TRANSCATHETER TRICUSPID INTERVENTION: SHORT PERSPECTIVE

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ABSTRAK

Pendahuluan Pendahuluan Sekitar 4% individu yang berusia 75 tahun atau lebih menunjukkan regurgitasi trikuspid (TR) yang signifikan secara klinis. Regurgitasi trikuspid primer disebabkan oleh kelainan struktural katup trikuspid dan terjadi pada 8-10% pasien dengan masalah katup trikuspid. Regurgitasi trikuspid sekunder sering terlihat akibat peregangan anulus yang diakibatkan oleh pembesaran ventrikel kanan dan disfungsi akibat hipertensi paru, yang umumnya dikaitkan dengan penyakit jantung sisi kiri atau fibrilasi atrium. Terlepas dari penyebabnya, TR menyebabkan volume yang berlebihan dan tekanan dinding yang meningkat, yang berkontribusi negatif terhadap remodeling yang berbahaya dan memburuknya TR. Intervensi untuk mengatasi TR tidak cukup digunakan dalam praktik klinis sehari-hari karena risiko pembedahan yang lebih tinggi dan pasien yang datang terlambat. **Metodologi** Pencarian elektronik yang ekstensif dilakukan menggunakan *PubMed, Google Scholar*, dan *ScienceDirect.* Penyelidikan dibatasi pada publikasi berbahasa Inggris. Pencarian manual dari berbagai publikasi dan daftar referensi yang relevan telah dilakukan. **Hasil** Intervensi katup trikuspid transkateter yang baru diperkenalkan dirancang untuk memenuhi persyaratan yang belum terpenuhi ini. Lebih jauh, evaluasi komprehensif dari perawatan transkateter yang tersedia saat ini, termasuk faktor-faktor utama untuk memilih pasien dan perangkat, serta rincian tentang ketidakpastian yang masih ada, didiskusikan pada artikel ini **Diskusi** Keahlian khusus dan evaluasi komprehensif oleh Tim Jantung multidisiplin sangat penting dalam menggabungkan teknik-teknik baru ini secara efektif dan memilih pasien yang sesuai—metode yang mapan untuk menilai pasien dengan TR yang merupakan kandidat potensial untuk prosedur transkateter

Kata Kunci : anatomi, klasifikasi, tingkat keparahan TR, pemilihan pasien, intervensi transkateter

ABSTRACT

Introduction Around 4% of individuals who are 75 years old or older demonstrate clinically significant tricuspid regurgitation (TR). Primary tricuspid regurgitation is caused by a structural abnormality of the tricuspid valve and is present in 8-10% of patients with tricuspid valve issues. Secondary tricuspid regurgitation is frequently seen due to annular stretching resulting from right ventricular enlargement and dysfunction due to pulmonary hypertension, which is commonly associated with left-sided heart disease or atrial fibrillation. Regardless of its cause, TR results in excessive volume and heightened wall pressure, which contribute negatively to harmful remodeling and worsening of TR. Interventions to address TR are not being used enough in daily clinical practice due to higher surgical risk and patients presenting late. An extensive electronic search was performed using PubMed, Google Scholar, and ScienceDirect. The inquiry was confined to English-language publications. A manual search of relevant publications and reference lists was conducted.. Result The newly introduced transcatheter tricuspid valve interventions are designed to meet this unfulfilled requirement. Furthermore, a comprehensive evaluation of the currently available transcatheter treatments, including the primary factors for choosing patients and devices, as well as details on lingering uncertainties, is presented **Discussion** Both dedicated expertise and a comprehensive evaluation by a multidisciplinary Heart Team are crucial in effectively incorporating these new techniques and choosing suitable patients—an established method to assess patients with TR who are potential candidates for transcatheter procedures.

Keyword : anatomy, classification, severity TR, patient selection, transcatheter intervention

INTRODUCTION

Tricuspid regurgitation (TR) is a frequently seen echocardiographic discovery found in 70-90% of the general populace (Nishimura et al., 2014). Although mild TR is common in healthy people, moderate or severe TR has a prevalence of 0.55% after adjusting for age and sex, showing a higher occurrence in females and a significant increase with age - around 4% of individuals aged 75 or older have clinically significant TR (Topilsky et al., 2019). The invention of transcatheter aortic valve implantation and its successful outcomes, followed by transcatheter therapies for mitral valve disease, have created numerous opportunities for transcatheter treatment of TR, a valvular heart disease that has historically been regarded as benign and frequently goes untreated (Praz et al., 2021).

Prolonged and serious TR results in the right ventricle (RV) being overloaded with volume and experiencing increased wall stress, leading to harmful remodeling and a deterioration of TR. This cycle of events leads to reduced survival and worsened heart failure symptoms in both patients with and without decreased left ventricular ejection fraction (Chorin et al., 2020; Topilsky et al., 2014). Hence, there is a pressing clinical requirement that necessitates immediate intervention. Yet, numerous uncertainties and inconsistencies persist, including a lack of systematic approach to evaluating tricuspid valve (TV) disease, unclear terminology regarding anatomy and causes, and difficulties in identifying the mechanism and extent of TR and its impact

METHODS

An extensive electronic search was conducted using PubMed, Google Scholar, and ScienceDirect. The inquiry was confined to English-language publications. A direct examination of relevant publications and reference lists was also performed. Searches include reviews, original articles, and case reports. The exclusion criteria included publications not written in English and those without full access.

The collected papers were organized and administered via Mendeley software. The search was conducted across many databases, resulting in some duplicate citations, which were eliminated using Mendeley software. Based on the title and abstract, the search results were sorted. The full text was then read, and articles that met the exclusion criteria were eliminated.

DISCUSSION

Anatomy, Classification, and Severity of Tricuspid Valve (TV)

The TV has the most significant size and is positioned towards the front of the heart, with intricate and diverse anatomy (Hołda et al., 2019). Despite its name suggesting three distinct leaflets, many different anatomical variations are present (Huttin et al., 2015; Xanthos et al., 2011). Transgastric short-axis view transesophageal echocardiography (TEE) imaging or 3D volume-rendered equivalent allows for visualization of TV morphology (Hahn et al., 2021; Huttin et al., 2015; Xanthos et al., 2011).

Identifying the primary morphologic and/or functional abnormalities leading to TR is a crucial factor in choosing transcatheter TV devices (Besler et al., 2018; Song et al., 2009). Primary tricuspid regurgitation is caused by a structural abnormality in the tricuspid valve and is found in just 8-10% of individuals with tricuspid valve disease. Secondary TR (STR) is more prevalent and results from atrial fibrillation (AF) with normal RV pressures (atrial/atriogenic or isolated TR) or annular dilatation brought on by RV enlargement and dysfunction as a result of pressure/volume overload as a result of pulmonary hypertension (PHT), which is frequently brought on by left-sided heart disease. Following left-sided valve surgery, STR may also appear, most likely as a result of silent ischemic RV damage (Praz et al., 2021). STR can also occur following surgery on the left-sided valves, potentially because of unnoticed damage to the right ventricle from lack of oxygen. 20-30% of patients experience significant TR following the placement of CIED RV leads, a condition that often worsens as time goes on (Anvardeen et al., 2019; Höke et al., 2014).

Carpentier's functional classification of leaflet mobility was intended to guide mitral valve surgical repair or replacement and its application to the TV is less well established (Antunes et al., 2017; Prihadi et al., 2018). In addition to differences in TV leaflet mobility, patients with STR also demonstrate variable remodeling of the TV annulus, right atrium (RA), and RV secondary to the underlying pathology (Antunes et al., 2017). The definition of different TR groups is prognostically important since disease etiology determines long-term outcomes. Accordingly, we propose a novel integrative classification of TR that accounts for the pathophysiology, imaging characteristics, clinical management, and outcome. We also recognize that differentiation of the initial etiology based on valve and chamber morphology/function may be challenging as TV disease progresses (Muraru et al., 2020).

Quantitative assessments of TR are crucial to determine severity, such as calculating anatomical regurgitant orifice area through vena contracta measurement and measuring physiological effective regurgitant orifice area (EROA) and regurgitant volume (RVol). A vena contracta of 7 mm or more typically signals severe TR, although some research

proposes a threshold of 9 mm calculated from two different 2D views (Lancellotti et al., 2013; Zoghbi et al., 2017). Measurements of vena contracta width, based on single 2D imaging, may not be accurate due to the non-circular shape of the TR coaptation zone. Therefore, utilizing 3D color assessment for planimetry could be more suitable in theory (Dahou et al., 2019).

Right heart catheterization is considered the best method for evaluating the severity and cause of PHT, pulmonary vascular resistance, the ratio of RA pressure to pulmonary capillary wedge pressure, pulmonary artery pulsatility index, and the potential for PHT to be reversed (Tsukashita et al., 2015). Additionally, a reduced afterload-adjusted tricuspid annular plane systolic excursion (TAPSE) compared to invasive systolic pulmonary artery pressure (SPAP) measured during right heart catheterization and a conflicting diagnosis of PHT (with a difference of >10 mmHg between non-invasive and invasive SPAP) were both factors independently associated with poorer outcomes (including death, hospitalization for heart failure, and need for re-intervention) in individuals with severe TR (Kang et al., 2016; Lurz et al., 2020).

Patient Selection

STR can be linked to various medical issues and might be seen by different types of healthcare providers, not just cardiologists (Condello et al., 2021). Efforts need to be focused on raising clinical awareness about the consequences and new treatment options (Hahn et al., 2022). Patients with any of the following conditions (left-sided heart disease, atrial fibrillation, prior mitral valve procedure, pre-capillary pulmonary hypertension, cardiac implantable electronic device with right ventricular lead) exhibiting congestive heart failure symptoms (jugular vein congestion, shortness of breath, swelling in extremities, kidney issues, congested liver, and gut) should undergo a thorough assessment for significant tricuspid regurgitation (Adamo et al., 2024; Zahr et al., 2022). The first appointment and evaluation with an echocardiogram to verify the diagnosis and evaluate the severity of TR and RV function should be followed by a prompt referral to a specialized center for TV disease treatment, where further testing like right and left heart catheterization and advanced imaging studies can be done (Ambrosino et al., 2024; Lebehn and Hahn, 2023).

At present, over 90% of patients with clinically significant TR do not receive treatment because of the common belief that TR improves with treatment for left-sided heart disease, even though it can progress in up to 25% of patients after open heart surgery (Dhoble et al., 2019). Additionally, relatively high death rates (8.8%-9.7%) have been documented following traditional procedures for isolated TR, typically due to delayed referrals (Alqahtani et al., 2017; Dreyfus et al., 2020). Nonetheless, tricuspid surgery could be safe and successful in experienced centers, as suggested by single-center studies involving younger and healthier patients than those in the TTVI cohorts (Hamandi et al., 2019; Kadri et al., 2019).

When considering a TV intervention, it is important to consider various factors such as the patient's clinical features, the severity of the disease, the function of other organs, and anatomical considerations. Individuals with mild to moderate left ventricular dysfunction who show symptoms and fluid retention despite treatment with diuretics, have normal right ventricular function, do not have pre-capillary pulmonary hypertension, and only have mild to moderate kidney and liver problems may benefit the most from tricuspid valve intervention (Kavsur et al., 2021; Mehr et al., 2020). A combined approach may be appropriate for patients with concurrent mitral or aortic valve issues a step-by-step strategy is often recommended as tricuspid

regurgitation and right ventricle size may improve in approximately 40% of patients after three months of successful transcatheter treatment for mitral regurgitation (Taramasso et al., 2019). On the other hand, the process may not be effective for patients with advanced heart failure, untreated pre- and post-capillary pulmonary hypertension, or severe lung scarring. Though there may not be proof currently, it is important to consider severe end-organ damage, such as end-stage kidney failure or obvious liver cirrhosis, especially if the projected lifespan is under one year (Vahanian et al., 2022).

Transcatheter Intervention

According to the evidence, the 2021 Valvular Heart Disease guidelines of the European Society of Cardiology initially recommend transcatheter treatment for severe symptomatic TR in inoperable patients with an IIb level C recommendation. They also stress the significance of promptly referring patients with TV disease and treating the TV concomitantly during left-sided heart surgery (Vahanian et al., 2022).

Presently available transcatheter procedures imitate surgical methods and consist of approved techniques in Europe like leaflet approximation, direct annuloplasty, and heterotopic caval valve implantation, in addition to transcatheter TV replacement (TTVR) systems that have not yet been released for commercial use, utilizing orthotopic valve implantation (Schlotter et al., 2021). Increasing evidence backs the utilization of TTVI in patients who are either inoperable or at high risk for surgery: mortality rates were decreased after undergoing the intervention with different devices compared to receiving standard medical care in two similar cohorts, along with a decrease in the frequency of re-hospitalization due to heart failure (26±3% vs 47±3% $p<0.0001$) one year after treatment. Confirmation of these results is necessary through conducting randomized controlled trials (Schlotter et al., 2021; Taramasso et al., 2019).

The TriClip™ (Abbott Vascular) or PASCAL systems (Edwards Lifesciences) have been authorized in Europe for minimally invasive tricuspid valve repair, specifically for tricuspid transcatheter edge-to-edge repair (T-TEER) or leaflet approximation. Due to their safety, accessibility, and user-friendly features, these methods are widely used globally. Although originally done "off-label" with the MitraClip® system from Abbott Vascular, (Braun et al., 2016; Hammerstingl et al., 2016) a new device called TriClip, specifically designed for tricuspid valve (TV) access, has been created with a shorter curved guide catheter and an extra steerable motion plane (septal to lateral) (Braun et al., 2016). In the TRILUMINATE study, T-TEER in 85 patients showed a significant decrease in severe TR, with 71% achieving moderate TR or less after one year. Symptomatic improvement was seen in 83% of patients, who were mostly in NYHA Class I or II, and there was a 40% decrease in the re-hospitalisation rate (Lurz et al., 2021; Nickenig et al., 2019).

The LuX-Valve, manufactured by Ningbo Jenscare Biotechnology Co. Ltd. in Ningbo, China, is a 32 Fr system that is implanted using transatrial access, able to attach to the septum and capture the anterior TV leaflet at the same time. The first encounter in forty-six patients showed a high technical success rate of 97.8%, with one patient experiencing a fatal RV perforation, and an in-hospital mortality rate of 13% (Lu et al., 2021).

Implanting a heterotopic caval valve can relieve symptoms caused by TR and RV failure in patients who cannot undergo other procedures, but does not address the underlying cause. It is a valuable option for symptom management. Traditional aortic

bioprostheses that expand with a balloon are too undersized in this situation, leading to harmful embolic issues. This development resulted in the creation of specialized devices called TricValve® (P+F Products+Features GmbH, Wessling, Germany) and TRICENTOM2M (MEDIRA GmbH, Balingen, Germany) (Donà et al., 2021; Dreger et al., 2020). TricValve has two valves placed in the superior and inferior vena cava individually, while TRICENTOM2M comprises a specially designed stent with a valve that connects both venae cavae. Both devices can currently be used to treat patients with inferior vena cava (IVC) diameters of 40-43 mm, while there needs to be a minimum distance of 10 mm from the RA junction to the hepatic veins (Toggweiler et al., 2018). Reported successful implantations of both devices have occurred in single patients, but recent fractures of the TRICENTOM2M stent frame in patients with severe TR have prompted design adjustments and modifications in clinical selection criteria. Additional analysis in more extensive groups is necessary in order to have a deeper understanding of the significance and impact of this treatment (Montorfano et al., 2019; Toggweiler et al., 2018).

An expert Heart Valve Centre specializing in TV treatment should establish a referral and educational network with partners, and provide easily accessible digital (imaging) data transfer options for remote consultations and case discussions. Participating in multicenter studies evaluating new treatment strategies for TR is crucial to improve our understanding of the indications, timing, and success rate of invasive TV treatments. Addressing the wide range of practices in diagnosing, assessing, and managing TV disease should be the top priority, with efforts focused on raising awareness among primary and secondary care providers. Progress in deep learning for analyzing echocardiographic, CCT, and CMR images could enhance the standardization and improve the precision of TR grading and assessment of RV function. These advancements are expected to speed up quickly in the upcoming stage of transcatheter valve interventions evolution.

CONCLUSION

TR is a valvular condition that is fairly prevalent. In the past, the use of loop diuretics in managing right HF symptoms did not offer any improvement in morbidity or mortality outcomes. Interventions are not commonly performed on patients with TR. Surgery for TR is not often done because of the belief in high death rates. Nevertheless, more recent information indicates improved results, especially in patients with only TR. The transcatheter procedure is still in its initial phases for the advancement and evaluation of new devices in clinical trials. Effective outcomes in patients with TR may be achieved by utilizing clinical assessment and imaging for proper patient selection, and subsequently choosing the most suitable intervention based on anatomic and physiologic factors

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