Transcatheter Tricuspid Valve-in-Valve Procedure

Severe tricuspid commitment is no longer understood as merely a marker of disease but is now widely thought of as a significant contributor to cardiac morbidity and mortality. However, isolated tricuspid valve surgery remains rare and to this day continues to be associated with the highest surgical risk among all valve procedures and high operative mortality rates, especially in reoperations. Therefore, the development of tricuspid transcatheter procedures is as necessary as it was for the other valves a couple of years ago. Recently, multiple percutaneous therapies have been developed for the management of severe tricuspid disease, initially only repair and more recently replacement, thus creating a new branch for the management of patients who have already undergone surgery and who present with dysfunctional bioprostheses.

1. Introduction

The tricuspid valve (TV) is the largest and most apically positioned of the four cardiac valves [1]: its normal orifice area lies between 7 and 9 cm^2 with an average gradient between the right atrium (RA) and right ventricular (RV) being typically <2 mm Hg [2]. Although TV is also an atrioventricular valve, its anatomy and function have several dissimilarities to the corresponding mitral valve (MV), in part due to the lower pressures in the right heart chambers.

The functional abnormalities resulting from TV disease are classified as primary and secondary, the first being relatively rare, and it is the consequence of a primitive lesion of the TV due to congenital or acquired disease processes that affect the leaflets or chordal structures, or both. Secondary TV disease is more common and is a consequence of other diseases such as left-side heart diseases, pulmonary hypertension, RV dilation, and dysfunction from any cause, without intrinsic lesion of the TV itself [1][3]. The most common TV disease in adults is tricuspid regurgitation (TR) and functional tricuspid regurgitation (FTR), with or without tricuspid leaflet tethering, secondary to left heart disease, either myocardial, valvular, or mixed, is responsible for more than 90% of TR in adults [3][4]. Irrespective of the specific initial etiology, TR is a progressive disease in the setting of RV and RA remodeling. Tricuspid stenosis (TS) is even more rarely described, accounting for about 2.4% of all cases of organic tricuspid valve disease, and most often coexists with mitral valve pathology, especially in patients with rheumatic heart disease [5].

TR is a common finding in most individuals, being found in up to 80–90% of them, and for long it was falsely considered a benign condition with a prolonged clinical latency [6]. Because of this, it has been relatively neglected both in the literature and clinically as compared to the primary left-sided diseases [3]. Furthermore, the rarity of TV surgical management, and its high post-operative mortality and morbidity [7][8][9], in addition to the lack of evidence proving the superiority of surgical treatment over medical therapy in severe TR [10], has led it to be called the "forgotten valve" for a long time [3][11].

Nonetheless, in the last few years, the pathophysiology and impact of TR on the outcome of various heart diseases has been increasingly understood and thus its non-benignity is already established in literature [12][13][14][15]. Long-term, higher FTR severity is associated with considerably worse survival, independently of other features [13], and despite TR providing no additive value in advanced congestive heart failure (CHF), it is associated with excess mortality in mild to moderate CHF [15]. Therefore, severe TR is associated with a poor prognosis, independent of age, biventricular systolic function, RV size, and dilation of the inferior vena cava [12].

Hence, a myriad of new research and surgical techniques has been developed aiming to establish the optimal treatment and to ensure perfect surgical timing [16]. Yet, to this day, TV surgery concomitant to left-sided heart surgery is the only Class I guideline recommended therapy for TR [17]. The remaining recommendations of the American and European societies lack both stronger evidence and clear benefits, whereas the current recommendation for isolated TV is restricted only to patients with severe TR who are either symptomatic or are developing progressive RV dilatation/dysfunction [17][18]. However, such patients with severe TR are often asymptomatic for a long period of time and symptoms may not specific, contributing to surgery's delay [16].

Nonetheless, despite the renewed interest in earlier surgery for patients with severe isolated TR before the onset of severe RV dysfunction or end-organ damage and recent improvement in mid to long-term results [19][20][21], isolated TV surgery remains rare and to this day continues to be associated with the highest surgical risk among all valve procedures and high operative mortality rates, especially in reoperations [7][8][9]. In this framework, catheter-based therapies for patients with severe isolated TR has become an area of rapid evolution and growing interest [22], furthermore following the trend of valvular heart disease towards less invasive surgical and percutaneous therapies. As a result, multiple transcatheter tricuspid valve interventions (TTVI) have been developed for treating severe TR, at first aiming at TV repair and, more recently, transcatheter tricuspid valve replacement (TTVR) that allowed a new branch of possibilities in the management of TV disease.

As the TV is being treated more often, also by surgical replacement, prostheses malfunctioning should be expected. Solutions as valve-in-valve and valve-in-ring with transcatheter aortic valve (TAVI) devices are in some way applicable to the tricuspid position. Some case reports have already been published and the most frequently used devices are the Melody™ (Medtronic, Minneapolis, MN, USA) transcatheter pulmonary valve (TPV) from Medtronic and the TAVI XT® and SAPIEN 3® (Edwards Lifesciences, Irvine, CA, USA) [23][24][25][26]. The first one has a major limitation as the maximum diameter size is 22 mm, and for the TV, it is too small. The procedures of valve-in-valve and valve-in-ring have been shown to be safe and feasible.

▌ 2. Imaging Assessment of the TV

2.1. Echocardiography

The goals of imaging in patients with TR are the assessment of severity, etiology, and consequences (RV size and function, pulmonary artery dimension, and pressure) and the detection of concomitant left-sided valvular disease (including the assessment of prosthetic valve function, where appropriate). In that regard, echocardiography remains the cornerstone imaging modality for initial assessment of the etiology and severity of TR. Clinically relevant measurements include an assessment of TR severity, tricuspid annular diameter, leaflet tenting measurements, and RV size and function [27].

Assessing the severity of TR by echocardiography remains challenging and controversial. Although the American Society of Echocardiography and the European Association of Cardiovascular Imaging guidelines considers three stages of FTR (mild, moderate, and severe) [28], the need has been felt for a more sensitive grading system [29]. A vena contracta ≥ 0.7 cm, effective regurgitant orifice area (EROA) of ≥0.40 cm^2, and regurgitant volume ≥ 45 mL, qualify it as severe; however, no distinction is made after these particular parameters. The TriValve registry showed that most of the TTVI patients have really severe TR (often called massive or torrential TR), and furthermore, it was noted that even after a significant TR improvement, in some cases it was still considered severe [30]. This is of particular importance for the evaluation of procedural results and residual TR, since it has been observed that a significant reduction in TR (although still severe according to the current guidelines) is associated with meaningful clinical benefits after TTVI [27]. Thus, a more sensitive five-stage TR severity assessment (mild, moderate, severe, massive, and torrential) has recently been proposed aiming to further assist the optimal therapy choice [31]. Massive and torrential TR gradings may have implications regarding selecting of patients eligible for percutaneous treatment [29]. Nevertheless, this new grading system is not yet present in the guidelines of the main international societies.

In the setting of TS, the echocardiographic view also provides the most useful information [18]. Echocardiographic evaluation of the anatomy of the valve and its subvalvular apparatus is important to assess valve reparability. The mean transvalvular pressure gradient is usually lower in TS than in mitral stenosis (MS), ranging between 2 and 10 mm Hg, and averaging around 5 mm Hg [5]. Despite no generally accepted grading of tricuspid stenosis severity existing, a mean gradient ≥ 5 mm Hg at normal heart rate and a calculated TV area of less than 1 cm^2 is considered indicative of clinically significant TS [5][17][18]. Higher gradients may be seen with combined stenosis and regurgitation.

To this day, transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) represent the gold standard methods for preprocedural assessment of the TV [27], as well as tools for outcome prediction [4][32].

2.2. Cardiac Computed Tomography

Multislice computed tomography (CT) offers a comprehensive assessment of the real 3D anatomy, allowing the operator to assess the TV anatomy as well as the adjacent structures, including the proximity of the right coronary artery to the tricuspid annulus (TA), the coronary sinus, the hepatic veins, and vena cava [33]. Hence it has become the third-step imaging modality during pre-procedural planning for transcatheter TV interventions after TTE and TEE, as it provides

valuable anatomic spatial information of the TV apparatus sometimes hampered by echocardiography because of its complex geometry and anterior position in the chest [19][22][34].

Its application is imperative when evaluating devices that directly interact with the TV leaflets or during the screening process for TTVR, as it enables the accurate measurement of the TA, including maximal anteroposterior and septolateral diameters, perimeter, area, and right ventricular geometry. It also enables the targeting of anchoring sites by drawing a perpendicular line linking the annular plane with the right ventricular septal free wall on a sagittal reconstruction [34]. Similar to transaortic (TAVR) and transmitral valve replacement (TMVR), preimplant CT plays an important role in defining fluoroscopic angles of coplanarity to the TA to help guide the procedure [35].

2.3. Cardiac Magnetic Resonance

Cardiac magnetic resonance (CMR) is currently the gold standard method for the assessment of RV morphology and function, besides an additive to 3D echocardiography for both anatomic and functional analysis of the TV and its annulus. Its use is particularly interesting for a comprehensive evaluation of the right-sided chamber without the need for radiation or iodinated contrast, and especially useful for those that require an appropriate three-dimensional assessment but have suboptimal echocardiographic windows (e.g., obese patients or with lung disease, breast implants, etc.) [28].

The measurement of TR severity on MRI might be performed using the indirect method by calculating TR volume, TR fraction, or by direct measurement of the effective regurgitant orifice area, when possible. While the TR severity cutoffs in CMR have not yet been established, a tricuspid regurgitant fraction ≥ 40% is generally considered hemodynamically significant [28].

3. Transcatheter Tricuspid Anatomic Challenges

Many lessons have been learned in the past decades about transcatheter valve replacement and although many of the concepts of TAVR and TMVR can be transposed to the TV [22], a better comprehension of the anatomical and functional peculiarities of the tricuspid valve and right heart chambers is essential to develop new techniques and to improve those already available, thereby overcoming the specific challenges related to TTVI.

First, surrounding the TV are four four key anatomic structures: the conduction system (atrioventricular node and right bundle of His), the right coronary artery, the noncoronary sinus of valsalva, and the coronary sinus ostium [1]. Therefore, the possible injury risks during transcatheter tricuspid interventions are elevated and with potential severe complications. Moreover, due to the trabeculated and thin RV wall, other approaches, such as the transapical, become hindering [22].

Compared with the MV, the tricuspid annulus is larger, with regurgitant orifice areas often twice those in the mitral position (up to 9 cm^2 area in normal condition, much larger in the presence of functional TR); in addition, its leaflets are thinner and more fragile [22][27]. Hence, the major interventional issue related to the TV compared to the MV lies in its larger orifice. As such, a complete occlusion of the regurgitant area can be very troublesome with the current repair devices that were originally intended for smaller gaps. For the same reason, a replacement device would also have to be extremely large to cover and seal the entire TV area, especially in the absence of any type of annular calcification or leaflet—which is almost never seen in native tricuspid valves—to aid its anchoring [27].

The TA is a saddle-shaped ellipsoid that becomes planar and circular as it dilates [1][22]. Peculiarly, TA dilation does not occur symmetrically, occurring primarily in the anterolateral free wall in patients with left-sided heart disease with sinus rhythm, expanding mostly along the posterior border with less prominent leaflet tethering in patients with functional TR secondary to chronic atrial fibrillation (AF). Therefore, its preferential dilation of the anterior and posterior leaflets allows malcoaptation between the anteroposterior and posteroseptal commissures, rather than the anteroseptal commissure. This organic pattern has important therapeutic implications for TV repair, especially for leaflet-based approaches [22].

Similarly to the MV, the TV has a common antegrade approach. While the most used site is currently the transfemoral access, through the inferior vena cava (IVC), there are some devices that are delivered through a transjugular approach [22][31]. However, the absence of transseptal support and the short distance between the IVC orifice and the TV annulus, combined with the loss of anatomical landmarks under pathologic conditions (RA and RV dilation), makes catheter navigation even more cumbersome than in the setting of a mitral valve intervention, resulting in a complete lack of stabilization and difficult coaxiality, which can lead ultimately into an improper positioning of the repair/replacement device [22][31][32]. Besides the anatomical disadvantages, as tendency of cardiac implantable electrical devices (CIEDs) spreads, so will increase the difficulty of future TTVI. The presence of pacemakers, implantable cardioverter defibrillators (ICDs) or

cardiac resynchronization therapy (CRT) devices will make navigating the catheter and fixing it in an optimal position even more problematic.

In addition to its anatomical peculiarities, the tricuspid valve also presents its own unique challenges on the imaging side. Since the TV is located more anteriorly compared to the MV, intraprocedural TEE guidance is particularly difficult in tricuspid procedures. In some circumstances, a combination of TEE, TTE, and intracardiac echocardiography (ICE) is needed to obtain adequate imaging quality [22].

Despite differences and challenges, in contrast to the mitral and aortic valves, the right heart valves are open-angulated and widely separated by the crista supraventricularis, making the risk of obstruction of the right ventricular outflow tract almost insignificant [22], thereby decreasing one of the most feared complications of percutaneous procedures.

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