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THE PRESENT AND FUTURE

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Transcatheter Tricuspid Valve Interventions

Landscape, Challenges, and Future Directions

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ABSTRACT

Tricuspid regurgitation is a common finding in patients with left-sided valvular or myocardial disease, often being a marker for late-stage chronic heart failure with a grim prognosis. However, isolated tricuspid valve surgery remains infrequent and is associated with the highest mortality among all valve procedures. Hence, a largely unmet clinical need exists for less invasive therapeutic options in these patients. In recent times, multiple percutaneous therapies have been developed for treating severe tricuspid regurgitation, including tricuspid valve repair and, more recently replacement, opening an entirely new venue for managing tricuspid regurgitation. The aim of this review is to provide an updated overview and a clinical perspective on novel transcatheter tricuspid valve therapies, highlighting potential challenges and future directions. (J Am Coll Cardiol 2018;71:2935–56) © 2018 by the American College of Cardiology Foundation.

Tricuspid regurgitation (TR) is estimated to affect >1.5 million people in the United States (1), with a yearly incidence of about 200,000 and >300,000 patients in the United States and Europe, respectively. TR is most often functional, primarily due to annular dilatation and leaflet tethering from right ventricular remodeling caused by left-sided heart disease, atrial fibrillation, or pulmonary hypertension (2).

The prognosis of untreated TR remains poor (3), with most patients receiving lifetime medical therapy until intractable right heart failure and end-organ dysfunction appear. This is despite current guidelines favoring early tricuspid valve (TV) repair in patients with tricuspid annular dilatation undergoing left-sided cardiac surgery, even if TR is mild (4,5). Reluctance to perform tricuspid surgery stems from increased in-hospital mortality, particularly following prior left-sided heart valve surgery (6,7) or after initial tricuspid repair (8,9). Of note, isolated TV surgery remains rare—only 5,005 isolated tricuspid procedures were performed in a large contemporary U.S. nationwide registry over a 10-year period—and continues to be associated with the highest surgical risk among all valve procedures in contemporary practice, with operative mortality rates of 8.8% to 9.7% (**Figure 1**) (10,11).

In recent years, a growing body of knowledge along with multiple emerging transcatheter tricuspid technologies has spurred active investigation within the interventional and surgical communities alike, with ongoing rapid momentum. We provide an updated overview of the current landscape of transcatheter TV therapies, focusing on procedural

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ABBREVIATIONS AND ACRONYMS

CAVI = caval valve implantation

CE = Conformité Européenne

CT = computed tomographic

IVC = inferior vena cava

NYHA = New York Heart Association

QoL = quality of life

SVC = superior vena cava

TA = tricuspid annulus

TR = tricuspid regurgitation

TTVR = transcatheter tricuspid valve replacement

TTVr = transcatheter tricuspid valve repair

TV = tricuspid valve

and midterm outcomes, remaining caveats, and future directions.

PRE-PROCEDURAL SCREENING AND MULTIMODALITY IMAGING

TV ANATOMY. Accurate knowledge of the TV apparatus anatomy is key when planning transcatheter tricuspid interventions. The TV is a complex structure, with several anatomic peculiarities rendering it unique (**Figure 2**) (12). Compared with the mitral valve, the tricuspid annulus (TA) is larger—the largest of all valves, with regurgitant orifice areas often twice those in the mitral position—and its leaflets are thinner and more fragile. The TA is a saddle-shaped ellipsoid that becomes planar and circular as it dilates. Interestingly, dilatation of the TA occurs 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 (**Figure 3**) (13). Because of preferential dilation of the anterior and posterior leaflets, malcoaptation occurs primarily between the anteroposterior and posteroseptal commissures rather than the anteroseptal commissure, with important mechanistic and therapeutic implications for TV repair, especially for leaflet-based approaches (14).

Four chief anatomic structures surround the TV and are therefore at risk for impingement during transcatheter tricuspid interventions: the conduction system (atrioventricular node and right bundle of His) coursing the membranous septum at 3 to 5 mm from the anteroseptal commissure, the right coronary artery (encircling the right atrioventricular groove ~5.5 mm from the septal and posterior portions, 7 mm from the anterior portion), the noncoronary sinus of Valsalva, and the coronary sinus ostium being an important landmark of the posteroseptal commissure. The TV apparatus poses additional challenging issues to overcome: lack of calcium, angulation in relation to the superior vena cava (SVC) and inferior vena cava (IVC), a trabeculated and thin right ventricle hindering a transapical approach, or the presence of pre-existing cardiac implantable electronic devices (15).

ECHOCARDIOGRAPHIC EVALUATION OF TR

Echocardiography remains the cornerstone imaging modality for initial assessment of the etiology and severity of TR. Current guidelines establish an echocardiographic tricuspid annular threshold of ≥40 mm (21 mm/m^2) for combined TV repair (4,5,16), although a larger cutoff (70 mm) based on direct surgical measurements has also been proposed (17). However, surgical measurements are often performed under unloaded conditions and are highly dependent on the traction applied to the TA, and recent data cast doubt on their accuracy (18). Judging the severity of TR by echocardiography remains challenging and controversial. The American Society of Echocardiography and the European Association of Cardiovascular Imaging currently consider 3 stages of functional TR: mild, moderate, and severe (**Table 1**) (19,20). A comprehensive description of qualitative, semiquantitative, and quantitative echocardiographic assessment of functional TR can be found elsewhere (21).

PATIENT SELECTION. The silent yet progressive nature of functional TR consistently leads to delayed referral of patients with end-stage heart failure with extreme leaflet tethering and tricuspid annular enlargement, carrying high perioperative mortality and adverse outcomes following correction (22). Accurate patient screening by a multidisciplinary heart team is paramount to optimize procedural results and effectiveness of transcatheter tricuspid therapies. Invasive measurement of pulmonary artery pressures and resistances can be useful when clinical and noninvasive data are inconsistent, because laminar TR and dynamic right atrial pressure in the presence of a prominent V wave may preclude reliable noninvasive estimates (23). Clinical and echocardiographic predictors of TR recurrence (TV tethering distance >0.76 cm or tethering area >1.63 cm^2 [24], higher pre-operative regurgitation grade, left and right ventricular dysfunction, permanent pacemaker, suture annuloplasty [8], increasing pulmonary pressure [25]) or worse survival (right ventricular end-systolic area ≥20 cm^2 [6], age, end-stage renal disease, and TV replacement [10]) after TV surgery are important factors to consider when assessing potential candidates for transcatheter TV interventions. First and foremost, efforts should focus on identifying those patients in whom transcatheter TV repair (TTVr) or transcatheter TV replacement (TTVR) is likely to be futile, heeding the dictum of primum non nocere. At this early stage of the technology, TTVr and TTVR should probably be reserved for patients with isolated TR deemed at too high surgical risk because of prior open heart surgery or multiple comorbidities, in the absence of severe right or left ventricular dysfunction and severe pulmonary hypertension.