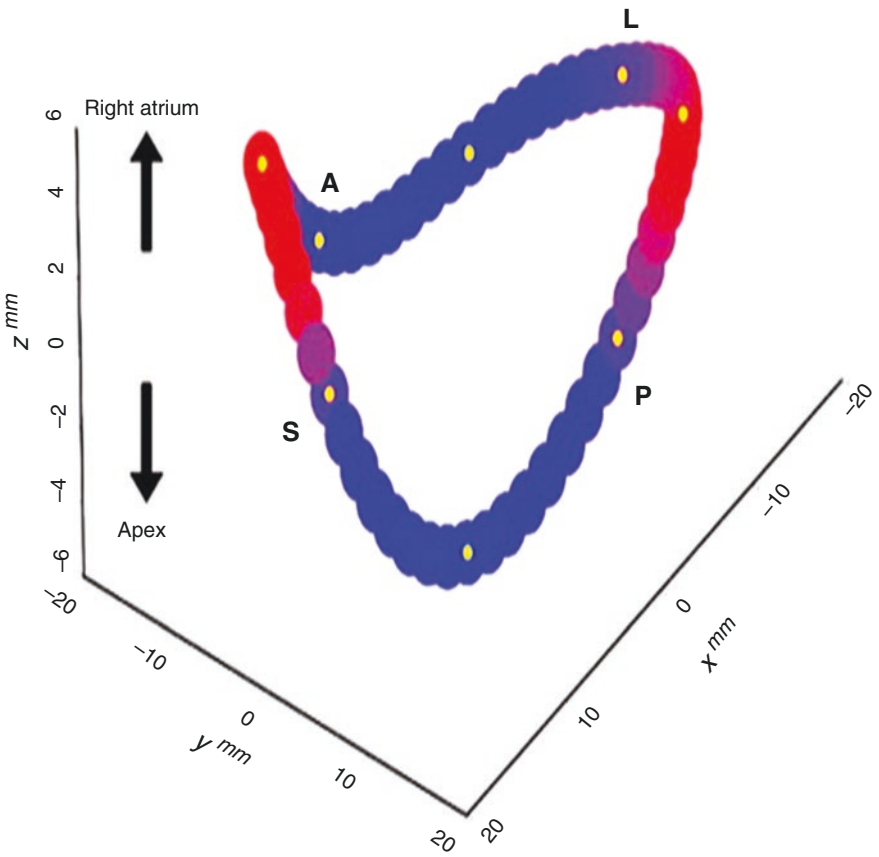

Fig. 1.5 The reconstructed ring shape for tricuspid annuloplasty, based on the average results obtained in healthy subjects at the time of minimum TA area. The positive x–y–z axis indicates the respective directions toward the septum, the posterior wall, and the right atrium. At the yellow dot, the average of each of the manually selected TA locations is shown. The reconstructed TA locations were color coded by assigning shades of red to points located above the best-fit plane toward the atrium and shades of blue to points located below the best-fit plane toward the apex. A anterior, L lateral, P posterior, S septum. (Reprinted from Fukuda et al. [12], Copyright (2006), with permission from Wolters Kluwer Health)

Tricuspid Tensor Apparatus

The tricuspid valve is attached to the right ventricle via papillary muscles and chordae that together comprise the tensor apparatus of the tricuspid valve (Fig. 1.6). Attachments of the valve leaflet tissue can vary along a spectrum from connection with a large, discrete papillary muscle to connection with a small, rudimentary papillary muscle to connect directly with the right ventricular wall.

There are typically three major papillary muscles, though this number can vary greatly [4, 14, 16]. The anterior papillary muscle is the largest and attaches to both

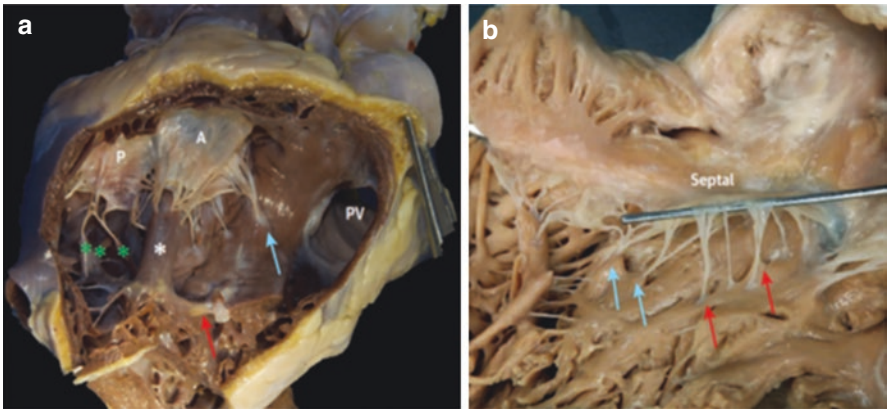

Fig. 1.6 Tricuspid valve tensor apparatus. (**a**) Typical papillary muscle distribution for the tricuspid valve. The anterior papillary muscle is typically the target (white asterisk), which provides chordal support for the A and P leaflets. The moderator band (orange arrows) may join this papillary muscle. The posterior papillary muscle is often bifid or trifid (green asterisks) and lends chordal support to the posterior and septal leaflets. The septal papillary muscle is variable (blue arrows). (**b**) Septal leaflet chordal attachments to the septal papillary muscle are shown (blue arrows) and directly from the septal myocardium (orange arrows). A anterior leaflet, P posterior leaflet. (Reprinted from Dahou et al. [10], Copyright (2019), with permission from Elsevier)

the anterior and posterior leaflets. The anterior papillary muscle can be bifid or be multiple in some cases. The posterior papillary muscle often has multiple heads and attaches to the septal and posterior leaflets. A septal papillary muscle is rudimentary and may be absent or multiple in many cases.

Chordae connect valve leaflets to the papillary muscles and typically arise from the apical third of the papillary muscle and branch soon after their origin. Accessory chordae can also connect directly from leaflet tissue to the right ventricular free wall, the interventricular septum, or the moderator band. Chordae that do not attach to leaflet tissue ("false chordae") also exist and can connect different points on ventricular walls or papillary muscles.

There are five distinct types of chordae of the tricuspid valve: fan-shaped, rough zone, basal, free edge, and deep chordae [7]. Fan-shaped chordae insert into the commissures between leaflets and into clefts in the posterior leaflet and may have threadlike communications between their branches in a lace-like pattern. Rough zone chordae split into three branches soon after their origin and insert into the rough zone on each leaflet: one branch on the free margin of each leaflet, one branch on the line of closure, and a third branch between the two. Basal chordae are directly attached to the ventricular wall. Free edge and deep chordae are unique to the tricuspid valve. Free edge chordae are often long and form a delta-shaped insertion into a leaflet's free edge. Deep chordae are also long and pass deep to the leaflet's free margin inserting in the upper part of the rough zone or the clear zone, providing a second layer of chordal attachment.

The number of chordae can vary significantly, ranging from 17 to 36 in one study [7]. Tricuspid valve chordae are composed of 80% collagen organized in straight

bundles and networks of fibrils, which have less extensibility than chordae of the mitral valve [17].

Adjacent Structures

Knowledge of the anatomy of structures adjacent to the tricuspid valve can give one a better understanding of tricuspid valvular pathologies as well as potential therapeutic options (Fig. 1.7).

The noncoronary sinus of Valsalva is a particularly important clinical landmark that lies immediately adjacent to the tricuspid valve annulus and marks the commissure of the anterior and septal leaflets. Additionally, the opening of the coronary sinus lies just superior to the tricuspid valve annulus and marks the commissure of the posterior and septal tricuspid valve leaflets.

The AV node and the bundle of His are also clinically relevant structures adjacent to the tricuspid valve. The bundle of His crosses the septal leaflet attachment 3–5 mm posterior to the commissure of the anterior and septal leaflets [10]. Cavotricuspid isthmus is another electrically important area of slow conduction that is anteromedial to the inferior vena cava and posterolateral to the tricuspid valve [18].

The right coronary artery is also adjacent to the tricuspid valve. The right coronary artery courses through the AV groove, which approximates the location of the tricuspid valve anulus. However, the right coronary artery begins its course relatively distant from the annulus and gradually becomes closer to the endocardium as it progresses. The right coronary artery runs particularly close to the annulus in the inferior segment where it lies <3 mm from the endocardial surface [19].

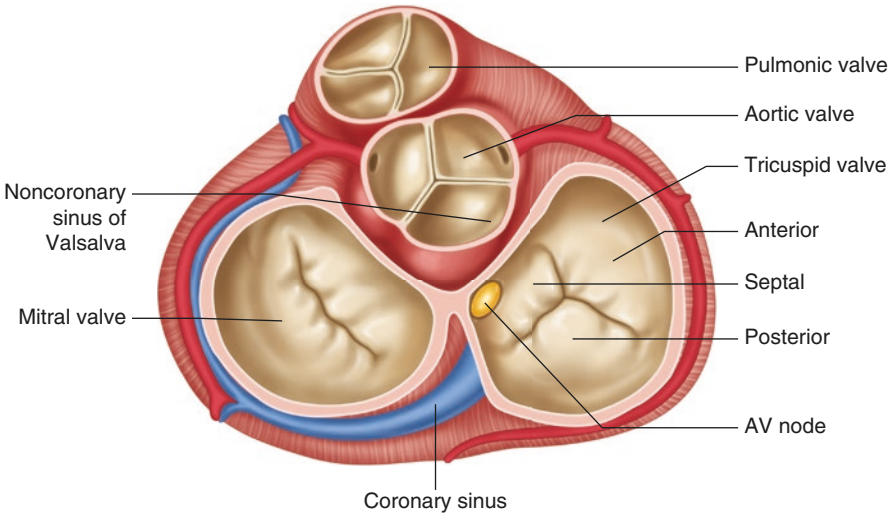

Fig. 1.7 Structures adjacent to the tricuspid valve

The venae cavae feed the right atrium and are also important structures with respect to the tricuspid valve. The inferior vena cava is formed from the confluence of the right and left common iliac veins in the retroperitoneal space and runs along the right side of the vertebral column. The superior vena cava is formed from the confluence of the right and left brachiocephalic veins and courses along the right middle mediastinum.

Implications for Tricuspid Valve Intervention

Many of the key features of tricuspid valve anatomy detailed above are important when considering surgical or transcatheter intervention to treat tricuspid valve pathology, particularly in comparison to mitral valve anatomy and intervention.

The anterior location of the tricuspid valve in the heart can make imaging guidance for procedures with transesophageal echocardiography challenging. In some cases, transthoracic echocardiography or intracardiac echocardiography may be an appropriate adjunct or substitute to obtain adequate image quality [20].

The tricuspid valve leaflets have unique features that make tricuspid valve intervention challenging. The leaflets themselves are thinner compared to the mitral valve, which makes it difficult to anchor devices to them and can make the leaflets easier to damage during manipulation. In particular, this can become an important issue with transcatheter leaflet gripping systems to address tricuspid regurgitation where tearing of the leaflets may make regurgitation worse.

The tricuspid annulus also has unique features that can make tricuspid valve intervention difficult. First, the lack of a definitive fibrous annulus or annular calcification makes it difficult to locate the annulus fluoroscopically and to seat a valve completely in the annulus. Second, the complex three-dimensional shape of the annulus can make it challenging to create annuloplasty devices that mimic a normal anatomic tricuspid annulus. Third, the larger orifice of the tricuspid valve relative to the mitral valve makes it challenging to overcome a large coaptation gap, and residual regurgitation may remain. Finally, annular devices must be designed to account for the wide variation in annular size during the cardiac cycle [10].

The complex and variable tricuspid tensor apparatus also presents unique challenges for tricuspid intervention. The multiplicity of chordae can make it challenging to manipulate transcatheter devices. This is particularly relevant for devices that attempt to attach to leaflet tips, where the majority of chordae insert. The risk of impingement of chordae is high and can lead to difficulty in device retrieval or chordal rupture and subsequent worsening of tricuspid regurgitation. Tricuspid chordal tissue is also thinner compared to the mitral valve and may be easier to damage. Finally, the presence of false chordae, which connect two spots on ventricular walls, can further increase the risk of device entanglement in the right ventricle.

Anatomy of structures adjacent to the tricuspid valve also has implications for tricuspid intervention. Any devices manipulating the tricuspid annulus near the anteroseptal commissure can run the risk of perforation into the aorta. Additionally,

any devices manipulating the septal aspect of the annulus can compress the AV node or His bundle and can lead to complete heart block. Furthermore, manipulation of the inferior annulus in particular can run the risk of injury to the right coronary artery.

Access to the tricuspid valve in some respects is easier than access to the mitral valve, as the vena cavae are large and distensible and transseptal puncture is not required for transcatheter therapies. However, devices designed for trans-septal delivery to the mitral valve may not necessarily reach the tricuspid valve in the appropriate angle. Furthermore, transapical access for the right ventricle may be challenging given the thin right ventricular wall, particularly for patients with a dilated right ventricle from tricuspid regurgitation [20].

Finally, the lack of any continuity between the tricuspid valve and the pulmonic valve decreases the risk of outflow obstruction, which is otherwise an important consideration for mitral valve intervention.

Conclusion

Through careful review of the development of the tricuspid valve, anatomy of its distinct components, and its relationship with adjacent structures, one can understand the complex and unique morphology of the tricuspid valve. This knowledge can serve as a foundation for understanding the clinical, hemodynamic, and multimodality imaging assessment of the tricuspid valve and the current and future management for tricuspid valve disease.

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Chapter 2
Epidemiology, Pathophysiology, and Natural History of Tricuspid Valve Regurgitation and Stenosis

James N. Kirkpatrick and Andrew S. Perry

Epidemiology of Tricuspid Valve Regurgitation

Tricuspid regurgitation is common. In a population-based study of 3589 persons (1696 men and 1893 women) enrolled in the Framingham study, tricuspid regurgitation (of any degree) was present in 82.0% of men and 85.7% of women [1]. However, only 14.8% of men and 18.4% of women had tricuspid regurgitation of mild severity or greater, indicating that trace (or physiologic) tricuspid regurgitation is common in normal hearts. In the United States, it was estimated that a total of 1.6 million people had moderate to severe tricuspid regurgitation in the early 2000s [2].

The majority of tricuspid regurgitation (>80%) is secondary, or functional, in etiology. Any process that results in right ventricular volume and/or pressure overload may cause tricuspid annular dilation and thereby regurgitation. Examples include mitral valve stenosis or regurgitation, left ventricular myocardial disease, pulmonary hypertension, right ventricular infarction, dilated cardiomyopathies, right ventricular pacing, and atrial fibrillation [3].

Primary tricuspid regurgitation may result from congenital or acquired means. Congenital heart conditions that predispose to tricuspid valve disease include Ebstein's anomaly, atrioventricular prolapse, and tricuspid valve dysplasia, cleft, or prolapse. Acquired causes include infective endocarditis, trauma from intracardiac devices (implantable cardio-defibrillator and pacemaker leads) or endomyocardial biopsy, rheumatic heart disease, carcinoid syndrome, sarcoidosis, systemic lupus erythematosus, radiation, chest wall trauma, and use of anorectic drugs such as fenfluramine or phentermine. In a study of 132 patients with carcinoid syndrome

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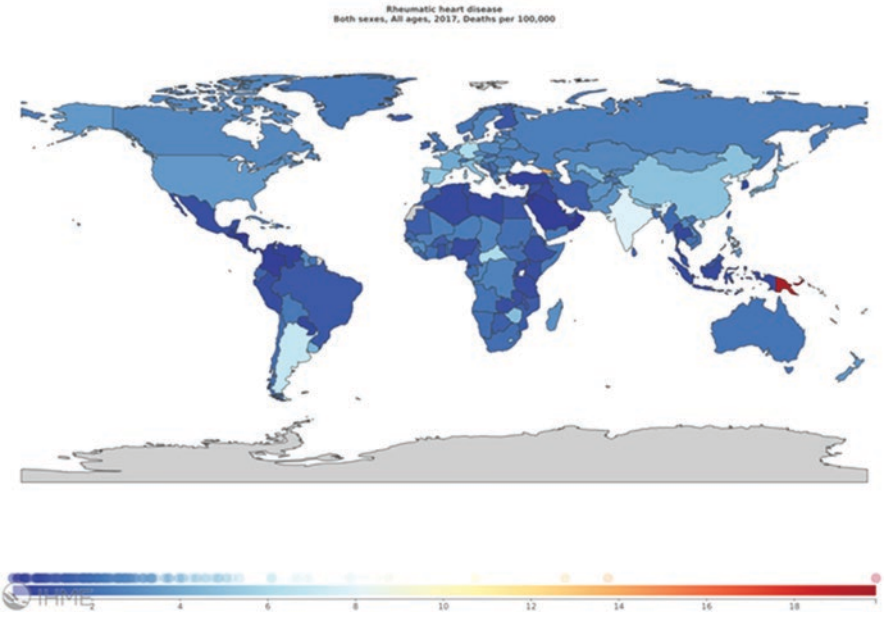

Fig. 2.1 Prevalence of rheumatic heart disease, 2017. (Institute for Health Metrics and Evaluation (IHME) [37])

who had an echocardiogram, 74 (56%) patients had cardiac involvement, the majority manifesting as tricuspid valve pathology (72, 55%) [4].

Rheumatic heart disease (not just tricuspid involvement) is uncommon in the developed world and wealthy nations but remains a major cause of cardiovascular morbidity and mortality in developing nations [5]. Worldwide, an estimated 30 million people are affected by rheumatic heart disease with the heaviest burdens in Africa, Southeast Asia, and the Western Pacific (Fig. 2.1) [6]. Direct tricuspid valve involvement in rheumatic heart disease is common, in some pathological studies ranging from 30% to 50%. However, in a study of 372 patients with echocardiographically detected rheumatic mitral valve disease, 23 (6%) had tricuspid valve involvement [7]. This study was published in 1983, though with the improvements in contemporary imaging, the prevalence detected today by echocardiography may be higher. The incidence of tricuspid regurgitation in rheumatic heart disease is likely around 10% [8].

Tricuspid valve endocarditis is much less common than left-sided endocarditis and comprises 15% of all infective endocarditis cases. Among those patients who require surgery, tricuspid regurgitation is commonly found, being present in 78% of patients in one study [9]. The majority of patients with tricuspid valve endocarditis are persons who inject drugs, and the main organism isolated is *Staphylococcus aureus* [10].

While anorectic drugs such as fenfluramine and dexfenfluramine are associated with an increased risk of valvular heart disease, the risk is low. Short-term exposure

to these medications (less than 4 months) is associated with a 5-year incidence of 7.1 per 10,000 persons exposed. Longer exposure (over 4 months) is associated with a 5-year incidence of 35 per 10,000 persons exposed [11]. Tricuspid valve involvement is likely even rarer. In the seminal paper by Jick et al., of the 11 patients discovered with medication-induced valve disease, none of them had tricuspid valve involvement [11].

The prevalence of tricuspid regurgitation among patients undergoing mitral valve surgery has been well studied and is quite common. Accordingly, mitral valve or "left-sided" heart disease has been implicated as a common etiology of tricuspid regurgitation. In a large retrospective cohort of 5168 patients undergoing mitral valve surgery, about 40% of patients had moderate to severe tricuspid regurgitation at the time of mitral valve surgery [12]. In a smaller study of patients undergoing surgical revascularization and mitral valve repair with ring, of the 70 patients studied, 21 (30%) had moderate to severe tricuspid regurgitation [13]. In a study of 318 patients undergoing balloon mitral valvuloplasty, 97 (31%) had moderate to severe tricuspid regurgitation [14].

Tricuspid regurgitation may manifest many years after mitral valve surgery. This is referred to in the literature as "late tricuspid regurgitation." Whether or not this is due to residual elevations in left atrial or pulmonary arterial pressures or a separate process is a matter of debate. Between 4 and 24 years after mitral valve surgery for rheumatic mitral valve disease, 14% of patients were found to have severe tricuspid regurgitation, all of whom had atrial fibrillation [15]. In patients who had mitral valve repair for ischemic mitral regurgitation, 74% developed moderate to severe tricuspid regurgitation by 3 years after surgery [13].

Development of moderate to severe tricuspid regurgitation after intracardiac lead implantation is common, with an incidence of 38% reported in one series [16]. Finally, there are patients with idiopathic tricuspid regurgitation who have tricuspid annular dilation without an apparent underlying cause [17]. See Table 2.1 for causes of tricuspid regurgitation.

Epidemiology of Tricuspid Valve Stenosis

Tricuspid valve stenosis is a rare entity, affecting less than 1% of patients [18]. There are a few causes of native tricuspid valve stenosis. These include rheumatic heart disease (often mixed tricuspid stenosis and tricuspid regurgitation), carcinoid, systemic lupus erythematosus, congenital abnormalities (tricuspid atresia or stenosis), or right atrial masses (such as in infective endocarditis or large, prolapsing myxomas). In some cases of metabolic and enzymatic disorders, leaflet thickening and stenosis can occur such as in Fabry's disease and Whipple's disease. Most commonly encountered is rheumatic heart disease, which generally has concurrent left-sided valve disease (mitral valve stenosis with or without aortic valve stenosis), although rare cases of isolated rheumatic tricuspid valve disease have been reported [19]. While Ebstein's anomaly is also more commonly known to produce tricuspid

Table 2.1 Causes of tricuspid regurgitation

Secondary (functional) regurgitation (>80%)
Mitral valve disease
Left ventricular dysfunction
Pulmonary hypertension
Right ventricular infarction
Dilated cardiomyopathies
Right ventricular pacing
Atrial fibrillation
Primary regurgitation
Congenital
Cleft valve, dysplasia
Ebstein's anomaly
Atrioventricular prolapse
Acquired
Rheumatic heart disease
Endocarditis
Carcinoid
Sarcoidosis
Systemic lupus erythematosus
Anorectic drugs
Blunt chest trauma
Iatrogenic
Intracardiac devices
Endomyocardial biopsy
Radiation

regurgitation, there are reports of tricuspid stenosis associated with Ebstein's [20]. Tricuspid stenosis is an uncommon consequence of infective endocarditis, being present in only 3.5% of patients undergoing surgery for tricuspid valve endocarditis [9].

Pathophysiology of Tricuspid Regurgitation

The tricuspid valve naturally has a half-moon shape because of the way the right ventricle wraps around the left ventricle. Generally, there are three leaflets (septal, posterior, and anterior), but there are descriptions of valves with as few as two and as many as six leaflets. As stated previously, most tricuspid regurgitation is secondary to right ventricular pressure or volume overload, and the leaflets are structurally normal. In secondary tricuspid regurgitation, there are three identifiable stages of disease progression. First, as the right ventricle dilates in response to volume or pressure overload, the tricuspid annulus flattens, dilates, and begins to become more

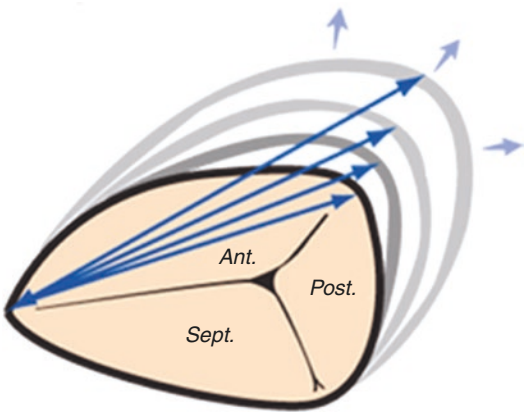

Fig. 2.2 Tricuspid dilatation occurs with outward movement of the anterior and posterior leaflets. (Republished with permission of McGraw Hill Education, from Cohn and Adams [38]; permission conveyed through Copyright Clearance Center, Inc. Available at: https://accesssurgery.mhmedical.com/content.aspx?bookid=2157§ionid=164304336. Accessed: January 31, 2022)

circle shaped. Annular dilation mainly occurs with outward movement of the anterior and posterior leaflets, as the septal leaflet is attached to the fibrous septum, which constrains septal annular dilatation (Fig. 2.2) [21]. Second, as the right ventricle continues to dilate and the tricuspid annulus correspondingly enlarges, the leaflets fail to coapt. Third, with severe right ventricle dilation, tethering of the leaflets may occur, but tethering is generally limited to the anterior and posterior leaflet since the papillary muscles are attached to the right ventricle free wall [22]. Tethering of the septal leaflet is unlikely to occur as the septal papillary muscles are inserted high on the wall. Overall, the dominant mechanism of tricuspid regurgitation in the setting of right ventricular enlargement is felt to be from annular dilation.

Because of the relationship between left-sided heart disease and significant tricuspid regurgitation, it was long thought that elevated pulmonary pressures are a necessary prerequisite to tricuspid regurgitation. There are data that suggest tricuspid regurgitation may occur with or without the presence of pulmonary hypertension, and not all patients with pulmonary hypertension have significant tricuspid regurgitation [1, 23]. Tricuspid regurgitation related to pulmonary hypertension has a different overall mechanism compared to that seen in primary right ventricular enlargement. Patients with tricuspid regurgitation in the setting of pulmonary hypertension have increased tenting height of the leaflets. This indicates that the driving mechanism behind tricuspid regurgitation in the setting of pulmonary hypertension (irrespective of WHO Class of pulmonary hypertension) is leaflet tethering that results from right ventricular lengthening, rather than true annular dilation [24].

Annular dilation, rather than leaflet tethering, is the predominant mechanism among patients with idiopathic tricuspid regurgitation. Interestingly, idiopathic tricuspid regurgitation is seen in older patients, many of whom have atrial fibrillation. Tricuspid annular dilation is a known consequence of atrial fibrillation, and thus

preexisting atrial fibrillation may be causative for the development of tricuspid regurgitation rather than a consequence as previously thought [24].

Primary tricuspid regurgitation occurs by mechanisms unique to the disease. Ebstein's anomaly is the most common congenital heart disease affecting the tricuspid valve. Ebstein's anomaly is an apical displacement of the posterior and septal leaflets in the right ventricle resulting in atrialization of the right ventricle. Specifically, this means these leaflets are attached not at the atrial-ventricular junction, but rather on the ventricular walls. While the anterior leaflet attachment is generally not apically displaced, all three leaflets are structurally abnormal. Each leaflet can have aberrant papillary muscles or chordae tendinae attaching to the ventricular wall, impairing its closure. This significant tethering of the leaflets leads to regurgitation [20].

Tricuspid regurgitation associated with rheumatic heart disease can have one of two mechanisms. First, the regurgitation may be functional, secondary to the elevated pulmonary pressures caused by rheumatic mitral valve stenosis. Second, there can be direct involvement of the tricuspid valve with fibrous thickening of valve leaflets. The thickening is due to an autoimmune response after group A streptococcal infection (rheumatic fever). The streptococcal M protein has molecular mimicry with many native cardiac proteins such as myosin, keratin, and laminin [25]. As in rheumatic mitral valve disease, there is a fusion of the commissures with diastolic doming of the valve causing tricuspid stenosis [25]. During ventricular systole, the thickened valves fail to coapt normally during closure resulting in regurgitation. When presenting between the ages of 20 and 50 with dyspnea, many patients may not recall their childhood history of pharyngitis, followed by a fever, with or without polyarthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules [5].

Carcinoid syndrome results in fibrous plaques, usually on the ventricular side of the valve and endocardium of the right ventricle (Fig. 2.3). The leaflets become thickened, shortened, and less mobile. Additionally, the plaques on the valve may adhere to those on the ventricular wall preventing normal coaptation. In a small study of 74 patients with carcinoid disease, the leaflets were "thickened, shortened, retracted and hypomobile" resulting in a fixed in a semi-open position. The anterior and septal leaflets were the most involved. Carcinoid syndrome involves the pulmonic valve in half of the patients with tricuspid valve involvement, causing pulmonic stenosis. This obstruction raises the right ventricular pressure and contributes to the amount of tricuspid regurgitation. The degree of tricuspid regurgitation in carcinoid disease is not trivial, with almost all patients having moderate to severe grades [4].

Infective endocarditis may result in direct damage to the valve leaflets. While the exact mechanisms behind tricuspid valve involvement in such patients have not been clarified, there is likely a combination of damage from particulate and a high bacterial load with IV drug injection, with a minor contribution from slight immunologic derangements. Vegetations more commonly affect the atrial side of the valve. Large and destructive vegetations (*Staphylococcus aureus*) may cause leaflet perforation, or the vegetation may be anatomically situated to impair normal coaptation [10].

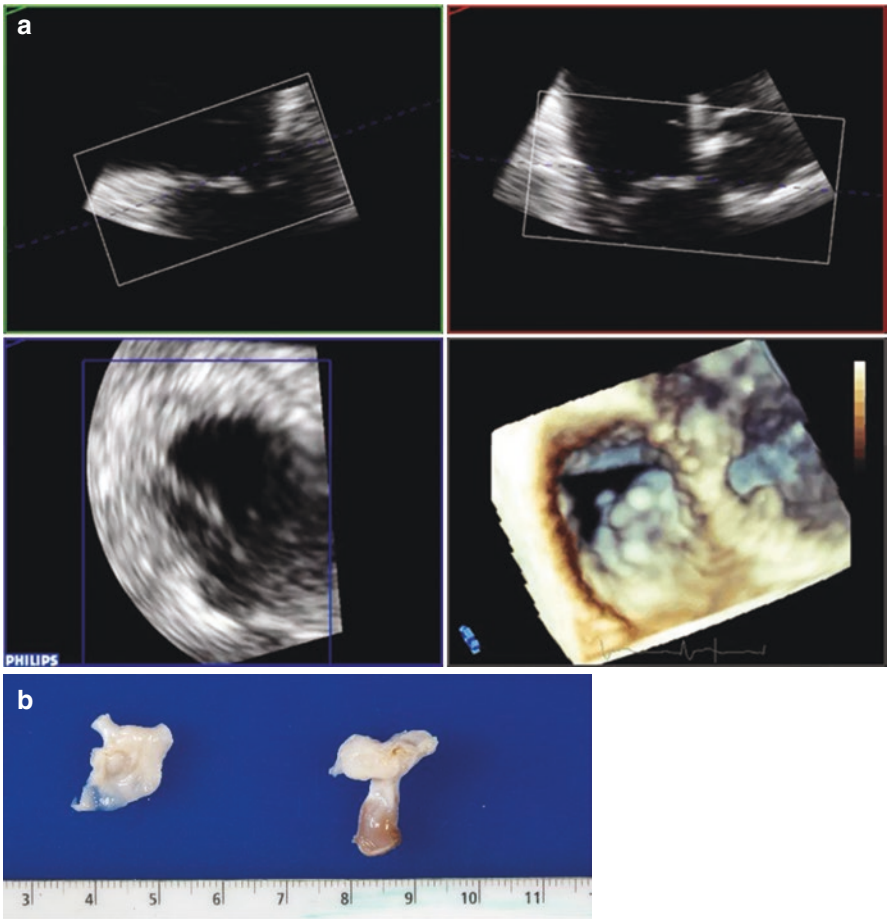

Fig. 2.3 Carcinoid tricuspid valve. Carcinoid plaques generally develop on the ventricular side of the valve causing leaflet thickening and restricted motion. (**a**) Pictured is a transesophageal echocardiogram of the tricuspid valve in a patient with carcinoid disease. Note the nodularity on the 3D-echo demonstrating the carcinoid plaques. (**b**) Pictured is a pathological specimen of carcinoid disease affecting the tricuspid valve. (Image courtesy of Haodong Xu, MD, Department of Pathology, University of Washington)

There is an increasing awareness of iatrogenic causes of tricuspid regurgitation. During implantation of pacemaker or implantable cardio-defibrillator leads, there may be perforation of a leaflet or rupture of the chordae tendinae [26]. Rupture of the chordae can result in a flail leaflet and severe, eccentric regurgitation. After implantation, the wire may abut one of the leaflets and impair the normal closure of the valve (Fig. 2.4). This usually occurs against the anterior or posterior leaflets. The wire may also become entangled within the chordal apparatus, leading to leaflet tethering. Similar to the risks with intracardiac lead insertion, there may be direct leaflet injury and/or chordal rupture during endomyocardial biopsy.

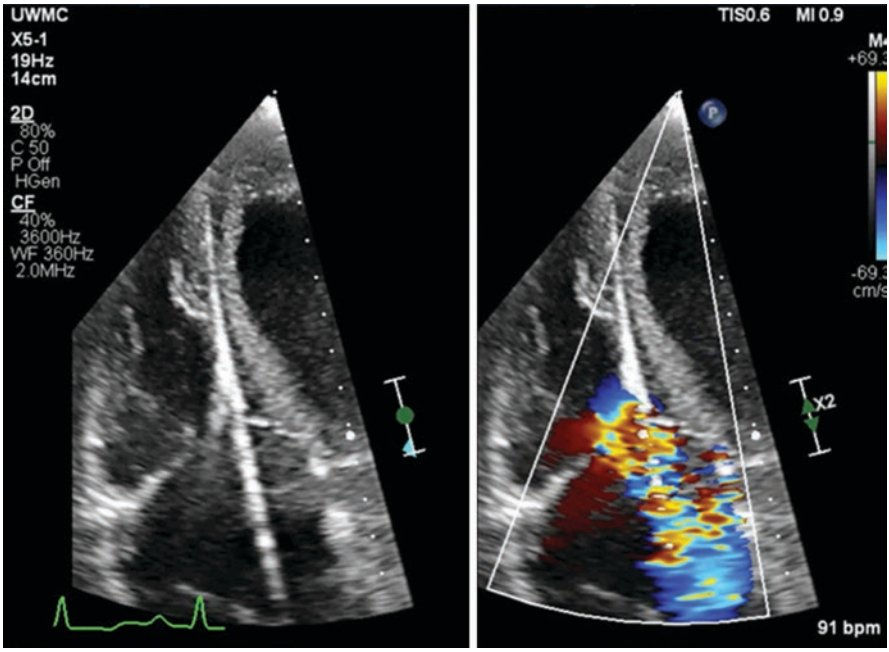

Fig. 2.4 Intracardiac lead associated tricuspid regurgitation. Up to 38% of patients with a right ventricular lead have tricuspid regurgitation. As demonstrated in this apical view of tricuspid valve, the most common mechanism is the impingement of the septal leaflet

Pathophysiology of Tricuspid Valve Stenosis

Tricuspid stenosis is defined as narrowing of the valve opening; this creates a gradient between the right atrium and ventricle during diastole, resulting in elevated right atrial pressures and right atrial dilation. Right atrial hypertension and dilation subsequently lead to signs of right heart failure, including hepatic congestion and peripheral edema. Lesions that cause tricuspid stenosis frequently cause concomitant tricuspid regurgitation. In rheumatic valve disease, the leaflets are thickened with a fusion of the commissures, and valve doming during diastole creates a narrowed valve orifice [7]. There are rarely any calcific deposits, unlike in rheumatic mitral valve stenosis [27].

Systemic lupus erythematosus may also cause tricuspid stenosis. Immune deposits and fibrous plaques may develop in addition to Libman–Sacks endocarditis. The fibrous reaction may lead to thickening and commissural fusion, while the Libman–Sacks endocarditis may cause valve obstruction [28].

Natural History of Tricuspid Regurgitation

Irrespective of the underlying cause of tricuspid regurgitation, the severity of regurgitation correlates with mortality. In a study of 5223 patients receiving care within the Veteran's Affairs healthcare system, increasing severity of tricuspid regurgitation was associated with increased mortality independent of age, left ventricular ejection fraction, and right ventricular systolic function [29]. Severe tricuspid regurgitation has been identified as an independent predictor of mortality in patients with left ventricular ejection fraction ≤35% [30]. In a study of 289 patients with isolated tricuspid regurgitation (normal leaflets, normal LVEF, and absence of pulmonary hypertension), the 5-year mortality was higher than that of age-matched controls [31].

Mild or moderate tricuspid regurgitation with mild or moderate degrees of right atrial enlargement is unlikely to be of hemodynamic consequence. Pulmonary hypertension and atrial fibrillation are risk factors for the progression of regurgitation [32]. In severe tricuspid regurgitation, there can be a long asymptomatic period with progressive dilation of the right atrium and ventricle [33]. Eventually, right atrial pressure and volume increase beyond the capacitance of the atrium, and the increased pressure is transmitted to the liver, manifesting as hepatomegaly, ascites, and, more distally, peripheral edema. This process can lead to renal insufficiency and over many years may progress to hepatic cirrhosis.

There are limited data about the rate of progression of tricuspid regurgitation. Specifically, data on progression from mild to moderate or moderate to severe are scarce. In a study of tricuspid regurgitation before and after mitral valve surgery, only 11/128 patients with 0 or 1+ tricuspid regurgitation developed 3+ or greater tricuspid regurgitation at follow-up (mean follow-up of 8 years). For patients who had 2+ tricuspid regurgitation on the preoperative study, 17/46 developed 3+ or greater tricuspid regurgitation at follow-up [34]. Thus, it seems that mild regurgitation is unlikely to progress to moderate regurgitation, and while moderate regurgitation may progress toward severe, the progression period is likely many years.

For acquired causes of tricuspid regurgitation, control of the underlying process is essential. Antibiotic treatment is obviously crucial for endocarditis and in prophylaxis against recurrent rheumatic disease damage. In patients with systemic lupus erythematosus, valve disease may regress with successful control of lupus [28]. Unfortunately, patients with carcinoid valve disease do not have regression of disease despite control of carcinoid [28]. For those patients with appetite suppressant–induced valve disease, cessation of exposure usually leads to regression of valve disease [35].

Tricuspid regurgitation by itself leads to right ventricular dilation, right ventricular dysfunction, tricuspid valve annular dilation, and leaflet tethering. While treatment guidelines state that tricuspid valve interventions should be performed well in advance to prevent the development of right ventricular dysfunction, the timing and rate of progression of right ventricular dysfunction from tricuspid regurgitation have not been well described [36].

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Chapter 3
Assessment and Management of Tricuspid Valve Regurgitation

Lindsey Trutter

Physical Exam in Tricuspid Regurgitation

Clinical evaluation of tricuspid regurgitation (TR) begins with cardiac auscultation. Classically, a pansystolic murmur at the left lower sternal border that increases with inspiration (Carvallo sign) is apparent with TR. The Carvallo sign, first described in 1946, is due to augmented venous return that accompanies inspiration and consequently intensifies regurgitant tricuspid flow. Maneuvers that increase venous return, such as hepatic compression, leg raise, and exercise, will also intensify the murmur. This has been demonstrated via phonocardiography tracings in the right atrium (RA) (Fig. 3.1) [1]. The presence of the Carvallo sign is a specific, not sensitive exam finding, as 20% of patients with moderate to severe TR were negative for this clinical finding in a sampled population [2]. In contrast, maneuvers that decrease venous return (Valsalva, standing) will reduce the intensity of the murmur.

With the progression of TR valvulopathy, the right ventricle (RV) can dilate. The murmur may then extend to the right lower sternal border, subxiphoid region, and toward the apex. In the setting of a dilated, failing RV, an S3 gallop can often be appreciated in the subxiphoid area.

Lancisi's sign, or jugular venous distension (JVD), with exaggerated "cv" wave, is visualized on neck exam. It is a consequence of the TR jet occurring during right ventricular systole with simultaneous venous return to the right atrium. The cv wave represents an exaggerated and broadened v wave usurping the normal c wave (closure of the tricuspid valve) and x descent (atrial relaxation) rendering the jugular venous pulsation monophasic (Fig. 3.2). Given this appearance and the fact that it is occasionally palpable, the cv wave may be mistaken for a carotid pulsation. However, the comparably latent upstroke, prominent y descent, and respirophasic changes that characterize jugular venous pressures can be recognized with a trained

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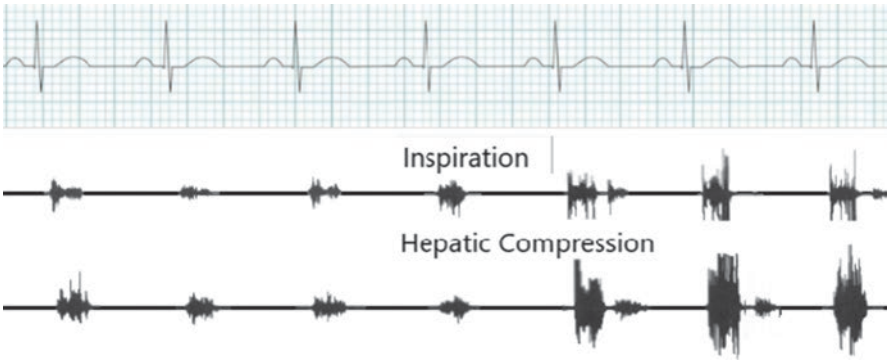

Fig. 3.1 Representation of phonocardiography tracing in the right atrium of a patient with TR demonstrating intensifying murmur with inspiration and applied hepatic pressure

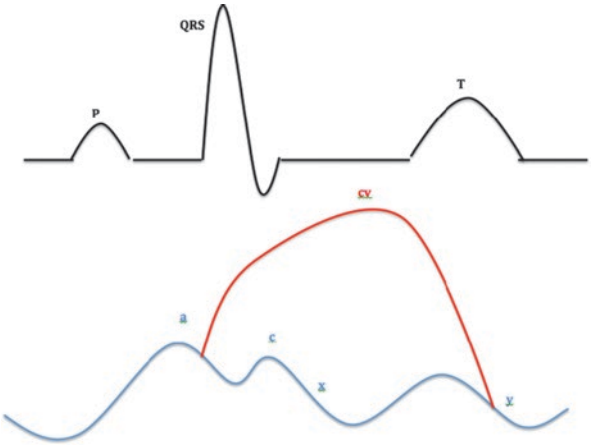

Fig. 3.2 Normal central venous pressure waveform (blue line) and change in waveform seen in severe tricuspid regurgitation (red line) with a fusion of c and v waves and absence of the x descent

Table 3.1 Commonly described physical exam findings in advanced tricuspid regurgitation

Maneuver	Description
Carvallo sign	Increase in TR murmur with deep inspiratory hold [3]
Lancisi's sign	JVD with exaggerated cv wave during systole [4]
Kussmaul's sign	Increase in jugular venous pulse with inspiration [5]
Augmented Carvallo	Increase in TR murmur with manual liver compression [6]

eye. Kussmaul's sign is another abnormality of the jugular venous waveform due to TR. It is the increase in the jugular venous pulse with maneuvers increasing venous flow (inspiration, hepatic compression, exercise, and leg raise) (Table 3.1).

Assessment of volume status is integral to characterizing the consequences of TR and guides clinical management. Patients may present with hepatomegaly, ascites, and peripheral edema that reflect both the severity and chronicity of TR

Table 3.2 Numerical rating of lower extremity edema and associated exam findings

Grades of pitting edema	
0+	No pitting edema
1+	Mild; small depression that disappears immediately
2+	Moderate; depression disappears <10 seconds
3+	Moderate-severe; depression disappears 10–20 seconds
4+	Severe; depression that lasts >20 seconds

(Table 3.2). Liver congestion may progress to the point the liver is tender and pulsatile upon palpation. In rare cases, this pulsatility can be visualized in lower extremity varicose veins [7].

Despite a number of characteristic physical findings, these are generally insensitive for TR. Indeed, clinical findings are often subtle or absent in mild or moderate TR, and these cases are most often diagnosed incidentally via echocardiography [8]. Early investigation to delineate the prevalence of diagnostic features relied on invasive measurements such as intracardiac phonography and right ventriculography due to the lack of noninvasive imaging. In these studies, the triad of the Carvallo sign, prominent v waves, and pulsatile liver was specific but not sensitive. All patients with this triad were found to have severe TR; however, only 30% of patients with severe TR displayed all three physical exam findings. Sensitivity improved when the Carvallo sign was used alone or in conjunction with prominent v waves or pulsatile liver [1]. Addition of manual hepatic pressure increases the murmur of TR, identifying the Carvallo sign in an additional 17.6% of patients who lacked inspiratory murmur augmentation at baseline [6].

Medical Management of Tricuspid Regurgitation

Conventional medical therapy for patients with TR is reflected in a recent review of patients with severe TR at a tertiary care center. A total of 87 patients were identified over the preceding 2 years, with the majority receiving medical therapy ($n = 65$) rather than valve repair or replacement ($n = 22$). Of the entire cohort, nearly all were on diuretics (98%), while a minority were treated with aldosterone antagonists (35%). It is important to note that frequently implicated causes of secondary TR, namely atrial fibrillation and mitral regurgitation, were prevalent in this cohort [9].

Diuretics Diuretics decrease renal sodium reabsorption and encourage the movement of fluid into the urine, thereby reducing total body water. They are broadly classified into one of three categories depending on their site of action within the nephron (loop, thiazide, or potassium-sparing diuretics). While there is little randomized data on diuretics in heart failure, they relieve congestion and improve symptoms and exercise capacity [10].

There are no trials that address the effect of diuretic therapy on TR severity or subsequent outcomes. However, in patients with TR and evidence of congestion (hepatomegaly, ascites, lower extremity edema), diuretics are reasonable in an effort to achieve symptomatic relief. For maintenance therapy, an agent with greater oral bioavailability (torsemide, bumetanide) may be preferable to furosemide, although the efficacy of this strategy is not established. Other measures, such as salt and fluid restriction, daily weights, and tailored diuretic dosing, are also reasonable in these cases.

Potassium-sparing diuretics such as aldosterone antagonists are occasionally employed in patients with significant TR. These are often used in tandem with loop diuretics when hypokalemia is encountered. The hyperaldosteronism that accompanies liver cirrhosis or chronic right ventricular volume and pressure overload make this class of diuretic reasonable to prescribe when TR is accompanied by these conditions [9, 11]. Although being logical based on pathophysiology, inhibition of the renin–angiotensin–aldosterone system has not been established to preserve right ventricular or tricuspid valve function.

Pulmonary Hypertension Moderate or greater TR is observed in 20–50% of patients with pulmonary hypertension (PH), and portends a worse overall prognosis [11–14]. When TR is encountered in the setting of pulmonary hypertension, therapies that address the underlying cause of PH (Groups 2–5) or pulmonary pressures directly (Group 1 or recalcitrant PH) have variable reported effects on TR severity [13]. It is important to keep in mind when reviewing these studies, however, that a reduction in pulmonary pressures, not grade of TR, was the primary goal. Accordingly, the analyses regarding the effects of these agents on TR are often underpowered, or not reported.

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Chapter 4
Hemodynamic Assessment of Tricuspid Valve Disease

Thomas J. Atchison and Sitaramesh Emani

Introduction

Traditionally, the tricuspid valve (TV), and diseases thereof, have not garnered as much attention as other valves, relegating it as the "forgotten valve "of the heart [1, 2]. Much of the tricuspid valve's second-tier status can be attributed to the frequency with which TV disease results from other diseases, especially left-sided valvular disease [3]. As such, TV disorders have been largely addressed in the context of these other diseases, and therapies for TV disease have typically focused on treating those concurrent conditions with the assumption that the TV would itself improve accordingly [1, 3]. However, significant tricuspid valve disease itself can lead to worsening outcomes, including right heart failure [4]. In response, a number of exciting new techniques and technologies have emerged to help combat tricuspid valve disease. Successfully treating tricuspid valve disease is dependent on understanding TV anatomy, mechanics of blood flow through the valve, and appropriate ways to assess physiology.

Anatomy and Physiology of the Tricuspid Valve

Located between the right atrium and right ventricle, the tricuspid valve is the largest of the four valves in the heart and is the most apical. It can be divided into four parts: the annulus, the leaflets, the papillary muscles, and the chordal attachments. The tricuspid valve has three leaflets typically classified as septal, anterior, and posterior. The leaflets are unequal in size, with anterior leaflet typically having the largest area, and therefore the greatest range of motion. The annulus is a D-shaped,

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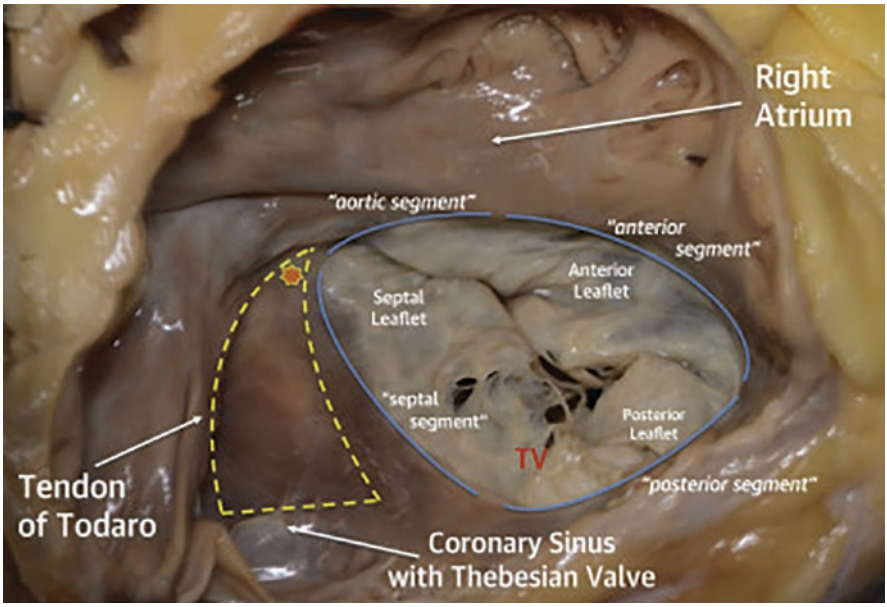

Fig. 4.1 Anatomical layout of the tricuspid valve showing the D-shape annulus and related structures. (With permission) (Asmarats et al. [30])

nonplanar structure made up of two separate parts: a large C-shape section that corresponds to the right atrium and the right ventricle, and a smaller, straighter section that corresponds to the septal leaflet and ventricular septum (Fig. 4.1). Of note, the annulus is a dynamic structure that can increase its area up to 30% during the cardiac cycle under normal loading conditions [5].

The atrioventricular node and the bundle of His cross the septal leaflet attachments 3–5 mm posterior to the antero-septal commissure [5]. Additionally, the noncoronary sinus of Valsalva is adjacent to the area between the septal and anterior leaflets. The septal leaflet of the tricuspid valve is also one of the landmarks used to identify the triangle of Koch (along with the tendon of Todaro and the coronary sinus) (see Fig. 4.1). From the exterior of the heart, the right coronary artery can be used to estimate the location of the tricuspid valve as it courses through the atrioventricular groove.

The majority of right ventricular filling, and therefore flow across the tricuspid valve, occurs during the passive phase of diastole and is driven by the pressure gradient between the right atrium in the right ventricle. Given the large size and relatively low pressures of the right atrium and right ventricle, diastolic velocities across the tricuspid valve are typically low, with a peak transannular velocity of less than 1 m/s and a mean velocity gradient of less than 2 m/s [3]. Active atrial contraction, and the resultant increase in right atrial pressure, results in additional blood flow into the right ventricle. Normal pressure waveforms of the right atrium and right ventricle including the "c-wave," which represents the bulging of the tricuspid valve

back into the right atrium following valve closure [6]. Disturbances to valve anatomy and function will significantly alter the normal pressure relationship between the right atrium and right ventricle, resulting in abnormal pressures, gradients, and flow across the TV.

Diseases of the Tricuspid Valve

Tricuspid Stenosis

Tricuspid stenosis (TS) results from a narrowing of the valvular opening and is a rare disease, most commonly resulting from rheumatoid fever. TS is almost always found in conjunction with mitral stenosis [7, 8]. Using first-pass principles, narrowing of the tricuspid valve causes an increased impedance to blood flow from the right atrium to the right ventricle, particularly during active atrial contraction. The result is an enlarged a-wave seen on right atrial tracings [4, 9]. More specifically, the change in right atrial pressure is governed by Poiseuille's law [$Q = \frac{\pi P r^4}{8 \mu l}$, where Q = flow rate, P = pressure, r = radius, μ = fluid viscosity, and l = length of tubing]. Rearranging the equation shows that pressure is inversely proportional to the size of the opening [$P \propto \frac{1}{r^4}$] and reveals why pressures increase markedly with reduction in the valve area. Clinical assessment of TS can be done either invasively with cardiac catheterization or noninvasively with Doppler echocardiography.

Cardiac Catheterization

Tricuspid stenosis can be evaluated invasively through a right heart catheterization. Simultaneous recordings of the right atrial and right ventricular pressures using a dual lumen catheter will yield pressure differences between the two chambers [10]. Due to the smaller orifice of a stenotic TV, passive blood flow during early diastole will be reduced, resulting in a larger blood volume in the right atrium during atrial systole, ultimately resulting in higher atrial systolic pressures. Concurrently, the stenotic obstruction will result in the right ventricular diastolic pressure being lower than normal conditions. These changes result in a significantly increased A-wave and a more gradual Y-descent in right atrial pressure tracings [11]. Right ventricular waveforms are normal except for reduced end-diastolic pressures due to incomplete filling of the right ventricle [12] (Fig. 4.2).

As previously noted, an elevated pressure gradient will occur across the stenotic tricuspid valve proportional to the inverse of the valve area. Severity of tricuspid stenosis, therefore, can be evaluated based on the resultant gradient. Because the gradient across the TV is dynamic throughout the cardiac cycle, the mean gradient during ventricular diastole is used to evaluate the TV [13]. Severe tricuspid stenosis

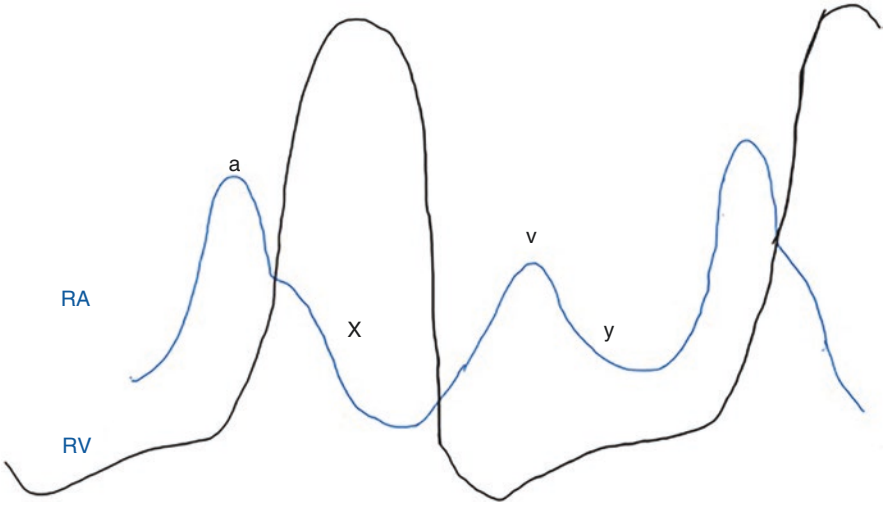

Fig. 4.2 Simultaneous right atrial and right ventricular waveforms in tricuspid stenosis. The "a-wave" is increased, the "y-descent" is more gradual, and the right ventricular end-diastolic pressure is reduced

correlates with a mean gradient of ≥5 mmHg; however, calculation of the gradient is affected by heart rate, with higher gradients occurring with faster heart rates and/or the simultaneous presence of tricuspid regurgitation [4, 13].

Historically, severe tricuspid stenosis is defined as a TV area of ≤1.0 cm^2 [4]. Although Poiseuille's law describes the general relationship between valve area and pressure gradients, the more accepted formula to calculate TV is the equation originally described by Gorlin and Gorlin,

$$\text{TV Area} = \frac{\text{Cardiac Output}}{(\text{Diastolic Filling Period})(44.5)(\sqrt{\text{mean RAP} - \text{mean RV diastolic pressure}})}$$ [14].

Utilization of this equation requires measurement of cardiac output and definition of the diastolic filling period across the TV. Current practice typically employs the use of catheterization lab software to calculate the valve area using this formula.

Doppler Echocardiography

Doppler echocardiography provides a noninvasive method for assessing tricuspid valve disease. Although echocardiographic analysis does not provide direct measurements of pressures, blood flow velocities can be assessed using Doppler signals. Translating velocities into pressure estimates can then be achieved using the law of conservation of energy, and namely the Bernoulli equation. The Bernoulli equation defines the relationship between potential energy and kinetic energy within a closed system, stating that the total energy remains constant [15]. In its full version, the Bernoulli equation is expressed as $P_{0_1} + \rho g h_1 + \frac{1}{2}\rho v_1^2 = P_{0_2} + \rho g h_2 + \frac{1}{2}\rho v_2^2$. In this

equation, potential energy is expressed in the term ρgh, where ρ is the density of the fluid, g is gravitational acceleration, and h is the height of the fluid column. Within the heart, it is assumed that differences in height are negligible, and therefore this potential energy term mathematically cancels out. This assumption leads to the simplified Bernoulli equation, $\Delta P = \frac{1}{2}\rho\left(v_2^2 - v_1^2\right)$, where v is velocity and ΔP represents the pressure gradient of interest. Of note, due to the relatively small values of v_1 compared to v_2, the term v_1^2 is assumed to approach zero and is ignored [15]. Using the density of blood ($1060\frac{\text{kg}}{\text{m}^3}$) and velocity ($\frac{\text{m}}{\text{s}}$) results in pressures measured by Paschal units. Converting to Paschal units into standard mmHg units reveals the commonly used Doppler derived pressure gradient formula $\Delta P = 4v^2$, with v being the maximal velocity measured across the valve [16, 17]. Mean gradient values of ≥5 mmHg generally signify severe stenosis [7].

In significant tricuspid stenosis, resting cardiac output is reduced and does not increase with exercise due to the fixed obstruction to flow [4, 9]. Physiologically, the decrease in cardiac output translates to a longer period of time for pressures to equalize across the tricuspid valve, with longer times being resulting from more severe stenosis. This concept can be quantified using the pressure half time (PHT), which is the time needed for maximal velocity to reduce by 50%. PHT values of ≥190 ms correspond to severe TS [18].

The use of noninvasive techniques to evaluate tricuspid stenosis is often sufficient to establish severity, and the use of invasive measures is generally recommended only when noninvasive measurements are inconclusive or inadequate [4].

Treatment of Tricuspid Stenosis

Therapeutic interventions upon a stenotic tricuspid valve are generally reserved for cases of severe TS. Because most cases of TS occur in the setting of left-sided valve disease, current guideline recommendations suggest surgical intervention on a severely stenotic TV at the time of left-sided valve surgery. Isolated tricuspid stenosis warrants surgical intervention when patients are considered significantly symptomatic, but outcomes are dependent on postoperative right ventricular function [4, 19]. For patients with severe, symptomatic TS without associated tricuspid regurgitation, percutaneous balloon commissurotomy can be considered [4].

Tricuspid Regurgitation

Tricuspid regurgitation (TR) is characterized by the backflow of blood from the right ventricle into the right atrium during ventricular systole. Tricuspid regurgitation is generally categorized as either primary or secondary. Primary TR results from a structural malfunction of the tricuspid valve, such as perforation (seen with

rheumatoid heart disease or infectious endocarditis), Ebstein's abnormality, the presence of wires for cardiac rhythm devices, and several other causes [1, 3, 4]. Secondary TR results from loss of TV functionality related to changes in the TV annular geometry, but not the valve leaflets themselves. Although quantification methods do exist to characterize TR severity, the clinical presence of right heart failure symptoms alone signals poor outcomes regardless of TR quantification. In cases of severe TR, outcomes also tend to be poor and are independent of other cardiac performance measures [20].

Cardiac Catheterization

Catheter evaluation of tricuspid regurgitation is often confounded by the presence of atrial fibrillation. The presence of atrial fibrillation will significantly alter right atrial pressure tracings and greatly reduce the interpretability of waveform analysis, particularly when trying to evaluate A-wave and x-descent contours [21]. Because the major flow abnormality in tricuspid regurgitation occurs during ventricular systole, contraction of the right ventricle against an incompetent valve will result in increased flow back into the right atrium. This pattern manifests as tall V-waves on right atrial pressure tracings and results in increased volume within the right atrium at the end of atrial filling. The excess volume then rapidly flows back into the ventricle during early diastolic filling and can be seen in the form of a rapid y-descent. The combination of large V-waves ("ventricularization" pattern) and an elevated mean right atrial pressure does correlate, however, with significant TR [21]. Overall, the utility of isolated invasive hemodynamics to diagnose severe TR is limited and generally not used as a primary tool.

Doppler Echocardiography

Doppler echocardiography is the primary tool used to evaluate tricuspid regurgitation. An extensive and detailed review of the many parameters used to quantify TR is beyond the scope of this text but can be found elsewhere [22]. Core principles are reviewed here, however, with a focus on severe TR given the general recommendations for intervention at that level of valve dysfunction [4, 22].

In severe TR, the additional volume within the right atrium should result in increased flow across the TV during ventricular filling. Because diastolic filling time should not be affected by TR, the velocity of flow across the TV should increase with larger volumes (i.e., worsening TR). Criteria define tricuspid valve inflow velocities of $\geq$1 m/s as correlating with severe TR [23].

Quantification of regurgitant blood volume across the tricuspid valve can be used to identify severe TR. Operating from the conservation of mass principle, the volume entering the right ventricle during diastolic filling will equal the forward flow volume plus the regurgitant volume during systole [TV inflow volume = Right ventricular forward flow volume + TV regurgitant volume] [23]. Using the principle of

time-velocity integral (TVI), both the TV inflow volume and the right ventricular outflow tract volume (right ventricular forward flow volume) can be estimated (detailed methodology of TVI calculation described elsewhere) [24, 25]. Therefore, TV regurgitant volume = TV inflow volume − Right ventircular outflow volume. Regurgitant volumes of ≥45 mL are indicative of severe TR; however, technical challenges with signal acquisition can affect the accuracy of this calculation [23].

Adopting the concept of proximal isovelocity surface area (PISA) measurements from mitral valve evaluations provides another method of TR quantification [26]. Although more thorough descriptions of PISA measurements are available [23], a brief description is provided here. Again, derived from the basis of conservation of mass, the volume of blood per time unit (known as flux) flowing through two points should be equal. Fluid volume is represented by area × velocty; as such, the continuity equation can be represented as $A_1v_1 = A_2v_2$. By allowing A_1 to be the regurgitant area of the TV, v_1 becomes the velocity through the valve, which is acquired by Doppler velocity measurement at the regurgitant orifice. The second area of flux is then identified as the hemisphere through which regurgitant flow passes at an identified velocity. This second velocity is identified using the Nyquist limit, which represents the maximal frequency shift detectable by Doppler based on acquisition settings [15, 26]. Visually, adjusting the Nyquist limit allows a hemisphere to be defined on color Doppler images, the radius of which can be measured and used to calculate surface area [23, 26]. Mathematical rearrangement then allows the regurgitant area to be calculated ($A_1 = \frac{A_2 v_2}{v_1}$). A regurgitant area of ≥0.4 cm^2 is used to define severe TR, although PISA quantification may underestimate severity of TR [23, 27].

Treatment of Tricuspid Regurgitation

Guideline recommendations suggest that severe tricuspid regurgitation be addressed in the presence of symptoms or in the event of right ventricular dysfunction [4]. Similar to tricuspid stenosis, the presence of severe TR typically occurs in the context of left-sided valve disease [3]; therefore, the surgical therapies upon a regurgitant tricuspid valve (repair or replacement) are often tied to operative plans for the left-sided valve lesion, if at all [4]. Traditionally, treatment of the left-sided valve lesion was thought to be sufficient to allow improvement in TR [1]. For isolated, severe secondary TR, surgical valve repair or replacement is not commonly performed and may be due to the operative risk associated with open valve procedures in the presence of right ventricular dysfunction [1, 19]. For this latter scenario, newer percutaneous approaches may mitigate operative risks and provide therapeutic strategies in generally untreated cohort by using novel technologies and approaches [28, 29]. These newer methods are currently investigational and are undergoing clinical testing to prove safety and efficacy.

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Chapter 5
Echocardiographic Assessment of Tricuspid Valve Disease

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Tricuspid Valve Anatomy for Echo Imaging

Knowledge of the basic tricuspid valve anatomy is essential to proper imaging of the valve to determine sites of pathology and to guide interventions. Tricuspid valve apparatus anatomy is covered in detail in Chap. 1; however, it is worthwhile to highlight several points that play a key role in imaging.

Tricuspid Leaflet Variation

The tricuspid leaflets can vary significantly in size. The septal and anterior leaflets are usually the largest in circumference compared to the posterior leaflet and are often the easiest to visualize [1]. Some individuals may have more than three leaflets, and others may functionally have two leaflets (fused or diminutive posterior leaflet). The posterior leaflet is positioned along the RV inferior wall [2].

The tricuspid leaflets are thinner than the mitral leaflets, which makes imaging more challenging [2, 3], especially when it comes to 3D imaging. Therefore,

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Fig. 5.1 Transthoracic echocardiographic imaging of the tricuspid valve. (**a**) Right ventricular parasternal inflow. The transducer is angled inferiorly and to the right from a standard parasternal long-axis view. If the coronary sinus ostium or the muscular interventricular ventricular septum are visualized, then the leaflets imaged are the anterior (red) and septal (yellow). (**b**) Right ventricular parasternal inflow. Angling the transducer more sharply inferiorly and to the right, the posterior (blue) leaflet can be visualized instead of the septal. (**c**) Parasternal short-axis. The anterior leaflet (red) is imaged closest to the aortic valve. The posterior leaflet (blue) is most commonly the additional leaflet visualized. (**d**) Parasternal short-axis. When a single leaflet is visualized, it represents an anterior leaflet (red). (**e**, **f**) Apical four-chamber. The septal leaflet (yellow) is easily identified as the leaflet closest to the interventricular septum. However, the opposing leaflet can be either the anterior or posterior leaflet depending on angulation. Angling to include the aorta or LVOT will select for the anterior leaflet (red), whereas angling to include the coronary sinus (*) will select the posterior leaflet (blue)

knowledge of anatomy in different 2D views in both transthoracic (TTE) and transesophageal (TEE) imaging is paramount.

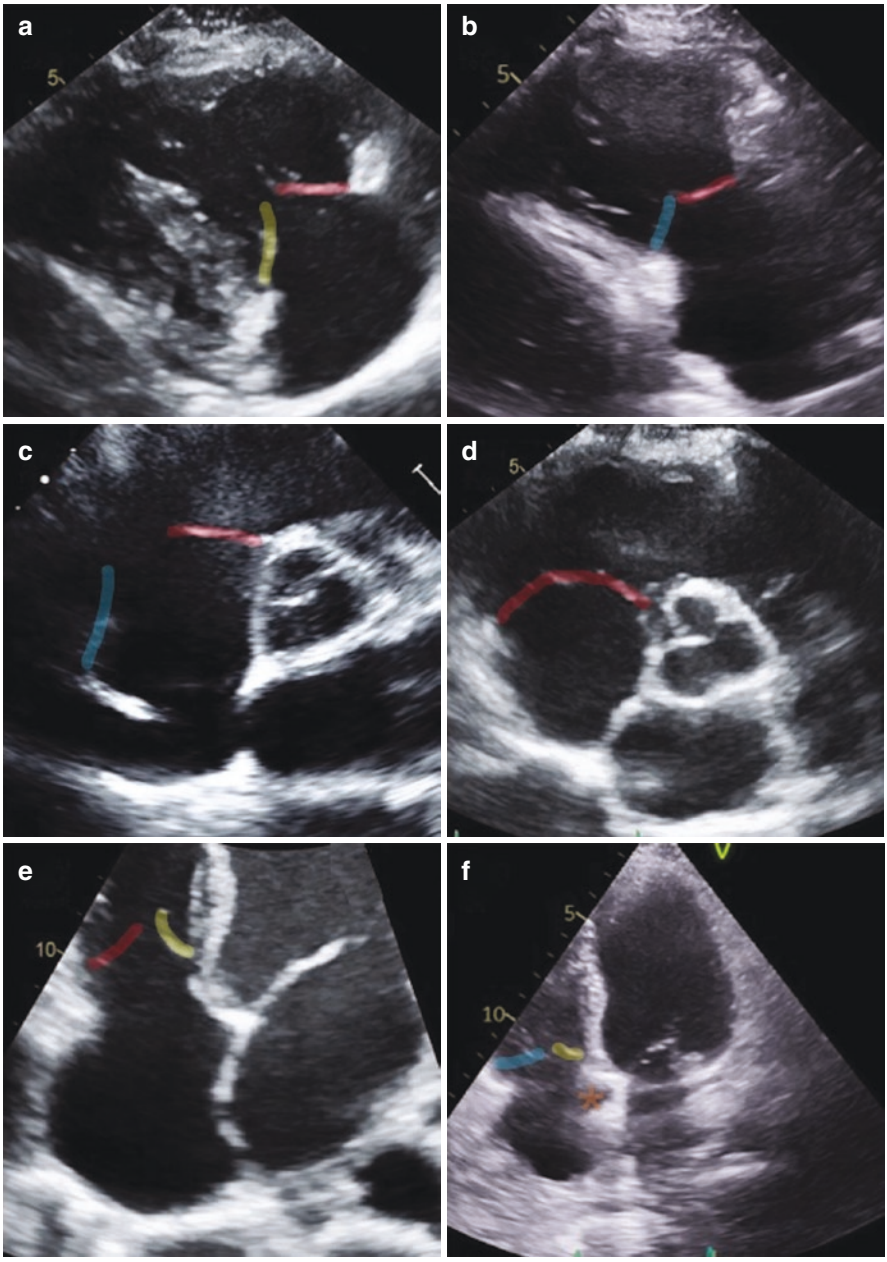
Standard 2D TTE Views

It is important to use multiple 2D views to identify all three leaflets and their pathology (Figs. 5.1 and 5.2) as 3D en face images may not be ideal in everyone or the view may be obscured by device leads. Only one 2D view allows one to visualize all three leaflets: the transgastric short-axis view (see Fig. 5.2f). All other 2D views allow visualization of one (typically the anterior leaflet in short-axis views) or two leaflets (either anterior-posterior, septal-anterior, or septal-posterior leaflets).

The leaflets seen in 2D views for TTE and TEE can often vary significantly in shape and position due to RV size and shape, changes in orientation of the heart within the chest, and tricuspid valve anatomical variation. However, neighboring structures can help identify each leaflet. In planes that visualize the ventricular septum, the septal leaflet should be in view; in planes that visualize the aorta, the anterior leaflet should be in view; and in planes where the coronary sinus is seen, the posterior leaflet should be seen.

Four standard TTE views are commonly utilized; these include right ventricular inflow (RVIF), parasternal short-axis (PSAX), apical four-chamber (A4C), and RV-focused (RVF) views [4]. Slight angulation changes between these views can lead to different combinations of leaflet visualization [5].

In the RVIF view, either the anterior-posterior leaflets or anterior-septal leaflets are seen. Visualization of the septum best defines the septal leaflet. If the septum is in view (incomplete rotation to remove LV and septum), then it is the septal and anterior leaflets that are seen (see Fig. 5.1a). If the LV is completely out of view, it is the posterior and anterior leaflets that are seen (see Fig. 5.1b).



In the PSAX view, most commonly the anterior and posterior leaflets are seen, particularly when there is central coaptation (see Fig. 5.1c) [4]. If a single leaflet is seen with the aortic valve, that is the anterior leaflet, as the aorta is an anterior structure (see Fig. 5.1d) [4].

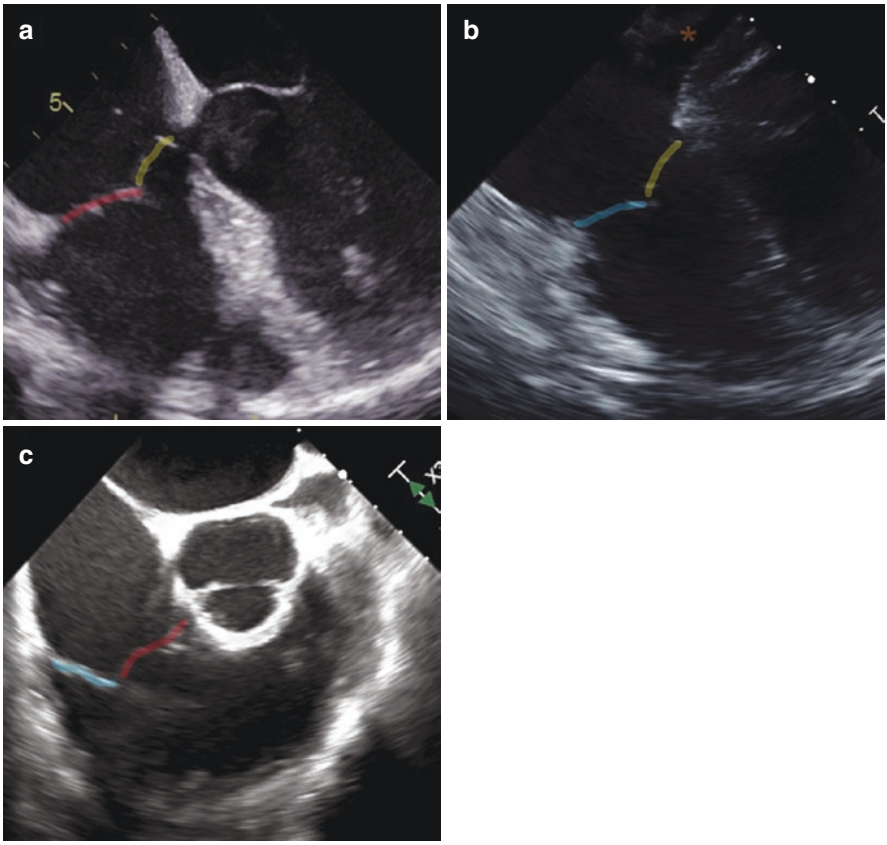
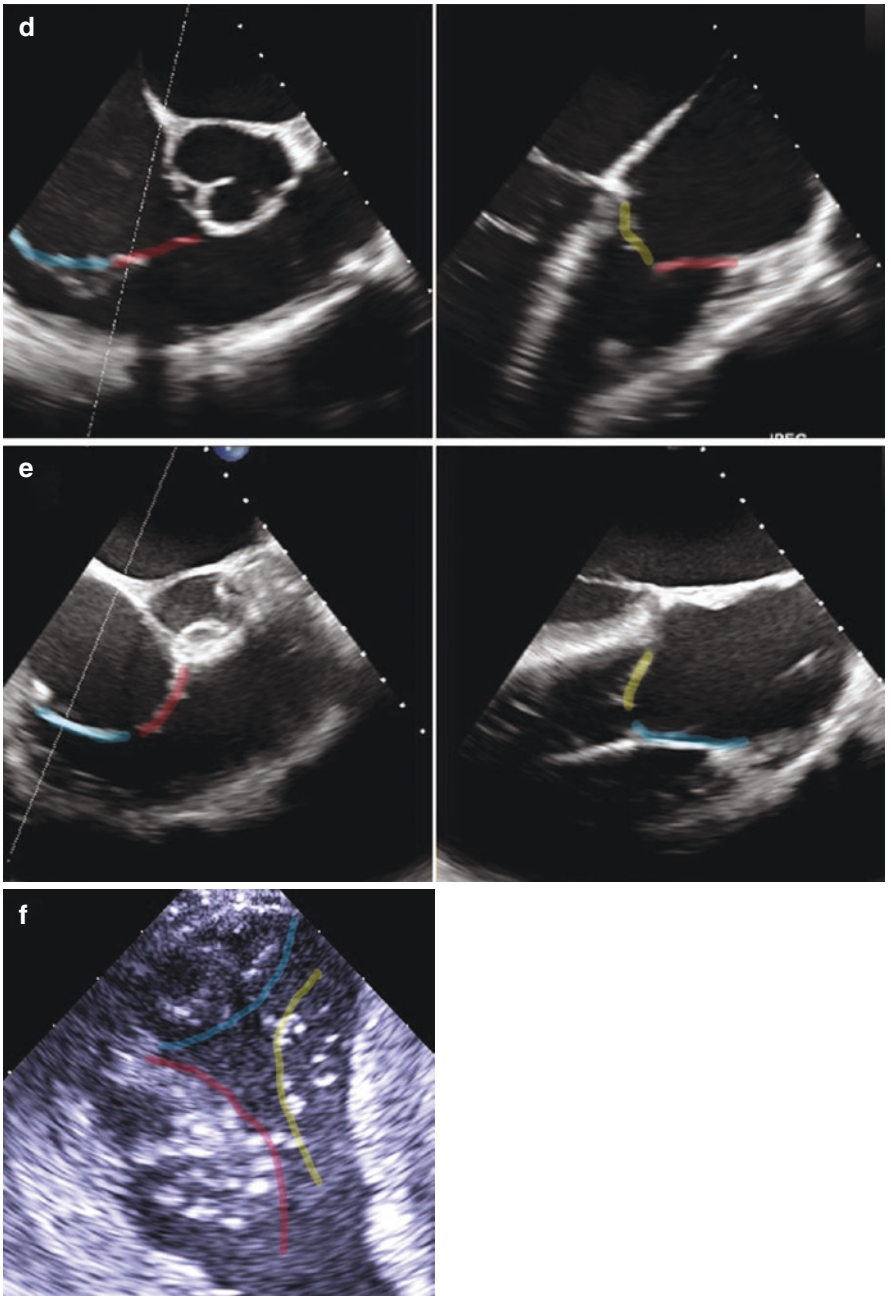


Fig. 5.2 Transesophageal echocardiographic imaging of the tricuspid valve. (**a**, **b**) Four-chamber. At 0°, either the septal-anterior leaflets or the septal-posterior leaflets are visualized. Inclusion of the LVOT or aortic valve helps identify the anterior leaflet (**a**). Inclusion of the coronary sinus (*) helps identify the posterior leaflet (**b**). (**c**) 30–70° short axis. Often it is the anterior (red) and posterior (blue) leaflets that are visualized. The septal leaflet is typically not seen in the view; however, use of multiple plane imaging can help identify this leaflet. (**d**, **e**) 30–70° short-axis orthogonal views. Orthogonal imaging through the anterior leaflet (**d**) shows the apposition of the septal (yellow) and anterior (red) leaflets. Orthogonal imaging through the posterior leaflet (**e**) identifies the apposition of the septal (yellow) and posterior (blue) leaflets. (**f**) Transgastric short axis. This 2D TEE view identifies all three leaflets en face simultaneously: anterior (red), septal (yellow), and posterior (blue). (**g**, **h**) Transgastric orthogonal views. Orthogonal imaging through the anterior leaflet (**g**) shows the apposition of the anterior (red) and posterior (blue) leaflets. Orthogonal imaging through the septal leaflet (**h**) identifies the apposition of the septal (yellow) and posterior (blue) leaflets. (**i**) Deep transgastric. In the deep transgastric view, often the septal (yellow) and anterior (red) leaflets are seen, given that this view is obtained with anteflexion when the aortic valve is in view. (**j**, **k**) Deep transgastric orthogonal views. Orthogonal imaging through the septal leaflet (**j**) shows the apposition of the septal (yellow) and posterior (blue) leaflets. Orthogonal imaging through the anterior leaflet (**k**) identifies the apposition of the anterior (red) and posterior (blue) leaflets



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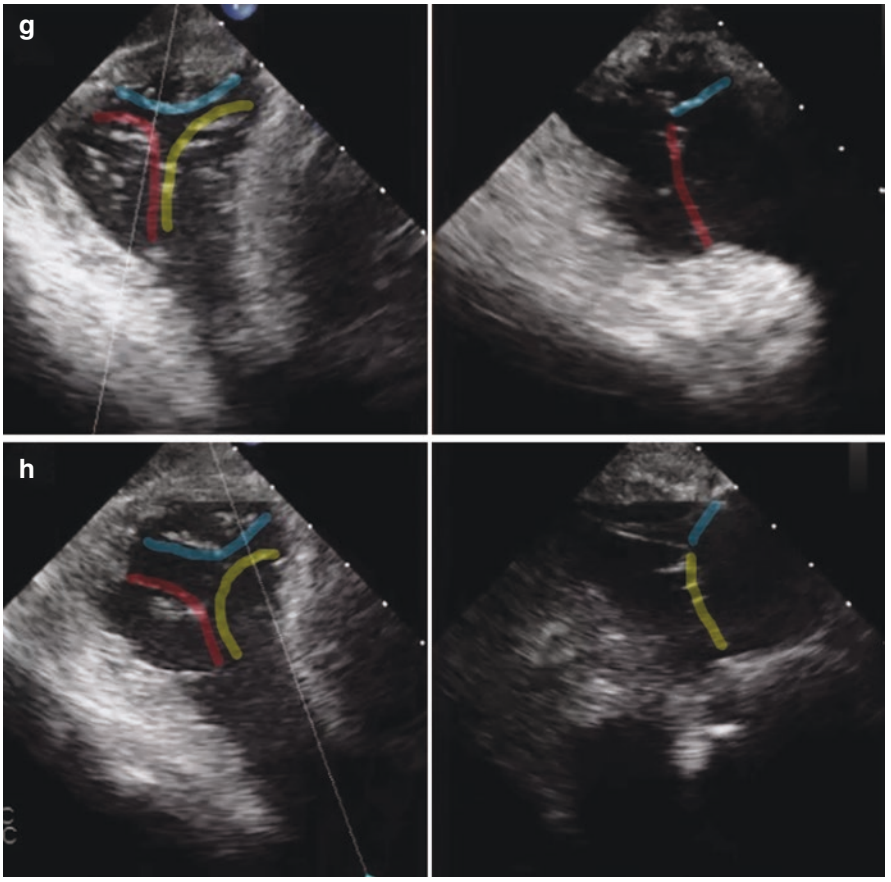

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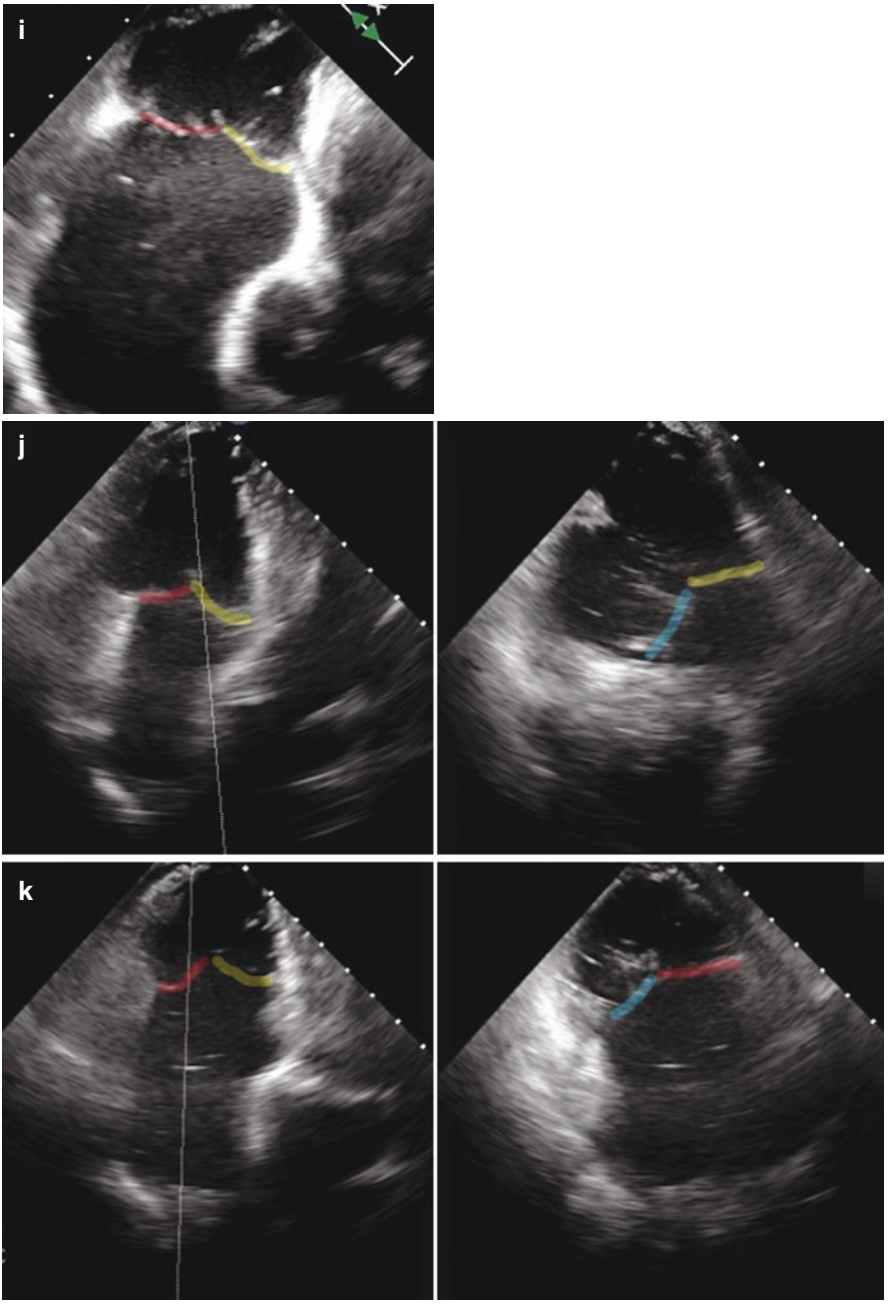


Fig. 5.2 (continued)

In the A4C window, the septal leaflet should be clearly seen—whether the other leaflet is the posterior or anterior leaflet depends on whether the probe is more anterior (visualizing part of the LV outflow tract, Fig. 5.1e) or posterior (visualizing the coronary sinus, Fig. 5.1f) [4]. The presence of the coronary sinus best defines the posterior-septal leaflets since the coronary sinus empties into the RA at the commissure of these leaflets [4]. Sweeping through the valve in real time is often helpful to discern the leaflets.

Standard 2D TEE Views

Similar principles regarding which neighboring structures are visible help identify the individual leaflets seen in the standard 2D TEE views. In the four-chamber view at 0°, either the septal-anterior leaflets or the septal-posterior leaflets are visualized. Use of anteflexion and withdrawal of the probe such that the LVOT and aortic valve starts to be seen (5-chamber view) help identify the anterior leaflet (Fig. 5.2a). Insertion and retroflexion of the probe help identify the posterior leaflet, especially when the coronary sinus comes into view (Fig. 5.2b).

In the short-axis view (30–70°) just as in the parasternal short-axis view for TTE, often it is the anterior and posterior leaflets that are visualized (Fig. 5.2c). The septal leaflet is typically not seen in the view; however, use of multiple plane imaging can help identify this leaflet as well as associated pathology (lack of coaptation, tethering). Orthogonal imaging through the anterior leaflet (closest to the aorta) shows the apposition of the septal and anterior leaflets, and orthogonal imaging through the posterior leaflet identifies the apposition of the septal and posterior leaflets (Fig. 5.2d, e). These views can then be individually assessed in corresponding planes (110–150°) if needed.

The transgastric views are often the most helpful to identify leaflets in patients with devices or leads since shadowing from these structures is less of an issue. The short axis here is the only 2D TEE view that clearly identifies all three leaflets en face simultaneously (Fig. 5.2f). From here, additional orthogonal plane imaging can be used to visualize either anterior-posterior (Fig. 5.2g) or septal-posterior leaflets (Fig. 5.2h). In the deep transgastric view, which is similar to a TTE four-chamber view, often the septal-anterior leaflets are seen, given that this view is obtained with anteflexion and often the aortic valve is in view (Fig. 5.2i). Orthogonal planes show the septal and posterior leaflets and the anterior and septal leaflets (Fig. 5.2j, k).

3D Views

It is important to decide on a convention when imaging the tricuspid valve en face in 3D. This is critical when working with a team to plan interventional procedures. Some advocate for displaying the interatrial septum, and thus septal leaflet, inferiorly in the far field at 6 o'clock [5]; however, others display this leaflet at 9 o'clock

similar to a surgeon's view, in keeping with the convention for mitral valve views. The general rule of thumb is to start with the best 2D image (whether at 0°, short axis, or possibly even deep transgastric) in the mid-esophageal views and then to acquire the 3D images. Including a neighboring structure, such as the aortic valve as a landmark, helps one to better rotate and orient the image into an ideal view. Figure 5.3 shows several examples of 3D en face views that help identify some of

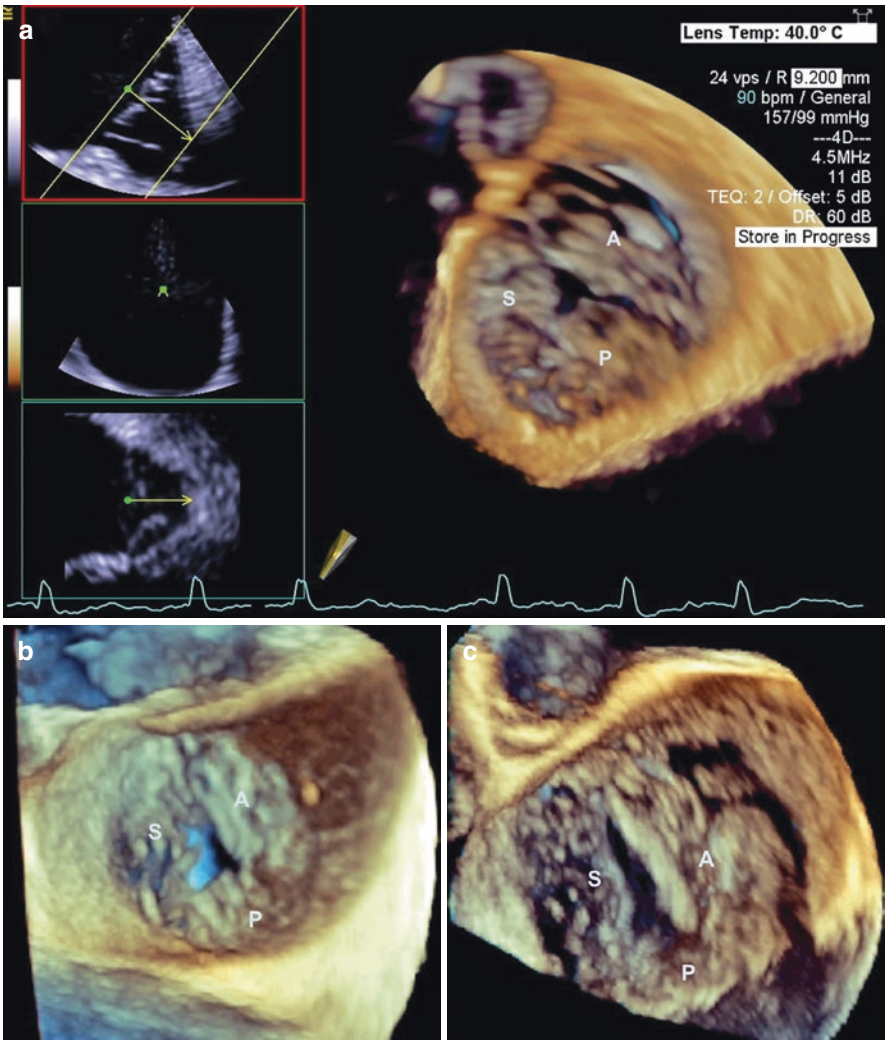


Fig. 5.3 3D en face views of the tricuspid valve. (**a**) An example where all three tricuspid leaflets are of similar size and their commissures are easy to identify. (**b**) Partially fused anterior and posterior leaflets. (**c**) Diminutive posterior leaflet with large anterior and septal leaflets. (**d**) Reconstructed en face view from 3D data set showing orthogonal 2D views that bisect the leaflets at their point of coaptation

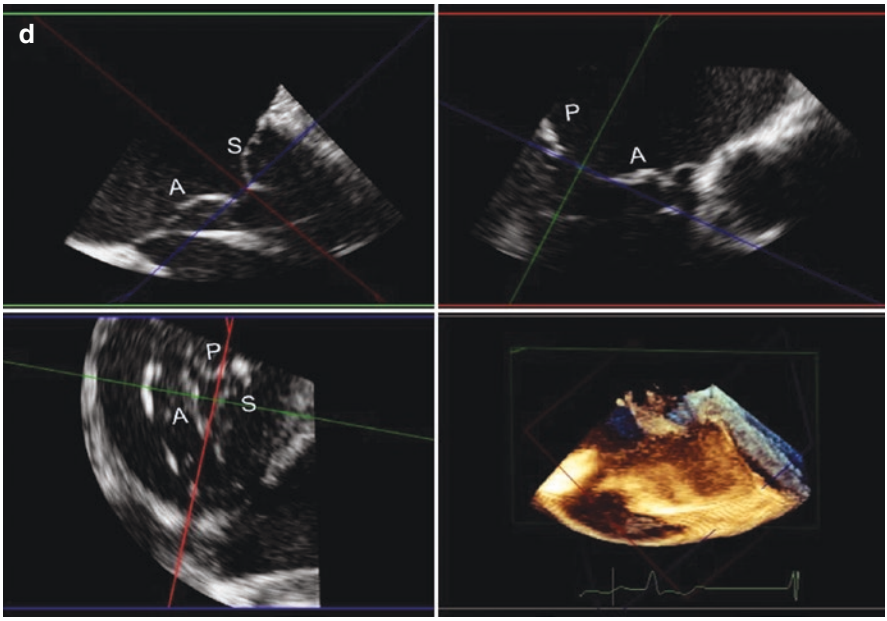


Fig. 5.3 (continued)

the variations in leaflet anatomy mentioned above. Figure 5.3d shows reconstruction of orthogonal planes from a 3D data set to help create an en face view similar to the transgastric image. This reconstruction can be useful for making annular and valvular measurements.

Annulus Sizing

Similar to the mitral annulus, the tricuspid annulus (TA) is nonplanar and has a dynamic shape during the cardiac cycle [1]. An understanding of shape changes helps make the appropriate measurements needed to identify pathological enlargement. In RV diastole, the TA takes on an elliptical, saddle shape with peaks at the anteroseptal and posterolateral portions and conversely, lower points at its anterolateral and posteroseptal portions [3]. In normal hearts, the TA morphology flattens and becomes more circular during RV systole [1, 6].

The diameter and the circumference of the TA are also dynamic so that measurements vary within the cardiac cycle [2]. Change in size largely occurs in the septolateral direction since the septal leaflet is relatively fixed and dilation occurs with gaps between the septal-anterior or septal-posterior leaflets. The TA appears largest in end RV diastole and smallest in RV systole [1, 2, 7]. Multiple publications note that normal TA size is affected by gender and body surface area (BSA) [1, 2, 7].

These alterations have led to some disagreement across publications on normal size, as well as when and in which plane to make optimal measurements [7]. The European guidelines currently describe a normal TA diameter in an adult as 28 ± 5 mm at *end diastole* in the A4C echocardiographic view [1, 8]. The European and American guidelines are in agreement and define a dilated TA diameter in an adult at >40 mm (>21 mm/m^2) in diastole on the A4C echocardiographic view [1, 9]. However, these guidelines are not based on surgical outcomes, and studies have shown that 2D echocardiographic measurements underestimate TA size when compared to 3D echocardiography, MRI, or multidetector CT [2, 3, 7].

It is important with annular size measurements to decide whether the mechanism of tricuspid regurgitation is due to annular dilation, leaflet tethering, or both. Leaflet tethering often occurs in tandem with RV dilation in the mid and distal segments; this can be observed in processes such as pulmonary hypertension. Annular anatomy may be preserved, but leaflet tenting may exist. In primary annular pathologies, which may be seen in patients with enlarged atria, atrial fibrillation, or other causes of functional TR such as primary right ventricular cardiomyopathies, the base may dilate significantly, and the leaflets become flat and fail to coapt. The coaptation gap can often be much greater than that seen with the mitral valve; this results in torrential tricuspid regurgitation and is important to characterize to plan interventional procedures.

Assessing Mechanism of Tricuspid Regurgitation or Stenosis and Severity

The etiology of tricuspid valve pathology is diverse but predominantly results in regurgitation rather than stenosis. In a 25-year surgical pathology series from the Mayo clinic, 74% of tricuspid valves were purely regurgitant and 2% were purely stenotic [10]. The severity of regurgitation and stenosis dictates the presence and extent of clinical manifestations and predicts cardiovascular outcomes [11]. Hemodynamically significant tricuspid regurgitation or stenosis leads to right heart failure, which may manifest as peripheral edema, hepatomegaly with hepatic congestion, and distended neck veins. Echocardiography is critical to identify etiology and then appropriately classify the severity of tricuspid valve disease.

Tricuspid Regurgitation

In 80–90% of normal individuals, tricuspid regurgitation is identified on echocardiography [12]. However, <1% of these individuals have moderate or greater tricuspid regurgitation. Tricuspid regurgitation can be classified into primary and secondary etiologies (Table 5.1). In a series of patients with severe tricuspid regurgitation by echocardiography, only 9.5% of patients were found to have organic

Table 5.1 Causes of tricuspid regurgitation

Primary (20%)	Secondary (80%)
Myxomatous	Left heart disease (valve disease, LV dysfunction)
Rheumatic	Any cause of pulmonary hypertension
Endocarditis	Any cause of RV dysfunction
Carcinoid syndrome	
Drug-induced (anorectic drugs, fenfluramine)	*Idiopathic* (associated with atrial fibrillation)
Traumatic (blunt chest injury, laceration)	
Iatrogenic (device lead, RV biopsy)	
Congenital (Ebstein's anomaly)	

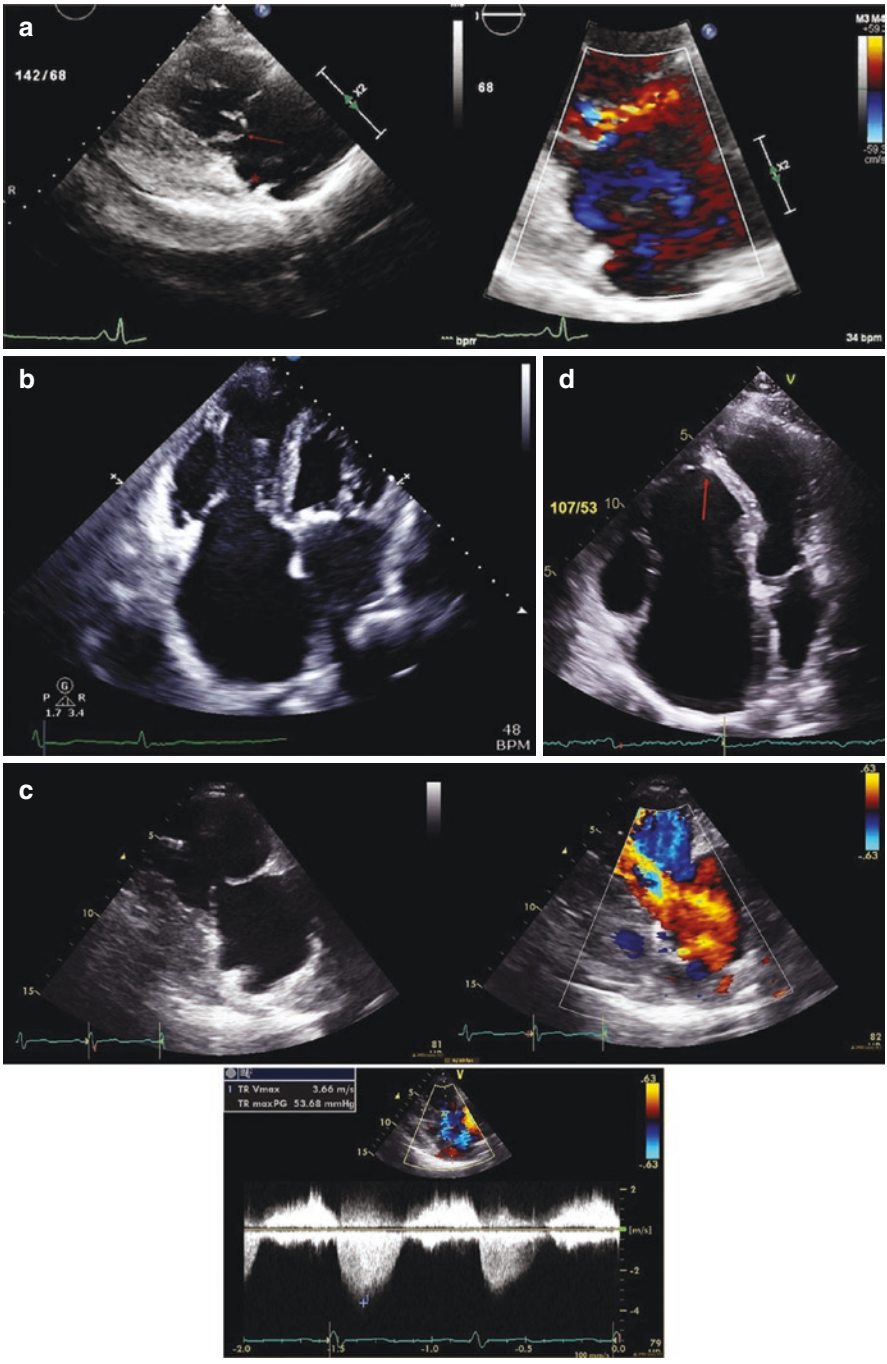
Adapted from Ref. [6]

tricuspid disease [13]. Approximately 75–80% of patients with significant tricuspid regurgitation were found to have a functional etiology for their disease [14].

Native Primary Tricuspid Regurgitation

Characteristic echocardiographic features distinguish the etiology of primary tricuspid regurgitation. The prevalence of concomitant myxomatous tricuspid and mitral disease is uncertain. In a study of patients with mitral valve prolapse, tricuspid prolapse was also present in 10–20% of patients [15]. Isolated myxomatous degeneration of the tricuspid valve is much less common than myxomatous degeneration of the mitral valve, with autopsy studies suggesting a prevalence of 0.3–3% [16]. Relative to left-sided valves, surgical intervention of primary myxomatous tricuspid disease is uncommon, seen in 4% of patients in a series from Beijing [14]. The appearance of myxomatous tricuspid valves on echocardiography is similar to features noted in mitral disease, which can include thickened and billowed leaflets with prolapse and flail segments (Fig. 5.4a).

Fig. 5.4 (**a**) Tricuspid valve prolapse. Left: Right ventricular parasternal inflow view showing prolapse and billowing (arrow) of the septal leaflet (Video 5.1a). The coronary sinus is also seen (*). Right: Zoomed right ventricular parasternal inflow view with color Doppler showing eccentric jet away from the prolapsed leaflet (see Video 5.1a). (**b**) Rheumatic heart disease. Apical four-chamber view showing thickening and restriction of the tricuspid leaflets as well as annular dilation and an enlarged large RA (Video 5.1b). There is also significant RV dilation and tethering of the tricuspid leaflets in the setting of pulmonary hypertension leading to a large coaptation gap between tricuspid leaflets. This patient also has severe mitral and aortic stenosis in the setting of rheumatic heart disease. (**c**) Carcinoid. Upper left: Right ventricular parasternal inflow view showing reduced mobility of the tricuspid valve in a patient with carcinoid tricuspid valve disease (Video 5.1c). Upper Right: Diastolic color flow acceleration through the tricuspid valve (see Video 5.1c). Bottom: Continuous wave Doppler through the tricuspid valve showing tricuspid regurgitation with pulmonary hypertension and tricuspid stenosis. (**d**) Ebstein's anomaly. Apical four-chamber view showing severe apical displacement of the septal leaflet of the tricuspid valve (arrow) and right-sided chamber dilation (Video 5.1d)


a
142/68
68
34 bpm
b
48
BPM
d
107/53
c
1 TR Vmax 3.66 m/s
TR maxPG 53.68 mmHg

Rheumatic disease is the most common cause of primary tricuspid regurgitation in developing countries. Rheumatic tricuspid disease can also manifest long after mitral valve replacement [17]. Surgical intervention for isolated tricuspid disease is rare. Of 328 consecutive patients who underwent tricuspid surgery for rheumatic disease in a Spanish series, only 4% had isolated tricuspid surgery [18]. The appearance of rheumatic disease in the tricuspid position on echocardiography is similar to its appearance on the mitral valve, with restricted leaflet motion and leaflet shortening and thickening. Often, many patients with rheumatic mitral valve disease will have atrial fibrillation with large RA and annular dilation as well as significant right ventricular dilation and dysfunction with pulmonary hypertension. This causes tricuspid regurgitation through multiple mechanisms as shown in Fig. 5.4b.

Carcinoid tumors, which constitute a rare form of malignancy that originates from enterochromaffin cells in the gastrointestinal tract, may secrete significant vasoactive substances such as serotonin. This process can lead to the deposition of fibrous tissue, or carcinoid plaque, onto the tricuspid valve [19]. The valve leaflets typically remain intact while the ventricular aspect of the tricuspid valve is often affected. On echocardiography, the tricuspid leaflets are thickened, and mobility is significantly reduced (Fig. 5.4c); usually, this causes combined regurgitation and stenosis [20].

The cause of primary tricuspid regurgitation in young adults is often congenital, with Ebstein's anomaly as the most common. Ebstein's anomaly, however, is rare, occurring in <1 per 200,000 live births [21]. It is characterized by adherence of the septal and posterior leaflets to the myocardium due to failure of delamination, as well as apical displacement of the functional annulus, dilation of the "atrialized" right ventricle with associated "true" annular dilation, and tethering and abnormalities of the anterior leaflet. An atrial communication is also almost always present; this occurs in up to 90% of patients [22]. The diagnosis is supported by >8 mm/m^2 apical displacement of the tricuspid valve as compared to the mitral valve [23]. Other common echocardiographic findings include exaggerated motion of the anterior leaflet, abnormal chordal attachments to the septal leaflet, right ventricular outflow tract dilation, significant tricuspid regurgitation, and interatrial shunt with right-to-left shunting due to increased right atrial pressures (Fig. 5.4d). Ebstein's anomaly may vary in the severity of anatomic derangement, correlating with the amount of leaflet displacement and tethering, as well as right ventricular dilation and dysfunction [21].

Primary tricuspid regurgitation can also be iatrogenic; this can occur following procedures that require traversing the tricuspid valve, such as right ventricular biopsy and cardiac electronic device (CED) implantation. The incidence of worsening tricuspid regurgitation after CED implantation varies; it can occur as frequently as in 45% of patients [24]. CED leads traversing the tricuspid valve can lead to leaflet impingement, adherence, perforation, laceration, and subvalvular interference [25], of which echocardiography may assist with diagnosis (Fig. 5.5). A tricuspid regurgitation jet that originates more apically than the coaptation point suggests lead interference. 3D echocardiography may improve the ability to determine lead trajectory [26, 27]. Leads located in the valve commissures or center of the valve

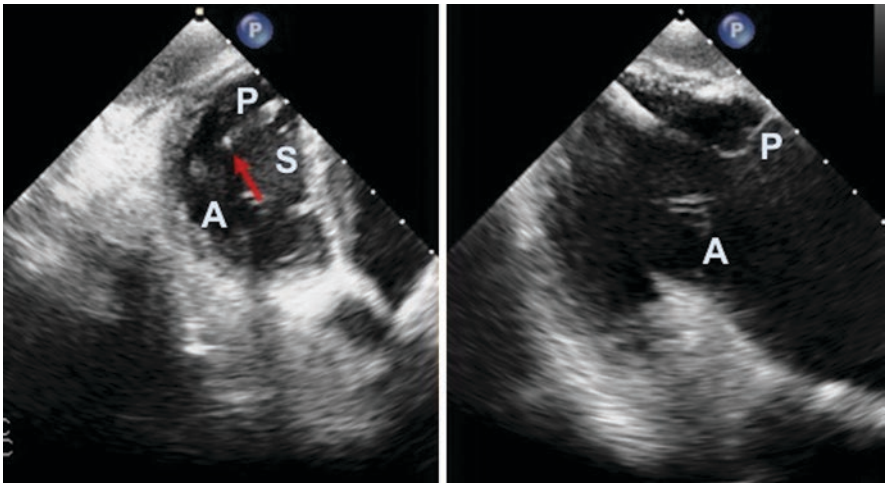


Fig. 5.5 Tricuspid regurgitation from cardiac electronic device lead impingement. Orthogonal transgastric views of the tricuspid valve (Video 5.2). A cardiac electronic device lead is seen tethering the posterior leaflet (arrow) and contributing to severe tricuspid regurgitation

were less associated with significant tricuspid regurgitation compared to leads adherent to the leaflets [27]. CEDs may also lead to right ventricular remodeling, another potential mechanism of CED-associated tricuspid regurgitation [28].

Native Secondary Tricuspid Regurgitation

Secondary or "functional" tricuspid regurgitation is more common than primary tricuspid regurgitation. Secondary tricuspid regurgitation can be further defined by etiology: left heart disease, pulmonary hypertension, idiopathic annular dilation in the setting of atrial myopathies and atrial fibrillation, and primary right ventricular dysfunction (see Table 5.1). In the setting of pulmonary hypertension, there is right ventricular remodeling and lengthening, often with dilation at the mid-wall and apical displacement of the tricuspid subvalvular apparatus leading to leaflet tethering and a coaptation gap (Fig. 5.6a). With primary RV cardiomyopathies as can be seen with ARVC, there can be tricuspid annular dilation, which causes the saddle-shaped annulus to become flat and circular, as there is progressive dilation in the direction of the free wall [29] (Fig. 5.6b). The degree of functional tricuspid regurgitation is independently prognostic in left heart disease [30], pulmonary hypertension [31], and right ventricular dysfunction [11].

Sometimes referred to as "idiopathic" or "isolated," tricuspid regurgitation associated with atrial fibrillation is another common functional cause [13]. In this condition, the predominant mechanism is excessive annular enlargement in the direction of the free wall (Fig. 5.6c), with isolated basal right ventricular enlargement and

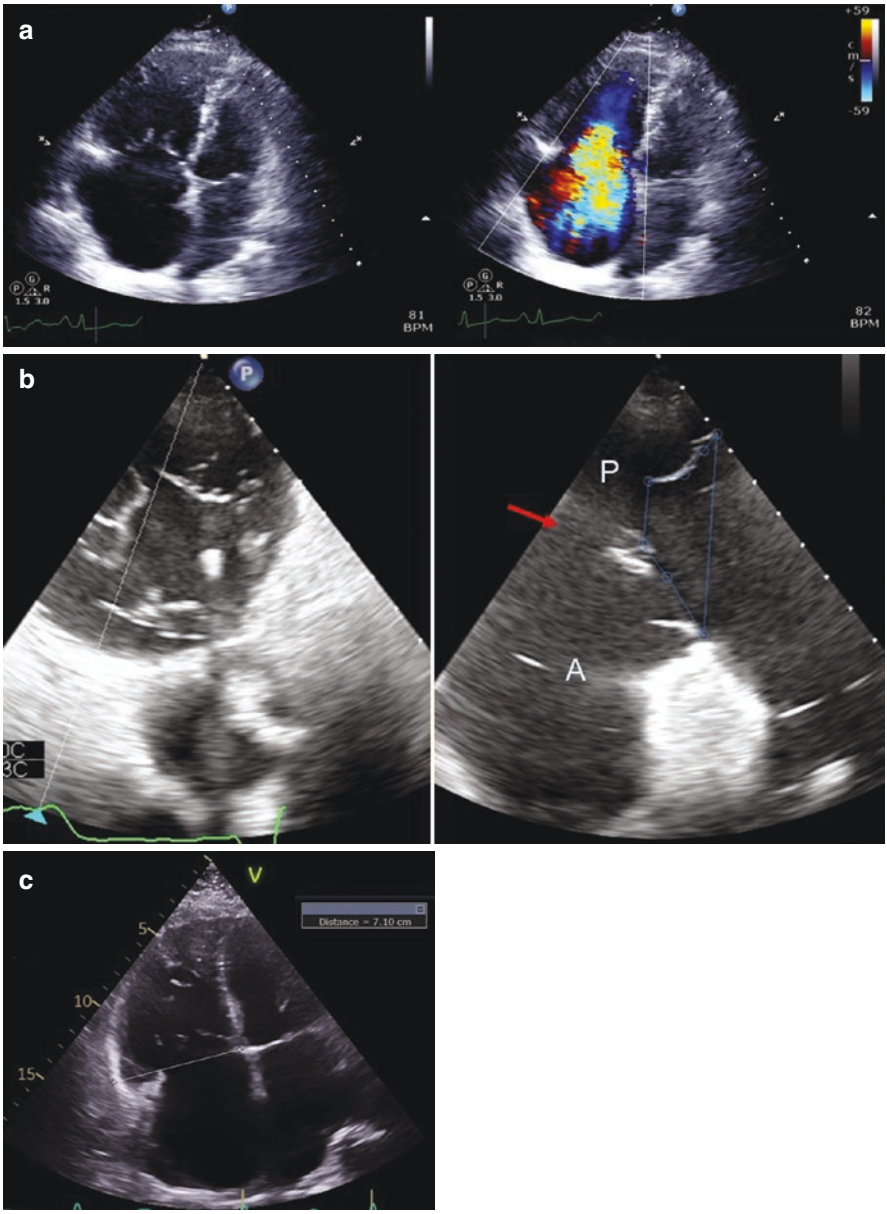


Fig. 5.6 Secondary tricuspid regurgitation examples. (**a**) Tricuspid regurgitation due to pulmonary hypertension. Note the tethering of the tricuspid leaflets and lack of significant annular dilation leading to severe tricuspid regurgitation, with the origin of the color jet well below the annular plane (Video 5.3a). (**b**) Tricuspid regurgitation due to arrhythmogenic right ventricular cardiomyopathy. Left: Transgastric view of the tricuspid valve during early systole (Video 5.3b). Right: Orthogonal view across the posterior and anterior leaflets (see Video 5.3b). This patient has severe RV dysfunction and torrential tricuspid regurgitation, with a significant tenting area (blue outline) and coaptation gap (red arrow). (**c**) Idiopathic tricuspid regurgitation. Right ventricular focused apical four-chamber view in early systole showing severe RV enlargement, tricuspid annular dilation, and tricuspid leaflet malcoaptation (Video 5.3c). This patient has idiopathic tricuspid regurgitation from atrial fibrillation

right atrial enlargement [29]. The tricuspid leaflet tethering area is typically negligible, in contrast to tricuspid regurgitation due to right ventricular dysfunction and lengthening. This etiology of tricuspid regurgitation is associated with advanced age, female gender, small body surface area, and hypertension [32]. Severe tricuspid regurgitation from idiopathic tricuspid regurgitation is also independently associated with increased morbidity and mortality [33, 34]. In secondary tricuspid regurgitation, a comprehensive echocardiographic evaluation involves assessing left heart chambers and valves, pulmonary vasculature, right ventricular remodeling and function, tricuspid leaflet tethering, tricuspid annulus assessment, and tricuspid regurgitation severity [35].

Echocardiographic Assessment of Tricuspid Regurgitation Severity

Echocardiography remains the most common and comprehensive method to assess the severity of tricuspid regurgitation. Cardiac magnetic resonance and computer tomography angiography are other noninvasive modalities that can be used to quantitate and assess tricuspid valve regurgitation, each with its own advantages and disadvantages. To characterize native tricuspid regurgitation severity, the American Society of Echocardiography guidelines [36] suggest a comprehensive assessment using structural, qualitative, semiquantitative, and quantitative parameters (Table 5.2).

Color Doppler jet area is affected by many parameters, including power, gain, tissue priority setting, aliasing velocity, and jet eccentricity [37]. Relative to a mitral regurgitant jet, the color jet area tends to be smaller in tricuspid regurgitation for a given EROA due to lower velocities and conservation of momentum [38]. The vena contracta, or a measurement of the color jet at its narrowest point, can be performed in 2D (width) or 3D (area) echocardiography. 3D analysis reveals that the vena contracta is often ellipsoid or crescent shape [39]; therefore, 2D methods may vary based on the imaging window. Continuous-wave velocity profile, another qualitative assessment using Doppler, is weak and incomplete in trivial or mild tricuspid regurgitation. The spectral envelope becomes dense, complete, and triangular with severe tricuspid regurgitation, as right atrial pressure rises early in systole.

Systolic flow reversal in the hepatic vein is a common sign of severe tricuspid regurgitation but is not specific and can also occur in ventricular or junctional rhythm with retrograde P-waves [37]. There is no regurgitation volume cutoff to produce systolic reversal of the hepatic vein. Small right atrial volume, elevated systemic venous pressure, and reduced right ventricular function require a lesser degree of tricuspid regurgitation to produce a systolic reversal of the hepatic vein [37].

Quantitative assessment can be performed using proximal convergence and volumetric quantification analysis [36]. The PISA method takes advantage of the aliasing velocity and assumes that blood approaches the regurgitant valve at hemispheric isovelocity shells, which allows for an estimate of flow. Using the conservation of mass, EROA can be calculated by dividing the flow into the maximal velocity from

Table 5.2 Grading the severity of tricuspid regurgitation by echocardiography

Structural	Mild	Moderate	Severe
TV morphology	**Normal or mildly abnormal leaflets**	Moderately abnormal leaflets	**Severe valve lesions** (e.g., flail leaflet, severe retraction, large perforation)
RV and RA size	Usually normal	Normal or mild dilation	Usually dilated[a]
IVC diameter	Normal <2 cm	Normal or mildly dilated (2.1–2.5 cm)	Dilated >2.5 cm
Qualitative Doppler			
Color flow jet area[b]	**Small, narrow, central**	Moderate central	**Large central jet** or eccentric wall-impinging jet of variable size
Flow convergence zone	**Not visible, transient or small**	Intermediate in size and duration	**Large throughout systole**
CWD jet	**Faint/partial/** parabolic	Dense, parabolic or triangular	Dense, often triangular
Semiquantitative			
Color flow jet area (cm^2)[b]	Not defined	Not defined	**>10**
VCW (cm)	<0.3	0.3–0.69	**≥0.7**
PISA radius (cm)[c]	≤0.5	0.6–0.9	**>0.9**
Hepatic vein flow[d]	Systolic dominance	Systolic blunting	**Systolic flow reversal**
Tricuspid inflow[d]	**A-wave dominant**	Variable	E-wave >1.0 m/s
Quantitative			
EROA (cm^2)	<0.20	0.20–0.39[e]	**≥0.40**
RVol (2D PISA) (mL)	<30	30–44[e]	≥0.45

Adapted from Ref. [29]
Bolded signs are considered specific for their TR grade
CWD continuous-wave Doppler, *EROA* effective regurgitant orifice area, *IVC* inferior vena cava, *PISA* proximal isovelocity surface area, *RA* right atrium, *RV* right ventricle, *RVol* regurgitant volume, *VCW* vena contracta width
[a]RV and RA size can be within the "normal" range in patients with acute severe TR
[b]With Nyquist limit >50–70 cm/s
[c]With baseline Nyquist limit shift of 28 cm/s
[d]Signs are nonspecific and are influenced by many other factors (RV diastolic function, atrial fibrillation, RA pressure)
[e]There are too little data to support further separation of these values

the continuous wave Doppler. Geometric and temporal assumptions limit the accuracy of the PISA method, as EROA is often underestimated. Volumetric assessment compares the stroke volume through the regurgitant valve with a reference stroke volume, often the LVOT [37]. The tricuspid valve annulus can be measured using 2D biplane or 3D. The EROA can also be estimated directly using 3D color vena contracta. The echocardiographic features of severe tricuspid regurgitation are

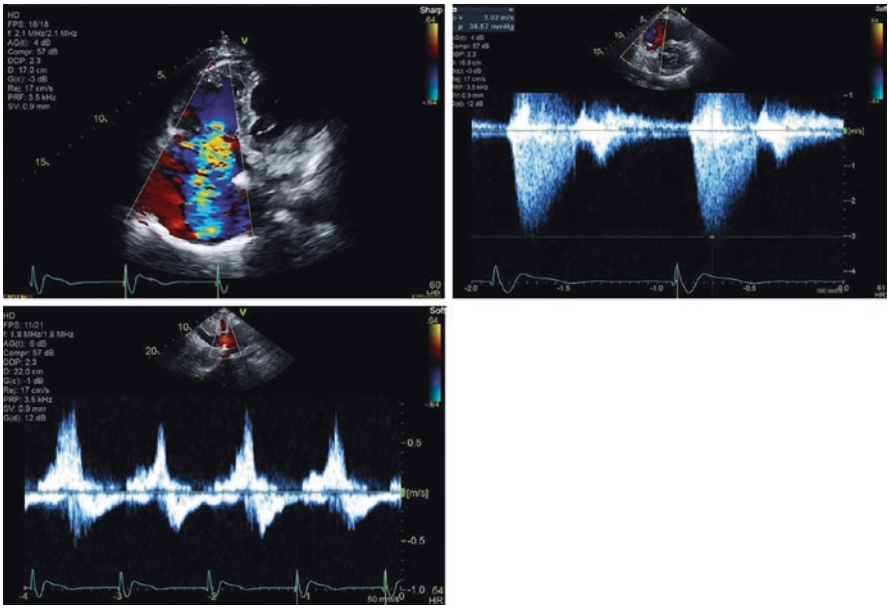


Fig. 5.7 Features of severe TR. Upper Left: Color Doppler jet area >10 cm^2 (Video 5.4). Upper Right: Triangular continuous-wave tricuspid regurgitation signal. Bottom: Systolic reversal of the hepatic vein flow in the subcostal window

Table 5.3 Proposed new grading system for tricuspid regurgitation

Parameters	Mild	Moderate	Severe	Massive	Torrential
VC width[a]	<3 mm	3–6.9 mm	7–13 mm	14–20 mm	≥21 mm
EROA (PISA)	<20 mm^2	20–39 mm^2	40–59 mm^2	60–79 mm^2	≥80 mm^2
3D VC area			75–94 mm^2	95–114 mm^2	≥115 mm^2

Adapted from Ref. [29]
EROA effective regurgitant orifice area, *PISA* proximal isovelocity surface area, *VC* vena contracta
[a]VC width calculated by the average of two orthogonal views

shown in Fig. 5.7. Due to the frequent late presentation of tricuspid regurgitation, a new proposed grading system for tricuspid regurgitation has been proposed (Table 5.3) but has not been validated [40]. Whereas the EROA can exceed 3–4 times the severe cutoff in tricuspid regurgitation with obvious non-coaptation, this is not compatible with life in mitral regurgitation.

Native Tricuspid Stenosis

Tricuspid valve obstruction is a rare entity. In adults, it is most commonly caused by rheumatic disease but is also caused by congenital abnormalities, metabolic disorders (carcinoid, Fabry's disease, Whipple's disease), and endocarditis [41]. Tricuspid

stenosis is rarely isolated when it is due to rheumatic disease. Echocardiographic findings that are consistent with severe tricuspid stenosis include mean pressure gradient ≥5 mmHg, inflow time-velocity integral >60 cm, pressure half time ≥190 ms, and valve area ≤1 cm^2 [42].

Prosthetic Tricuspid Disease

Bioprosthetic valves are more common than mechanical valves in the tricuspid position due to the risk of valve thrombosis. The echocardiographic assessment of prosthetic tricuspid valve is similar to that of native tricuspid disease. The complications of prosthetic tricuspid disease are similar to other prosthetic valve diseases, which include obstruction from pannus, thickening, or calcification, as well as paravalvular leak, leaflet tear, valve dehiscence, thrombus, or vegetation.

Given that prosthetic velocities vary with respiration, an average of five cardiac cycles should be used regardless of underlying rhythm [43]. Although limited data exist, prosthetic EOA can be calculated by measuring the LVOT stroke volume by the prosthesis VTI; however, the presence of significant tricuspid regurgitation will not be accurate. There is a suggestion of prosthetic tricuspid stenosis if peak velocity reaches >1.7 m/s and the mean gradient is ≥6 mmHg, with a pressure half time of ≥230 ms (Fig. 5.8). Prosthetic tricuspid regurgitation is suggested if jet area >10 cm^2, vena contracta width >0.7 cm, and systolic reversal of the hepatic vein is present, and if the jet contour and density are early peaking and dense. Conversely, bioprosthetic tricuspid parameters were obtained shortly after surgery in a Mayo Clinic series, with "normal values" that include pressure half time <200 ms, mean gradient <9 mmHg, E velocity <2.1 m/s, tricuspid VTI <66 cm, and VTI (TV)/VTI (LVOT) <3.3 [44]. Similarly, normal mechanical tricuspid prosthetic echocardiographic parameters shortly after surgery were pressure half time <130 ms, peak E velocity <1.9 m/s, and mean gradient <6 mmHg [45].

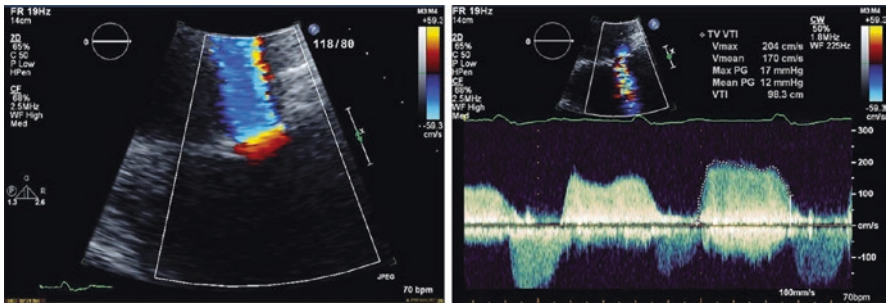


Fig. 5.8 Prosthetic tricuspid stenosis. Left: Zoomed apical four-chamber TTE view showing color flow acceleration across a 3-mm St. Jude tricuspid prosthetic valve during diastole, consistent with tricuspid stenosis (Video 5.5). Right: Transtricuspid prosthetic gradient shows a peak velocity of >2 m/s and a mean gradient of 12 mmHg, suggesting severe prosthetic stenosis

There is even less experience with the evaluation and assessment of tricuspid valves that were repaired percutaneously, as there are no FDA-approved devices at this time [46]. There are many devices that are currently in development, however. In the tricuspid edge-to-edge repair registry, the vena contracta, EROA, and regurgitant volume were calculated from multiple jets, and these methods will require validation [47].

Imaging for Tricuspid Valve Intervention

Emerging Therapies

Transcatheter therapies continue to evolve in light of the fact that a poor prognosis is associated with severe tricuspid regurgitation and also great morbidity and mortality associated with surgical intervention [48]. Percutaneous tricuspid valve procedures rely on accurate assessment of the tricuspid valve, both prior to and during the procedure, to determine correct placement. Imaging requirements vary based on the type of tricuspid regurgitation.

In order to determine which intervention is best, accurate assessment of tricuspid valve anatomy, mechanism of tricuspid regurgitation, and sizing of the annulus or vena cava is critical. Key features to take into account include the dimensions of the tricuspid annulus, the presence of a pacemaker lead across the valve and whether this is impacting valve function, and whether tricuspid valve leaflets prolapse or are fibrotic due to carcinoid or rheumatic disease [49].

Multimodality imaging is often needed in the face of complex pathology. Echocardiography is typically the first step to evaluate tricuspid valve anatomy and function, but assessment of the valve, annulus sizing, and right ventricular function is often complemented by the use of cardiac MRI (Chap. 6) and cardiac CT (Chap. 7).

Transcatheter Tricuspid Valve Interventions

Given the growing number of patients with severe tricuspid regurgitation who are at high surgical risk or inoperable, the emergence of transcatheter valve therapies may provide a feasible, durable, and safe solution [50]. At present, some key options available include heterotopic transcatheter valves within caval veins, tricuspid valve annuloplasty, the MitraClip device, and valve in valve/ring.

Heterotopic Transcatheter Valves

Tricuspid valve incompetence can lead to excess venous congestion so that implantation of balloon- or self-expandable transcatheter valves in the inferior vena cava and superior vena cava can decrease the backflow of blood. Therefore, patients with severe tricuspid regurgitation and systolic backflow reversal in the inferior vena cava may benefit from the placement of transcatheter valves. Distance between the cavoatrial junction and the first hepatic vein must be visualized as well as the caval vein dimensions and RV function prior to the procedure. This intervention was evaluated in the HOVER and TRICAVAL trials.

First, the severity of this tricuspid valve incompetence and RV function must be proven by TTE or CMR. Then, the dimensions of the caval veins and the distance from the inferior cavoatrial junction to the first hepatic vein must be determined by MDCT. If dimensions are smaller than desired, an obstruction could result upon tricuspid valve implantation. On the other hand, if the cavoatrial junction is too large, which may occur with right atrial dilation, there is a risk of device migration. Finally, if RV function is severely reduced, then further RA and RV remodeling, which can occur after device implantation due to elevated RA and RV pressures, may preclude symptomatic improvement [50].

Transcatheter Tricuspid Valve Annuloplasty Devices

Transcatheter tricuspid valve annuloplasty devices can be directly anchored into the tricuspid annulus (direct annuloplasty) or placed in the pericardial space along the atrioventricular groove (indirect annuloplasty). The PTVAS, SCOUT, and SCOUT II trials continue to evaluate both the safety and efficacy of direct annuloplasty approaches by way of the Trialign device. The PREVENT trial focuses on the safety and efficacy of an alternative direct annuloplasty device, the Tricinch device.

For direct annuloplasty, the first step is to determine the severity of functional tricuspid regurgitation by TTE or CMR. Then, MDCT is used to determine the course of the right coronary artery (RCA) along or, more rarely, across the atrioventricular groove. MDCT is also used in pre-procedure planning to obtain the distance between the RCA and the tricuspid annulus and to demarcate the atrioventricular groove. The course of the RCA and other epicardial coronary arteries is critical to prevent impingement during implantation of the device. If there is at least 2 mm between the RCA and tricuspid annulus, the anchors or pledgets of each device can safely avoid the RCA.

For indirect annuloplasty, it is important to locate the epicardial coronary arteries in relation to the atrioventricular groove to prevent impingement and ensure the coronary arteries do not cross the course of the transatrial intrapericardial tricuspid annuloplasty system. In addition, it must be confirmed that the lobe of the right atrial appendage is anterior since the pericardial space is accessed via the right atrial appendage [50].

In patients with secondary tricuspid regurgitation and only mild-moderate tricuspid annular dilation without significant tethering, an annuloplasty device remains a feasible option. These devices are currently being used in approximately 30% of patients. If there is more significant annular dilation and tethering, then annuloplasty could be used in combination with approaches such as the MitraClip device [51].

Edge-to-Edge Repair with the MitraClip Device

Since experimental models of functional tricuspid regurgitation demonstrated a significant reduction in EROA and regurgitant volume, which can concomitantly increase cardiac output, with clipping of septal and anterior leaflets, these techniques gained traction [52]. Tricuspid valve anatomy, localization of coaptation gap, and an assessment of which leaflets are most tethered are crucial to select the appropriate patients [50]. Planning prior to the procedure requires the determination of the largest vena contracta location and then the motion and length of the tricuspid leaflets.

Severity of tricuspid regurgitation must be assessed by TTE, TEE, or if needed CMR. Then to determine the largest EROA, TTE is crucial. To obtain further understanding of the coaptation gap and leaflet anatomy, 3D echo is critical due to high temporal and spatial resolution. If the coaptation gap between leaflets is too large or the tricuspid valve leaflets are excessively tethered, the procedure becomes more challenging. The MitraClip is best tolerated in those patients with primary tricuspid regurgitation due to tricuspid valve prolapse or pacemaker lead placement without severe tricuspid annular dilation. Secondary tricuspid regurgitation with only moderate tricuspid annular dilation or tethering may still benefit from the MitraClip. These devices currently represent the most common percutaneous transcatheter technology used, over 50% of the time. If the RV has remodeled significantly, and severe tricuspid annular dilation as well as tethering exists, then transcatheter valve replacement may be preferred [51].

Transcatheter Valve Replacement

If a patient has a failed tricuspid valve annuloplasty or a failed biological tricuspid prosthesis, there may be a benefit to a valve-in-ring or valve-in-valve procedure with the transcatheter Sapien valve or Melody valve.

Looking ahead prior to the procedure, first there must be an identification of the severity and mechanism of dysfunction by TTE. It is crucial to determine if there is paravalvular or valvular regurgitation. The dimensions of the ring or valve are also crucial—TTE, TEE, and MDCT can help accomplish these aims. If the sewing ring is incomplete, this leads to a shorter asymmetric landing zone for the deployment of transcatheter devices [50]. In addition, the size of the existing ring or prosthesis must be compatible with a transcatheter device. For those patients with primary TR due to rheumatic disease or lead placement with significant tricuspid annular

dilation, there is a role for transcatheter valve replacement. In patients with secondary tricuspid regurgitation but only moderate tricuspid annular dilation or with severe dilation but preserved or mildly reduced RV function, there can also be a role for transcatheter valve replacement. While various models of transcatheter valve replacement are developed, an adequately sized device can address significant annular dilation and also paravalvular leak found during planning stages [49].

Future Directions

In a recent study from the TriValve Registry of 312 high-risk patients with severe symptomatic tricuspid regurgitation, actuarial survival improved in those patients with successful device implantation. Furthermore, the main factor that was related to procedure failure was greater coaptation depth, a marker of valve tethering [53]. While this population was at increased risk and the registry enrolled patients with an eye toward the compassionate use of procedures, it helps provide insight into the potential for these procedures. The study also sheds light on the importance of patient selection; patients with late disease progression, with features such as RV remodeling and dysfunction, were less likely to experience procedural success. The field of transcatheter interventions for severe tricuspid regurgitation represents a new frontier, with questions such as scoring systems to predict eligibility, long-term durability, and anticoagulation, which remain under investigation. The novel devices explored here, alongside multimodality imaging techniques, will pave the way for innovative therapies to address a formidable disease process.

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Chapter 6
MRI Assessment of the Tricuspid Valve and Right Heart

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Introduction

Although there have been improvements in cardiac imaging, assessing the complex geometries of the right atrium (RA), tricuspid valve (TV), and right ventricle (RV) remains a challenge with strictly two-dimensional imaging. The substernal (anterior) position and complex morphology of these structures underlie much of this difficulty [1].

Transthoracic echocardiography, radionuclide ventriculography, and computed tomography are commonly used in clinical practice to qualitatively monitor RV size and systolic function. Given the complex shape, thin wall, and substernal location of the RV, echocardiography evaluation is limited. Computed tomography can circumnavigate some of these, though it exposes patients to ionizing radiation. CMR provides the most comprehensive evaluation of the RV. It is the gold standard for quantification of ventricular volume and ejection fraction with additional benefits of tissue characterization and accurate quantification of blood flow [2, 3]. CMR affords a reasonable compromise of high temporal, spatial, and contrast

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resolution with a wide field of view without radiation exposure. The interest in CMR is based on these features, as well as the reproducible nature of volumetric and flow measurements [2, 4]. The RV and TV can be evaluated from multiple planes using steady-state free precession (SSFP) sequences. SSFP techniques have been validated for the quantification of ventricular volumes and function and evaluating valvular structures [5]. Gradient echo (GRE) imaging allows for accurate visualization of stenotic and regurgitant flow [5]. Furthermore, quantification of flow across the TV and pulmonary valve can be evaluated using phase-contrast velocity-encoding [5]. RV systolic function is most commonly assessed by global metrics (e.g., ejection fraction, stroke volume, cavity volume, and myocardial thickness); however, regional assessment can also be obtained [3]. Recent research has shown regional changes in strain and strain rate were sensitive for detecting early manifestations of dysfunction and so may provide additional information when assessing RV systolic function [6, 7].

This chapter will provide a brief synopsis of the underlying principles of CMR assessment as it relates to RV function and the TV.

CMR Pulse Sequences and Strain: General Principles

There are a variety of CMR pulse sequences used in cardiac imaging. The most common pulse sequences for the assessment of ventricular function and heart valvular disease are summarized in Table 6.1 [8] and discussed in this section.

Table 6.1 CMR pulse sequences with utility in the evaluation of valvular heart disease

CMR pulse sequence	Utility
Steady-state free precession cine	Valve anatomy and leaflet motion Ventricular volumes and function Turbulent blood flow jet visualization
Gradient echo cine	Valve anatomy and leaflet motion Turbulent blood flow jet visualization Prosthetic valve assessment
Phase contrast	Flow velocity Forward and regurgitant volumes
Turbo spin echo	Evaluation of valve masses
Segmented inversion recovery gradient echo	Evaluation of valve masses

Steady-State Free Precession

Steady-state free precession (SSFP) sequences are gradient echo sequences with a short repetition time in which a steady residual transverse magnetization is maintained between successive cycles [9]. SSFP provides a high signal-to-noise ratio and excellent contrast between the blood pool and myocardium. RV volumes are measured from the plane of the TV to the RV apex using either axial or short-axis stacks [10]. Endocardial and epicardial contours are drawn at both end-diastolic and end-systolic phases of the cardiac cycle throughout the stack, allowing for accurate calculation of RV volumes, ejection fraction, and myocardial mass (Fig. 6.1). Although there are advantages of SSFP imaging, among the limitations is the possibility of signal loss. Marked signal loss can occur in regions of flow turbulence or susceptibility artifacts due to magnetic field inhomogeneities. To minimize any signal loss, echo times for SSFP imaging are kept relatively short. Furthermore, it is imperative to properly align planes when more than one jet is present in order to identify the mechanism of regurgitation and the location of the regurgitant jets.

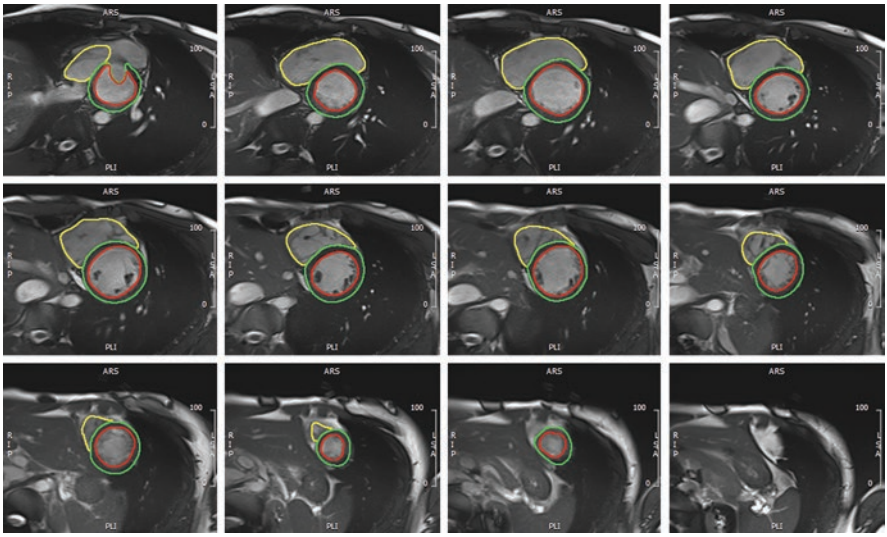

Fig. 6.1 Steady-state free precession sequence in short-axis view. RV volume, ejection fraction, and mass are calculated using an SSFP short-axis stack. Endocardial and epicardial contours are drawn at both end-diastole and end-systole throughout the stack. SSFP steady-state free precession sequence

GRE Imaging

GRE imaging uses increased spin dephasing, which improves the sensitivity of detecting abnormal flow, and is less subject to signal loss compared to SSFP imaging. GRE short-axis stacks can be used to measure valve orifice area. This can be performed by using slightly overlapped slices while giving attention to ensure there is complete visualization through the orifice. This technique is more accurate when the orifice has a simple shape, and the jet is coherent. Irregular regurgitant jet shapes with multiple components compromise the sensitivity of this technique.

Phase Contrast Mapping

Phase-contrast velocity mapping utilizes gradient velocity-encoding to generate a phase shift of moving protons within the magnetic field [11]. Velocity mapping imaging can be used to measure jet velocity and volume flow. The intensity of the phase images is directly proportional to the velocity of spins within each voxel, which allows for quantitative assessment of flow velocities. Directional components (*X*, *Y*, and *Z* planes) of velocity are encoded; however, the through plane (slice selection) is assigned to the *Z*-plane. Phase-contrast velocity mapping is susceptible to aliasing, which occurs when the maximum measurable encoding velocity (V_{ENC}) is set too low. In contrast, when the V_{ENC} is set too high, sensitivity is reduced. The optimal V_{ENC} is ~10% greater than the maximum velocity component in the image.

CMR-Derived Strain

Strain is defined as the deformation of an object in response to an applied force and is conventionally reported as a percent change. The speed at which the deformation occurs is termed as strain rate. Regional strain can be calculated using the Lagrangian formula: $[e = (L - Lo)/Lo]$, where e is strain, Lo is original length, and L is the length of the object after the applied force resulting in deformation. A negative strain value occurs when L is shorter than Lo, and a positive strain value occurs when L exceeds Lo. Strain is a tensor and can be calculated in three principal directions (longitudinal, circumferential, and radial). There are several CMR acquisition techniques that can be used to analyze strain, including myocardial tagging, displacement-encoding (DENSE), strain encoding (SENC), and feature tracking (FT) [12]. While myocardial tagging MRI is the gold standard for myocardial deformation, this method is time-consuming. This spurred the development of FT-CMR, which is less time-consuming (Fig. 6.2), and analogous to speckle-tracking echocardiography. FT-CMR is a post-processing technique in which myocardial tissue signatures in cine images are tracked to measure heart deformation. Endocardial

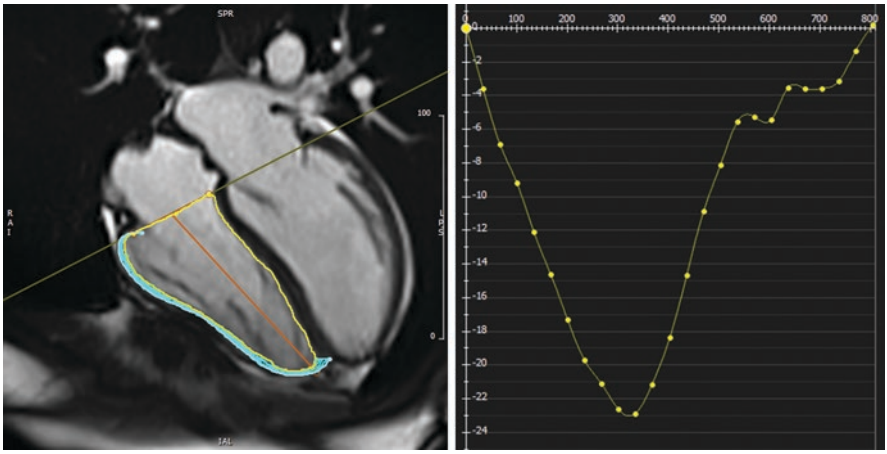

Fig. 6.2 Cardiovascular magnetic resonance-tissue tracking in the assessment of right ventricular function. Longitudinal strain in the apical four-chamber view with the strain curve demonstrated

and epicardial borders are delineated and tracked using cine imaging from short-axis and three long-axis views (four-chamber, two-chamber, and three-chamber) throughout the cardiac cycle. FT-CMR has good intra- and inter-observer reproducibility [13–15]. An important advantage is that it can be applied to SSFP imaging, which is commonly part of routine CMR protocols, thus requiring no additional sequences.

CMR Assessment in Tricuspid Valve and Right Heart Disease

Right Atrium Anatomy, Size, and Function

The RA is less uniform in thickness compared to the left atrium. The terminal crest demarcates the junction between the right atrial appendage and venous inflow. Pectinate muscles arise from the terminal crest and course in branched and often overlapping fashion toward the TV. The prominent RA musculature underlies the increased TV ring excursion compared to the mitral valve [16]. Atrial size and function, including atrial strain, can be measured by CMR. CMR offers advantages compared to echocardiography for evaluating the RA: wider field of view, greater signal-to-noise ratio with improved image quality, and border tracking for the RA [17]. Normal values for right atrial function are provided in Table 6.2. Similar to the assessment of ventricular deformation, the quantitative assessment of atrial deformation by feature tracking or tissue tracking is reproducible [18]. Regional deformation for both atria can be compared to measure inter-atrial dyssynchrony. In addition, assessment for late gadolinium enhancement as a measure of atrial wall

Table 6.2 Ventricular reference range for Caucasian adults

Parameters	Men	Women
RV EDV (ml)	124–248	85–168
RV ESV (ml)	47–123	27–77
RV SV (ml)	62–131	48–99
Indexed RV EDV (ml/m^2)	68–125	53–99
Indexed RV ESV (ml/m^2)	25–63	17–46
Indexed RV SV (ml/m^2)	34–67	30–59
RV EF (%)	45–65	47–68
Maximal RA volume (ml)	43–143	38–101
RA SV (ml)	10–66	14–52
Indexed maximal RA volume (ml)	22–74	23–59
Indexed RA SV (ml/m^2)	5–33	8–31
RA EF (%)	23–58	31–63
RV longitudinal strain (%)[a]	−19.71 to −22.73	−19.71 to −22.73
RV circumferential strain (%)[a]	−10.35 to −12.02	−11.14 to −13.04

EDV end-diastolic volume, *EF* ejection fraction, *ESV* end-systolic volume, *RA* right atrium, *RV* right ventricle, *SV* stroke volume. The normal ranges were defined as the range where the measured value fell within the 95% prediction interval

[a]Reprinted from Truong et al. [15]. Copyright 2017, with permission from Elsevier. Adapted from Ref. [81]

fibrosis is possible by CMR, although improved sequences with very good spatial resolution are required for this to be adopted widely in clinical practice due to the thin atrial wall [19].

Tricuspid Valve Anatomy and Function

When viewed using standard orthogonal body coordinates, the TV consists of the anterosuperior (often referred to as anterior), septal, and inferior (often referred to as posterior) leaflets [20]. For purposes of concordance with clinical literature, we will refer to the anterosuperior leaflet as "anterior" and inferior leaflet as "posterior." The TV is the largest cardiac valve with a wide variability in the number and morphology of the leaflets [1, 21]. Compared to the mitral valve, the TV annulus is located slightly closer to the apex and has papillary muscle and direct chordal attachments to the interventricular septum. One of the most consistent features of the TV and its supporting apparatus are the multiple direct chordal attachments tethering the septal leaflet to the interventricular septum (Fig. 6.3). In contrast, there is marked variability in the morphology and location of the supporting papillary muscles. The anterior and septal leaflets are usually the largest, and the posterior leaflets are generally the smallest of the three [1]. The normal tricuspid annulus is a complex nonplanar structure, measuring approximately 4–6 cm^2 in area in adults when fully open in diastole, with dynamic changes throughout the cardiac cycle and under varying loading conditions [22].

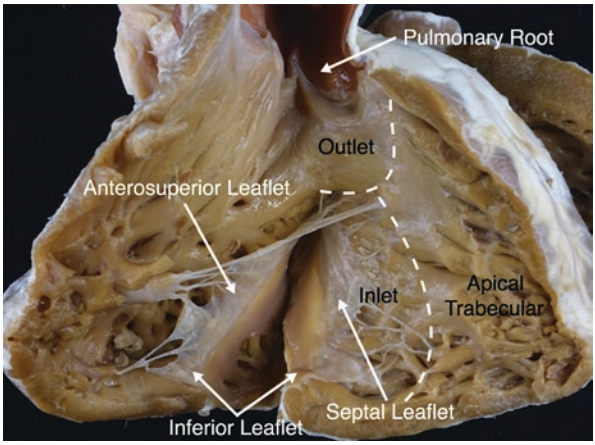

Fig. 6.3 Normal right ventricle and tricuspid valve. This normal heart specimen is opened to view the right ventricular cavity and tricuspid valve. The three leaflets of the tricuspid valve are visualized (anterior, septal, and posterior leaflets) guarding the inlet of the right ventricle. The tripartite right ventricle consists of inlet, apical trabecular, and outlet components with the hashed white lines marking the boundaries between each

CMR evaluation of TV leaflet morphology can be challenging because the normal leaflets are thin. Thin slice SSFP cine imaging is used to assess the anatomy and function of the TV. Common imaging planes include the four-chamber cine to assess the anterior and septal leaflets and the RV inflow or two-chamber and RV inflow/outflow cines, which can assess the anterior and posterior leaflets (Fig. 6.4). The short-axis cine stack slices through the TV en face. Conventional and time-resolved magnetic angiography allows for multiplanar reformatting and 3D CMR reconstruction, which can provide a detailed anatomical evaluation of the TV [23–25].

Right Ventricle Anatomy, Size, and Function

The normal RV is tripartite with an inlet, apical trabecular, and outlet component (see Fig. 6.4). The inlet of the RV extends from the TV annular plane to its chordal and papillary muscle attachments on the interventricular septum and RV free wall. The apical trabecular component has coarse trabeculations with the prominent and distinct moderator band coursing from the septum to RV free wall [26] (see Fig. 6.3). The normal RV outlet differs from the left ventricular outlet. In the RV, there is a free-standing muscular sleeve or infundibulum that lifts the pulmonary root away from the base of the heart resulting in fibrous discontinuity between the TV and pulmonary valve [27]. By two-dimensional imaging, the RV appears crescent shaped when viewed in its short axis and pyramidal shaped in its long axis.

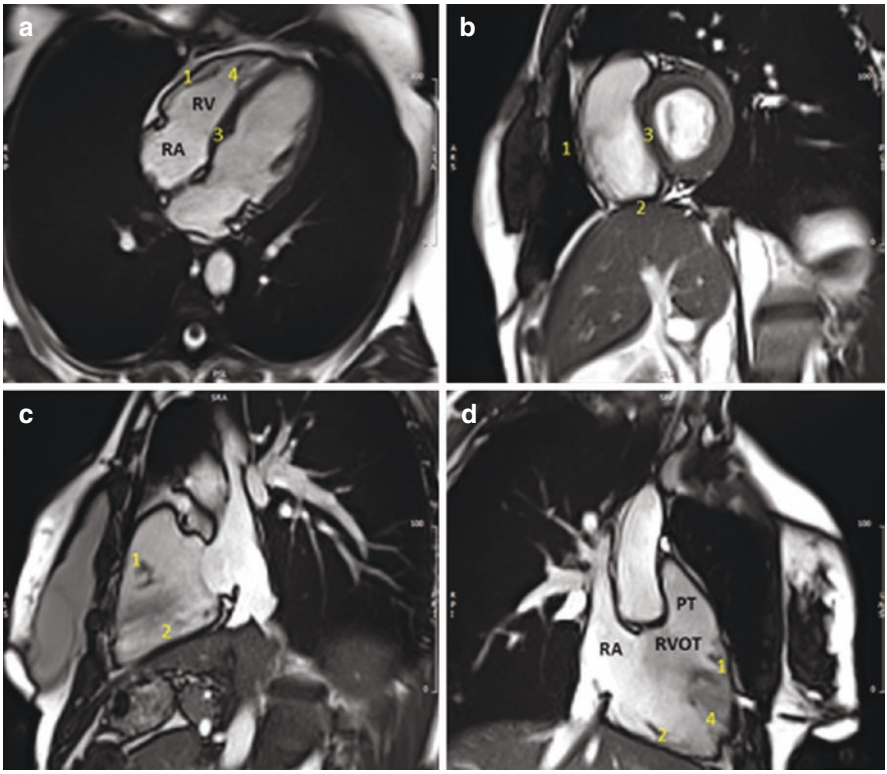

Fig. 6.4 Cardiovascular magnetic resonance in the assessment of right ventricle and tricuspid valve. (**a**) Four-chamber view: evaluates the inflow and the apical trabecular portion of the RV, the septal and anterior leaflets of the tricuspid valve; (**b**) Short-axis view: a stack can be obtained through the entire tripartite RV, viewing the three leaflets of the tricuspid valve en face at the base of the heart; (**c**) RV inflow: evaluates the inflow and the apical trabecular portion of the RV, and the anterior and posterior leaflets of the tricuspid valve; (**d**) RV inflow/outflow: evaluates the entire tripartite RV from the inlet to apical trabecular to outlet components, viewing the anterior and posterior leaflets of the tricuspid valve. RV right ventricle, TR tricuspid valve, RA right atrium, PT pulmonary trunk, RVOT right ventricular outflow tract; (1), anterior wall; (2), inferior wall; (3), interventricular septum; (4), trabecular bands

Contraction of the RV consists of a peristalsis-like motion with synchronized contraction occurring from the inlet and apex toward the outlet [28]. This predominately longitudinal shortening with delay in contraction from inlet to outlet of approximately 20–50 ms results in indistinct isovolumetric periods, in contrast to the left ventricular contraction pattern [28, 29]. The end-diastolic volume of the normal RV is on average 10–15% larger than that of the LV, with approximately 20% of its volume accounted for by the infundibulum. The RV free wall is thinner than that of the LV and is one-sixth to one-third the mass of the LV [28].

There are several methods used to measure RV systolic function, including volumetric and tissue tracking techniques. Ventricular systolic function can be estimated

by measuring the ejection fraction by CMR using the Simpson method. This method uses a stack of contiguous slices of the entire ventricle. The ventricular volume is the sum of the individual slice volumes (slice thickness × slice area). The RV stroke volume (SV) can be noninvasively calculated as the difference of end-diastolic volume (EDV) and end-systolic volume (ESV) (SV = EDV − ESV). The ejection fraction is the SV divided by EDV (SV/EDV). Normal reference values for RV function using CMR are provided in Table 6.2.

Right Atrial Pathology

Right Atrial Dysfunction

Right atrial dysfunction is now recognized as a distinct clinical entity [30]. RA dysfunction is important in pulmonary arterial hypertension, heart failure, and CHD. It has been shown to be a predictor of clinical outcomes in a variety of cardiovascular diseases [31–34]. CMR is the gold standard modality for the assessment of the RA function due to its excellent spatial resolution and endocardial border definition. CMR-derived RA strain allows identification of all phases of RA dynamics (reservoir, conduit, and booster function) [35], allowing for detection of subclinical dysfunction [36]. Whether or not RA function will be relevant to the success of individualized TV interventions remains to be determined.

Tricuspid Valve Pathology

Tricuspid Valve Regurgitation

Physiological TR, often termed trivial, is a common finding in healthy individuals, while pathological TR is commonly a consequence of annular dilation, increased RV pressure, or a leaflet abnormality. Left-sided heart failure resulting in RV hypertension is the most common cause of TR in adults. There are multiple congenital TV malformations, including leaflet dysplasia, annular hypoplasia, leaflet cleft, Ebstein anomaly, and leaflet prolapse. Annular dilation of the TV with resulting functional TR as a result of RV dilation is also common in many forms of congenital heart disease (CHD), such as repaired tetralogy of Fallot.

Velocity encoding can be used to directly quantify TR from a short-axis en face acquisition (Fig. 6.5). However, this technique is challenging due to the movement of tricuspid annulus. Dephasing allows for planimetry of a clearly delineated vena contracta, and >7 mm suggests the presence of severe TR [37]. There are quantitative techniques that allow for indirect quantification of TR. RV stroke volume (SV) can be compared to the pulmonary valve forward flow and can be used to calculate

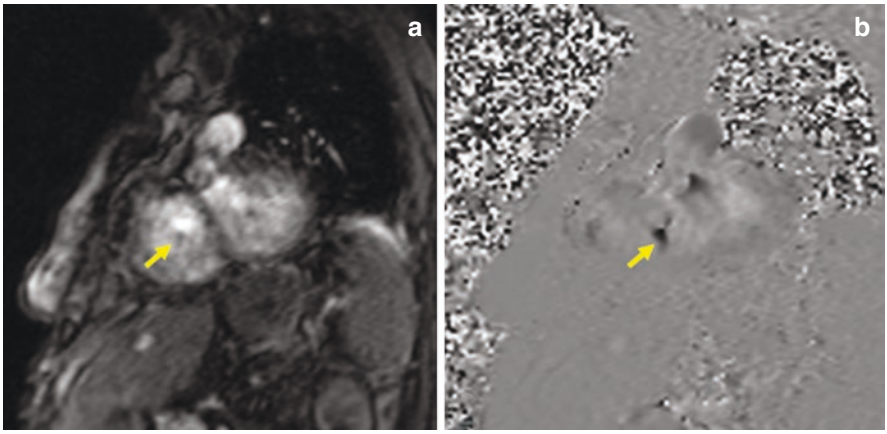

Fig. 6.5 Tricuspid regurgitation on gradient recalled echo and phase-contrast velocity imaging. (**a**) Gradient recalled echo imaging demonstrating non-coaptation of the tricuspid valve (yellow arrow); (**b**) phase-contrast velocity encoded imaging demonstrating tricuspid valve regurgitation (yellow arrow) at the level of valve orifice in short-axis view

TR: TR fraction = (RV SV − pulmonary valve forward flow)/RV SV × 100%. It should be noted that this technique is susceptible to error in any situation where there is significant intracardiac shunting, beat-to-beat variability of SV, such as an arrhythmia or significant pericardial effusion, since the RV stroke volume and pulmonary valve phase-contrast sequences are acquired over multiple heartbeats. Alternatively, ventricular SVs can be compared (RV SV − left ventricular SV)/RV SV × 100% [25]. This technique becomes difficult to use in the setting of polyvalvular regurgitation and also becomes less reliable in the face of arrhythmia. Finally, in the absence of significant atrial level shunting, the TR regurgitant fraction can be calculated using tricuspid and mitral valve antegrade diastolic flow using the following formula: TR regurgitant flow = TV diastolic flow – mitral valve diastolic inflow. This technique becomes less useful if there is mitral regurgitation.

CMR in Transcatheter Tricuspid Valve Interventions

Severe TR is associated with poor prognosis if left untreated. The current recommendations for TR intervention include (1) severe TR undergoing left-sided valve surgery, (2) mild or moderate functional TR at the time of left-sided valve surgery with tricuspid annular dilation or evidence of right heart failure, and (3) severe primary TR with symptoms unresponsive to medical therapy [38, 39]. The recent guidelines emphasize the importance of early treatment of TR [38]. Though still in clinical trials, transcatheter interventions have emerged as alternatives to conventional surgery in the management of TV disease because of the growing number of

high surgical risk elderly patients [25]. Recently, 6-month outcomes have suggested the safety of the transcatheter interventions in patients with symptomatic and moderate to severe functional TR with a decrease of annular dimensions, a significant reduction in regurgitant severity, improvements in heart failure symptoms, improved quality of life, and increased exercise capacity [40]. The primary imaging modality for diagnosis and longitudinal evaluation of tricuspid regurgitation is two-dimensional echocardiography with supplemental three-dimensional echocardiography; however, CMR imaging can be used to inform the timing of TV surgery and assess potential hemodynamic improvements after intervention [25, 41].

Tricuspid Valve Stenosis

Tricuspid stenosis is decreasing in incidence and, when diagnosed, is commonly attributed to rheumatic heart disease [38, 42]. Other causes include infective endocarditis, carcinoid, endomyocardial fibrosis, systemic lupus erythematous, and congenital TV lesions [42]. Varying degrees of TV hypoplasia and resulting stenosis are also seen in forms of congenital heart disease (CHD), such as pulmonary atresia with an intact ventricular septum.

CMR use in the setting of tricuspid stenosis has not been well studied. However, tricuspid stenosis by CMR will typically demonstrate thickened leaflets with restricted excursion during diastole [42, 43]. Tricuspid stenosis is often visualized as a signal void during the diastolic phase extending into the RV. CMR short-axis images and phase velocity maps can be aligned to transect the stenotic lesion close to the orifice. A valve orifice measured in diastole from short-axis images of <1 cm^2 is indicative of severe stenosis [42].

Right Ventricle Pathology

Ischemic Heart Disease

RV infarction has been reported in as many as 50% of cases involving inferior myocardial infarctions and 33% of all anterior myocardial infarctions [44–46]. RV systolic dysfunction resulting from concomitant left ventricular myocardial infarction is associated with higher rates of morbidity and mortality [47]. The RV ejection fraction and degree of regional wall motion abnormalities are important prognostic markers. RV infarction can be detected and evaluated by the use of late gadolinium enhancement (LGE) (Fig. 6.6) and T2-weighted imaging. Tissue characterization assessing myocardial edema and detection of LGE help differentiate reversible and irreversible injury.

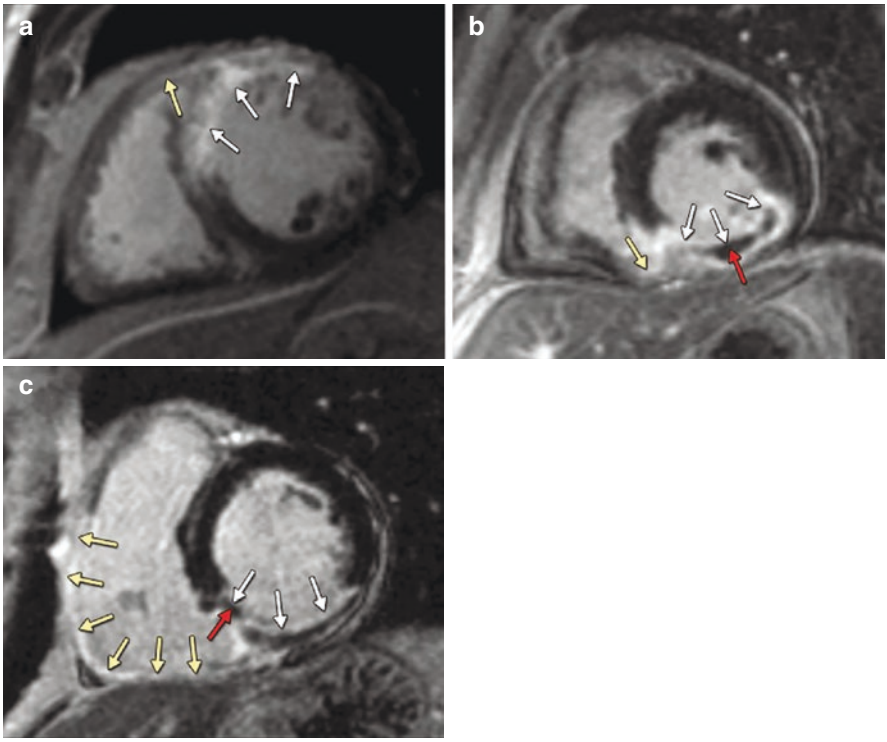

Fig. 6.6 Right ventricular myocardial infarction on late enhancement cardiovascular magnetic resonance imaging. (**a**) LGE is present in the anterior part of the RV free wall in a patient with anterior STEMI; (**b**, **c**) LGE is present in the inferior or both the inferior and the mid-part of RV free wall in patients with inferior STEMI. Yellow arrows indicate LGE in RV free wall, white arrows indicate LGE in left ventricular wall, and red arrows indicate microvascular obstruction. RV right ventricular, LGE late gadolinium enhancement, STEMI ST-segment elevation myocardial infarction. (Reprinted with permission from Miszalski-Jamka et al. [82])

Pulmonary Hypertension and Left-Sided Heart Failure

Accurate quantitation of RV volumes and systolic function provides important prognostic information and can be used for risk-stratification in both RV and LV heart failure with reduced and preserved ejection fraction [48–50] and pulmonary artery hypertension [51, 52]. Increased RV to LV volume ratio has been associated with increased all-cause mortality in patients with pulmonary hypertension [51]. Furthermore, CMR RV functional assessment (RV EDV, ESV, and ejection fraction) has contributed to improved medical management of pulmonary hypertension. CMR-derived septal curvature is associated with mortality and can be used to monitor response to pulmonary hypertension therapy [53].

Congenital Heart Disease

The TV and RV are involved in various forms of CHD. CMR is used for both the diagnosis and follow-up of pediatric and adult CHD patients (Table 6.3) [54, 55]. For example, tetralogy of Fallot is the most common form of cyanotic CHD and affects approximately 1 in 3600 live births [56]. With improving care, there are now more adults living with repaired or palliated CHD than their pediatric counterparts, including those with repaired tetralogy of Fallot [57]. CMR is an important tool for

Table 6.3 Right-heart CHD lesions commonly evaluated by CMR in alphabetical order

Lesion	CMR evaluation of right heart
Congenitally corrected transposition of the great arteries	Systemic RV volumes and systolic function Assessment of systemic ventricular fibrosis Quantification of TR If VSD present, useful for quantification of pulmonary versus systemic flow Evaluation of pulmonary stenosis if present Following double switch repair, similar utility as commented below regarding assessment following both arterial and atrial switches
Ebstein anomaly	Functional RV volumes and systolic function Atrialized RV volumes RA volumes Quantification of TR Following repair, evaluation of the TV, RV volumes, and systolic function can be necessary
Secundum atrial septal defect can be useful as an adjunct to echo	RV volume Quantify the shunt volume
Single ventricle with Fontan palliation	Systemic ventricular volumes and systolic function Assessment of systemic ventricular fibrosis Quantification of TR if systemic RV Evaluation of Fontan circuit anatomy and flows to branch pulmonary arteries Quantification of aortopulmonary and venovenous collateral flow
Sinus venosus defect (superior or inferior type)	Assessment of associated partial anomalous pulmonary venous drainage RV volumes Quantification of shunt fraction
Tetralogy of Fallot status post complete repair	Quantification of pulmonary regurgitation and pulmonary stenosis RV volumes and systolic function Assessment of biventricular fibrosis Quantification of associated TR RA volumes Assessment of branch pulmonary artery anatomy and flows

(continued)

Table 6.3 (continued)

Lesion	CMR evaluation of right heart
Transposition of the great arteries status post arterial switch	Quantification of pulmonary regurgitation and pulmonary stenosis RA volumes Quantification of associated TR RV volumes and systolic function Assessment of biventricular fibrosis Assessment of branch pulmonary artery anatomy and flows
Transposition of the great arteries status post atrial switch	Assessment of pulmonary and atrial venous baffles, including quantification of pulmonary versus systemic flow to assess for baffle leak RA volumes Quantification of associated TR RV volumes and systolic function Assessment of branch pulmonary artery anatomy and flows

RA right atrium, *RV* right ventricle, *TR* tricuspid regurgitation, *VSD* ventricular septal defect

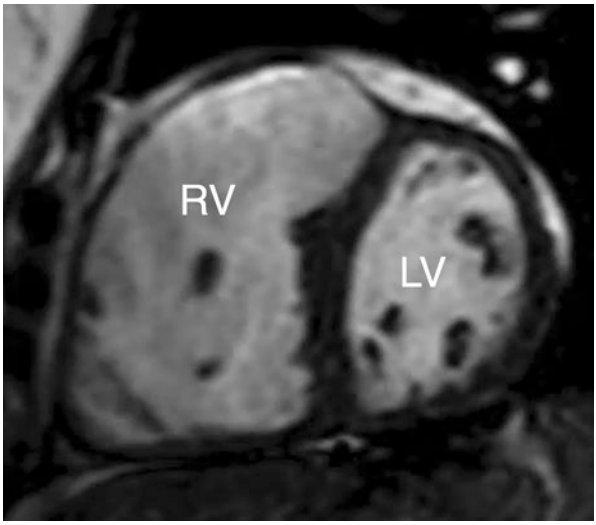

Fig. 6.7 Repaired tetralogy of Fallot with severe right ventricular dilation on cardiovascular magnetic resonance. This short-axis cine at the mid-ventricular level in a patient with repaired TOF demonstrates a severely dilated RV with diastolic flattening of the interventricular septum. TOF tetralogy of Fallot, RV right ventricular, LV left ventricle

follow-up of children and adults with repaired tetralogy of Fallot because the assessment of RV size and systolic function (Fig. 6.7) is important for guiding management and determining the need and timing of pulmonary valve replacement [58, 59]. In fact, both preoperative RV systolic dysfunction and RV-mass-to-volume ratio as determined by CMR relate to occurrence of death or sustained ventricular tachycardia following pulmonary valve replacement [60]. While there is no consensus on criteria for concomitant TV replacement at the time of PVR in repaired TOF [61], intervening on severe TR may be warranted, with CMR often being necessary for more objective quantification. Additionally, CMR affords assessment of the RV outflow tract, including the degree of stenosis and regurgitation, as well as the

branch pulmonary artery anatomy and differential flow. Similar evaluation is often necessary in other forms of repaired CHD leading to RV dilation and systolic dysfunction, such as any patient prone to pulmonary artery or RV-to-pulmonary artery conduit stenosis or regurgitation. Such patients include those with tetralogy of Fallot with pulmonary atresia following complete repair utilizing an RV-to-pulmonary artery conduit, transposition of the great arteries status post arterial switch, or those undergoing a Ross procedure where the native pulmonary root is surgically placed into the aortic position necessitating an RV-to-pulmonary artery conduit [62].

Ebstein's anomaly of the TV involves apical displacement, or in its severe form better described as the rotation of the septal and posterior leaflets of the TV into the RV outflow tract (Fig. 6.8). Both the degree of displacement and extent of development of the posterior and septal leaflet should be interrogated. In fact, a simple measure of the valve rotation angle by CMR prior to the cone surgical reconstruction has been shown to be predictive of unsuccessful repair with subsequent dehiscence [63]. The anterior leaflet retains its normal attachment at the true annulus; however, it is often large and sail-like and can have fenestrations and excessive chordal attachments to the RV free wall limiting its mobility. These are important surgical considerations that need to be meticulously described [64]. While echocardiography plays an important role in delineating the anatomy of the malformed TV, CMR can add value via a more accurate assessment of the degree of tricuspid regurgitation and RV size and function [65]. Additionally, CMR is important in assessing

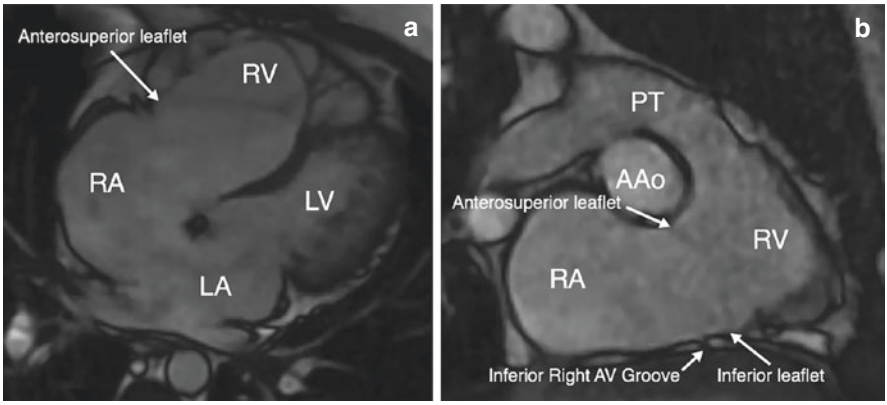

Fig. 6.8 Cardiovascular magnetic resonance imaging in Ebstein anomaly. (**a**) A four-chamber image in a patient with Ebstein's anomaly of the tricuspid valve demonstrates the large and sail-like anterior leaflet retaining its normal hinge with severe displacement and rotation of the septal leaflet toward the right ventricular outflow tract resulting in a large atrialized RV and dilated RA. The LV is heavily trabeculated and meets the criteria for LV noncompaction, a common finding present in up to one-fifth of those with Ebstein's anomaly. (**b**) This RV inflow–outflow cine image again demonstrates the normal hinge point of the anterior leaflet, with mild displacement of the posterior leaflet toward the RV apex. RV right ventricle, RA right atrium, LV left ventricle, AAo ascending aorta, AV atrioventricular, PT pulmonary trunk, LA left atrium

the atrialized RV volume, which relates to exercise capacity [66]. Hemodynamically significant TV abnormalities occur in up to one-third of patients with congenitally corrected transposition of the great arteries, with valvular dysplasia being the most common, followed by Ebstenoid malformation of the TV. In this lesion, the RV is now the systemic ventricle and the TV is exposed to systemic pressures and largely impacted by the interventricular septal position. Competence of the TV now becomes even more important, with the vicious circle of worsening TR and depressed RV systolic function linked to poorer overall outcomes [67]. There are other less common forms of malformation of the TV and RV, which similarly benefit from CMR assessment.

Hypoplastic left heart syndrome (HLHS) is the most common form of CHD with single ventricle physiology [68]. In this disease, patients are born with atretic or severely hypoplastic mitral and aortic valves and undergo serial surgical palliations, ending with the Fontan operation, which connects the systemic veins directly to the branch pulmonary arteries [69]. The RV in this disease is the systemic ventricle, and thus accurate evaluation of ventricular function is crucial as heart failure is a leading cause for mortality in this patient population [70]. CMR provides functional evaluation of the single ventricle, assessment of TR, and evaluation of the Fontan pathway and branch pulmonary arteries, all of which are proven to have a prognostic value in this population [71, 72]. TR can result from structural abnormalities in the TR, and the most common is a small septal leaflet and anterior leaflet prolapse [73]. In addition, frequently encountered abnormalities are valve leaflet dysplasia and leaflet prolapse that alter TV geometry resulting in abnormal coaptation [74–76]. Leaflet tethering can result in restricted leaflet motion, deficient coaptation, and regurgitation. A higher tethering volume has been correlated with increased TR [77]. Tethering can also occur as a consequence of the lateral displacement of the anterior papillary muscle due to the abnormal geometry and dilation of a single RV [73, 77–79]. Abnormal chordae tendinae, including elongation, deficiency, or malattachment, are pathologic findings that result in AVVR. Finally, functional TR occurs in the absence of structural abnormalities of the valve apparatus secondary to ventricular and annular dilation. This results in a stretched annulus and deficient coaptation of valve leaflets. CMR is better suited to evaluate flow and quantify TR in HLHS [80]. Serial CMR exams can assess the progression of ventricular dilation or systolic dysfunction, each of which predisposes to mortality after TR intervention post-Fontan [76]. Other diseases with a systemic RV, including congenitally corrected transposition, as discussed above, and transposition of the great arteries after atrial baffle require serial evaluation of the RV and TR with CMR.

Limitations of MRI

There are limitations to the use of CMR. Implantable devices that are not MRI compatible dictate patient selection. In CHD, the presence of stainless steel or ferromagnetic vascular coils, stents, or occlusion devices may cause imaging artifacts and

limit evaluation by CMR. Quantifying flow by two-dimensional imaging can be especially challenging given the fixed slice location and valvular movement relative to that slice results in through-plane motion. Additionally, image acquisition usually requires an appropriate breath-hold technique over multiple cardiac cycles. Contiguous stacks of cine images along with using a multiplanar approach to imaging the TV are essential to evaluate the anatomy in its entirety. Signal loss can occur when using phase velocity mapping secondary to partial volume averaging or when the size of the voxels (too large) in relation to the size and shape of a jet (narrow) do not match. Structural heterogeneity of the RV in the presence of CHD and arrhythmias can make volumetric analysis both challenging and time-consuming.

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Chapter 7
Computed Tomography Assessment of the Tricuspid Valve and the Right Heart

Saurav Uppal, Laurie Bossory, Michael Biersmith, and Thura T. Harfi

Introduction

In recent years, there has been renewed interest in the assessment and management of tricuspid valve (TV) disease, particularly tricuspid regurgitation (TR). Moderate-to-severe TR affects nearly 1.6 million patients in the United States, and is independently associated with increased cardiac events and overall mortality [1–4]. The majority of TR is functional in nature, often occurring in the context of left-sided heart disease, atrial fibrillation, or pulmonary hypertension (PHTN). Untreated severe symptomatic TR carries a poor prognosis, even after accounting for left-sided valvulopathy and congenital heart disease (CHD) [5]. Along with the renewed interest in TV disease, there has also been a growing awareness of right ventricular (RV) function.

In addition to left ventricular dysfunction, both PHTN and congenital heart disease can lead to progressive RV dysfunction and TR. With the improvements in the management of heart failure, patients with left ventricular (LV) dysfunction are living longer and into more advanced stages of their disease. Similar trends have been noted in the PHTN and congenital heart disease populations, particularly with the emergence and growth of dedicated PHTN and adult-congenital heart disease

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subspecialties. The prevalence of PHTN is estimated to be about 127 cases/100,000 population in 2012 based on a cohort study from Canada [6]. As of 2010, an estimated 2.4 million people have CHD in the United States, and this population continues to grow [7]. Though this increased survivorship is certainly commendable, there is a pressing need to better understand and mitigate the effects of progressive right heart failure often noted in these populations. Progressive RV dysfunction and dilation can lead to annular dilation of the TV causing TR. Many studies have shown that patients with RV dysfunction and severe TR tend to have worse outcomes [8–10]. Given the increasing prevalence of right-sided dysfunction and the correlation with clinical outcomes, it has become prudent to have better assessment of the RV and right-sided structures including the TV.

In this chapter we will discuss the utilization of multi-detector computed tomography (MDCT) as it relates to the assessment of RV function and TV and for planning various novel transcatheter TV interventions.

The Role of CT in the Assessment of the Right Heart: General Principles

Given the resurging interest in TV disease, as well as the rapid evolution in transcatheter TV devices, high-fidelity imaging assessment of the right heart anatomy is paramount. The right heart—including the RV, right atrium (RA), TV, and tricuspid annulus (TA)—is notoriously difficult to image and quantify due to its complex geometry. There are several imaging modalities used to evaluate the right heart, each with their own strengths and weaknesses.

Traditionally, echocardiography, particularly transthoracic echocardiography (TTE), has been the standard imaging modality to evaluate both LV and RV function. Given its high temporal resolution, TTE provides a good assessment of valvular function and morphology. Advantages include wide accessibility, relatively low cost, noninvasive nature, excellent temporal resolution, and shorter length of exam. Despite these advantages, TTE can be limited by acoustic shadowing secondary to patient characteristics such as obesity, chronic obstructive pulmonary disease, and small intercostal spaces. Moreover, the complex geometry of the RV and the TV can make the assessment more challenging.

Cardiac magnetic resonance (CMR) imaging is the current standard for evaluation of the RV. Despite this, there are several shortcomings that preclude utilization of this imaging modality for all patient populations. Owing largely to expense, the accessibility of CMR has traditionally been limited to tertiary-care academic centers. Additional barriers include longer scan times, patient's claustrophobia, contrast limitations for patients with end-stage kidney disease, and safe and/or effective image acquisition in patients with metallic implantable devices such as pacemakers and defibrillators. Due to these limitations, MDCT has emerged as a valuable alternate imaging modality.

Multi-detector computed tomography has excellent spatial resolution that is superior to both echocardiography and CMR. Currently, MDCT has spatial resolution around 0.5 mm in the *x*, *y*, and *z* axes, and continued improvements are expected with newer scanner technology. This is in contrast to CMR, which has a spatial resolution around 1–2 mm. High spatial resolution is one of the primary strengths of CT and is exceptionally useful in preprocedural planning for transcatheter valve therapies [11]. Claustrophobic patients can usually tolerate undergoing cardiac CT without difficulty. Additionally, with newer-generation cardiac CT scanners, the temporal resolution has improved significantly. For example, dual-source CT scanners can obtain images with a resolution <80–100 milliseconds [12]. Such advances have made it possible to obtain real-time evaluation of cardiac function, including ejection fractions of LV and RV. Furthermore, cardiac CT imaging is the only imaging modality that affords real 3D (or even 4D) datasets that provide multiplane reconstruction of images, which can facilitate procedural and surgical planning.

Although CMR is still considered the standard for left and right ventricular volume and ejection fraction measurements, cardiac CT offers accurate assessment of cardiac chambers comparable to CMR in a fraction of the time [13]. Studies have shown comparable assessment of ventricular function with CT compared to CMR [14]. MDCT is an imaging option for RV assessment in patients who have defibrillators or cardiac synchronization devices that are non-MRI compatible and offers an alternative for patients who struggle with anxiety or claustrophobia. The multisociety guidelines consider cardiac CT an appropriate test for evaluation of right and left heart function and structure [15].

Two important drawbacks of cardiac CT are the exposure to ionizing radiation and the use of iodinated contrast media, which are known to be nephrotoxic. Fortunately, the radiation exposure associated with cardiac CT has dramatically decreased over the past decade with newer generation CT scanners [16].

Utility of CT in Assessment of Right Heart

CT Acquisition Techniques to Optimize Right Heart Visualization

The traditional CT protocol for a coronary angiogram utilizes injection of contrast media followed by a saline bolus. This protocol results in optimal opacification of the left heart structures, but a varying degree of opacification of the right heart. Additionally, it leaves significant streaking artifact in the right atrium as the contrast from the superior vena cava (SVC) mixes with the blood coming from the inferior vena cava (IVC). In order to optimize left and right heart contrast opacification and avoid the streaking artifact in the RA, a triphasic contrast injection protocol is recommended. A triphasic contrast injection protocol includes a 60–65 ml of contrast media, followed by 20 ml of a 50–50 or 70–30 mixture of contrast–saline mixture

followed by a 40 ml saline flush. The recommended infusion rate is 5–6 ml per second. This protocol has been shown to optimize visualization of the TV and reduce streaking artifact in the RA [17, 18].

Typically, CT coronary imaging can be obtained in a prospective manner; however, cine images of the tricuspid valve and full RV functional assessments require retrospective ECG gating [19]. This method of image acquisition increases the radiation exposure to the patient. Dose modulation techniques and iterative reconstruction should be used and usually mitigate this increased radiation dose received during retrospective ECG gating.

Assessment of Right Ventricular Size and Function

Assessment of RV function with MDCT involves segmentation of the ventricle using several phases of the cardiac cycle, often 10 phases with a 64-slice CT scanner, or 20 phases with dual-source CT scanners. The end-systolic and end-diastolic volumes are determined by evaluating cardiac motion and volume changes by the reader. The endocardium is manually traced to delineate the RV volumes. Stroke volume (SV) is calculated from difference of end-diastolic volume (EDV) and end-systolic volume (ESV). The RV ejection fraction is calculated as the ratio between SV and EDV. Several studies have shown the high accuracy of MDCT for measurement of RV volume and RV ejection fraction compared to CMR [12, 13, 20, 21]. Automated tracing of the RV endocardial borders is available; however, manual corrections of the automated tracing are frequently needed due to complex RV geometry. Multiple views can be reconstructed to view the RV systolic function in four-chamber, two-chamber, and three-chamber views (Figs. 7.1, 7.2, 7.3, and 7.4). Global and regional wall motion abnormalities can also be assessed (Videos 7.1, 7.2, and 7.3). Normative values for the CT-derived cardiac chamber size and function have been reported (Table 7.1) [22].

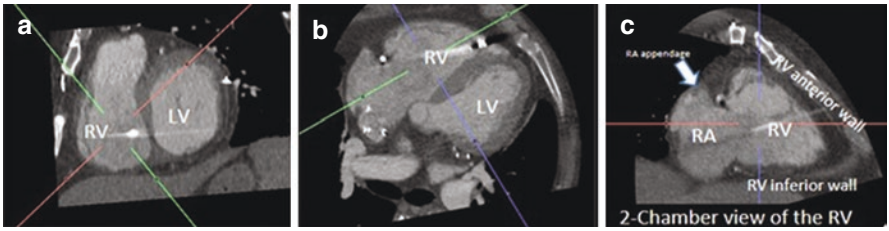

Fig. 7.1 Creating two-chamber view of the RV. From the short-axis view of the heart (panel **a**) move the center of the planes inside the RV. Then shift the green plane to cross the anterior (free) wall of the RV and the inferior (diaphragmatic) wall of the RV (panel **b**). Then in the modified four-chamber, have the green plane cross the RA (panel **b**). A two-chamber view of the RV will appear (panel **c**). RV right ventricle, RA right atrium, LV left ventricle

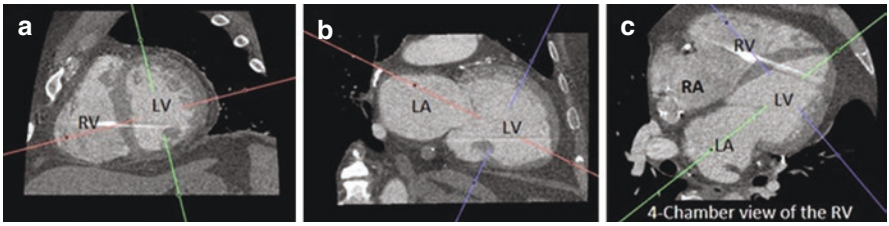

Fig. 7.2 Creating four-chamber view of the LV and RV. From the short-axis view of the heart (panel **a**), place the center planes inside the center of the left ventricle then orientate the red plane to cross the RV at its largest dimension. Next, place the red plane toward the LV apex (panel **b**). This will create a four-chamber view of the right and left ventricle (panel **c**). LV left ventricle, RV right ventricle, LA left atrium, RA right atrium

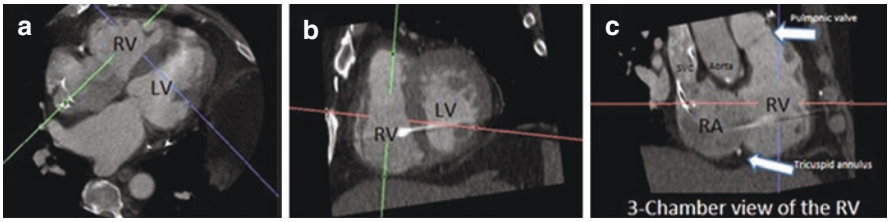

Fig. 7.3 Creating three-chamber view of the RV (RV inflow and outflow view). Move the center of the planes to be inside the center of the RV in the four-chamber view (panel **a**), then move the green plane extend along the long axis of the RV into the RVOT (panel **b**), optimize the planes to show both the pulmonic valve and the tricuspid annulus (three-chamber view) (panel **c**). Note the lack of tricuspid/pulmonic valve continuity which makes RVOT obstruction very rare in TV intervention. The area between the pulmonic valve and the tricuspid annulus is near the noncoronary aortic sinus. RV right ventricle, RVOT right ventricular outflow tract, TV tricuspid valve, SVC superior vena cava

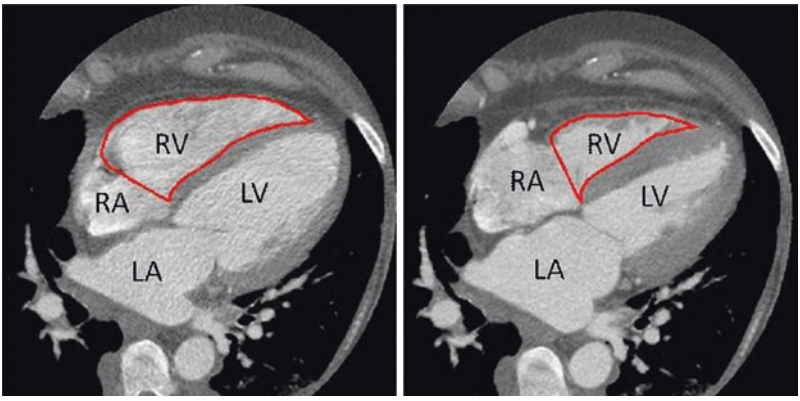

Fig. 7.4 Measuring of the right ventricular volumes using cardiac CT. Tracing the RV endocardial border to assess RV volume for assessment of EDV and ESV to calculate the RV ejection fraction. Notice the difference in the myocardial wall thickness and size of the right atrium in end diastole (left panel) and end systole (right panel). Only one slice in shown; however, ES and ED volumes measurement requires tracing the RV endocardial border on multiple slices. RV right ventricle, LV left ventricle, LA left atrium, RA right atrium, EDV end diastolic volume, ESV end systolic volume, ES end systolic, ED end diastolic

Table 7.1 Normative values for the CT-derived right ventricle chamber size, volume, and function

	End-systolic		End-diastolic				
RV dimensions	Mean (SD)	95% CI	Mean SD	95% CI	Other RV measures	Mean (SD)	95% CI
Linear (n = 103)					Remodeling		
Mid-cavity, septal–medial (mm)	29.6 (5.3)	19.2–40.0	37.0 (5.7)	25.8–48.2	RV free wall thickness	2.4 (0.7)	1.0–3.8
Mid-cavity, anterior–inferior (mm)	57.9 (8.0)	42.2–73.6	72.6 (9.0)	55.0–90.2			
Apical–annular length (mm)	62.0 (8.8)	44.8–79.2	77.7 (10.4)	57.3–98.1			
3D (n = 85)					Functional measures		
3D volume (ml)	82.1 (29.2)	24.9–139.2	174.9 (48.0)	80.0–269.0	Tricuspid annular excursion (mm)	29.6 (5.3)	19.2–40.0
3D volume index (m^l/m^2)			93.3 (20.3)	53.5–133.1	3D RVEF (%)	57.9 (8.0)	42.2–73.6

RV right ventricle, *RVEF* right ventricular ejection fraction
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MDCT Assessment of the Tricuspid Annulus

Functional TR occurs in the setting of right ventricular enlargement and annular dilation. In the assessment of functional TR, it is necessary to have accurate measurement of the TA and leaflet coaptation for possible procedural planning. MDCT TA measurements are taken during diastole at the leaflets most basal attachments (Fig. 7.5). In healthy individuals, the TA is oval shaped and appears approximately 30% longer in the medial to inferolateral direction. The average diameter of TA is 4.0 ± 0.7 cm. The TA area changes by 30% during the cardiac cycle [23–25]. In patients with mild or trace TR, the tricuspid annulus maintains its elliptical shape. In moderate to severe TR, the annulus becomes more circular [26]. As may be expected, the TA area becomes larger with worsening regurgitation and is proportional to TR severity [27]. MDCT can also measure the distance between each leaflet commissure, tethering heights, and tethering angles of each leaflet, each correlating to severity of TR and with prognostic value in patients with severe TR [28]. Tethering height is the distance of commissural displacement into the RV in patients with TR. Tethering area is the area between the annular plane of the TV and the displaced leaflets of the TV. Tethering area greater than 1.6 cm^2 and leaflet coaptation distance greater than 8 mm represent significant tethering and are significant predictors of recurrent TR following TV annuloplasty [29].

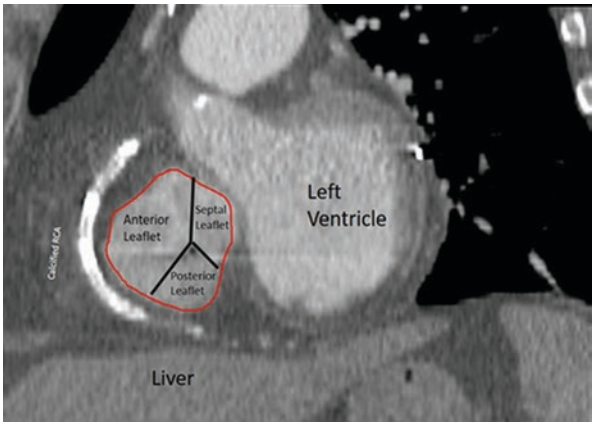


Fig. 7.5 Tricuspid valve annulus with associated tricuspid valve leaflets orientation. Leaflet coaptation lines are marked by the black lines. Note that the largest leaflet is the anterior leaflet. Note the proximity of the RCA (heavily calcified) to the annulus. The red line represents the perimeter of the annulus. RCA, right coronary artery

Assessment of Right Ventricular Strain with CT

Right ventricular strain is a term that is often used to describe the magnitude of right ventricular myocardial deformation. Excessive strain can be caused by acute pulmonary embolism, PHTN, chronic lung disease, or RV infarction. Right ventricular strain has been studied for its prognostic value in patients with heart failure and acute pulmonary embolism and often helps guide management [30, 31]. Both CT and echocardiography can be used to assess RV strain. Right ventricular strain by echocardiography is often measured with either tissue doppler imaging or 2D speckle tracking. Using CT, RV strain is identified using RV-to-LV diameter ratio calculated from a four-chamber image, measuring the maximum distance from the interventricular septum to the endocardium. A normal RV / LV ratio is 0.9–1, moderate RV dilation corresponds to a RV/LV diameter ratio of $\geq$1.3 [32, 33]. Additional studies have shown that even in patients with a normal RV/LV ratio, an RV size greater than 45 mm on CT predicts the presence of increased RV strain in patients with acute PE and identifies a subset of patients with poorer overall outcomes [34].

Utility of CT in Emerging Transcatheter Tricuspid Valve Interventions

Traditionally, surgical management of TR had limited scope owing to early data suggesting that isolated left-sided valve repair or replacement led to improvement of TR, and thus, addressing the TV through surgical means was seldom necessary [35]. This was further supported by surgical case series where tricuspid valvulectomy without valve replacement in the setting of recurrent endocarditis led to a low incidence of ensuing treatment-refractory right heart failure [36]. Right ventricular dysfunction, liver cirrhosis, and renal disease are common comorbidities in patients

with severe TR and isolated TV repair or replacement confers an operative mortality on the order of 8–11% [37]. Due to this high perioperative risk and uncertainty surrounding patient selection, surgical volumes have remained low with approximately 5000 cases performed annually [37, 38]. However, more recent appreciation of the morbidity and mortality associated with severe TR has led to expanded surgical indications [39]. This paradigm shift in management has occurred in concert with rapid advances in transcutaneous valve repair and replacement devices that offer promising alternatives to surgical approaches.

Multimodality imaging has been essential to successful left-sided transcatheter interventions, and these imaging techniques are being adapted for use during right-sided procedures. While echocardiography is the cornerstone of preoperative and intraoperative imaging, MDCT has proven to be an important adjunctive modality as it offers an accurate assessment of TA and right chamber dimensions, landing zone geometry, caval size assessment, and analyses of possible anatomic impediments to intervention [40]. Two-dimensional (2D) echo and transesophageal echocardiography may provide incomplete assessments of right-sided cardiac structures owing to the unique geometry of the right ventricle, relative anterior positioning, and potential for acoustic shadowing in certain patient populations. MDCT is not bound by these restrictions and offers high-fidelity volumetric assessments via planimetered axial slices. Compared with CMR, MDCT offers superior spatial resolution and comparable chamber quantification when retrospective ECG-gated protocols are employed [41]. Lastly, CT data can be employed in 3D printing software applications to recreate the tricuspid valve apparatus as an adjunct to intervention planning [42].

Several transcatheter tricuspid valve repair and replacement devices have been developed and are in various phases of clinical testing. Broadly speaking, these systems target coaptation, annular reduction, leaflet edge-to-edge repair, heterotopic caval valve implantation, and orthotopic valve replacement (Fig. 7.6) [43, 44]. The complex and dynamic nature of the tricuspid valve apparatus and neighboring critical structures demand the high spatial resolution imaging afforded by CT. These anatomic considerations influence the choice in transcatheter device. In approximately two-thirds of patients with significant TR, the right coronary artery (RCA)

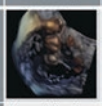
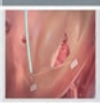
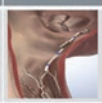
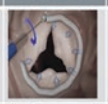
	A	B	C	D	E	F	G	H
Device Name	MitraClip	Trialign	TriCinch	Cardioband	Millipede	FORMA Repair System	Caval valve implantation	TRAIPTA
Device Image								
Description	Bicuspidisation of the TV by plicating	Bicuspidisation of the TV by plicating	Bicuspidisation of the TV by cinching	direct annuloplasty device	Complete semi rigid ring	Spacer to occupy the regurgitant orifice area	caval valve implantion in vena cava	Pericardial circumferential device
Access	Transfemoral	Transjugular	Transfemoral	Transfemoral	Transfemoral	Transsubclavian	Transjugular/ transfemoral	Transjugular/ transfemoral

Fig. 7.6 Major categories of transcatheter tricuspid valve repair technologies including direct suture annuloplasty, direct ring annuloplasty, indirect annuloplasty, coaptation enhancement, and valve replacement. TV tricuspid valve. (Reprinted with permission from Kuwata et al. [44])

courses within the atrioventricular groove adjacent to the anterior and posterior regions of the TA. In the remaining population, the RCA either courses superior to the tricuspid valve or crosses the horizontal plane of the TA [45]. The mean horizontal distance from the annulus to the RCA at the level of the anterior and posterior tricuspid leaflets is 6.8 mm and 2.1 mm, respectively [46]. The close proximity of RCA to the annulus poses a risk of coronary impingement and acute ischemia, particularly with the deployment annular reduction devices and when the RCA courses <2.0 mm from the annular ring [45]. As the noncoronary sinus of Valsalva is adjacent to the anteroseptal commissure, there is a risk of aortic perforation should a device be anchored at this level. The His bundle is located approximately 3–5 mm posterior to the anteroseptal commissure adjacent to the TV septal leaflet attachment on the membranous septum posing a risk of conduction block should this region be damaged. The TA sizing is important for plication, annular reduction, and valve replacement systems. Defining RV anatomy including RV apex-tricuspid annular distance is important for proper deployment of spacer devices. Delineating the caval borders is essential for sizing of heterotopic caval implants (Fig. 7.7) [45]. In transcatheter mitral valve replacement, left ventricular outflow obstruction is a feared complication and a major focus in preoperative CT imaging [41]. Unlike the continuity between the aortic valve and anterior leaflet of the mitral valve, the tricuspid and pulmonary valves are separated by a ventriculo-infundibular fold. This separation minimizes the risk of neo-right ventricular outflow obstruction during tricuspid valve replacement [41]. While no established imaging guidelines exist,

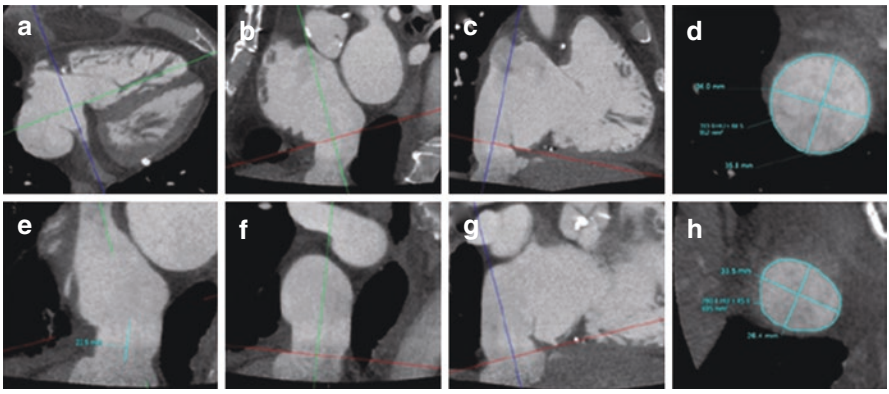


Fig. 7.7 Multi-planar CT reconstructions planes for assessment of the IVC dimensions prior to heterotopic caval implantation. (**a**) Orthogonal axial views of the right ventricular apex and the coronary sinus. (**b**) Single-oblique sagittal and coronal (**c**) views, aligned along the transition of right atrium and inferior vena cava parallel to the basal part of the coronary sinus to reconstruct a double-oblique transverse plane of the IVC at the entrance into the right atrium (**d**). Axial reconstructions positioned at the lower level of the IVC. The distance between the IVC at that point and the first hepatic vein can be measured (**e**). Using the single-oblique sagittal (**f**) and coronal (**g**) views, a double-oblique transverse plane of the IVC can be reconstructed to measure the maximal and minimal diameter, perimeter and area (**h**). IVC inferior vena cava. (Reprinted by permission of Oxford University Press from van Rosendael et al. [45])

device-specific CT imaging considerations are summarized in Table 7.2 and described in detail below [40]. Of note, interventions employing leaflet edge-to-edge repair devices such as Mitral Clip (Abbott, Abbott Park, IL) are heavily reliant on echocardiography and CT has a limited role in the preoperative planning.

CT Imaging of Transcutaneous Spacer Devices

Spacer devices, such as the Forma Repair System (Edwards Lifesciences, Irvine, CA), occupy the TV regurgitant orifice area to increase native leaflet coaptation, thereby reducing regurgitant volume (see Figs. 7.6 and 7.8) [47]. This particular device is a foam-filled polymer balloon spacer that is advanced via the left subclavian or axillary vein and placed through the TA over a rail that is subsequently anchored at the septal portion of the right ventricular apex. As detailed in early feasibility studies, ECG-gated MDCT is used to measure TA dimensions, RV diameters, TA–RV apex distance, and subclavian and axillary vein dimensions to ensure compatibility with the device and introducer sheath [47]. The configuration of the subvalvular apparatus including papillary muscles, the moderator band, and positioning of pacing leads (if present) are also assessed. Anchoring targets are selected by drawing a perpendicular line between the tricuspid plane and the RV septal free wall groove in a sagittal MDCT reconstruction perpendicular to the TA (Fig. 7.9). Based on this projection, fluoroscopic angles of coplanarity to the TA are created to assist in preoperative planning. Lastly, CT is also used in follow-up assessments to confirm rail system integrity and positioning [48].

CT Imaging of Transcutaneous Annular Reduction Devices

Annular reduction devices currently under investigation include the TriCinch (4Tech Cardio Ltd., Galway, Ireland), Millipede IRIS (Millipede, Inc., Santa Rosa, CA), Cardioband (Edwards Lifesciences, Irvine, CA), Trialign (Mitralign, Inc., Tewksbury, MA), and transatrial intrapericardial tricuspid annuloplasty (TRAIPTA) systems (see Fig. 7.6). Computed tomography has an important role in defining the course and distance of the RCA in relationship to the annulus as well as optimizing target positioning through short axis, long two- and four-chamber axis, and volume-rendered reconstruction views [45]. Damage to the RCA with annuloplasty devices is proportional to the distance and course of the RCA with respect to the annulus.

The TriCinch system is comprised of a stainless-steel corkscrew that is anchored in the anterior–posterior TA and linked via a Dacron band to a self-expanding nitinol stent deployed in the IVC between the hepatic and right renal veins. When tension is applied, the septal–lateral annular dimensions are reduced improving the degree of functional TR. First-in-human and feasibility studies have employed CT to identify the optimal anchoring site at the anterior aspect of the TA between the

Table 7.2 Key anatomic considerations during computed tomographic pre-procedural assessment according to anatomic therapeutic target

Device	Anatomic features	Imaging views
Coaptation devices	• Tricuspid annular dimensions (anteroposterior and septal-lateral diameter, perimeter, area), midventricular diameter • Distance from the TA to the right ventricular apex • Target anchoring site • Left subclavian and axillary vein	• Short axis of the TA • Long-axis 4-chamber • RV long-axis 2-chamber • Coronal reconstruction
Annuloplasty devices	• Course of the RCA relative to the TA • Distance from RCA to the anterior and posterior tricuspid leaflet insertion • Optimal anchoring target	• Volume-rendered reconstruction, long-axis 2- and 4-chamber, short-axis • Short-axis of the TA and long-axis 4-chamber • Short-axis of the TA
Heterotopic CAVI	• IVC size at the cavoatrial junction and at the level of the first hepatic vein • Distance between the cavoatrial junction and the first hepatic vein	• Double oblique transverse plane of the inferior cavoatrial junction and at the level of the first hepatic vein • Single oblique sagittal plane of the IVC
Orthotopic TTVR	• Tricuspid annular dimensions (anteroposterior and septal-lateral diameters, perimeter, area) • Right internal jugular vein and SVC size • Course of the RCA relative to the TA • Distance from RCA to the anterior and posterior tricuspid leaflet insertion • Risk for ROVT obstruction	• Short axis of the TA Double oblique transverse plane • Volume-rendered reconstrucion, long-axis 2- and 4-chamber. short-axis • Short-axis of the TA and long-axis 4-chamber • Sagittal oblique reconstruction and short axis of the RVOT

CAVI **caval valve implantation,** *RCA* **right coronary artery,** *RVOT* **right ventricular outflow tract,** *SVC* **superior vena cava,** *TA* **tricuspid annulus,** *TTVR* **transcatheter tricuspid valve replacement**

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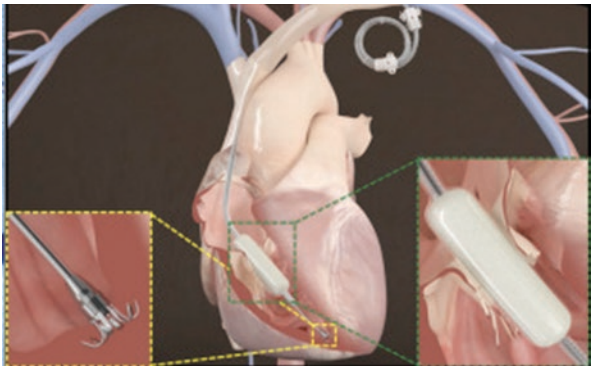

Fig. 7.8 The FORMA Repair System [47]. A foam-filled polymer balloon spacer that is advanced via the left subclavian vein and placed within the tricuspid annulus anchored at the septal portion of the right ventricular apex. (Reprinted from Campelo-Parada et al. [47], Copyright 2015, with permission from Elsevier)

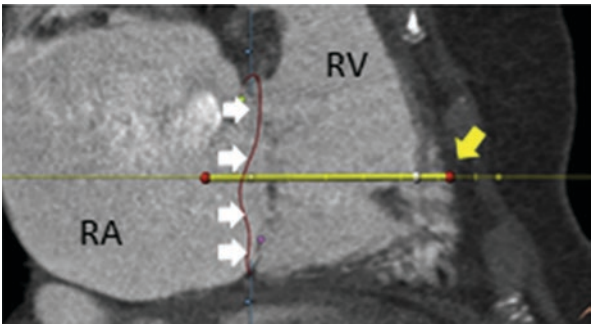

Fig. 7.9 Contrast CT–derived reconstructions of the right heart in preparation for FORMA device placement. Sagittal reconstruction delineating the annular plane (white arrows) and the planned anchoring site (yellow arrow). (Reprinted from Perlman et al. [48], Copyright 2017, with permission from Elsevier)

RCA and anterior leaflet hinge point to avoid coronary impingement. CT is also used to ensure appropriate IVC stent sizing (see Fig. 7.7) [49, 50].

The Millipede IRIS transcatheter system consists of a semi-rigid closed annular ring anchored via stainless steel screws on the atrial aspect of the TA. Once placed, adjustable sliding collars are cinched over the collapsible zig-zag nitinol frame to reduce the annular dimension. Initially, the device was surgically placed in the mitral position with the subsequent development of a transcatheter delivery system [51]. The device has since been surgically implanted in the tricuspid valve position and a dedicated transcatheter delivery catheter is currently under development [52]. MDCT is used to define pre- and post-procedure atrial and ventricular volumes as well as annular dimensions (see Fig. 7.6).

The Cardioband system consists of a contraction wire embedded in a polyester sleeve implanted on the atrial side of the TA from the anteroseptal to the septo-posterior commissures via a series of anchors. Once the device is placed, the contraction wire is then cinched, decreasing annular dimensions and reducing TR mimicking the surgical placement of an incomplete annuloplasty ring [53]. Based on initial imaging experience in the mitral space, CT-guided preoperative planning

has been adopted in the tricuspid valve for use in assessing annular size and width, planning of fluoroscopic views, and mitigating risk to injury to the RCA [54, 55].

The Trialign system is a transcutaneous mimic of the modified Kay procedure that leads to bicuspidization of the tricuspid valve via pledgeted sutures that are subsequently cinched to decrease annular dimensions (see Fig. 7.6). First-in-human and early feasibility studies did not rely heavily on CT imaging; however, CT can be used as an adjunctive modality to define tricuspid anatomy and to localize the RCA course to avoid injury [41, 56, 57].

The TRAIPTA device is an indirect annuloplasty system that consists of a nitinol loop introduced inside the pericardium via the right atrial appendage, and encircling the heart along the atrioventricular groove to reduce annular dimension. Preclinical animal testing studies utilized CT to study the presence of a discrete right atrial lobe to facilitate access, clearly demarcate the atrioventricular groove, and define coronary artery course to assess deployment feasibility [58, 59].

CT Imaging of Heterotopic Caval Valve Implantation

Heterotopic caval valve implantation involves the deployment a bioprosthetic valve in the IVC and/or SVC and has been demonstrated to reduce venous pressure overload and to improve clinical symptoms [60]. Commercially available balloon expandable transcatheter aortic valve replacement (TAVR) valves have also been employed for this purpose with the assistance of pre-implantation caval stents to ensure stable positioning [61]. Compared with patients who have mild-to-moderate TR, those with severe TR can have variably larger IVC diameters that may not be compatible with these repurposed devices [45]. Diameters of the IVC and SVC may reach 35 and 40 mm, respectively, and the mean distance between the inferior cavoatrial junction and the most superior hepatic vein is 14.1 ± 5.4 mm, which is shorter than the width of some existing TAVR valves [62–64]. Thus, tailored bioprosthetic caval implants, that is, TricValve (P&F Products & Features Vertriebs GmbH, Vienna, Austria), have been developed. With these systems, CT plays an important role in caval dimension assessments to assist in prosthetic device customization, if needed, and to avoid complications such as hepatic vein obstruction or device embolization. Necessary imaging information includes obtaining IVC maximal and minimal diameter, perimeter, and area at the cavoatrial junction and at the level of the first hepatic vein as well as the distance between these two anatomical landmarks during mid-diastole (see Fig. 7.7). In the SVC, the diameter of the vein is measured at the superior cavoatrial junction. These dimensions can be obtained via double-oblique transverse and single-oblique sagittal reconstructions at these three respective anatomical positions [45].

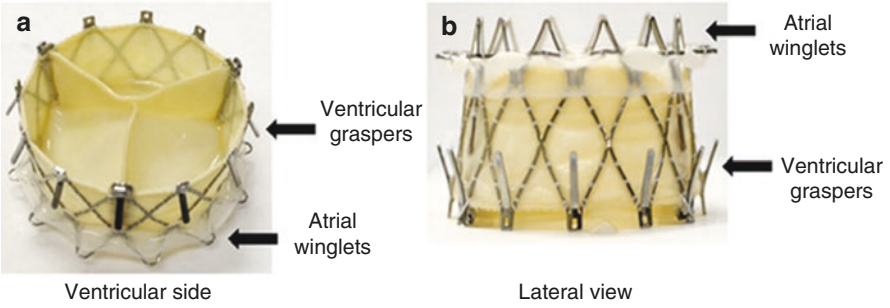

Fig. 7.10 NaviGate-valved stent (**a**) ventricular side and (**b**) lateral view showing nitinol frame with atrial winglets and ventricular graspers to secure positioning. (Reprinted with permission from Navia et al. [67])

CT Imaging of Orthotopic Transcatheter Tricuspid Valve Implantation

Total transcatheter bioprosthetic valve replacement represents an exciting evolution in the management of structural heart disease. For the tricuspid valve, this option had previously been limited to patients who had a prior surgical TV repair with a ring (valve-in-ring) and those with prior bioprosthetic TV (valve-in-valve) implants for failed TV annuloplasty and degenerative bioprosthetic valves, respectively. Cross-sectional imaging with CT has been variably used in these procedures [65, 66]. This area is rapidly evolving with the advent of dedicated fully orthotopic transcatheter tricuspid valve replacement options, that is, Navigate (NaviGate Cardiac Structures, Lake Forest, CA). This device consists of a self-expanding tapered nitinol stent with atrial winglets and ventricular graspers to allow for secure anchoring in the tricuspid annulus (Fig. 7.10). First-in-human studies detail the importance of CT in the pre- and postoperative assessments [67]. Four-dimensional (respiration-correlated) CT provides a phase-resolved visualization of tissue motion, effectively providing 3D cine imaging. This can be used to create a 3D printing model of right heart structures to simulate procedural implantation. As with other transcutaneous devices, CT is used to assess chamber quantification, tricuspid annulus, and vascular assess structures. Similar to heterotopic caval devices, CT image acquisition may include short axis views of the TA and RVOT, long-axis two- and four-chamber views, volume-rendered reconstructions, and sagittal- and double-oblique reconstructions (see Figs. 7.1, 7.2, and 7.3). Multiple additional devices are in development and various stages of clinical testing [40, 43].

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Chapter 8
Carcinoid Heart Disease

Lavanya Kondapalli, Amber Berning, Suparna C. Clasen, and Rhonda Miyasaka

Abbreviations

3D	three-dimensional
CHD	carcinoid heart disease
CW	continuous wave
MPR	multiplanar reconstruction
MRI	magnetic resonance imaging
NT-proBNP	pro-B-type natriuretic peptide
TEE	transesophageal echocardiography
TTE	transthoracic echocardiography

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Case Presentation

A 55-year-old male with no significant past medical history presents for evaluation of progressive shortness of breath and new onset leg swelling. He is a regular exerciser and has new windedness 20 min into a workout for the past several months. In the past few weeks, he has developed new bilateral lower extremity swelling, notes occasional palpitations, and has lightheadedness upon bending down to tie his shoes. He denies angina, orthopnea, paroxysmal nocturnal dyspnea, syncope. Review of systems notable for diarrhea. His vitals are within normal limits and his electrocardiogram is unremarkable. On exam, he is compensated, jugular venous pressure is estimated at 12 mm Hg with a prominent V-wave, he has a prominent right ventricular heave, a III/VI systolic ejection murmur at the left sternal border which increases with inspiration is heard, and he has 2+ bilateral lower extremity edema. You suspect carcinoid heart disease and N-terminal pro-B-type natriuretic peptide (NT-proBNP) of 510 ng/mL, urine 5-H1AA of 791 μmol/24 h and transthoracic echocardiogram (Fig. 8.1) confirm your diagnosis.

Incidence and Epidemiology of Carcinoid Heart Disease

Heart disease and cancer are leading causes of morbidity and mortality in the United States. In 2019, the prevalence of cardiovascular disease in people ≥20 years old was estimated at 48.0% which in 2016 amounted to 121.5 million adults [1]. In 2018, it was estimated that 1.74 million new cases of cancer were diagnosed [2]. In contrast, neuroendocrine tumors like carcinoid are rare with an incidence of 2.5 to

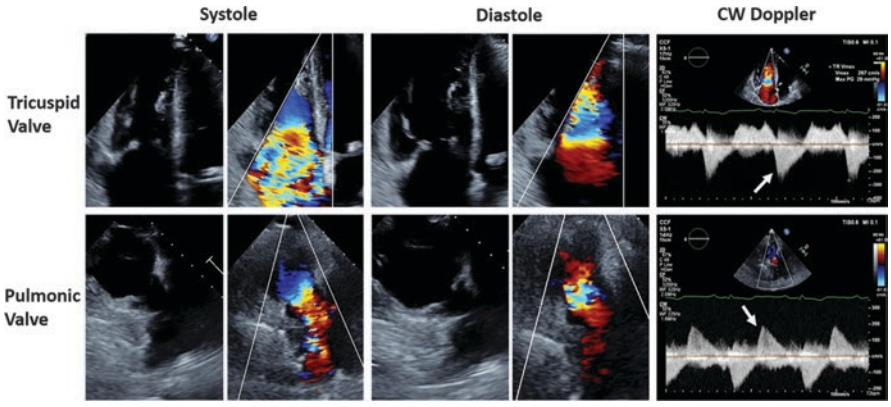

Fig. 8.1 Transthoracic echocardiography of classic tricuspid and pulmonic carcinoid valve disease. Note the thickened and retracted leaflets with lack of coaptation causing severe tricuspid and pulmonic regurgitation. CW Doppler of tricuspid regurgitation and pulmonic regurgitation jets shows a dense, triangular waveform consistent with severe regurgitation (arrows)

5 cases per 100,000 people although incidence is increasing and a small subset of these cases will have carcinoid heart disease [3].

Neuroendocrine tumors are neoplasms that have characteristic neuroendocrine differentiation, can arise in various locations, and may cause symptoms related to vasoactive peptide release [3]. "Carcinoid" refers to neuroendocrine tumors arising from the gastrointestinal tract. Carcinoid tumors are indolent and typically do not cause symptoms until the tumor is large or metastasized. Carcinoid syndrome refers to the presence of a constellation of symptoms including secretory diarrhea, bronchospasm, and episodes of vasomotor changes (e.g., flushing and hypotension, rarely hypertension). Typically, carcinoid syndrome is thought to occur when vasoactive substances originating from the carcinoid tumor or metastases reach the systemic circulation through the hepatic vein. It is estimated that of people with neuroendocrine tumors, 30–40% will have carcinoid syndrome and 20–50% of patients with carcinoid syndrome will have carcinoid heart disease [4].

Carcinoid heart disease (CHD) is associated with high morbidity and mortality. In 1993, Pellikka et al. reported on 74 patients with carcinoid syndrome and found that those with echocardiographic evidence of carcinoid heart disease had a median survival of 1.6 years, which was significantly worse than patients without cardiac involvement [5]. A more recent retrospective study on 200 patients with carcinoid heart disease also at the Mayo Clinic found that that the median survival for patients diagnosed between 1981 and June 1989 was 1.5 years (95% CI 1.1–1.9 years), for patients diagnosed in July 1989–May 1995 it was 3.2 years (95% CI 1.3–5.1 years), and for patients diagnosed in June 1995–2000 it was 4.4 years (95% CI 2.4–7.1 years) [6]. Survival rates have likely improved due to use of somatostatin analogues and surgical intervention.

Pathophysiology of Carcinoid Heart Disease

Carcinoid heart disease is characterized by the development of plaques along the endocardial surface of the valve leaflet, and primarily affects the right-sided valves; the left side is seldom affected, owing to inactivation of vasoactive substances by the lung vasculature. Grossly, the plaques present as thickening of the valve with focal commissural fusion and associated thickening of the subvalvular apparatus, like findings seen in rheumatic heart disease (Fig. 8.2). Microscopically, the plaques are composed of a proliferation of bland-appearing myofibroblasts; extracellular components such as collagen, myxoid matrix, and elastin; and an overlying endothelial layer. Chronic inflammation as well as neovascularization can be seen within the plaques. Damage to the underlying valve is not characteristic (Fig. 8.3). The elaboration of serotonin by the primary or metastatic tumor is implicated in the development of CHD. Activation of 5-hydroxytryptamine 2B receptors has been shown to promote myofibroblast deposition and the activation of valvular interstitial cells, which results in the fibrosis seen in CHD [7–9].

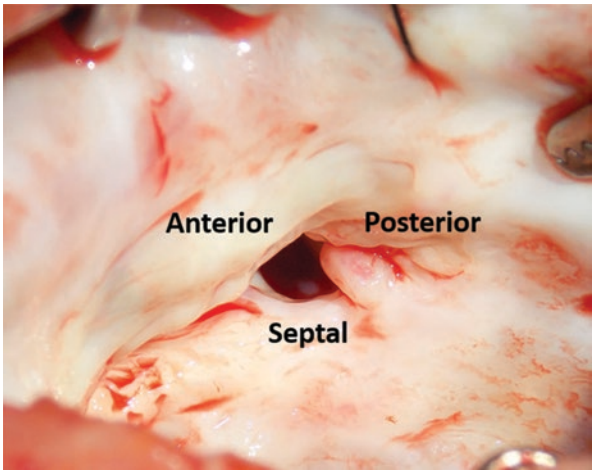

Fig. 8.2 Surgical photo of a tricuspid valve with severe carcinoid involvement. Note the leaflets are thickened, retracted, and fixed in a semi-open position

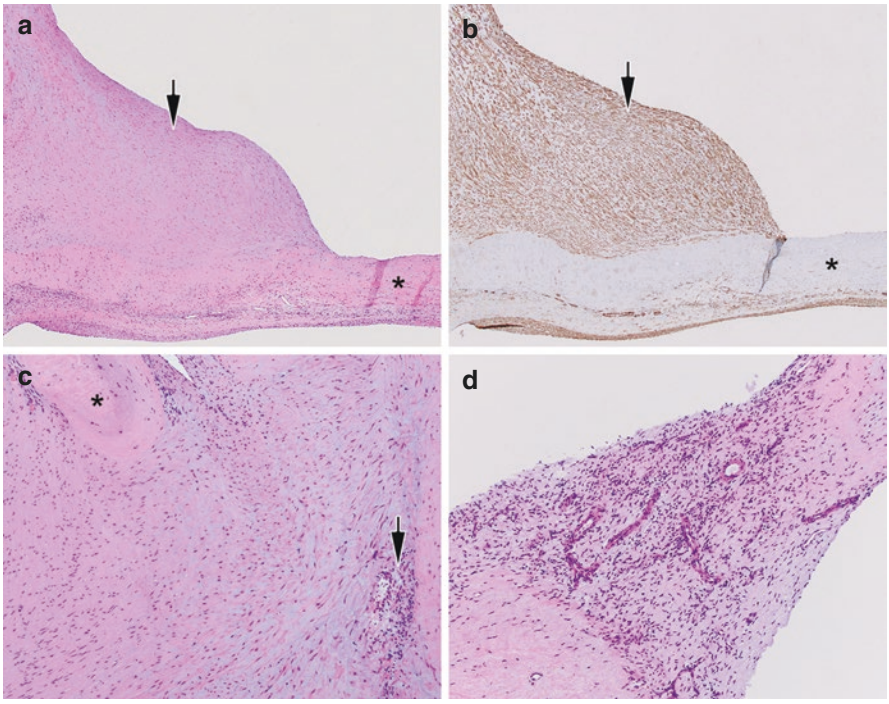

Fig. 8.3 Histology of carcinoid heart disease. (**a**) Myofibroblastic proliferation (carcinoid plaque) involving the left side of the tricuspid valve (arrow); the strip of valve on the right is uninvolved (*). (**b**) Smooth muscle actin immunohistochemistry highlighting the myofibroblastic proliferation (arrow); the uninvolved valve is negative (*). (**c**) Bland proliferation of spindled myofibroblasts with associated extracellular matrix; underlying cardiac valve is present in the upper left-hand corner (*) and chronic inflammation in the lower right-hand corner (arrow). (**d**) Neovascularization within the carcinoid plaque

Surveillance and Diagnosis of Carcinoid Heart Disease

Several biomarkers have been correlated to carcinoid heart disease including NT-proBNP, urinary or plasma 5-HIAA, chromogranin A, and actin A. In 2017, an expert consensus statement on carcinoid heart disease recommended that NT-proBNP was the best biomarker available for screening patients with carcinoid syndrome for carcinoid heart disease. This expert panel proposed that patients with metastatic neuroendocrine tumors undergo a clinical assessment and check NT-proBNP every 6 months. If the NT-proBNP is greater than 260 ng/mL or there are clinical suggestions of carcinoid heart disease, then a transthoracic echocardiogram should be performed. It can be useful to also keep track of a patient's urinary 5-HIAA level since values >300 μmol/24 h increase a patient's risk of developing carcinoid heart disease [4]. Unfortunately, carcinoid heart disease can progress quickly so regular follow up of patients with carcinoid syndrome is critical. Bhattacharyya et al. prospectively followed 252 patients with carcinoid syndrome at 6-month intervals and noted progression of carcinoid heart disease if the echocardiographic score they utilized increased by ≥25% from the prior 6 months. With a median follow-up for 29 months, 44 patients had progression of existing carcinoid heart disease or new carcinoid heart disease diagnosed [10].

Echocardiographic scoring systems have been developed to characterize carcinoid heart disease and predict progression. For example, in patients with carcinoid heart disease, a score which graded the following features from 0 (normal) to 3 (severe): leaflet thickening/mobility/morphology, valvular stenosis/regurgitation and right ventricular diameter/function correlated with NT-pro-BNP levels [11]. In a study of 137 patients with metastatic neuroendocrine tumors, a 5-point increase in echocardiographic score correlated with increased risk of CHD progression (OR 2.95, 95% CI 1.71–5.09, $p < 0.005$) and death (OR 2.66, 95% CI 1.63–4.35, $p < 0.005$) [12]. A comparison of six available echocardiographic scoring systems found all had similar sensitivity and specificity for identifying CHD however more complex scores may be better for patients with CHD who may need surgery [13].

Imaging

Echocardiography is the gold standard diagnostic test for the screening and serial evaluation of carcinoid heart disease [4]. As the right-sided heart chambers are anteriorly located, close to the chest wall, transthoracic echocardiography (TTE) typically provides excellent imaging of the right ventricle, tricuspid valve, and pulmonic valve. Two-dimensional and three-dimensional imaging provides information on valvular structure and function, and Doppler assessment is used to quantitate the severity of valve dysfunction. Echocardiographic evaluation of right ventricular size and function is also essential. If TTE does not provide adequate valvular evaluation, transesophageal echocardiography (TEE) may also be a useful imaging modality.

As previously mentioned, carcinoid heart disease is characterized by the deposition of carcinoid plaques, primarily on the right-sided heart structures. There is a wide spectrum of imaging findings that have been described [14], ranging from mild valvular thickening to severe valvular dysfunction. On echocardiography, there is a classic appearance of the tricuspid and pulmonic valves. The leaflets and subvalvular apparatus appear thickened and retracted, and in the case of severe disease, the valves appear rigid and stuck in a semi-open position (Fig. 8.1). This leads to a combination of stenosis and regurgitation. Valvular function is assessed with the use of color flow Doppler and continuous wave (CW) doppler, and the severity of stenosis or regurgitation should be graded accorded to guidelines [15]. With severe carcinoid tricuspid valve disease, color Doppler will reveal turbulent diastolic inflow suggestive of tricuspid stenosis as well as severe tricuspid regurgitation. CW Doppler through the tricuspid valve will reveal a dense, triangular-shaped regurgitant jet consistent with severe tricuspid regurgitation, as well as elevated inflow gradients indicative of tricuspid stenosis. The combination of stenosis and regurgitation will often show "to and fro" flow across the valve.

With three-dimensional (3D) imaging, the valves can be visualized *en face* and, in the case of severe disease, may reveal a triangular-shaped orifice with no central coaptation, and little change in systole or diastole (Fig. 8.4). Multiplanar reconstruction (MPR) can be used to evaluate all leaflets and 3D planimetry can be performed to estimate valve area or regurgitant orifice area (Fig. 8.4) [16].

Although carcinoid disease most commonly involves the tricuspid and pulmonic valves, left-sided structures, such as the mitral and aortic valves, may also be

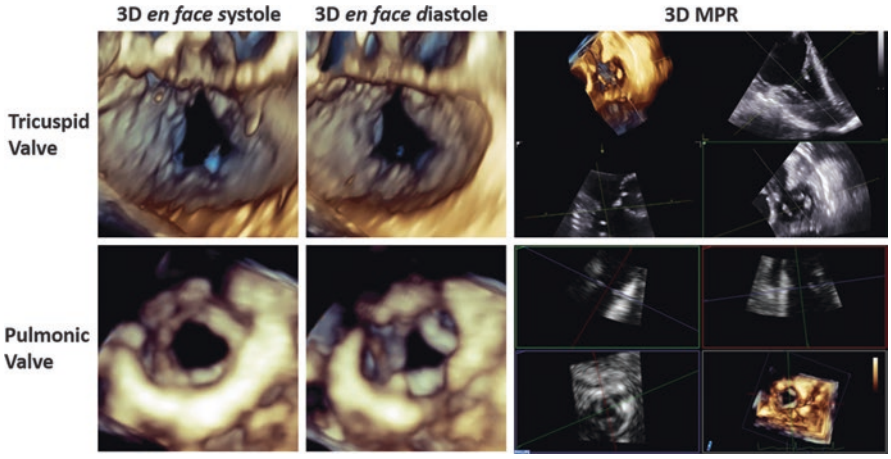

Fig. 8.4 Three-dimensional transesophageal echocardiography (3D TEE) of the tricuspid and pulmonic valves. 3D *en face* views allow simultaneous visualization of all three leaflets and highlight minimal leaflet excursion in systole versus diastole. 3D multiplanar reconstruction (MPR) allows simultaneous visualization of long axis and short axis views. 3D planimetry of the short axis view can be performed to measure valve area or regurgitant orifice area

affected, particularly in the presence of a patent foramen ovale [14]. Rarely, carcinoid tumors may metastasize to the heart, which is characterized by a well-circumscribed mass that may be seen in either of the ventricular walls or interventricular septum [7]. For this reason, a comprehensive echocardiographic exam is necessary, including evaluation for right to left shunt with agitated saline contrast study.

In addition to echocardiography, cardiac magnetic resonance imaging (MRI) may be helpful in the evaluation of patients with carcinoid heart disease. Cardiac MRI can provide a quantitative assessment of right ventricular size and function, evaluate for the presence of metastases, and can also provide information on valvular structure and function [7].

Management of Carcinoid Heart Disease

Successful management of carcinoid heart disease relies on a team-based approach. Key members of the team include the patient, cardio-oncologist, oncologist, cardiothoracic surgeon, and cardiothoracic anesthesiologist. From a cardiac standpoint, the focus of care is on management of right heart failure and identification of the need for cardiac surgery. Daily weights, fluid restriction, and careful diuretic administration are necessary given the side effects of decreasing preload in right heart failure. Compression stockings and salt restriction are also important. Spironolactone can be considered given the potential benefit to the right heart [17].

Somatostatin analogues are the cornerstone of carcinoid treatment and prevent the development and/or progression of carcinoid heart disease [4]. Somatostatin analogues decrease circulating levels of serotonin and bioactive metabolites. The two currently available somatostatin analogues are octreotide and lanreotide and long-acting formulations are used for treatment of symptomatic carcinoid. Use of these analogues is expanding as studies have shown benefit in asymptomatic patients with carcinoid with regards to progression-free survival [18, 19]. Telotristat ethyl is approved by the Food and Drug Administration for refractory symptoms and interferon alfa is an approved agent in Europe. Everolimus, an mTOR inhibitor, should be used with caution in carcinoid heart disease and held for 2–4 weeks prior to procedures, including heart surgery [4]. Peptide receptor radionucleotide therapy (PRRT) is a type of treatment in which radionucleotide therapy is delivered systemically to tumor cells and is contraindicated in patients with decompensated heart failure due to the administration of intravenous fluids involved with the treatment [4, 20]. Transcatheter arterial embolization or chemoembolization of hepatic metastases should be used with caution in severe carcinoid heart disease and right ventricular dysfunction. Surgical debulking of hepatic metastases may be an option after valve replacement for carcinoid heart disease [4].

Carcinoid Crisis

Carcinoid crisis is of concern in the peri-procedure period [21]. Carcinoid crisis refers to the constellation of flushing, hypotension, and bronchospasm, which can result from administration of catecholamines and histamine-releasing drugs or from events that trigger catecholamine release like emotional stress, hypercapnia, hypothermia, hypotension, or hypertension [22]. Octreotide administration prior to and during the procedure can provide hemodynamic stability and should be readily available during procedures for patients with carcinoid. Patients should be educated on their potential need for octreotide prior to procedures and encouraged to proactively discuss the sedation plan with the anesthesiology team at preoperative visits. Cardiac surgery in patients with carcinoid heart disease can be particularly challenging given the need to manage low cardiac output secondary to right heart failure on top of carcinoid crisis. Cardiothoracic anesthesiologists with experience managing carcinoid heart disease may be best suited to provide anesthesia support in these cases. Many institutions have octreotide protocols in place to manage carcinoid crisis in the perioperative period.

Surgery

Surgical timing depends on heart failure symptoms, right heart function, and how well-controlled carcinoid syndrome is. Cardiac surgery for carcinoid heart disease typically focuses on tricuspid valve replacement. However patients may also need pulmonic valve replacement, closure of a patent foramen ovale to avoid transmission of vasoactive substances to the left-sided valves, replacement of other valves, bypass grafting, removal of intramyocardial carcinoid metastases, and patch enlargement of the right ventricular outflow tract. Optimal timing of surgery is not clear and requires a collaborative discussion between members of the patient's care team. Current consensus guidelines recommend referral to cardiac surgery when symptoms or ventricular dysfunction are present, anticipated survival of at least 12 months postoperatively, and rarely as a precursor to hepatic surgery [4]. The decision of mechanical versus bioprosthetic valves should be individualized with considerations given to the need for future oncologic procedures, bleeding risks associated with liver disease and structural valve deterioration [23]. The oncologist should weigh in regarding how controlled a patient's carcinoid syndrome is in the presurgical period and recommendations for somatostatin analogue dosing in the perioperative period.

Cardiac surgery can improve heart failure functional class and lengthen survival. A study of 22 patients who underwent valve replacement between 2006 and 2010 showed that those who survived surgery had significant improvement in New York Heart Association functional class at 3 months [24]. A contemporary review of 240

patients who underwent valve replacement for carcinoid heart disease between November 1985 and January 2018 revealed survival estimates at 1 year was 69%, 3 years was 48%, and 5 years was 34%. Early mortality rate after valve surgery also decreased over time, 29% between 1985 and 1994, 7% between 1995 and 2004, and 5% since 2005 [25].

Bioprosthetic Valve Deterioration

Bioprosthetic valve deterioration has been reported after valve replacement to treat carcinoid heart disease. Castillo et al. reported the need for redo tricuspid and pulmonic valve replacement at 25 months in a 47-year-old male with carcinoid heart disease who underwent resection of the primary carcinoid tumor in the ileum and liver lobectomy after his initial cardiac surgery. These authors surmise that high levels of serotonin and 5-HIAA despite optimal medical therapy contributed to the early deterioration of the initial prosthetic valves. They performed the patient's redo surgery with mechanical tricuspid and pulmonic valves [26]. In Bhattacharya et al.'s aforementioned study of 22 patients undergoing cardiac surgery, 2 developed bioprosthetic valve degeneration [24]. Another surgical outcomes study of 39 patients treated with surgery for CHD reported 2 had valve deterioration treated with valve-in-valve transcatheter aortic valve replacement [27].

Percutaneous Interventions in Carcinoid Heart Disease

Percutaneous interventions to treat carcinoid heart disease is a burgeoning area. Percutaneous native pulmonic valve replacement with the Melody valve and the Edwards Sapien XT have been reported to treat CHD in patients who were considered high surgical risk [28–30]. Conradi et al. reported on two patients who previously had bioprosthetic tricuspid and pulmonic valve replacements who were treated with valve-in-valve replacement of the pulmonic valve [31]. Transcatheter, transapical tricuspid, and pulmonary valve-in-valve replacements with the Edwards Sapien XT valves has been described to treat failing bioprosthetic tricuspid and pulmonic valves in carcinoid heart disease [32]. Transcatheter treatment of native tricuspid valve disease (without CHD) is challenging due to the large tricuspid annular size, lack of fibrous skeleton for support, highly variable tricuspid anatomy, and complex subvalvular apparatus. There are several transcatheter tricuspid valve replacement devices under investigation for the treatment of native tricuspid valve regurgitation; however, to date, percutaneous valve replacement of the native tricuspid valve affected by carcinoid heart disease has not yet been reported, but this is an area of great interest for future investigation.

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Part II
Current Management of Tricuspid Valve Disease

Chapter 9
The Surgical Management of Tricuspid Valve Disease

Aaron M. Williams, Alexander A. Brescia, Tessa M. F. Watt, Curtis S. Bergquist, and Steven F. Bolling

Introduction

Although previously considered the "forgotten valve," there has been increasing interest in the surgical management of patients with tricuspid valve (TV) pathology [1]. Moderate-to-severe tricuspid regurgitation (TR) impacts nearly 1.6 million people in the United States (US) [2]. Despite an incidence of nearly 200,000 TR cases per year, only 8000 tricuspid valve (TV) operations are performed annually in the US [3]. As a result, the TV has also been considered the "undertreated valve."

The most common TV pathology in developed countries is TR, while tricuspid stenosis (TS) remains a rare but complex disease. Primary TR can be from a leaflet pathology or congenital disorder, while functional or secondary TR remains the primary etiology of tricuspid insufficiency. In functional TR, left-sided heart disease can lead to right ventricle (RV) overload resulting in RV dilation, tricuspid annulus (TA) dilatation, and, eventually, functional TR. After onset, patients can develop significant life-limiting symptoms and decreased quality of life [4]. TR patients have also been shown to have increased morbidity, prolonged hospitalization, higher rates of rehospitalization, and worse long-term survival [5–7]. As such, providers must be well versed to manage TV pathologies by understanding the history, anatomy, pathophysiology, and current surgical options for addressing TV disease.

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Historical Perspective

Historically, the TV was considered the "forgotten" or "untreated valve" [8]. There are many reasons contributing to this historical perspective. First, patients with right-sided endocarditis were classically treated with TV excision, which would secondarily leave patients with torrential TR. This was thought to be well tolerated, although true long-term data in this population remained limited. Second, many surgeons previously believed that TR was simply a bystander of left-sided heart pathologies that required surgical correction. Third, many surgeons and cardiologists focused primarily on the presence of TR alone, rather than other risk factors suggestive of worsening TR including annular dilatation. Lastly, the impact of TR on morbidity and mortality was often hidden behind the outcomes of a patient's left-sided heart pathology.

In recent years, however, we now know that TR does not improve following left-sided heart surgery alone and the presence of TR can impact a patient's long-term survival [5–7]. We have also been able to better study the impact of TR on clinical outcomes now that patient's survival from left-sided heart disease has improved. It has also been demonstrated that other independent risk factors, such as annular dilatation, are better predictors of late TR. As we been able to better study the impact of TV pathologies in recent years, the importance of surgical management has reemerged.

Tricuspid Valve Anatomy

To provide optimal surgical management for patients with TV pathology, surgeons must understand relevant surgical anatomy. The TV apparatus consists of three distinct leaflets including the anterior, posterior, and septal leaflets. These leaflets are highly variable in size, although generally the anterior leaflet is the largest, while the septal is the smallest. The anterior and posterior leaflets are anchored to an anterior papillary muscle, while the septal and posterior leaflets are attached to the posterior papillary muscle. The interventricular septum is responsible for anchoring both the anterior and septal leaflets to the chordae tendinae, as there is no septal papillary muscle [4]. Accessory chordal attachments involving the RV free wall and moderator band are also present [4]. Despite this anatomy, these chordal attachments remain highly variable and can potentially result in improper leaflet coaptation during TV pathology [8].

Numerous important nearby structures also require recognition during surgery. The atrioventricular (AV) node is located adjacent to the atrial septum near the septal leaflet. The bundle of His, which is an extension of the AV node, runs along the crest of the interventricular muscular septum. The right coronary artery (RCA) runs just anterior to the anterior tricuspid leaflet annulus. These structures are important to be aware of as no sutures should be placed in these regions to prevent myocardial

ischemia and conduction block. Furthermore, the near proximity of the AV node to the TV apparatus has also led to the widespread use of incomplete annular rings to minimize risk of developing iatrogenic arrhythmias.

The geometry of the TV apparatus also requires highlighting. The tricuspid annulus (TA) is collagenous ring that serves as the line of attachment for the TV leaflets. It is often a thin ring, but plays a key role in affording the dynamic shape and size of the TA. In normal physiologic conditions, the TA has a non-planar, semi-lunar, three-dimensional (3D) saddle-shape configuration [9]. In this setting, the anteroseptal TA portion remains at the highest location in the TA, while the postero-septal portion is seated in the lowest position. During each cardiac cycle, the TA is highly dynamic as the annular circumference can decrease by 19% during atrial systole [10]. When TV pathology occurs, this nonplanar TA orientation becomes disrupted and can cause a more planar and circular shape, resulting in TA dilatation. As such, restoring the TA configuration through annular reduction remains crucial to restoring the standard anatomy for patients who develop TR.

Tricuspid Valve Pathophysiology and Clinical Features

Tricuspid Regurgitation

Tricuspid regurgitation can result from primary valve pathology in nearly 25% of cases and can involve rheumatic, myxomatous, congenital, endocarditis, and other etiologies (Table 9.1). However, TR is most commonly considered functional or secondary, which has been shown in 75% of cases [11]. A left-side heart pathology, such as left ventricle (LV) dysfunction, valve disease, or atrial fibrillation, can ultimately result in RV dysfunction, TA dilation, and subsequent TR development. The development of functional TR can be classified into three stages of progressive disease [12]:

Stage I: Early TA Dilation
In stage I, regardless of etiology, the TA exhibits early dilation, typically secondary to RV enlargement. Secondary or functional TR may or may not be present in this early of the disease process.

Stage II: Moderate TA Dilation and Abnormal Leaflet Coaptation
TA dilation worsens as the RV function and dilation progressively worsening. The anterior and posterior leaflets are predominately affected in this process. As this happens, malcoaptation occurs secondarily between the anteroposterior and posterolateral commissures. The severity of functional TR also worsens accordingly.

Stage III: Severe TA Dilatation and Tricuspid Leaflet Tethering
As RV dilation continues to worsen, the TA dilation becomes so severe that it causes tethering of the tricuspid leaflets. This can severely impact leaflet attachments and cause severe or worse TR.

Table 9.1 Primary and secondary etiologies of tricuspid regurgitation

Primary etiologies (25%)
Rheumatic
Myxomatous
Ebstein's anomaly or other congenital disease
Endomyocardial fibrosis
Endocarditis
Traumatic
Iatrogenic (pacemaker/defibrillator lead, RV biopsy)
Secondary etiologies (75%)
Left heart disease (LV dysfunction or valve disease)
Any cause of pulmonary hypertension
Any cause of RV dysfunction (myocardial disease, RV ischemia/infarction)

LV left ventricular, *RV* right ventricular

Clinically, patients with moderate-to-severe TR often present with symptoms secondary to decreased cardiac output including weakness and fatigue. Jugular venous distention can be common when an increase in venous return in accentuated through inspiration. Once it develops, right-sided heart failure can lead to ascites, hepatomegaly, cirrhosis, and peripheral edema. In the latter stages of the disease, patients often develop cyanosis and even hepatic cardiac cirrhosis. Patients with mild TR are often asymptomatic.

Tricuspid Stenosis

Tricuspid stenosis is a pathology classically related to rheumatic heart disease, although other etiologies exist (Table 9.2). Even in this setting, isolated TS is rare and more commonly a varying degree of concurrent TR. Similar to mitral valve disease, TS most commonly affects young women. In the early stages, TS involves shortening of the chordae and leaflet thickening, while in later stages involves fusion of the free edges and calcified deposits on the TV.

After TS begins, the diastolic gradient between the RA and RV begins to increase. As the RA pressure increases, venous congestion occurs and the right atrial wall can even thicken and become dilated.

Clinically, patients may present with decreased cardiac output, resulting in malaise and fatigue, along with ascites, peripheral edema, and anasarca. These symptoms can even mask or impact symptoms of patients with decreased left-sided blood flow secondary to mitral stenosis.

Table 9.2 Etiologies of tricuspid stenosis

Immunological disease
Rheumatic heart disease
Antiphospholipid syndrome
Systemic lupus erythematosus
Infective endocarditis
Tumors
Myxoma
Carcinoid syndrome
Others
Congenital abnormalities
Ebstein's anomaly
Iatrogenic
Ventriculoatrial shunts
Fusion of ICD or PPM leads to subvalvular structures
Metabolic, enzymatic, or drug related

ICD implantable cardioverter defibrillator, *PPM* permanent pacemaker

Table 9.3 2014 ACA/AHA recommendations

Recommendation	Class	Level of Evidence
Tricuspid valve surgery is recommended for patients with severe TR (stages C and D) undergoing left-sided valve surgery	I	C
Tricuspid valve repair can be beneficial for patients with mild, moderate, or greater functional TR (stage B) at the time of left-sided valve surgery with either (1) tricuspid annular dilation or (2) prior evidence or right HF	IIa	B
Tricuspid valve surgery can be beneficial for patients with symptoms due to severe primary TR that are unresponsive to medical therapy (stage D)	IIa	C
Tricuspid valve repair may be considered for patients with moderate functional TR (stage B) and pulmonary artery hypertension at the time of left-sided valve surgery	IIb	C
Tricuspid valve surgery may be considered for asymptomatic or minimally symptomatic patients with severe primary TR (stage C) and progressive degrees of moderate or greater RV dilation and/or systolic dysfunction	IIb	C
Reoperation for isolated tricuspid valve repair or replacement may be considered for persistent symptoms due to severe TR (stage D) in patients who have undergone previous left-sided valve surgery and who do not have severe pulmonary hypertension or significant RV systolic dysfunction	IIb	C

Indications for Tricuspid Valve Surgery

Recommendations on the indications for TV surgery in the current era involve both the American College of Cardiology (ACA)/American Heart Association (AHA) 2014 Practice Guidelines [13] and the European Society of Cardiology (ESC)/European Association for Cardiothoracic Surgery (EACTS) 2017 Guidelines [14]. All current guidelines and recommendations are listed in Tables 9.3 and 9.4.

Table 9.4 ESC/EACTS 2017 recommendations

Recommendations on tricuspid stenosis	Class	Level
Surgery is indicated in symptomatic patients with severe tricuspid stenosis	I	C
Surgery is indicated in patients with severe tricuspid stenosis undergoing left-sided valve intervention	I	C
Recommendations on primary tricuspid regurgitation		
Surgery is indicated in patients with severe primary tricuspid regurgitation undergoing left-sided valve surgery	I	C
Surgery is indicated in symptomatic patients with severe isolated primary tricuspid regurgitation without severe RV dysfunction	I	C
Surgery should be considered in patients with moderate primary tricuspid regurgitation undergoing left-sided valve surgery	IIa	C
Surgery should be considered in asymptomatic or mildly symptomatic patients with severe isolated primary tricuspid regurgitation and progressive RV dilatation or deterioration of RV function	IIa	C
Recommendations on secondary tricuspid regurgitation		
Surgery is indicated in patients with severe secondary tricuspid regurgitation undergoing left-sided valve surgery.	I	C
Surgery should be considered in patients with mild or moderate secondary tricuspid regurgitation with a dilated annulus (≥40 mm or >21 mm/m2 by 2D echocardiography) undergoing left-sided valve surgery	IIa	C
Surgery may be considered in patients undergoing left-sided valve surgery with mild or moderate secondary tricuspid regurgitation even in the absence of annular dilatation when previous recent right-heart failure has been documented	IIb	C
After previous left-sided surgery and in absence of recurrent left-sided valve dysfunction, surgery should be considered in patients with severe tricuspid regurgitation who are symptomatic or have progressive RV dilatation/dysfunction, in the absence of severe RV or LV dysfunction and severe pulmonary vascular disease/hypertension.	IIa	C

Primary Tricuspid Regurgitation

The ACA/AHA 2014 guidelines recommend TV surgery for patients with severe primary TR undergoing left-sided valve surgery (Class I) [13]. However, TV surgery may also be considered for patients with severe primary TR unresponsive to medical therapy (Class IIa) and those with asymptomatic or minimally symptomatic severe primary TR with moderate or greater RV dilatation or systolic dysfunction (Class IIb) [13]. The ESC/EACTS 2017 Practice Guidelines have more aggressive recommendations and list a Class I recommendation for patients with severe symptomatic primary TR without severe RV dysfunction [14]. This is an instance where valve disease with symptoms is not listed as a Class I indication in the ACA/AHA 2014 guidelines, which may reflect hesitance to operate on patients with irreversible RV dysfunction. The ESC/EACTS guidelines also recommend surgical consideration for patients with moderate primary TR undergoing left-sided heart surgery (Class IIa) [14].

Secondary Tricuspid Regurgitation

Similarly, the ACA/AHA recommends TV surgery for patients with severe functional TR who are planned to undergo left-sided valve surgery (Class I) [13]. TV repair should also be considered for mild or greater secondary TR with evidence of TA dilation or prior evidence of right heart failure (Class IIa) and for patients with moderate TR and pulmonary hypertension (Class IIb) at the time of left-sided valve surgery. Reoperation for repair or replacement for patients with severe TR with prior left-sided valve surgery without pulmonary hypertension or RV dysfunction can also be considered (Class IIb).

The ESC/EACTS 2017 Practice Guidelines provide many similar recommendations and are considered even more aggressive to target patients earlier in the disease course [14]. TV surgery may even be considered in patients with mild-or-moderate TR undergoing left-sided valve surgery when prior recent right-heart failure has been shown even without the presence of TA dilation (Class IIb) [14].

As the guidelines are written currently, patients with a potential indication for surgical management are older, have more comorbidities, usually have had prior cardiac surgery, and suffer from severe RV dysfunction. In fact, patients with functional TR are often asymptomatic despite impaired RV dysfunction. As such, surgical management of patients earlier in the disease process, which is a technically easier operation with lower operative risk, are missed at this time. In the future, additional consideration for these patients should be taken into account in the next generation of guidelines.

Tricuspid Stenosis

According to the ACA/AHA 2014 guidelines, TV surgery is indicated for patients with symptomatic, isolated severe TS (Class I) [13]. Furthermore, TV surgery is indicated for all patients with severe TS undergoing left-sided valve interventions regardless of the presence of symptoms (Class I). A TV commissurotomy may also be considered in patients with symptomatic, isolated severe TS without accompanying TR (Class IIb). The ESC/EACTS 2017 guidelines have the same recommendations [14]. Both guidelines have defined severe TS as having thick, distorted, calcified leaflets, right atrial and inferior vena cava enlargement, a valve area $<1.0\ cm^2$, and a mean pressure gradient of greater than 5–10 mm Hg.

Surgical Exposure

TV surgery can be performed concurrently with aortic and/or mitral valve operations using conventional or mini-sternotomy approach or a right mini-thoracotomy exposure for mitral valve procedures. Obtaining bicaval cannulation with snares is required to fully isolate the RA. Vacuum-assisted drainage is often very helpful. Left-sided valve surgery can be performed using blood cardioplegic arrest with either antegrade and/or retrograde administration and systemic hypothermia. The mitral valve can be exposed via a left atrial incision or right atrial incision followed by a transseptal incision. After performing the mitral procedure, the TV procedure may be performed during rewarming and reperfusion with the hearting beating.

Isolated TV surgery can also be performed using a sternotomy or right mini-thoracotomy. In a beating heart technique, the bicaval snares are tightened around the venous drainage and a right atriotomy is performed to expose the TV. For an approach through a right mini-thoracotomy, femoral and internal jugular vein cannulas are positioned outside of the right atrium and snares are used to ensure venous drainage.

Tricuspid Valve Repair

Numerous surgical techniques exist for the various TV pathologies that may be encountered. Basic repair techniques include the rigid ring–based annuloplasty, which is the surgical gold standard of TV repair, along with suture-based annuloplasty, leaflet repair, leaflet augmentation, and other surgical repair techniques (Table 9.5). If repair is not possible or will result in a non-satisfactory result, TV replacement should be performed.

Table 9.5 Current surgical techniques for tricuspid valve disease

Category	Techniques
Ring-based annuloplasty	Rigid
	Semi-rigid
	Flexible
Suture-based annuloplasty	De Vega
	Kay
	Modified De Vega
	Others
Leaflet repair	Clover
	Tricuspid leaflet
Leaflet augmentation	Pericardial patch with ring annuloplasty
Other repairs	Double orifice
	Posterior annular bicuspidization
Valve replacement	Prosthetic
	Mechanical

Surgical Planning

According to the three pathophysiologic phases of TR development, surgical repair of the TV will require tailored strategies. In general, the tricuspid annuloplasty alone will yield excellent results for patients with stage I and II TR. However, stage III requires more of a tailored approach as patients will have both TA dilation and leaflet tethering. This may require a combination of ring-based annuloplasty along with leaflet reconstruction to address the leaflet tethering. There are many adjunctive options available including bicuspidalization, patch augmentation, double orifice valve, and other approaches.

Ring-Based Annuloplasty Techniques

The mainstay of surgical repair for TR involves the placement of annular ring or band to reduce TA size and to achieve normal leaflet coaptation. These can include rigid rings (e.g., Carpentier–Edwards), flexible rings (e.g., Duran), or flexible bands (e.g., Cosgrove annuloplasty rings). To avoid injuring the AV node and Bundle of His near the apex of the triangle of Koch, annuloplasty rings are typically incomplete circumferentially. After choosing a ring or band, Ethibond annuloplasty sutures are placed in a horizontal mattress fashion circumferentially around the TA with a 1 cm width and 1 mm apart. These sutures are initially placed along the lateral half of the septal annulus and then along the entire anterior and posterior TV annulus.

In recent years, significant data has emerged to suggest that rigid annuloplasty rings offer the most durability compared to other rings, bands, and suture-based annuloplasty. In a study comparing 790 patients who underwent concomitant TV annuloplasty for TR, recurrent regurgitation severity was lowest among patients with the semi-rigid Carpentier–Edwards ring compared to flexible rings and suture-based annuloplasty at 8 years following surgery [15]. Even at longer-term follow-up out to 21 years, freedom from recurrent TR and long-term survival were higher in the rigid ring group compared to other ring groups [16]. Although randomized controlled trials are currently underway, most surgeons consider ring-based annuloplasty, which directly addresses the TA dilation associated with TR, to be the gold standard surgical treatment.

Although most surgeons agree on rigid ring–based annuloplasty for functional TR, controversy still remains regarding sizing of annuloplasty rings. Some recommend using the length of the base of the septal leaflet or the intertrigonal distance to determine the size of the ring or band. Others favor undersizing the tricuspid annuloplasty ring by at least two ring sizes. Others even argue for oversizing to prevent subsequent TS development.

Our group and others recommend a general guideline of undersizing the annuloplasty ring by at least two sizes when the annular diameter is greater than 40 mm

[17]. In actuality, this is renormalizing the TA to its original size, which is 2.8 ± 0.5 cm. This can even be simplified in the setting of concurrent mitral valve repair for mitral regurgitation along with TV repair using similar-sized annuloplasty rings. Using the same sized ring for both mitral and TV repair can be effective and does not result in any TS or any negative impact on RV function [18].

Suture-Based Annuloplasty

Although ring-based annuloplasty has become the standard surgical repair in recent years, the classic De Vega suture–based annuloplasty, which was originally described in the 1970s, is a historic technique still commonly used across world [19]. This technique involves plication of the posterior TA using a double continuous suture, which allows preservation of the septal portion of the TA [19]. This allows downsizing of the TA to reduce the effective valvular orifice area to increase leaflet coaptation. Another classic technique, the Kay annuloplasty, uses a pledgeted-horizontal mattress annuloplasty to plicate the posterior TV annulus [19]. This essentially creates a "bi-leaflet" TV by excluding the posterior leaflet from the effective valve orifice. The benefits of these techniques are that they are fast and cost-effective. However, they have been criticized as being unreliable. The De Vega annuloplasty is prone to suture migration and dehiscence, while the Kay annuloplasty fails to address anterior TA dilitation, thereby making both annuloplasty techniques prone to progressive TA dilation and recurrent TR [19]. Many modifications have been made in recent years including the modified De Vega technique, which involves using Teflon felt pledgets to help minimize the risk of the suture tearing through tissue causing recurrent TR [19].

Originally, the final orifice size was gauged by two fingers, a practice which has now been replaced by annular sizers. After sizing, the purse-string suture is tied down, cinching to the appropriate degree of TA reduction. Careful attention is also needed when performing suture-based annuloplasty techniques for TR. Awareness of the triangle of Koch and AV node is required while stiches are placed. As the TA has often been considered to be underdeveloped compared to the mitral annulus, annuloplasty sutures should be placed in a horizontal mattress fashion advancing parallel and within the annulus to ensure optimal patient outcomes.

Leaflet Repair Techniques

Several leaflet repair techniques also exist to address TR with leaflet abnormalities. The edge-to-edge repair also known as the "clover technique," which is very similar to the Alfieri repair technique for mitral regurgitation, was originally described by De Bonis et al. [20]. The technique involves suturing together the central free edges of the tricuspid leaflets. This is often combined along with a ring-based annuloplasty, although it has been performed independently [20].

Leaflet augmentation techniques have also been described to address leaflet tethering that is commonly associated with advanced TR. Dreyfus et al. described increasing the surface leaflet coaptation by threefold by advancing the zone of coaptation into the RV at the level of the tethered posterior and septal leaflets [21, 22]. This technique involves detaching the anterior leaflet from the anteroseptal to the anteroposterior commissure. An autologous pericardial patch is then placed to facilitate leaflet enlargement. When performing this technique, it is crucial to oversize the patch to minimize any tension which could restrict motion of the leaflets.

Chordal Replacement Techniques

Chordal replacement may be required in patients with a prolapsed TV leaflet or flail leaflet secondary to chordal elongation or rupture. Gore-Tex polytetrafluoroethylene (PTFE) neochord sutures can be used to replaced diseased or injured chordae. Both limbs of a CV-4 Gore-Tex neochord can be passed through the fibrinous part of the papillary muscle of interest and then through the prolapsed leaflet approximately 4–5 mm from the free edge. Functional evaluation using saline to distend the RV while occluding the pulmonary artery can then be used to determine the appropriate height of the Gore-Tex neochord. The neochord height can be adjusted as needed.

Leaflet Reconstruction

In patients with severe leaflet destruction secondary to pathologies like endocarditis, leaflet reconstruction may need to be considered. Repair of an involved damaged leaflet may be reconstructed (up to 50% of leaflet surface) as long as the edge along the coaptation line remains intact. In general, stay sutures (5/0 Prolene) are placed around the chordate tendinae of the perforated leaflet facilitating proper visualization with gentle traction. If the valve is considered repairable, any vegetations or unhealthy tissue are resected allowing only healthy tissue to remain for repair. A bovine pericardial patch can be placed using a locking 5/0 continuous Prolene suture, which will help minimize any purse-stringing of the patch. The pericardial patch should also be slightly oversized to minimize the risk of any tension causing restricted leaflet motion. After repair, the TA can then be stabilized using a rigid annuloplasty ring.

Other Surgical Repair Strategies

One of the major underlying issues in secondary TR is dilatation of the posterior tricuspid annulus. As such, the posterior annular bicuspidization technique can be performed by placing a pledgeted-supported mattress suture from the anteroposterior to the posterolateral commissure along the posterior annulus. Several groups have reported that this technique can be effective in select cases [23].

Other techniques exist including the double-orifice valve technique, which can help reduce regurgitant flow. This technique involves passing two pledgeted-supported mattress sutures from the middle of the anterior annulus across to the septal annulus [20]. These sutures should be aimed toward an area two-thirds the length of the septal annulus from the anteroseptal commissure. This will help minimize injury to the bundle of His.

Intraoperative Assessment of Valve Repair

After surgical repair, intraoperative assessment of TV competence remains crucial to ensuring an optimal TV repair. Intraoperative evaluation involves filling the RV with saline and evaluating leaflet coaptation. As the pulmonary artery is occluded, the RV volume can generate enough pressure to close the TV. If TV competence appears inadequate, the TV repair may require further ring downsizing, or a valve replacement should then potentially be considered.

Acute Complications of Tricuspid Valve Repair

Surgeons performing TV repair must also be aware of potential acute complications that can occur. These include both AV node and RCA injury. To minimize risk of AV node injury, it is often advocated to placed sutures in the "10 o'clock to 6 o'clock" positions along the TA from the primary surgeon's view. To minimize risk of RCA injury, stitches should be placed evenly along the TA. RCA injury is almost never complete occlusion of the RCA, but usually occurs as a partial injury secondary to bending or twisting of the RCA. Again, even stitch placement can help minimize this injury.

Tricuspid Valve Replacement

For patients with TV leaflets not amenable for repair, TV replacement is considered the gold standard technique and has been highly successful. This technique addresses both severe valvular disease and helps minimize disease progression leading to recurrent TR.

At present, there are two major categories of valves that may be selected for TV replacement, including mechanical or bioprosthetic valves. The choice remains controversial at this time, although many guidelines favor the use of large-size bioprosthetic valves over mechanical valves [14]. Although both have demonstrate similar long-term survival outcomes, mechanical valves have been shown to be prone to thromboembolic complications in the setting of a low-pressure right-sided heart. Biologic valves, however, have been shown to have good long-term durability, although they are at risk for degeneration over time. As such, the decision between mechanical and biologic prosthetic valves must be weight carefully based on the patient's age, comorbidities, patient preferences, and tolerability of anticoagulation.

To perform the TV replacement, non-everting, interrupted pledgeted 2/0 Ethibond sutures are anchored circumferentially along the TA with 1 cm between each suture limb and 1 mm between each adjacent suture. The sutures should be placed vertically upwards to minimize risk of including atrial or septal tissue. At the superior-medial aspect of the septal annulus, the sutures are plicated through the septal leaflet tissue to minimize risk of penetrating the nearby conduction tissue. Care should also be taken near important anatomical structures including the aortic valve, the coronary sinus, right coronary artery, and conduction tissue. After sizing the valve orifice, sutures are put through the valve ring and the sutures are tied down. A mechanical valve should be oriented in the anti-anatomical position with maximum flow directed into the RV outflow tract, while a bioprosthetic valve should be oriented with the stents aligned with the posteroseptal and anteroseptal commissures.

When compared with repair, TV replacement affords decreased survival at 10 years postoperatively, although no differences in valve-related mortality or reoperation has been noted [24]. This may be secondary to a rigid valve prosthesis causing decreased cardiac output and RV function which may contribute to decreased overall survival, while not affecting other valve-related morbidity or reoperation [24].

Recurrent Tricuspid Regurgitation

Recurrent TR after surgical repair also remains a problem that surgeons need to be aware of. Risk factors for recurrent or residual TR include the severity of preoperative TR, leaflet tethering, poor left ventricular and RV function, and higher pulmonary artery pressures [25]. Some studies have highlighted that in patients with grade 3–4 TR, 14% had recurrent TR at 1 week postoperatively and at 23% out to 5 years [15].

Interestingly, patients with transvalvular or implantable cardioverter defibrillator (ICD) leads are also at high risk for late recurrence of TR. At 5 years following TV annuloplasty, 42% of patients with transvalvular pacemaker leads were shown to have recurrent TR compared to 23% without leads [15]. Such findings suggest that patients with transvalvular leads may be better served by conversion to epicardial

leads or transverse coronary sinus leads at the time of TV surgery to minimize recurrent TR [26].

As targeting no to minimal recurrent TR is the goal following surgery, TR patients undergoing surgical management may require additional options to improve short- and long-term results and require close monitoring after surgery.

Minimally Invasive Tricuspid Valve Surgery

In the last decade, a minimally invasive approach to TV surgery has emerged [27]. Several studies have highlighted the benefit of a minimally invasive right thoracotomy in recent years. In a retrospective propensity-match study evaluating a right-mini thoracotomy versus conventional sternotomy for patients undergoing mitral or TV surgery, patients who underwent the right mini-thoracotomy had decreased length of stay, operative time, and blood product transfusions compared to conventional thoracotomy [28]. In a large case series of patients undergoing TV surgery without cross-clamping and using a beating or fibrillating heart, a TV repair was attained in 61% of patients with a 2.1% 30-day mortality despite nearly half of the patients having undergone a prior sternotomy [29]. Although further prospective studies are required, a right mini-thoracotomy may be an alternative approach for high-risk patients with a prior history of sternotomy.

Conclusion

In conclusion, the TV no longer remains the "forgotten valve" as studies in recent years have highlighted the association between morbidity, mortality, and prolonged hospitalization related to TV pathologies. In developed countries, functional TR remains the most prevalent TV pathology. At present, rigid ring–based annuloplasty remains the gold standard surgical treatment, although additional leaflet augmentation may be required in select cases. TV replacement remains an option when needed. In recent years, minimally invasive TV surgery using a right mini-thoracotomy has also emerged as a potential treatment option for high-risk patients. In the current era, as TR has not been shown to regress following left-sided surgery and reoperation for TR carries high risk, surgeons must be more aggressive in management of TR with annular dilation when performing cardiac surgery. Overall, surgeons should be well versed in the anatomy, pathology, and surgical management options for addressing TV pathologies to provide optimal outcomes for patients.

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Chapter 10
Evaluation and Management of Tricuspid Regurgitation in Patients with Cardiac Implantable Electronic Devices

Donya Mohebali and James D. Chang

Introduction

Approximately 200,000 permanent pacemakers (PPMs) and 120,000 implantable cardioverter defibrillators (ICDs) are implanted annually in the United States [1]. Cardiac implantable electronic devices (CIEDs) have increased the quality and duration of life for millions of patients by providing support of heart rate, atrioventricular and interventricular synchrony, and prevention of sudden cardiac death [1, 2]. Until recently, with the advent of leadless pacing systems and His bundle pacing, the near-universal requirement for an endocardial lead to provide pacing or defibrillation, or both, in the right side of the heart has led to the recognition of adverse consequences of these leads with respect to tricuspid valve (TV) structure and function.

Tricuspid regurgitation (TR), of even moderate grade and of any etiology (primary or secondary), is associated with increased mortality rates, even after accounting for factors known to contribute to secondary, or functional, TR such as left ventricular (LV) dysfunction, right ventricular (RV) dilation and dysfunction, and pulmonary hypertension [3]. In patients with CIEDs, moderate-or-severe TR occurs at significantly higher rates [4, 5], and has been shown to be associated with increased heart failure hospitalizations and mortality [6–9].

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Tricuspid valve dysfunction after CIED implantation can manifest clinically as right-sided heart failure secondary to TR (or less often to tricuspid stenosis) or as left-sided heart failure when RV volume overload impairs LV filling by direct ventricular interaction through the interventricular septum. Other structural consequences can include mechanical interference with normal leaflet coaptation, leaflet entrapment, subvalvular support structure entanglement, endocarditis, and damage during lead placement or manipulation, or at the time of lead extraction of infected or malfunctioning leads.

The diagnosis and differentiation of lead-related primary TR, as distinct from secondary/functional TR, poses unique challenges, but constitute a critical distinction in the management of patients with a CIED and right heart failure. Routine diagnostic imaging can be fraught with pitfalls and therefore a high level of clinical suspicion in conjunction with 3D echocardiography can alert the clinician to the possibility of worsening heart failure as a consequence of mechanical interference with TV leaflet mobility or coaptation. This form of TV dysfunction may be amenable to lead extraction or valve repair or replacement when performed in a timely fashion to avoid severe annular and chamber dilation as well as severe RV dysfunction that when present may preclude the desired outcome even if the TV is technically repairable or replaceable. Thus, corrective intervention for suspected lead-related TR should be undertaken ONLY when all five of the following conditions are met: (1) the RV (tricuspid annulus) is neither severely dilated nor severely dysfunctional, (2) there is robust echocardiographic and hemodynamic evidence supporting a primary lead-related etiology of TR, (3) the requirement for stroke work production is not expected to exceed the capacity of the RV if and when it is forced to eject its entire stroke volume in an antegrade direction, (4) any left-sided cardiac dysfunction that may be contributing to TR is optimally managed, and (5) a TV replacement or repair strategy is available if transvenous lead extraction is the contemplated intervention.

Mechanisms of Lead-Induced Tricuspid Regurgitation

In order to understand the mechanism of lead-induced TR, it is important to understand the basic morphology and structure of the TV. Tricuspid valve morphology and attachments make it prone to insufficiency, as does any preexisting chamber dilation or LV dysfunction. The TV apparatus is comprised of a nonplanar elliptical annulus, three leaflets (anterior, posterior, and septal), chordae tendineae, and two papillary muscles (anterior and posterior). The mural portion of the annulus subtends the RV free wall, is not supported by the semirigid fibrous cardiac skeleton, and therefore can elongate under chronic pressure or volume overload leading to annular dilation. This is in contrast to the septal portion of the annulus that subtends the right fibrous trigone and is supported by the cardiac skeleton. Some of the TV chordae tendineae attach directly to the interventricular septum and free wall without an intervening papillary muscle. As a result of this underlying structure, TR

tends to beget more TR as the effects of a chronically volume overloaded state leads to chamber and annular dilation, tethering of the leaflets, and loss of leaflet coaptation. Pre-existing left-sided cardiac dysfunction (including systolic or diastolic myocardial dysfunction, valvular dysfunction, and dyssynchrony) predisposes the patient to functional or secondary TR, and as a result even a modest increment in TR associated with CIED implantation can over time result in severe TR and right-sided heart failure due to the combined effect of primary lead-related and secondary factors.

Mechanisms of CIED-induced TR can be classified as implantation-related, device-mediated, and pacing-related. Damage to the TV leaflets and subvalvular structures can occur during lead implantation, removal, or manipulation. These include leaflet perforation, laceration, or avulsion (primarily occurring during lead extraction) (Video 10.1), and transection of papillary muscles or chordae tendinae [10–14].

Device-mediated TR results from mechanical interference with TV leaflet mobility and coaptation. This occurs by the presence of a lead traversing the TV, which can prevent leaflet coaptation by direct contact with the leaflets, impingement on leaflet mobility, or by entanglement with the chordae tendinae. Absent direct mechanical interference with leaflet coaptation, over the long term even intermittent contact between the endocardial leads and leaflet or chordal structure can result in a foreign body inflammatory and fibrotic response leading to encapsulation or entrapment of the lead with subsequent loss of leaflet mobility (Videos 10.2 and 10.3).

Additionally, the presence of hardware in the circulatory system in combination with damage to the TV predisposes the patient with a CIED to thrombosis and endocarditis, both of which can lead to TV dysfunction – TR or stenosis [15–20]. There has been an increase in device infections, representing an emerging problem. Infection due to CIED necessitates lead extraction almost all of the time. Tricuspid valve dysfunction in this setting can occur as a result of leaflet destruction by the infectious process itself or during lead extraction. It is estimated that up to 24,000 lead extractions occur annually worldwide, and device infections remain the leading indication for extraction [21, 22]. Over time, leaflet and/or supporting structures adhere to and encapsulate CIED leads. As a result, transvenous lead extractions can cause TV damage, including leaflet avulsion [23–27] (see Video 10.1). Tricuspid valve damage can also result from surgical lead extraction [28].

Pacing-related TV dysfunction can occur by way of various mechanisms. Dyssynchronous LV electromechanical activation induced by left bundle branch block or RV pacing can result in systolic or diastolic dysfunction of the LV or in mitral regurgitation. This results in increased left-sided filling pressure and pulmonary artery pressure, leading to functional TR [29, 30]. Among 89 consecutive patients undergoing their first PPM implantation, TR increased after dual-chamber, but not after biventricular, PPM implantation further supporting this mechanism [31]. Other studies suggest that the physical presence of the lead itself, and not pacing per se, plays the major role in TV dysfunction, as the percentage of paced beats does not correlate with worsening TR [8, 32, 33].

Diagnosis of Tricuspid Valve Dysfunction Associated with CIED Leads

Echocardiographic assessment, two-dimensional (2D), three-dimensional (3D), and Doppler, are the mainstays for diagnosis of CIED-associated TV dysfunction. The diagnosis of TR in patients with CIEDs is similar to that in patients without endocardial leads. The CIED leads can result in echocardiographic imaging artifacts and signal attenuation because of their high acoustic impedance and reflectivity, resulting in underestimation of TR by Doppler color-flow mapping [34]. Other associated artifacts include scattering and acoustic shadowing, similar phenomena that are encountered in Doppler echocardiographic assessment of prosthetic valve regurgitation. This is somewhat mitigated with the use of transesophageal echocardiography (TEE). When TR is caused by an asymmetric impairment of leaflet mobility, which is usually the case with lead-related TR, the regurgitant jet can assume an eccentric or wall-hugging rather than central trajectory, resulting in loss of Doppler color-flow signal—known as the Coanda effect—and therefore underestimation of TR, as is similarly the case with mitral regurgitation caused by asymmetric leaflet tethering or prolapse.

A high index of clinical suspicion is required in conjunction with a careful physical assessment in patients in whom CIED lead-induced severe TR is suspected, as routine echocardiographic assessment may miss this, for the reasons stated above. In patients found to have severe TR from CIED leads, only 63% had a correct diagnosis based upon routine preoperative TTE [34], whereas all were found to have severe TR by preoperative or intraoperative TEE. In cases of suspected CIED-associated TR, it is important to inspect the pattern of hepatic vein flow by spectral and color-flow Doppler assessments, which are not affected by lead-induced acoustic artifacts. Holosystolic hepatic vein flow reversal is diagnostic of severe TR, whereas normal antegrade systolic flow excludes moderate and severe TR, although if the right atrium is severely dilated, the negative predictive value of hepatic vein systolic flow reversal may be reduced [35]. Therefore, Doppler assessment of the hepatic vein is essential in all patients with a CIED and will reveal many instances of severe TR not disclosed by standard color-flow imaging of the valve itself.

Treatment of Lead-Related Tricuspid Regurgitation

Surgical corrective intervention of severe TR induced by CIED leads includes suture (DeVega) annuloplasty, ring annuloplasty, and valve replacement with or without lead retention. For valve repair with lead retention, the lead is first surgically detached from any adherent interaction with valve leaflets or chordae tendineae.

The lead is repositioned by securing it in a location abutting the tricuspid annulus in a cleft created by suture-bicuspidization of the TV, to prevent leaflet impingement. Lastly, DeVega-type suture or ring annuloplasty can be performed in cases where the annulus is dilated [36–39].

On the one hand, ring annuloplasty can be done with an open C-ring (band), rather than a closed O-ring, in order to accommodate the lead within the ring [40–43]. On the other hand, a circumferential O-ring, providing superior support of the entire tricuspid annulus, can be deployed. However, the use of a circumferential annuloplasty ring requires displacement of the lead outside of the annulus, thereby entrapping it. The majority of case series describing TV repair or replacement resulting in an entrapped lead report normal function of both the valve implant and device following surgery. However, this method can lead to the possibility of damage to the lead or adverse effects on pacing or defibrillation in addition to precluding subsequent performance of transvenous lead extraction in the case of a future device infection.

Transvenous Lead Extraction to Treat Lead-Related Tricuspid Regurgitation

Over time, leaflets and supporting structures can adhere to and encapsulate CIED leads (see Videos 10.2 and 10.3). RV lead extraction can therefore result in TV damage, including leaflet avulsion (see Video 10.1). Current lead extraction methods employing sheath extraction with mechanical and laser-assisted dissection allow for extrication of the lead from encapsulating or ensheathing valve material with a low incidence of complications, such as worsening TR (0–5.6%), and a high procedural success rate (94–100%) [44–46]. Predictors of worsening TR after RV lead extraction include removal of greater than 1 lead, endocarditis involving the TV as the reason for explantation, and longer dwell time [45, 47].

Ultimately, whether lead extraction alone, without valve repair or replacement, is adequate to improve lead-related TR cannot be determined a priori with certainty. Because further damage may occur as a result of lead extraction, a valve replacement or repair strategy must be in place prior to RV lead extraction.

Lastly, there are no prospectively acquired data to support TR, in the absence of TV or device infection, as an indication for transvenous lead extraction [48]. However, when operative risk is low and patients have severe symptomatic TR with compelling three-dimensional (3D) echocardiographic evidence of valve dysfunction attributable to the lead, extraction should be considered, since the significant increment in morbidity and mortality associated with TR, with or without an interfering CIED lead, is now widely recognized.

Future Directions Including Leadless Pacemakers and his Bundle Pacing

Lead-related TV dysfunction can be eliminated by foregoing the use of transvalvular leads altogether. Strategies to provide pacing to the heart without crossing the TV include placement of a coronary sinus pacing lead, surgical epicardial placement of leads, and leadless pacing systems.

His bundle pacing results in a physiological activation sequence in the ventricles, thus leading to a narrow QRS complex, and minimizes the deleterious effects of RV pacing [49]. Additionally, because the His bundle penetrates the membranous septum on the atrial side of the TV leaflet insertion, His bundle pacing can occur without affecting TV closure and function. Importantly, effective and direct His bundle pacing may result in (1) a narrower QRS complex compared to biventricular pacing; (2) improvement of LV dimension, functional status, ejection fraction, and quality of life; (3) reduction of heart failure hospitalization frequency [50–56], and (4) avoidance of LV dyssynchrony caused by RV pacing as well as of the need to upgrade an RV pacing system to a biventricular pacing system in patients with pacing-induced dyssynchrony. Tricuspid valve function has not been directly assessed, but the absence of a lead that interferes with leaflet coaptation and the improved electromechanical coupling obtained with His bundle pacing compared with RV pacing should, in principle, preserve TV function [57].

Other novel approaches to reduce or eliminate many of the complications of conventional pacemakers, like TR, include leadless pacemakers. At present, these are transvenous single-chamber devices implanted in the RV apex (Nanostim, St. Jude Medical, St. Paul, Minnesota; and Micra pacing system, Medtronic, Minneapolis, Minnesota) [58, 59]. Initial data suggest that they are associated with a 99.2% rate of successful implantation and a 4% complication rate at 6-month follow-up [58, 60].

Conclusion

Clinical consequences of tricuspid valve dysfunction secondary to CIED leads are developing increasing recognition in parallel with recognition of those of RV and TV dysfunction in general. A higher level of clinical suspicion than has prevailed in the past, in conjunction with 3D echocardiography, may alert the clinician to the possibility that worsening heart failure may be a consequence of mechanical interference with TV leaflet mobility or coaptation and therefore amenable to lead extraction or valve repair or replacement. When clinical, hemodynamic, and echocardiographic assessment provides compelling evidence of lead-related severe TR, corrective intervention should be provided in a timely fashion, before the onset of severe annular and chamber dilation and severe RV dysfunction because, by that time, the lead itself will no longer be the problem, and the extant problem may not

be as amenable to corrective intervention. The future of CIEDs in which endocardial leads are absent or non-transvalvular is likely to be associated with a reduction in lead-related cardiac dysfunction.

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Chapter 11
Tricuspid Valve: A Heart Team Approach

Janet Fredal Wyman and Marcus Ryan Burns

The Heart Team Evolves for Tricuspid Valve Disease Management

The multidisciplinary heart team (MDHT) has become recognized as essential in the management of patients with complex valvular heart disease (VHD) and has been incorporated into valvular disease management guidelines worldwide [1–3]. The concept of a multidisciplinary team of healthcare professionals is well established in the care of patients with malignancies and organ failure that requires transplantation. Recognition of the "heart team" in the cardiac world emerged with the Syntax trial in 2006, where the combined opinion of the cardiac surgeon and the interventional cardiologist determined the patient's eligibility for the trial, followed by appropriateness for percutaneous coronary intervention (PCI) and/or coronary artery bypass graft (CABG) [4]. Over the next decade, the "heart team" moved from the coronary disease setting into valvular disease. The MDHT was incorporated into major valve research protocols, requiring collaboration in decision-making [5–11]. Although the "heart team" was initially defined as the interventional cardiologist and the cardiac surgeon [12], the advanced decision-making process for the treatment of complex valve disease found that the treatment discussion

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reached beyond the procedure itself. The team expanded to include an advanced echocardiographer, imaging specialists, anesthesiologists, the valve nurse clinician, and others who have unique contributions to make to the patient's care. This larger MDHT has been shown to improve clinical and economic outcomes in aortic valve procedures [13–17].

As transcatheter therapies moved to treatment of the other heart valves, the composition of the MDHT evolved. The most recently published recommendations for operator and institutional requirements for mitral valve intervention included the heart failure specialist and specified that the echocardiographer should have advanced training per American Society of Echocardiography standards [18]. Core to the clinical management of secondary or mixed mitral regurgitation is guideline-directed medial therapy (GDMT), which is generally led by the heart failure specialist [19]. Standardized echocardiographic assessment for mitral valve regurgitation analysis alone includes 14 qualitative parameters, 12 quantitative parameters, and hemodynamic and rhythm parameters [19]. Full evaluation of the regurgitant mitral valve with consideration of the various repair versus replacement options requires knowledge of both advanced echocardiographic interpretation and interventional imaging. An interventional imager with level III training is an essential component of the MDHT, providing indispensable direction throughout the diagnostic period and guidance for and during transcatheter procedures [18]. Decisions regarding surgical versus transcatheter treatment strategies require assessment of concomitant valvular and structural disease [19]. Surgical mitral valve treatment generally requires definition of all indications for intervention to allow a single "all at once" procedure. A transcatheter approach, however, generally adopts staged interventions, allowing for medical treatment of concomitant diseases and time for ventricular remodeling or patient conditioning between procedures. The history of disease progression of mitral valve disease extends over years; the patient and family report diminished activity over time to avoid symptoms, unaware that the decline is disease related. The advanced valve clinician and nurse coordinators provide ongoing navigation and treatment adjustments for the patient with mitral valve disease [19].

The MDHT for the tricuspid valve (TV-MDHT) has taken direction from its "sister" atrio-ventricular mitral valve. The etiology of tricuspid regurgitation (TR) is divided into primary and secondary causes, with an emerging population of adult patients showing isolated TR not associated with congenital disease, the presence of left heart failure, or pulmonary hypertension. The TV-MDHT comprises the same members as the mitral valve team, with the addition of specialists from the other associated disease processes. Tricuspid valve trials have incorporated these key members into their research protocols.

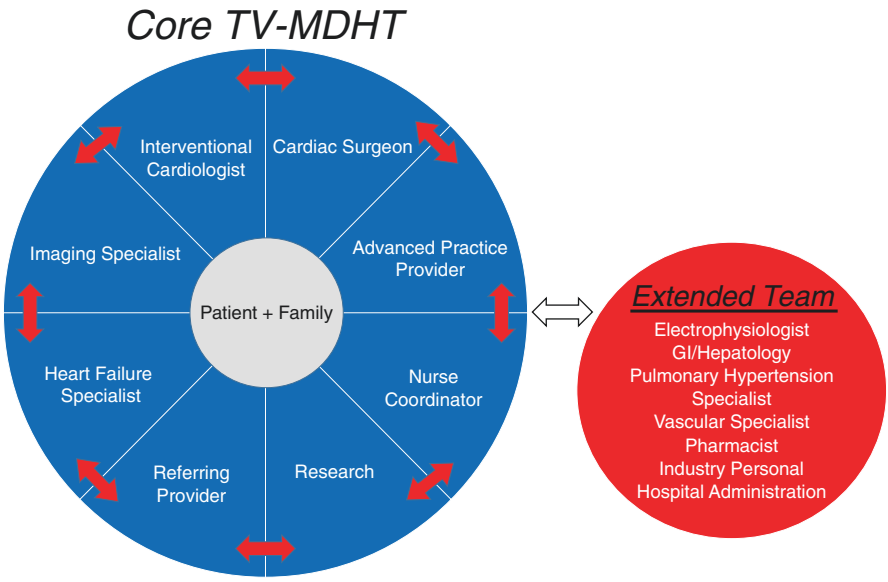

Fig. 11.1 Tricuspid valve multidisciplinary heart team

An Overview of the Multidisciplinary Team for the Tricuspid Valve

The Core Members of the TV-MDHT

A core group of healthcare professionals are intimately involved in the evaluation and management of patients with TV disease. From initial presentation and throughout the continuum of treatment, each of these key specialists is integral to the care in every patient with TV disease. Figure 11.1 provides an illustration of the TV-MDHT.

Interventional Cardiologist

Interventional cardiology has grown to bridge many cardiac specialties that were once separate. Broadly, interventional cardiologists who have gathered experience as well as special interest within the subspecialty of VHD often are referred to as "heart valve specialists." This first generation of structural interventional cardiologists (SIC) has more recently helped establish dedicated, formalized training programs for interventional cardiology fellows who aspire to incorporate SHD treatments into their individual practice. In many ways, SICs are the champions of the contemporary TV-MDHT. Screening, selection, and optimization remain critical in high-risk subsets of patients in whom protocol-based TV treatments may be

indicated. These professionals must collaborate with all members of the MDHT to provide coordinated, comprehensive, high-quality care.

Given the relative infancy of percutaneous treatments for TR, the specific diagnosis and treatment of TR patients require particular expertise and learned experiences on the behalf of IC. Deep knowledge and understanding of the complex TV anatomy as well as novel transcatheter-based TV technologies to include annuloplasty systems, coaptation devices, leaflet devices, caval valve implantation, and TV replacement are fundamental. Patient selection remains dependent on many factors to include anatomy of the TV and its relationships with surrounding structures, severity and etiology of TR, right ventricular (RV) size and function, among others. SICs must incorporate consistent and deliberate dialogue with all members of the MDHT during pre-procedural planning as well as interventions in order to successfully implement, prevent, and anticipate procedural complications.

Cardiothoracic Surgeon

Surgery has long been and remains the only guideline-indicated therapy for TR patients who remain symptomatic on medical therapy. Current American and European guidelines for the management of patients with VHD recommend TV surgery in (1) patients with symptomatic severe organic TR despite optimal pharmacological treatment without severe RV dysfunction; (2) asymptomatic patients with severe organic TR and signs of RV remodeling or dysfunction; and (3) patients with moderate or severe organic TR, or functional TR who undergo surgical treatment of left-sided VHD [20, 21]. However, due to an increasing appreciation of the inherently complex TV pathology and high morbidity and mortality associated with TV surgery, a variety of innovative, less-invasive techniques have been developed and are an attractive alternative to surgical-based correction.

The primary role of cardiothoracic surgeons (CTS) on the TV-MDHT is to provide expert opinion regarding surgical risks, as well as to determine overall candidacy and/or operability for surgical treatment. In addition to open surgery, surgeons could be trained to offer transcatheter-based or minimally invasive treatment options alike. Not unlike SICs, many CTS have skilled understanding of anatomy, pathophysiology, and hemodynamics of SHD. Given CTS are uniquely positioned to offer the full spectrum of therapy in structural heart disease they too remain a central pillar of the TV-MDHT.

Interventional Imaging

The complexity of percutaneous transcatheter-based technologies and devices for structural interventions continues to evolve in parallel to the development of a new subspecialty of structural heart interventional imagers [22, 23]. Advanced structural imaging is crucial to accurate diagnosis of the pathology, patient selection, and procedural planning for specific interventions.

The inherent complexity of the TV and RV anatomy and function provides unique challenges for structural heart interventional imagers. Two-dimensional (2D) echocardiography has now been supplemented with three-dimensional (3D) imaging, and advanced imagers have been able to incorporate computed tomography and cardiovascular magnetic resonance imaging in procedural planning and execution. The use of these additional modalities has helped in the understanding of TR severity grading, and assessment of RV remodeling and function, which was limited, and in part has led to the under-recognition of the magnitude of the problem [24]. The expansion of new devices and technologies to percutaneously address TR has led to an improvement of understanding of the pathophysiology, but more work is necessary and will be a central component of the imaging specialist's responsibilities and of the multidisciplinary heart team discussion.

Beyond this, imagers meticulously guide pre-procedural planning and ultimately procedural implementation of TV interventions. Strong communication skills are an absolute essential throughout all phases of the care continuum however, paramount during an interventional procedure to ensure optimal and safe patient outcomes.

Advanced Practice Providers: The Valve Clinicians

Advanced practice providers (APPs) are uniquely positioned to participate in the care of patients across the entire spectrum of care delivery. This group, which comprises nurse practitioners and physician assistants, has continued to demonstrate the ability to deliver safe, cost-effective, efficient, and high-quality care [20, 21, 25] with complex patients. Their education and training provide knowledge and skills that are exceptionally suited to meet the needs of complex valve patients, permitting them autonomy that can greatly extend a MDHTs capabilities.

Many patients burdened with TV disease endure a long and sometimes rigorous journey. If effectively integrated, APPs offer a continuous link or bridge to care that crucially improves patient access and continuity of care. Advanced practice providers can function either independently or alongside a collaborating physician in care coordination or in the provision of direct patient care.

Valve Program/Nurse Coordinator

Alongside the continuous, exponential growth of structural heart disease therapies, the role of valve program/nurse coordinators (VPCs), too, has evolved at an ineffable speed. Historically transcatheter aortic valve replacement patients were the initial focus population of the VPCs' efforts; however, VPCs now assist the MDHT in the management of mitral, tricuspid, and even pulmonic valve patients. Their contributions to the MDHT are endless. Mainly these individuals manage intake and keep the plan of care in constant motion. Consistent and clear communication is an essential skill to ensure all members of the MHDT are up to speed with the patient's individual care pathway. The VPCs spend a large amount of time interacting with

the patient and family and their insights are critical toward implementing treatment strategies. Particularly with TV patients, percutaneous treatment methods are focused on research protocol–based care. The VPC must closely collaborate with research coordinators and industry personal alike in order to ensure timely and adequate treatment.

Research Coordinators

Research coordinators involvement in the core TV-MDHT primarily starts with screening the TR patient populations for eligibility in protocol-based percutaneous TV treatments. Consideration of concomitant VHD treatments or percutaneous coronary intervention can affect eligibility and may require treatment prior to consideration for TV protocols. The research coordinators are responsible for having in-depth knowledge of research protocols, compliance with inclusion and exclusion criteria, guidance of diagnostic testing, and coordination of care to ensure adherence to research protocols. They oversee all communication with study sponsors, maintaining ongoing and final data collection, and reporting protocol deviations. They are the key resource for patients, ensuring they are fully informed of the purpose and requirements of protocol participation from initial consent, throughout the treatment process, until final data collection is completed.

Heart Failure Specialists

Severe TR disease is often associated with symptoms of right heart failure such as hepatosplenomegaly, ascites, and peripheral edema. Inclusion of the advanced heart failure specialist on the TV-MDHT is particularly valuable in managing the difficult right-sided fluid overload the TR patient experiences. Additionally, TR protocols typically mandate that advanced heart failure specialists be key members of the protocol, to independently verify that the TR patient is on stable goal-directed medical therapy prior to initiating any transcatheter or surgical-based definitive treatment.

Referring Provider

The referring provider could be identified as the initial or “frontline” TV-MDHT member. It is the referring provider who frequently recognizes the initial signs of TR and provides referral for advanced valve evaluation and treatment. It is imperative they are involved in or receive communication regarding treatment plans and implementation. The referring provider may be a valuable resource for the patient regarding titration of diuretics, as well as managing concomitant health issues that may impact TR management. Ultimately, they will provide the essential follow-up for the patient regardless of which treatment strategy is pursued.

Patient and Family

Finally, the most important member of core MDHT remains the patient. The patient and the patient's family should continuously be included in shared discussions surrounding diagnosis, treatment, and attune care plans specifically their individual goals of care. These goals should be clearly articulated and understood by all members of the MDHT.

The Extended Team Members of the TV-MDHT

Although the core TV-MDHT members serve as the principal team for the care and management of TR patients, the close collaboration and assistance of an extended care team may be needed in order to provide optimal care.

Electrophysiologist

Lead management and extraction are increasingly essential components of the comprehensive care of patients with device-related TR. During MDHT collaboration, cautious review of multimodality imaging for clear delineation of pacer lead impact on the tricuspid leaflet motion and contribution is essential prior to device modification. The procedure for lead extraction requires a careful risk and benefit discussion by the MDHT and with the patient.

Vascular Specialists

In patients with severe TR, the symptoms of fluid overload are treated with diuretic therapy. However, patients with refractory peripheral edema and lymphedema may benefit from management by vascular medicine specialists.

Hepatologist

Systolic flow reversal in the hepatic vessels is considered the strongest non-valvular metric for identifying severe TR [26]. Long-standing severe TR often leads to liver enlargement, ascites, and cirrhosis, from the passive congestion due to right heart failure. The hepatologist is a valuable TV-MDHT member because he or she can manage the recurring ascites and abnormal liver function that may develop with severe TR, perform a thorough workup for other etiologies of liver dysfunction, and help prognosticate outcomes for patients with severe liver disease.

Pulmonary Hypertension Specialist

Pulmonary hypertension (whether primary or secondary) may lead to symptoms of low cardiac output, including fatigue, weakness, shortness of breath, and exercise intolerance. Reduction of pulmonary pressures may reduce the severity of TR, associated symptoms, and need for valve treatment [12]. The pulmonary hypertension specialist plays a key role in managing pulmonary hypertension therapies for chronic disease management and providing key guidance during transcatheter procedures when rapid shifts in pressures during valve modifications can have significant impact on hemodynamics and cardiopulmonary function.

Pharmacist

As medication therapy for heart failure symptoms that occur with TV disease involves a combination of multiple medications [12], inclusion of a pharmacist on the MDHT is helpful in coordinating up-titration of medications, preventing drug–drug interactions, or strategically identifying complementary regimens [27]. When the valve issue occurs in association with other diseases that require an additional layer of therapy, or severe regurgitation has impacted liver or other organ function, pharmacist involvement becomes essential to creating a safe and effective medication regimen. Polypharmacy creates an increased risk for drug–drug interactions as well as creates a scenario conducive to poor adherence, compliance, and adverse events. A large body of evidence supports involvement of the pharmacist in management of heart failure. A systematic review has shown the pharmacist's significant impact with regard to a reduction in all-cause and heart failure admissions and improvement of medication adherence in the elderly with heart failure [28].

The Heart Team Collaboration

The complexity of TV disease prompts robust discussions during the MDHT conference. Tricuspid regurgitation is the most common form of tricuspid valve disease encountered in the clinical setting. Primary TR results from infective endocarditis, rheumatic disease, RV biopsy-related damage, PM wire–induced, prolapse, carcinoid, and Ebstein anomaly among other causes. Secondary TR is the most prevalent form; it occurs in association with other diseases, including left ventricular dysfunction, left-sided valve disease, pulmonary hypertension, atrial fibrillation, annular dilation, and/or RV dysfunction [29–31]. The diversity of the primary or secondary disease processes support the need for a more diverse team discussion. Recent guidelines support a systematic multimodality approach to diagnosis and treatment of tricuspid valve disease [32]. Comprehensive imaging is required to ascertain valve pathology, which provides understanding of the valve morphology and development of the symptom burden. Valve morphology provides a basis for assessing

transcatheter versus surgical treatment strategies. It also provides direction to the various members of the team who guide medical and lifestyle management. Surgical repair or replacement for TV disease is a Class I indication for severe TR for isolated primary disease that is symptomatic or with secondary disease when it occurs in conjunction with left-sided valve surgery. Isolated TV surgery is a Class IIa indication for asymptomatic or mildly symptomatic with RV enlargement or deteriorating RV function [32–34].

The association of secondary TR with left-sided valve dysfunction, RV dysfunction, pulmonary disease, and the complications of right heart overload including hepatic, abdominal, and peripheral edema calls for the involvement of a broader team than involved in the earlier aortic valve MDHT design. In transcatheter procedures for the patient with severe pulmonary hypertension, it may be necessary for a pulmonologist to be present in order to manage nitric oxide inhalation therapy. Chronic and recurring ascites may benefit from communication with the hepatologist regarding liver involvement.

The impact of tricuspid disease on functional status and quality of life of the patient is a long, insidious process. Patients and family members frequently do not recognize a decline has occurred until prompted by questions about previous activity levels. Continual reassessment and titration of diuretic therapy requires close collaboration between the patient and the team. Advanced practice provider valve clinicians, as integral members of the MDHT, play a key role in managing symptom burden on an ongoing basis. Pharmacy input to manage polypharmacy and drug–drug interactions is integral to discussions of ongoing pharmacologic care.

Community Awareness

Increasing both professional and public awareness of valve disease in general and TV specifically will result in improved care of these patients. Great progress has been made in the last 10 years regarding nonsurgical, catheter-based treatments, and the development of transcatheter aortic therapies has led to progress in the advancement of other transcatheter heart valve treatments. Access to nonsurgical repair or replacement procedures has brought hope for curative treatment and facilitates discussion with patients. Catheter-based treatments for the TV are currently in research stage, with patient access limited based on physical proximity to institutions with protocols, ability for patient-protocol "fit" based on inclusion/exclusion criteria, and finally the challenge of designing devices that address the various valve morphologies.

In order to move TV therapies forward, the first step lies in increasing professional awareness of TV disease. Historically, the impact of TR has been underappreciated with late diagnosis, treatments postponed until significant right-sided symptoms are present and right ventricular dysfunction has developed. Current guidelines recommend a direct path to surgical treatment only for symptomatic severe primary TR [12], yet secondary TR is a common form of the disease and both

have a long, subtle progression with a definitive diagnosis not occurring until well established. The timing of surgical treatment is often postponed until severe symptoms have developed, and at a point in time when additional comorbidities and right ventricular remodeling increase surgical mortality risk. Ultimately limiting the treatment options and long-term prognosis.

A second step to move treatment forward is to improve public awareness There has been public education regarding cardiac risk factors for coronary heart disease and stroke. Similar programs for valve disease and its contribution to development of heart failure are needed. Many elderly attribute their functional decline to the aging process when its true source is declining cardiac function from valve disease. Recommendations are for physicians and providers to see patients on a recurring basis, while paying attention to physical exam findings that identify valve disease and diagnostic testing that establishes severity. Educating patients regarding valve function and disease progression so that early referral before ventricular dysfunction occurs can help reduce the debilitating impact of severe TR.

The definitive road forward lies in research. More than 1.6 million Americans have at least moderate-to-severe TR, yet less than 8000 TV operations are performed annually in the USA [35]. The vast majority of these are done in combination with other valve surgeries; in the 10-year period, between 2004 and 2013, only 5005 were performed for isolated TR [36]. In 2020, the development of percutaneous treatments is still in the early stages, with no approved transcatheter devices for either tricuspid replacement or repair. Many protocols explore various transcatheter techniques for TV replacement or repair. The engagement of the MDHT will play an integral role in creating less invasive solutions for TV disease. The knowledge of advanced imagers, cardiac surgeons, and structural interventional cardiologists will be needed to understand device and procedural development to address the complex TV anatomy and pathoanatomy. The skills of our physicians, advanced practice providers, nurse coordinators, and pharmacists will be necessary to help guide the patient through the multistep evaluation process and to continue medical management while searching for curative solutions. The entire MDHT will need to be fully engaged in their team conference to create and implement a procedure plan that meets the unique needs of the patient.

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Part III
Future Management of Tricuspid Valve Disease

Chapter 12
Tricuspid Valve Disease: Annuloplasty-Based Therapies

Laura J. Davidson and Charles J. Davidson

Tricuspid valve disease is an extremely common, although often underrecognized and undertreated, disease, affecting 1.6 million people in the United States [1]. One-year survival of patients with severe tricuspid regurgitation (TR) is approximately 64% [2]. In patients who undergo left-sided valve surgeries that also have TR, survival is worse [3]. Furthermore, it is rare for a patient with isolated severe TR to undergo surgery, and the majority of surgical tricuspid interventions that occur happen within the context of an already planned surgery for other indications [4]. According to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, isolated tricuspid valve repair or replacement is a IIb recommendation for patients with previous left-sided surgery with severe symptomatic TR without signs of right ventricular dysfunction and a IIb recommendation for patients with asymptomatic, severe TR with progressive right ventricular dysfunction. Cardiac surgery is a IIa recommendation for isolated, severe symptomatic primary TR unresponsive to medical therapy [5].

Patients with severe, symptomatic TR often present late in the course of the disease or with multiple comorbidities contributing to relatively poor surgical outcomes. The reality is that mortality for isolated tricuspid valve surgery is quite high and approaching 20% at 30 days [6]. Additionally, eliminating TR with an annuloplasty repair is imperfect [7]. At 3 months post repair, 34% of patients still had moderate or severe TR, and at 5 years, 45% had moderate or severe TR [8]. ACC/AHA guidelines currently recommend medical therapy for TR, including the use of diuretics, but there is little indication that medical therapy for TR improves

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long-term outcomes. Therefore, prior to transcatheter tricuspid valve therapies, options for patients with severe TR were quite limited.

In order to perform transcatheter tricuspid valve procedures, knowledge of multimodality imaging is imperative. The traditional cornerstone of imaging for the tricuspid valve is transesophageal echocardiography. Grading the severity of TR can be challenging, since the tricuspid valve is anatomically complex, with varying number of leaflets, degrees of annular dilation, dynamic coaptation based on hemodynamics and fluid status, and variable tethering of leaflets [9]. Furthermore, anatomy varies such that a predefined view does not always visualize the same structures and all leaflets may not be visualized at the same time when 2D echo is used [10]. Anatomically, transcatheter tricuspid valve therapies face some specific challenges. First, severe TR is often functional and associated with extremely large annulus dimensions with concomitant right ventricular dysfunction. Therefore, with functional TR, tethering of the tricuspid valve is common and transcatheter repair may require large annular anchoring devices [6]. Also, many patients have severe TR due to pacemaker lead interference, and the presence of a pacemaker can make valve repair challenging due to anatomical limitations. Patients with pacemakers that impinge on the tricuspid valve leaflets are often excluded from valvular repair trials. Furthermore, the right coronary artery (RCA) lies adjacent to the tricuspid valve annulus, and annuloplasty can interfere with the patency of the right coronary when the technology requires contraction of the annulus [11]. Additionally, for many patients, transcatheter tricuspid valve therapies are recommended because the patient is high-risk for a reoperation, which often means that the patient has undergone previous left-sided valve replacement or repair that can significantly distort transesophageal echo (TEE) image quality during the procedure.

Transcatheter tricuspid valve devices that have been evaluated have generally enrolled only patients that are high risk or inoperable with severe TR that is refractory to medical therapy. Most patients have New York Heart Association (NYHA) class III or greater symptoms with the vast majority having massive or torrential functional TR and prior cardiac surgery [12]. The annuloplasty-based devices use either a suture annuloplasty or ring annuloplasty platform [12].

Direct Ring Annuloplasty Devices

The Cardioband Tricuspid Repair System (Edwards Lifesciences, Irvine, CA) is under clinical investigation in the US and is CE Mark approved in the EU for the treatment of functional TR (Figs. 12.1, 12.2, 12.3, and 12.4). The Cardioband procedure is performed via transfemoral venous access, using a 24F sheath. Anatomic suitability is determined by transthoracic echo (TTE), TEE, and cardiac CT. CTA is used to determine the appropriate band length and definition of the RCA proximity to the annulus. A series of up to 17 anchors are implanted on the atrial side where the leaflet inserts into the annulus, the so-called “hinge point.” The delivery guide sheath and implant catheters are navigated with TEE and fluoroscopy with a

Fig. 12.1 Cardioband Tricuspid Repair System (Edwards Lifesciences, Irvine, CA). Anchors are placed on the tricuspid annulus and a Dacron band is attached to the anchors (arrow). The Dacron band is then contracted to reduce annular size and TR grade

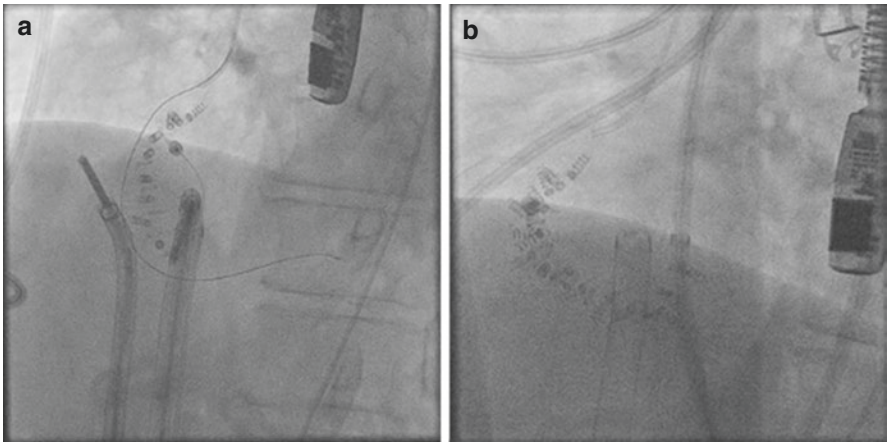

Fig. 12.2 (**a**) Fluoroscopic appearance of Cardioband anchors as they are placed along the tricuspid annulus (solid arrow). A coronary wire (dotted arrow) is placed in the right coronary artery to ensure patency during anchor deployment and contraction of the Dacron band. (**b**) Fluoroscopic appearance of Cardioband anchors following contraction of the Dacron band

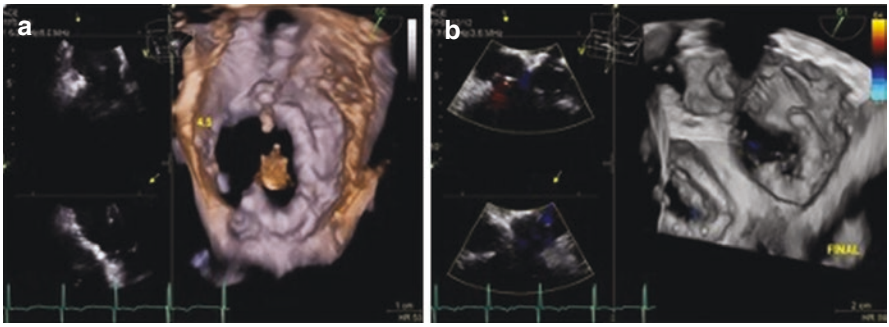

Fig. 12.3 (**a**, **b**) 3D Transesophageal echo images of Cardioband Tricuspid Repair System showing reduction in annular size and improvement in leaflet coaptation

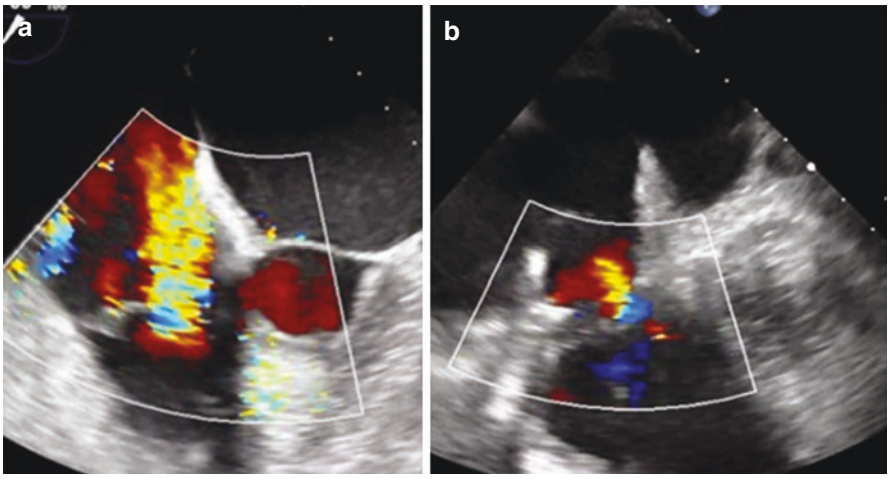

Fig. 12.4 Cardioband 2D Transesophageal Echo Baseline and Final Results. At baseline (**a**), patient has severe tricuspid regurgitation, which is reduced to mild following Cardioband (**b**). (From Davidson C, 2019. https://www.tctmd.com/)

right anterior oblique (RAO) and left anterior oblique (LAO) RCA roadmap. Three-dimensional (3D) intracardiac echo (ICE) has emerged as an important adjunct to help define the optimal implant location. A guide catheter and a coronary guidewire are placed into the RCA to allow periodic injections to assist with anchor placement and ensure lack of arterial interference during deployment and contraction. Implantation begins in the anteroseptal commissure and continues to the posterior annulus. After deployment of the anchors, the Dacron band containing a wire attached to the anchors is contracted. This results in improved leaflet coaptation and reduction of the septal lateral dimension of the tricuspid annulus.

Thirty-day outcomes for the US early feasibility study were reported for the 15 patients enrolled. There was a significant reduction in annular size and EROA at discharge and at 30-day follow up. Additionally, NYHA and Kansas City Cardiomyopathy Questionnaire (KCCQ) scores improved significantly [13]. Also, 6-month outcomes for 30 patients studied in the TRI-REPAIR study (Tricuspid Regurgitation RePAIr With CaRdioband Transcatheter System) demonstrated 100% technical success with a significant reduction in effective regurgitant orifice area, vena contracta width, and annular diameter. There was a corresponding significant improvement in NYHA class, 6-minute walk testing, and KCCQ scores [14].

Another transcatheter tricuspid annuloplasty system that is currently under investigation is the Millipede IRIS (Boston Scientific, Maple Grove, MN). The IRIS semirigid complete annuloplasty ring has anchors which are pre-attached to the base of a nitinol ring. Anchors can be repositioned as needed. It mimics a surgical ring by reducing annular dimensions and improving leaflet coaptation. The device offers the ability to customize the region of annular size reduction to the most dilated area. The three steps to deployment are placement, anchoring, and actuation (Fig. 12.5).

Similar to Cardioband or a surgical annuloplasty ring, it preserves native anatomy, allowing for future interventions including leaflet modification or valve replacement. The Millipede IRIS has been successfully implanted via a transcatheter route in the mitral position [15]. In the tricuspid position, the device has been implanted surgically in two patients who were also undergoing mitral regurgitation surgery. In these two patients, there was a significant reduction in the grade of TR that persisted at 12-month follow-up [16]. A transvenous delivery system for this device is being developed.

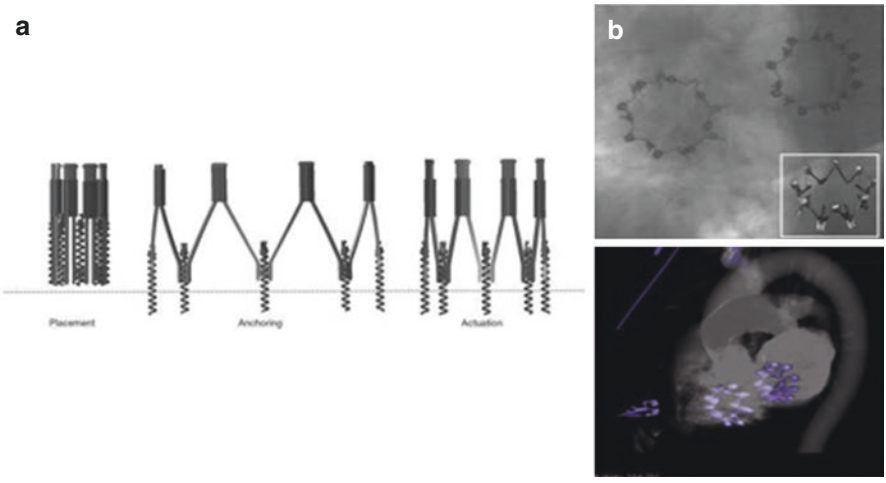

Fig. 12.5 (**a**) Millipede (Boston Scientific). There are three steps to Millipede deployment including placement, anchoring, and actuation. (**b**) Millipede device in the tricuspid and mitral position. (Reprinted with permission from Asmarats et al. [12])

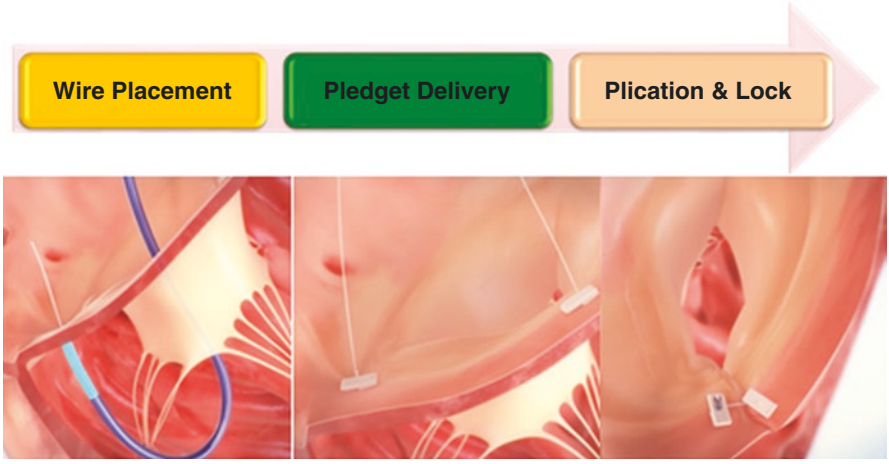

Fig. 12.6 Trialign procedure, 3 main steps. (From Davidson CJ, Hahn R, Meduri C et al., 2015. https://www.tctmd.com/)

Suture Annuloplasty Devices

The Trialign device (Fig. 12.6) is a suture annuloplasty transcatheter tricuspid valve repair system that has been evaluated in clinical trials. The first transcatheter tricuspid valve repair trial utilizing the Trialign device was evaluated in the SCOUT (Percutaneous Tricuspid Valve Annuloplasty System for Symptomatic Chronic Functional Tricuspid Regurgitation) trial. This device was predicated on a modification of the surgical Kay procedure with the goal of making the trileaflet tricuspid valve into a bicuspid valve. The procedure is performed via right internal jugular access under TEE guidance. Using a steerable guide catheter, a wire is delivered from the ventricular side of the tricuspid valve annulus and radiofrequency energy is used to deliver the wire through the annulus and onto the atrial side of the valve. This wire is then snared and a pledget is delivered onto the annulus. This sequence is first performed typically in the posteroseptal commissure and then repeated in the anteroposterior commissure. Next, a plication device is used to cinch the two pledgets together, conforming the trileaflet valve into a bicuspid valve, and reducing the annular size. The SCOUT I trial evaluated 45 patients who underwent device implantation. There was 97% procedural success without any instances of death, stroke, bleeding, or valve reintervention at 30 days. At 30 days, there was significant improvement in NYHA functional class, 6-minute walk distance, and the Minnesota Living with Heart Failure Questionnaire. There was also a significant decrease in TR assessed interprocedurally [17, 18]. At 1 year, there was 95% freedom from all-cause mortality. This technology is not currently being evaluated in clinical trials.

The TriCinch system (4Tech Cardio, Galway, Ireland) (Fig. 12.7) is a technology that also uses a transcatheter annuloplasty to reduce tricuspid annular size. The first generation of this device was evaluated in the PREVENT (Percutaneous Treatment

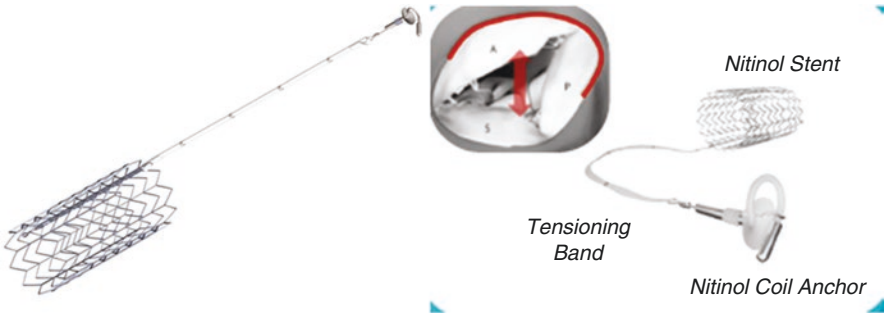

Fig. 12.7 TriCinch Coil Implant system. (From Nietlispach F, 2017. https://www.tctmd.com/)

Fig. 12.8 Minimally invasive annuloplasty, micro interventional devices. (From Williams M, 2018. https://www.tctmd.com/)

of Tricuspid Valve Regurgitation with the TriCinch System). This device is deployed via the femoral vein and the first-generation device deployed a corkscrew anchor to the anteroposterior commissure of the tricuspid valve. The anchor is connected to a Dacron band and a nitinol stent. Tension is then applied to the device, which reduces the septolateral dimension of the tricuspid valve. Once confirmed that the diameter has been reduced, the nitinol stent is deployed in the inferior vena cava [19]. In PREVENT, the procedure was successful in 81% of cases, but two procedures in the trial were complicated by hemopericardium and four patients experienced late detachment of the corkscrew anchor. At 6 months, patients had significant improvement in 6-minute walk testing and improvement in NYHA class [20]. The second-generation device replaces the corkscrew anchor and instead utilizes an epicardial coil that is placed in the mid-anterior tricuspid annulus [21]. This device is currently in clinical trials.

Minimally invasive annuloplasty (MIA, Micro Interventional Devices, Newtown, Pennsylvania) (Fig. 12.8) is another technology used for transcatheter tricuspid valve annuloplasty that was evaluated in the Study of Transcatheter Tricuspid Annular Repair (STTAR) study. The surgical implantation of the device was first evaluated and consists of deploying PolyCor anchors (compliant, self-tensioning,

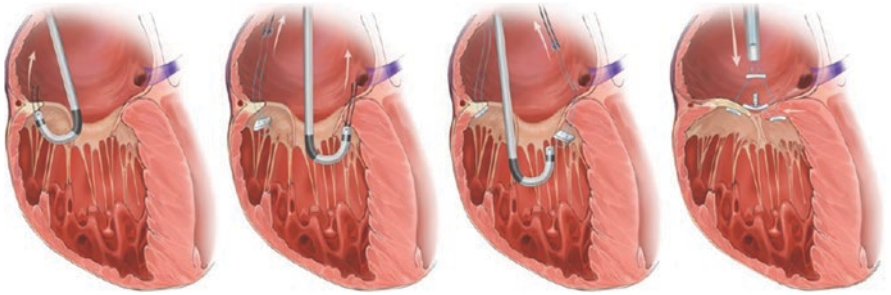

Fig. 12.9 Pledget-assisted suture tricuspid annuloplasty. (From Khan J et al., 2017. https://www.tctmd.com/)

polymeric anchors) and a MyoLast polymer (thermoplastic elastomer). The device aims to place multiple anchors between the posteroseptal and anteroposterior commissures and subsequently create tension between the commissures to exclude the posterior leaflet and result in bicuspidization of the tricuspid valve. The percutaneous arm of the study is now enrolling. Preliminary data in five patients treated with the percutaneous device demonstrated no adverse events related to the device. Tricuspid valve area decreased by an average of 43% and TR decreased by 1–2+ grade in four of the patients. Two of the patients enrolled had pacemaker leads at the time of implantation, indicating that the MIA device can be successfully implanted with pacemaker leads in place [22].

Pledget-assisted suture tricuspid annuloplasty (PASTA) (Fig. 12.9) is another technology that is under investigation. This device requires pledgets to be placed in the anterior and posterior-septal annulus and sutures are used to pull the pledgets together, creating a double-orifice valve. The device aims to mimic Hetzer's double-orifice suture technique. The procedure has been performed in 22 pigs via transapical or transjugular access with technical success and reduction in annular dimensions and quantitative TR. There were complications related to transapical access and pledget pull-through [23]. First in human experience has been reported in one patient with dehiscence pre-discharge and survival at 6 months [24].

Transcatheter tricuspid annuloplasty has multiple rapidly evolving innovative technologies that demonstrate great clinical potential. While most of the current trials have focused on patients who are at increased surgical risk, future studies will need to evaluate whether these technologies demonstrate similar outcomes to surgery in low-to-intermediate risk cohorts. To date, the annular technologies have consistently shown a high safety signal with substantial benefit in quality of life, correlating with a quantitative reduction in TR.

It is likely that one technology will not be suitable for all anatomy. Thus, there is a critical need for alternative tricuspid valve therapies, including tricuspid valve coaptation devices and transcatheter tricuspid valve replacement. Currently, there are no trials that directly compare transcatheter tricuspid annuloplasty, leaflet coaptation, or valve replacement. Coaptation devices for functional TR require appropriate leaflet anatomy, where there is not severe leaflet tethering, coaptation gaps, or

large chordal structures that prevent proper leaflet grasping and deployment. Leaflet modification devices are particularly suitable for degenerative TR with prolapse.

Similar to surgery, patients that present late in their disease course and have severe annular dilation, non-coaptation, or adherent pacemaker leads will be anatomically difficult for transcatheter repair and are likely more suitable for valve replacement. Durability of these technologies will need to be assessed and will influence decisions in device selection for each individual patient. As these various technologies evolve, it is imperative that each individual patient's complex and unique anatomy is taken into account while selecting the proper therapy, aided by superb imaging including TEE, ICE, coronary angiography, and CT.

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Chapter 13
Transcatheter Tricuspid Valve Intervention: Coaptation-Based Strategies

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Introduction

Tricuspid valve disease, specifically tricuspid regurgitation (TR), affects at least 1.5 million people in the United States, with an annual incidence of approximately 200,000 new cases [1]. Tricuspid valve disease is most often functional in the setting of left-sided heart disease, atrial fibrillation (AF), and pulmonary hypertension, where right ventricular remodeling leads to annular dilatation and leaflet tethering [2, 3]. As TR becomes moderate to severe, it becomes an independent predictor of increased mortality, even when patients are asymptomatic [4, 5]. Furthermore, untreated TR carries a grim prognosis, especially when irreversible right heart failure and end-organ dysfunction develop [6]. Tricuspid valve surgery (TVS) is currently the standard of care in symptomatic patients on maximal medical therapy, but it results in significant operative mortality and morbidities [7, 8]. In addition, isolated TVS is associated with the highest mortality among all contemporary valve procedures at 8.8–9.7% [8, 9]. TR, therefore, remains perceptibly undertreated despite guidelines urging prophylactic tricuspid valve repair (TVr) at the time of left-sided cardiac surgery under specific circumstances [10, 11].

To meet this clinical need, a number of transcatheter tricuspid valve interventions (TTVI) have been developed over the past decade. Patients currently referred for TTVI generally present with refractory heart failure. In the multicenter, international TriValve registry, the vast majority of patients were in New York Heart Association (NYHA) class III–IV, with a mean EuroSCORE II surgical mortality risk of 7.6 ± 5.7% [12].

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Transcatheter tricuspid valve intervention technologies can be broadly categorized into devices for coaptation, annuloplasty, caval valve implantation (CAVI), and transcatheter tricuspid valve replacement (TTVR) [11]. Almost all these technologies are investigational with very limited clinical evidence, but early feasibility and safety trials have shown promise. Here, we critically review the various coaptation-based strategies in the context of their evolving clinical indications. Interventions other than leaflet approximation techniques, including TTVR, are covered elsewhere.

Pre-procedural Imaging and Assessment

Transthoracic (TTE) and transesophageal echocardiographic (TEE) evaluation remain the mainstay of pre-procedural pathoanatomical evaluation of the tricuspid valve, especially for predicting the feasibility of repair with a coaptation-based device. As seen in Fig. 13.1, critical TEE views include the four-chamber view, the tricuspid valve right ventricular inflow-outflow X-plane to grasping view (to visualize the septal and anterior/posterior leaflets for leaflet grasping), and the transgastric basal short-axis view (to evaluate the TR jet and assess septal leaflet mobility) [13]. Computed tomography (CT) is also helpful for defining the anatomy of the tricuspid apparatus (see Chap. 7). All coaptation-based strategies require accurate

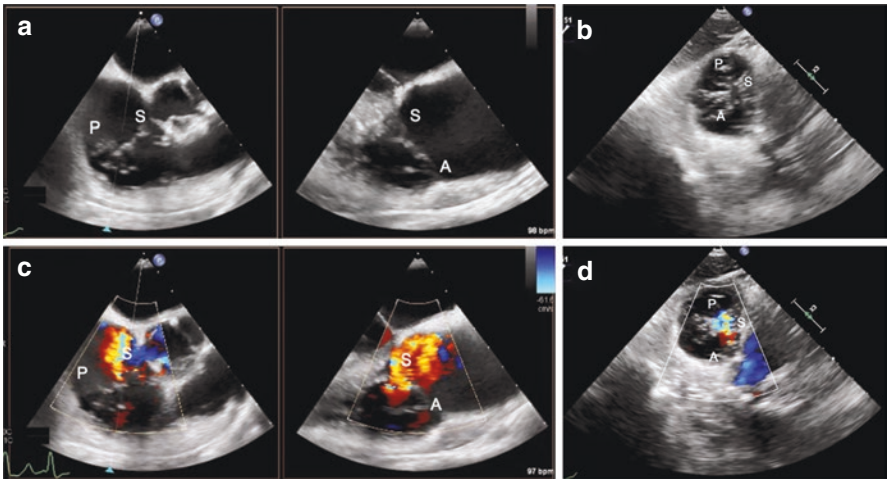

Fig. 13.1 Preoperative transesophageal echocardiographic evaluation of tricuspid valve and regurgitation. Preoperative TEE is essential in defining the pathoanatomy of the tricuspid valve apparatus. (**a**) RV inflow (left) and X-plane-to-grasping (right) views. (**b**) Transgastric view showing a central coaptation defect due to annular dilatation. (**c**, **d**) Doppler color flow mapping of the aforementioned views showing severe TR. A, anterior leaflet of the tricuspid valve; P, posterior leaflet of the tricuspid valve; RV, right ventricular; S, septal leaflet of the tricuspid valve; TEE, transesophageal echocardiography; TR, tricuspid regurgitation

measurements of the maximal anteroposterior and septolateral diameters, right ventricular geometry, and the maximal distance from the tricuspid valve to the right ventricular apex [14]. The target anchoring site of a spacer-type coaptation device can also be selected using CT imaging by drawing a perpendicular line linking the annular plane with the right ventricular septal free wall on a sagittal reconstruction [15]. Furthermore, CT imaging can also assess the size of the venous access site (e.g., left subclavian or axillary vein) for spacer-based coaptation devices [3].

Although there is a dearth of strict guidelines on TTVI repair strategy selection, expert consensus suggests that coaptation-based devices should be used in patients with annular dilatation with mild-to-moderate leaflet tethering. This is particularly true when the regurgitant jet is predominantly anteroseptal or central [16]. Evidence also suggests that the probability of successful repair with this strategy increases when the largest measured coaptation gap is no greater than 7 mm [17, 18], thus underscoring the importance of precise echocardiographic assessment. In contrast, an annular device is likely to be sufficient when minimal leaflet tethering is present. Advanced right ventricular remodeling with severe leaflet tethering and/or large coaptation gaps often requires TTVR or CAVI [16].

Coaptation-Based Devices

Coaptation-based strategies are currently the most commonly used transcatheter techniques in treating functional TR. Numerous devices exist, including the TriClip (Abbott Structural Heart, Santa Clara, CA), PASCAL (Edwards Lifesciences LLC, Irvine, CA), and FORMA (Edwards Lifesciences LLC) systems.

TriClip

Given its widespread availability and operator familiarity, the MitraClip system (Abbott Structural Heart, Santa Clara, CA), typically used to treat mitral regurgitation, has become the leading choice in patients with functional TR undergoing TTVI (off-label application) (Fig. 13.2a). In fact, MitraClip was used in 66% of patients in the TriValve registry [19]. One or more clips may be used to bicuspidize the valve by approximating, most commonly, the anterior and septal leaflets (Fig. 13.3). Clips may also be used to create a triple orifice by connecting the septal leaflet to the anterior and posterior leaflets, thus directly reducing the coaptation gap and counteracting annular dilatation [20, 21]. Early studies have shown that the latter might be more efficient in reducing the septolateral tricuspid annular diameter [21]. In addition to patients with functional TR, the MitraClip system has been used, with varying degrees of success, in patients with degenerative and lead-associated TR, as well as in those with large leaflet notches [22–24].

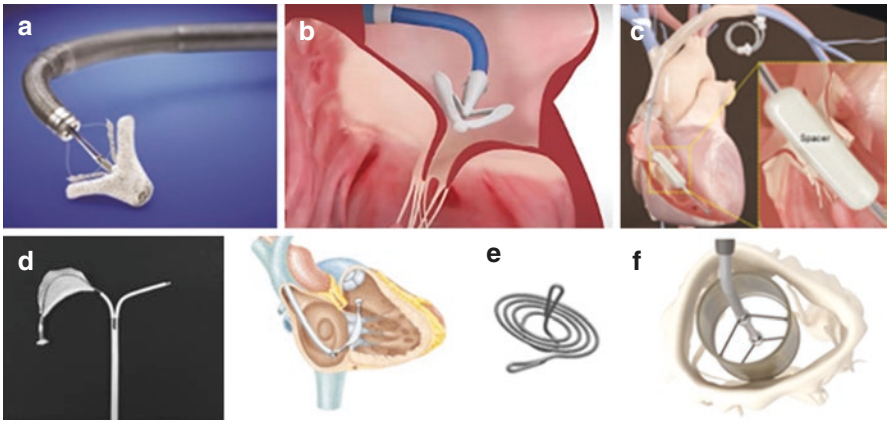

Fig. 13.2 Coaptation-based devices in various stages of clinical use and development. Specifically shown are the TriClip (**a**), PASCAL (**b**), Forma (**c**), Cerclage-TR Block (**d**), Mistral (**e**), and CroíValve (**f**) systems

Outcomes of MitraClip TTVI show early promise. In a multicenter European registry, Nickenig et al. reported on 64 high-risk patients with moderate or greater TR who were treated with the MitraClip system. There were no intra-procedural deaths, strokes, or major vascular complications, and successful device implantation was achieved in 97% of patients. In-hospital mortality was 5%. TR was reduced by at least one grade in 91% of patients, with concurrent improvements in NYHA class and 6-minute walking distance [25]. These results were corroborated by Orban et al., where 50 patients with severe TR underwent edge-to-edge repair. At 6 months, mortality was 16%, and 90% of patients had achieved a persistent reduction of at least one echocardiographic TR grade [26].

The 1-year outcomes of the TRILUMINATE trial (which used the tricuspid valve-specific TriClip system) were recently reported. This was a prospective, multicenter, early feasibility study that assessed 85 patients, with symptomatic moderate or greater TR, who underwent TriClip implantation [27]. TR reduction was achieved in 87% of subjects at 1 year, and the proportion of patients in NYHA class I/II increased from 22% at baseline to 80% at 1 year. All-cause mortality was 5.9% and there were no device-related safety events beyond the 30-day mark, thus validating the safety and durability of repair with the TriClip system [28]. The TRILUMINATE Pivotal Trial (NCT03904147), a prospective, multicenter, randomized controlled trial comparing the efficacy of TriClip to medical therapy is currently underway.

There are certain limitations, however, with the TriClip system. First, the anterior location of the tricuspid valve may hamper intraprocedural TEE assessment. In these cases, intracardiac echocardiography may be considered to ensure coaxial alignment with the device to avoid acoustic shadowing of the delivery catheter against the tricuspid leaflets, thus improving confirmation of leaflet insertion after grasping [29]. Steering of the Clip system within the right atrium can sometimes

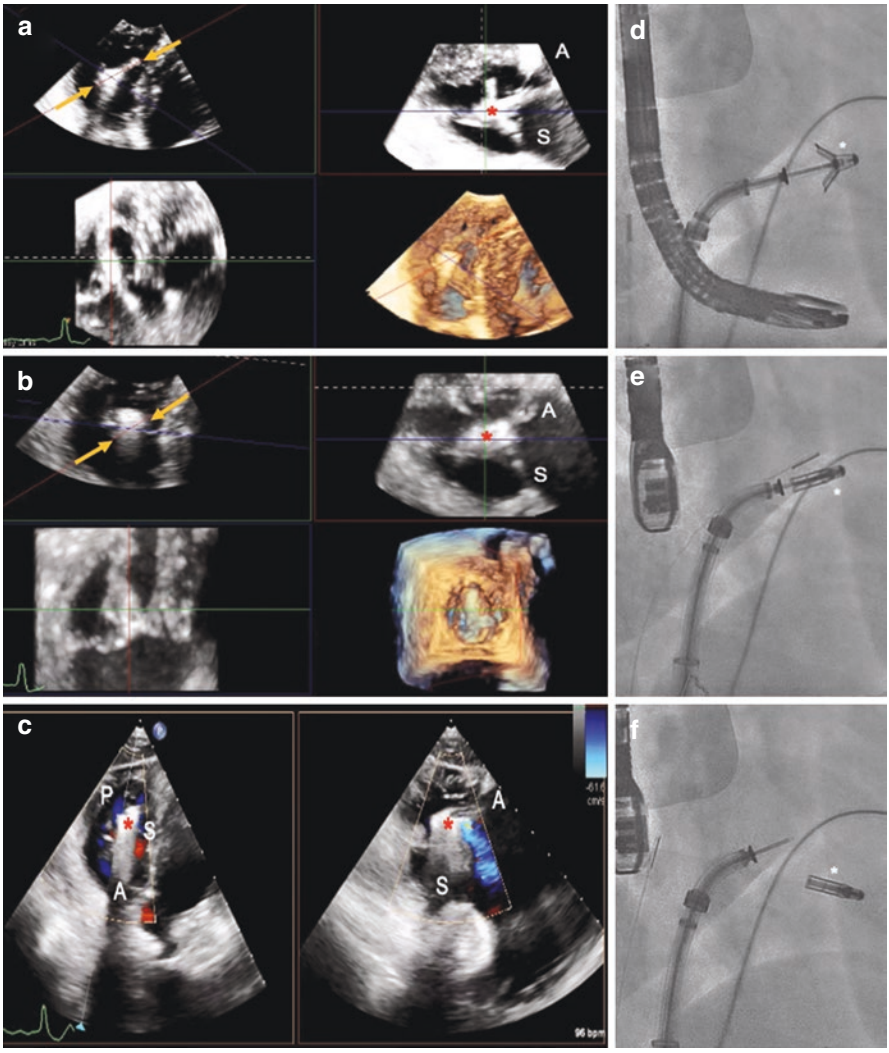

Fig. 13.3 Intraoperative transesophageal echocardiography and fluoroscopy of transcatheter tricuspid valve repair with the MitraClip System. The MitraClip device, which uses one or more clips to bicuspidize the tricuspid valve, is shown here via intraoperative TEE. (**a**, **b**) The device (yellow arrows and red asterisk) is seen to be grasping the anterior and septal leaflets. (**c**) Post-deployment TEE shows mild residual TR. Also shown are fluoroscopic images of (**d**) the device open in the right ventricle for grasping, (**e**) the anterior and septal leaflets being grasped, and (**f**) device deployment. A, anterior leaflet of the tricuspid valve; P, posterior leaflet of the tricuspid valve; S, septal leaflet of the tricuspid valve; TEE, transesophageal echocardiography; TR, tricuspid regurgitation

also be limited with the MitraClip system, requiring use of alternative strategies such as the "miskey" technique with 90° counterclockwise insertion [23]. Additionally, patients with functional TR often have large coaptation gaps that

necessitate multiple grasping attempts and clips. Pacemaker leads may also pose significant challenges due to acoustic shadowing against the tricuspid leaflets, leaflet tethering, or interference with the Clip delivery system. Finally, the relatively smaller subvalvular space within the right ventricle may cause the Clip delivery system to entangle with the tricuspid valve or its chordae [3, 30].

With pending CE mark approval of the TriClip system, the growing experience with the next-generation TriClip NT_R and XT_R devices will undoubtedly improve clinical and procedural outcomes. Given that the tricuspid valve, as well as its associated coaptation gap, tends to be larger compared to its mitral counterpart, the longer device arms of the XT_R system may be especially effective in reducing TR [16].

PASCAL

The PASCAL system constitutes two paddle-shaped, independently closeable, clasps (~25 mm width, ~10 mm length) and a central spacer (Fig. 13.2b) that was originally intended for the treatment of mitral regurgitation [31]. It is delivered via a 22-French steerable guide sheath, a steerable catheter, and an implantation catheter, and it is repositionable and recapturable if required [3]. The larger and wider device arms, presence of a central spacer, and the ability to grasp leaflets independently may all contribute to this system's unique applications within TTVI [32].

The feasibility, safety, short-term durability, and clinical outcomes of PASCAL were recently reported in a multicenter, observational study. Twenty-eight patients with severe TR and heart failure underwent compassionate use of this system. Procedural success was 86% with no intra-procedural complications. Overall, 30-day mortality was 7.1%. Furthermore, the incidence of patients in NYHA functional class ≥III was reduced from 100% at baseline to 12% at 1 month. In addition, 85% had less than moderate TR at the 30-day post-repair follow-up [33]. Although this early report demonstrated significant clinical improvements with the PASCAL system, larger prospective studies and clinical trials are required to assess its long-term safety and durability.

FORMA

The FORMA device treats TR by using a passively expanding, foam-filled balloon to occupy the regurgitant orifice area and reduce the leaflet coaptation gap (Fig. 13.2c). It is delivered via a left subclavian-axillary approach (using a 20–24 French sheath introducer) through a rail anchored at the right ventricular apex. The device, currently available in three sizes (12, 15, and 18 mm), is completely retrievable and unique in its ability to treat very large coaptation gaps not amenable to repair with other systems [11].

Much progress has been made since the first-in-human FORMA experience in 2015 [34]. Perlman et al. reported the 1-year outcomes of treatment of severe TR with FORMA system in 18 patients. Procedural success was 89% (the two unsuccessful procedures were right ventricular perforation requiring open surgery and device dislocation). There was no mortality at 1 year. Furthermore, 79% of patients were in NYHA class I/II with similar improvements in the average 6-minute walk test. Finally, 46% of patients had moderate or less TR, thus demonstrating mid-term safety and efficacy of the FORMA system [14].

More recently, the short- and mid-term outcomes on 29 patients with severe functional TR from the FORMA US Early Feasibility Study (US EFS) were reported [35]. Mortality was 7% at 30 days and 31% at 1 year. Also, 20% and 31% of patients were in NYHA class I at 30 days and 1 year, respectively, with similar improvements in mean vena contracta and effective regurgitant orifice area in paired analyses. Despite demonstration of feasibility and improvements in heart failure symptoms and quality of life, the US EFS raised several safety concerns that have yet to be addressed [36]. Interestingly, these results were in contrast to those reported by Asmarats et al. in their study of 19 patients who underwent TTVI with the FORMA system. The long-term outcomes from this study suggested a favorable safety profile in high-surgical-risk patients with sustained functional improvements and reductions in TR severity [37].

The aforementioned initial findings have spurred a number of modifications within the second-generation FORMA system. For instance, larger spacers are now available that address "torrential" forms of TR. Additionally, device anchoring is improved by a new sheath and a radiopaque apposition indicator [38]. The ongoing Repair of Tricuspid Valve Regurgitation Using the Edwards TricuSPid TrAnsCatheter REpaiR System (SPACER) trial (NCT02787408), with 78 enrolled participants, will shed further light on the safety, efficacy, and durability of this technology.

Experimental Devices

Three experimental, coaptation-based devices – the Cerclage-TR block (Tau-PNU Medical), Mistral device (Mitralix), and CroíValve system (CroíValve) – will be briefly discussed here.

Cerclage-TR Block

This system uses a septal leaflet extension (a soft membrane attached to a backbone column that crosses the tricuspid valve obliquely) to compensate for the regurgitant orifice (Fig. 13.2d). In preclinical studies, this technology was shown to reduce the severity of TR by at least one grade in four of five swine models [39]. However, further research and clinical first-in-human studies are needed to validate these promising results.

Mistral

This is a spiral-shaped device that targets the subvalvular chordae tendineae of the tricuspid valve apparatus (Fig. 13.2e). Delivered through an 8.5-French delivery system, this device is rotated within the right ventricle to grasp the chordae of two adjacent leaflets, thus pulling them together to enhance coaptation [40]. Eight first-in-human and four compassionate-use cases have been reported with variable amounts of follow-up (1–12 months). Procedural success was obtained in 10 out of the 12 patients with significant improvements in reduction of TR severity seen in 5 out of the 12 patients [41]. As with the Cerclage-TR block system, further clinical evaluation is necessary to affirm the safety and efficacy of this device.

CroíValve

The CroíValve system is a coaptation-based strategy that is anchored in the superior vena cava and placed, as a spacer, among the leaflets of the tricuspid valve, thus reducing the size of the regurgitant orifice (Fig. 13.2f). This device also consists of an inner apparatus that augments diastolic flow through the valve, thus mitigating the risk of device thrombosis. Preclinical studies showed early promise, and acute and chronic feasibility studies are ongoing [42].

Conclusion

Transcatheter tricuspid valve intervention is quickly emerging as a viable alternative to tricuspid valve surgery in high-risk surgical patients. Within TTVI repair strategies, coaptation-based devices are particularly efficacious for patients with tricuspid annular dilatation with mild-to-moderate leaflet tethering. Preoperative TEE and CT imaging are essential for procedural planning and success. Three main coaptation technologies, namely the TriClip, PASCAL, and FORMA systems, have emerged this past decade, with varying clinical and echocardiographic outcomes at short- and mid-term follow-up. The results of ongoing clinical trials will undoubtedly shed light on the long-term efficacy and durability of these devices.

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