Comprehensive Review

The Current Landscape of Transcatheter Tricuspid Valve Intervention

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ABSTRACT

Tricuspid regurgitation (TR) is common, and its prevalence increases with age. It was previously estimated that there are 1.6 million patients in the United States with moderate or worse TR, and more contemporary data suggest the age-adjusted prevalence of TR is 0.55%. Increasing TR severity is associated with an adverse prognosis independent of the pulmonary artery pressure and the degree of right heart failure. In heart failure with reduced ejection fraction, survival is significantly worsened when moderate or severe TR is present. The mainstay of therapy has traditionally been surgery, but outcomes are poor. There has been increasing attention on the potential role of transcatheter interventions for TR. Numerous platforms are in developmental evolution, which broadly fall into 3 categories: valve replacement, valve repair (subdivided into annular, leaflet, and chordal platforms), and caval valve implantation. In this review, we examine all these strategies and devices, including guidance on how to appropriately select patients who can benefit from intervention.

Introduction

Tricuspid regurgitation (TR) is common, and its prevalence increases with age.[1] It was previously estimated that there are 1.6 million patients in the United States with moderate or worse TR,[2] and more contemporary data suggest that the age-adjusted prevalence of TR is 0.55%.[1] Increasing TR severity is associated with an adverse prognosis[3,4] independent of the pulmonary artery pressure and the degree of right heart failure.[5] Left untreated, isolated TR significantly worsens survival,[6,7] and in a contemporary cohort, 5-year event-free survival was only ~60%.[8] In heart failure with reduced ejection fraction, survival is significantly worsened when moderate or severe TR is present.[6] In patients with severe secondary mitral regurgitation, the presence of moderate or worse TR was associated with worse clinical and echocardiographic characteristics and worse clinical outcomes when compared with patients with mild or no TR.[9]

The mainstay therapy for TR has traditionally been surgical repair or replacement. Current American guidelines suggest tricuspid valve (TV) surgery, a class I recommendation for patients undergoing left-sided valve surgery who experience severe TR regardless of symptoms.[10] There are

class IIa recommendations for TV surgery for severe primary TR with right-sided heart failure, medically refractory severe functional TR from annular dilatation (in the absence of pulmonary hypertension or left-sided disease), and mild-moderate TR with annular dilation or previous right heart failure if planning a left-sided valve surgery. Finally, there are IIb recommendations for TV surgery in asymptomatic, severe, primary TR with progressive right ventricle (RV) dilation or dysfunction and severe TR after left-sided valve surgery when associated with right heart failure (without severe pulmonary hypertension or RV systolic dysfunction). The European guidelines are similar but notably carry an additional IIb recommendation for experienced heart valve centers to consider transcatheter TV therapies "in symptomatic, inoperable, and anatomically eligible patients in whom symptomatic or prognostic improvement can be expected."[11]

Despite the prevalence or TR and broad indications for TR surgery, there remains a disconnect where only 8000 to 10,000 TV surgical procedures are performed annually in the United States.[12] Potential reasons for this discrepancy include challenges with diagnosis, leading to patients being systematically undertreated, and late referral, in which patients become poor surgical candidates owing to late manifestations of TR (RV

dysfunction, irreversible pulmonary hypertension, and hepatic and renal insufficiency). Poor uptake of TV surgery might also be explained by the poor results of TV surgery reported in the literature. Operative mortality has been reported as high as 30% in some series,[13] although more contemporary data using nationwide databases suggest 30-day mortality rates in the 8% to 10% range. Notably, these rates appear unchanged in the past decade despite an increased procedural volume during this timeframe.[14–16] In expert centers, highly selected patients undergoing isolated TV surgery had an operative mortality of 3.2%,[17] although it is clear that there is significant variability in observed outcomes.[8]

These combination of factors—a highly prevalent condition, an adverse impact on mortality, and effective therapies being applied only to a small fraction of patients with variable outcomes achieved—fulfills the criteria of an important unmet clinical need and is the ideal setting for the pursuance of novel therapeutic strategies. Furthermore, there has been notable success in the development of transcatheter therapies for aortic and mitral valvular heart disease. To that end, there has been increasing attention on the potential role of transcatheter interventions for TR (Central Illustration). Numerous platforms are in developmental evolution, which broadly fall into 3 categories: valve replacement, valve repair (subdivided into annular, leaflet, and chordal platforms), and caval valve implantation (Table 1).

Transcatheter TV replacement

There remains significant recent interest in transcatheter TV replacement (TTVR). The interest stems from the potential for eradication of TR (rather than just the 1-2 grade reductions seen with other transcatheter repair techniques), the ability to treat a wider range of anatomies and pathologies, and the potential to offer downstream valve-in-valve procedures. These potential benefits need to be weighed against the necessity of postprocedural therapeutic anticoagulation, a more invasive procedure, potential inducement of atrioventricular block, the risk of interaction with, or damage to, indwelling pacemaker or defibrillator leads, difficulties implanting pacemakers in the future, long-term durability, and a risk of worsening RV function due to loss of the "pop-off" phenomenon.

NaviGate

The NaviGate system (NaviGate Cardiac Structures) is a nitinol self-expanding stent with a trileaflet pericardial valve that was available in 5 sizes (36.0, 40.0, 44.0, 48.0, and 52.0 mm), with <10% oversizing to the tricuspid annulus size recommended.[18] The last iteration of the device had an outer diameter of 42F catheter and
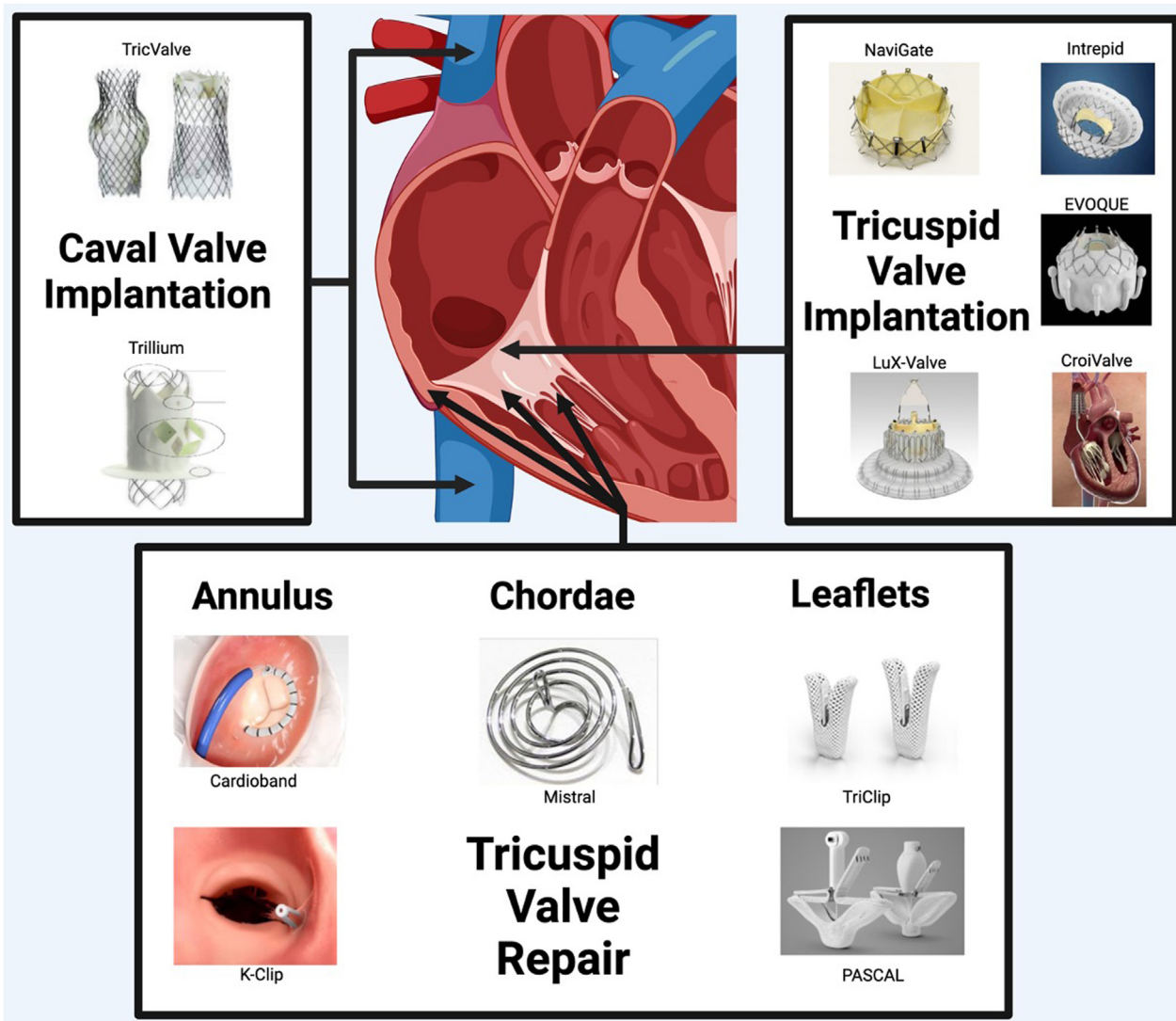
Central illustration.
A summary of the models and types of device currently available for transcatheter treatment of severe tricuspid regurgitation.

Table 1. A summary of the details of devices for the transcatheter treatment of severe tricuspid valve regurgitation.

Device name	Device category	Sizes (mm)	Frame height	Construction	Sheath size	Access route	CE Mark
TricValve	Caval (heterotopic)	SVC 25.0/29.0, inferior vena cava 31.0/35.0	SVC 67.0 mm/69.0 mm, inferior vena cava 65.0 mm	SVC and inferior vena cava valves, nitinol frame, bovine pericardium leaflets	27F	Jugular and femoral veins	Yes
Tricento	Caval (heterotopic)	Custom made	Custom made	Nitinol frame, porcine pericardium	24F	Femoral vein	No
SAPIEN XT	Caval (heterotopic)	20.0-29.0	NA	Cobalt cromium and pericardium	16-20F	Femoral vein	Yes
Croívalve	Caval (heterotopic)	Unknown	Unknown	Pericardium	26F	Unknown	No
Trillium	Caval (heterotopic)	NA	NA	Bare metal stent with multiple valves and sealing skirt	24F	Femoral vein	No
PASCAL	Coaptation enhancement	6.0-10.0	NA	Nitinol	22F	Femoral vein	Yes
TriClip	Coaptation enhancement	9.0-12.0	NA	Cobalt-chromium and nitinol construction, polyester cover mesh	22F	Femoral vein	Yes
Intrepid	Valve replacement	43.0-50.0	18.0 mm	Bovine pericardium, nitinol frame	35F	Femoral vein	No
EVOQUE	Valve replacement	44.0-52.0	Unknown	Bovine pericardium, nitinol frame	28F	Femoral vein	No
NAVIGATE	Valve replacement	36.0-52.0	Unknown	Equine pericardium, nitinol frame	24F	Transatrial	No
LuX-Valve	Valve replacement	50.0-70.0	Unknown	Bovine pericardium, nitinol frame	34.0 mm	Transatrial	No
Cardioband	Annular reduction	80.0-81.0 to 113.0-130.0	NA	Stainless steel	25F	Femoral vein	Yes

NA, not applicable; PH, pulmonary hypertension; SVC, superior vena cava.

was implanted transatrially using thoracotomy. A transjugular approach was abandoned owing to issues with size and coaxiality. The collective early experience with this device was summarized in a study of 30 consecutive patients treated on a compassionate-use basis at 10 institutions globally.[19] Of these 30 patients, 26 underwent technically successful implantations; 4 experienced malpositioning, and 2 required conversion to open surgery. All successfully treated patients experienced good TR reduction, with 75% experienced ≥2 grade reduction and 76% of patients having mild or less TR at discharge. This high-risk patient cohort had an in-hospital mortality of 10%, but there were no late device-related events.

LuX-Valve

The LuX-Valve system (Jenscare Biotechnology) was initially implanted transatrially through a thoracotomy and comprised a self-expanding bovine pericardial valve on a nitinol stent with leaflet clampers that attach to the native valve and a septal anchor. This mechanism of fixation (dependent on anchoring to the anteroposterior leaflet and the interventricular septum) means that sizing is based on the effective tricuspid orifice area (as opposed to the tricuspid annulus); therefore, fixation is not dependent on radial force. The annulus (50.0, 60.0, and 70.0 mm) and inner valve (26.0 and 28.0 mm) are sized separately. The majority of the experience has been in China on a compassionate-use basis, and an initial report of 12 patients has been published.[20] There was a 100% procedural success rate with no conversion to open surgery. There was 1 in-hospital death, but all others survived to 30 days, and all but 1 patient experienced less than or equal to mild residual TR. The second-generation platform, LuX-Valve Plus, is implanted via a transjugular approach, with the first-in-human study being reported.[21] Compassionate-use cases have also been done in the United States, Canada, and Europe. A European study has started enrollment.

Intrepid

The Intrepid valve (Medtronic) was initially implanted via a transapical approach for mitral valve disease[22] but can now be implanted via a transfemorally using a 35F catheter delivery system for both mitral[23]

and tricuspid[24] valves. This valve system is a trileaflet bovine pericardial valve mounted on a self-expanding nitinol stent; the main unique feature of Intrepid is that it is fully recapturable and retrievable. The valve itself is 27.0 mm with annular stent sizes of 43.0, 46.0, or 50.0 mm. The first-in-man experience has been presented and an early feasibility study is underway (NCT04433065).

EVOQUE

Similar to the Intrepid valve, the EVOQUE system (Edwards Lifesciences) was initially developed for the mitral position but has been adapted for the TV. EVOQUE has the greatest amount of clinical data of all valve replacement technologies. The valve is implanted via the transfemoral route with a 28F catheter delivery system, which facilitates fully percutaneous treatment without the need for vascular cutdown. The system comprised bovine pericardial leaflets with subannular anchors and an intraannular sealing skirt. The valve frame is designed to conform to the patient's tricuspid annulus, thereby respecting the native anatomy and achieving optimal retention force. There is a dedicated multiplanar steering system that aids in steering and facilitates coaxial delivery of the valve in a wide range of anatomies, including patients with pacemaker leads. The available sizes are 44.0, 48.0, and 52.0 mm.

The initial published data set on EVOQUE comes from the compassionate-use experience of 25 patients.[25] These high-risk patients had 0% 30-day mortality, and 92% procedural success ≤2+ TR in 96% of patients. Major bleeding occurred in 3 patients (12%), 2 patients (8%) required pacemaker implantation, and 1 patient (4%) required dialysis. In the 1-year results of this cohort,[26] 2 patients died between 30 days and 1 year; there were no valve-related deaths and only 1 new pacemaker after 30 days. There were also only 2 (7%) heart failure hospitalizations out to 1 year. At the 1-year time point, 92% of patients had mild or trace TR and no patient who received a valve had greater than moderate TR. There were also durable functional improvements with 68% of patients being in New York Heart Association (NYHA) class of ≤2.

This experience has been expanded in the TRISCEND early feasibility study (NCT04482062), enrolling patients with symptomatic TR who were symptomatic despite medical therapy. Screening was performed with transesophageal echocardiogram (TEE) and computed

tomography (CT) scanning, and screening was performed by the central screening committee. There was also an echocardiographic corelab, clinical events committee, and data and safety monitoring board. The early results of 56 patients have been published.[27] The median length of stay was 3.0 days, emphasizing the quick recovery from a fully percutaneous transcatheter procedure despite a high-risk population (mean Society of Thoracic Surgeons score patients-reported outcome measure, 7.7%). Device success was excellent (98%); procedural success was defined as device success without clinically significant paravalvular regurgitation at time of discharge. The procedural success was also excellent at 94%. The relative technical ease with which this valve can be implanted is also highlighted by an average device time of 70 minutes, which is particularly noteworthy considering that this is a report of early procedural experience with the platform. This ease of use was also associated with reproducibly good procedural results, with 98% of patients achieving a reduction in TR severity to trace or mild at 30 days; furthermore, all patients experienced ≥1 grade reduction and 95% experienced ≥2 grade reduction. This underlies that good TR reduction was achieved despite more than or equal to severe TR at baseline in 92% of patients. The 30-day all-cause mortality was 3.8% (2 patients), cardiac mortality was 1.9% (1 patient), and 3.8% (2 patients) required open surgery. The most common periprocedural complication was severe bleeding seen in 22.6% (12 patients); only 1 case had a major access site vascular complication. There were significant improvements in all functional metrics (NYHA class, 6-minute walk test [6MWT], and Kansas City Quality of Life Score [KCCQ] score). More recently, 1-year outcomes were presented at PCR London Valves 2022, with 90.1% survival, 88.4% freedom from heart failure hospitalizations, 97.6% with mild or trace TR, 93% NYHA class I or II (vs 26% at baseline), and a 26-point increase in KCCQ score over baseline.

Two-year outcomes were recently published from a retrospective analysis of 38 patients.[28] The 2-year survival was 71%, and there were significant improvements in right heart failure symptoms. RV reverse remodeling was maintained at this longer-term follow-up. Adverse events were also uncommon, with 11% major bleeding, 8% pacemaker rate, and 1 patient requiring surgical TV replacement for early migration of the device.

On the strength of these early results, the TRISCEND II pivotal trial (NCT04482062) is currently enrolling 1070 patients for randomization to TTVR with EVOQUE plus medical therapy vs medical therapy alone. The trial is slated for completion in 2029.

CroíValve

CroíValve is a unique platform where a prosthetic valve is deployed without annular contact. The native leaflets coapt against the outer wall of the "floating" valve during ventricular systole (preventing paravalvular regurgitation) and open normally during ventricular diastole (allowing paravalvular inflow to the RV as to prevent tricuspid stenosis through a relatively small prosthetic valve). The valve is held in place by a support anchor attached to a stent deployed in the superior vena cava (SVC). Advantages include a short procedure time (<5 minutes in experienced hands), avoiding TEE with intracardiac echocardiography (ICE) guidance, the ability to treat very large annuli, and avoiding interactions with the conduction system and right coronary artery (RCA). A first-in-human study early feasibility study is currently enrolling (NCT05296148).

Valve repair

Transcatheter TV annuloplasty devices

Transcatheter annuloplasty devices attempt to recreate the principles of surgical annuloplasty using a suture, clip, or ring to reduce the size of the TV annulus. With annular reduction, TR improves by eliminating coaptation gaps and restoring leaflet approximation. Suture and clip-based systems mimic a Kay annuloplasty, in which annular reduction is achieved by plicating the posterior leaflet and "bicuspidizing" the TV. Ring-based systems mimic surgical ring annuloplasty, in which annular reduction is achieved by suturing an undersized ring to the annulus. These approaches have had challenges due to device stability and interaction with nearby cardiac structures, including the RCA, conduction system, and aortic and coronary sinuses. TriAlign and Tri-Cinch are historical devices in this category that have been abandoned.

K-Clip

K-Clip is a newer clip-based platform (K-Clip; Huihe Company) that uses a transjugular approach, an 18F catheter outer guide, and a 15F catheter steerable delivery catheter to screw an anchor 4.0 mm into the tricuspid annulus. The anchor is then retracted, which pulls annular tissue between 2 clip arms for grasping to reduce the annular area. The clips are available in 12.0-, 14.0-, 16.0-, and 18.0-mm sizes and are designed to achieve maximum annular reductions ranging from 24.0 to 36.0 mm. CT planning is used to mitigate the risk of RCA injury, and intraprocedural right coronary angiography is performed before clip release. The first-in-human study was recently reported.[29] In a compassionate-use, prospective, multicenter, single-arm study, 15 patients with severe, symptomatic, functional TR were enrolled. With an average annular area reduction of 25%, 87% of patients were NYHA I or II at 30 days (vs 7% at baseline). The complication rate was overall low, including 1 major access site complication, 3 arrhythmias, and 2 cases of clinical heart failure. Notably, there were no cardiac perforations or RCA injuries.

Cardioband

The Cardioband system (Edwards Lifesciences) is the most widely used ring annuloplasty device and uses a sutureless band, which attaches to the atrial side of the anterior and posterior portions of the TV annulus. The device is implanted via a 26F catheter transfemoral access sheath and is anchored to the atrial aspect of the annulus. After anchoring, the device is cinched, thereby effectively reducing the septolateral annular diameter and leading to improved leaflet coaptation. After cinching, RCA angiography should be performed. The 30-day outcomes of 30 patients enrolled in the early feasibility study were recently published.[30] In this study, device success was achieved in 93% of patients, and there was no 30-day mortality. The septolateral annular diameter was successfully reduced by 13% and 85% of patients had at least 1 grade in TR reduction with associated improvements in functional status. The 6-month results from this study were recently presented,[31] with 92% survival rate at 6 months and a 19% reduction in annular diameters. TR reduction was also durable with a >1 grade reduction in 93% of patients with improvements in functional status and quality-of-life metrics.

Transcatheter TV edge-to-edge repair devices

Leaflet-directed interventions enhance coaptation using a clip and are currently the most widely used transcatheter devices for the treatment of TR. Technical challenges with tricuspid clip placement (above mitral procedures) include challenging transesophageal imaging (owing to the anterior location of the TV and shadowing from neighboring cardiac structures), large coaptation gaps (making grasping challenging), limited subvalvular space (with the attendant hazards of entanglement in the chords and other subvalvular apparatus), and the frequent presence of pacemaker leads.[32,33]

TriClip

TriClip is a modified MitraClip platform with design iterations to improve steering in the right atrium. Developed after the initial experience of using the MitraClip device[34,35] (Abbott Vascular) in the tricuspid position, the aim of this therapy is to attach clips to leaflets with poor coaptation, thereby reducing the effective regurgitant orifice area. Two techniques have been described: bicuspidization (or zipping) and triple-orifice (or clover). The bicuspidization technique is a modification of the Kay annuloplasty and involves placing a clip between the anterior and septal leaflets at the commissure, in which the coaptation gap is smallest. Subsequent clips are then placed inward, from that point, along the anteroseptal coaptation line. The triple-orifice technique mirrors the "clover technique" described by Alfieri et al[36] in 2003 for the correction of complex posttraumatic TV lesions. The first clip is implanted between the anterior and septal leaflets and a second clip between the posterior and septal leaflets, with the resulting orifice resembling a 3-leaf clover.

The early reports from compassionate use of this device in 64 consecutive patients were promising,[35] with TR reduction of at least 1 grade in 91% of patients and no major intraprocedural complications, deaths, or need for emergency surgery. This led to the iterative TriClip device, which was initially evaluated in 85 high-surgical risk patients.[37] Implant success was 100%, and at 30 days, 86% of patients experienced TR reduction of at least 1 grade, similar to the foundational reports with the MitraClip device. Again, there was a good safety profile with no periprocedural deaths, conversions to surgery, device embolizations, or strokes. The 1-year report from this nonrandomized cohort suggested reasonable durability, demonstrating TR reductions to moderate or less in 71% of patients.[38] Subsequently, the TRILU-MINATE Pivotal randomized controlled trial (RCT), the first RCT for transcatheter TV intervention, randomized 350 patients with severe symptomatic TR to treatment with the TriClip device or medical therapy alone.[39] For the primary outcome, a hierarchical composite of all-cause mortality or TV surgery, heart failure hospitalizations, and assessment of quality-of-life improvement using the KCCQ at 12 months, TriClip was superior to medical therapy. The end point was driven by the quality-of-life improvement, in which a 15 or greater improvement in the KCCQ was observed in the 47.9% of the device group compared with 26.4% of the medical therapy group. There was no difference in the rate of mortality or TV surgery and heart failure hospitalizations. An improved rate of reduction to moderate or less TR at 30 days was observed in 87% of the device arm vs 4.8% in the control. There is an additional single-arm registry nested within this trial, for patients in which it is not believed that TR is going to be reduced to moderate or less with device therapy; all these patients receive the device therapy with TriClip.

PASCAL

The PASCAL system (Edwards Lifesciences) was initially developed for the treatment of mitral regurgitation but has also been utilized and evaluated for the treatment of TR. The PASCAL device shares elements of both the MitraClip and the related but now discontinued FORMA device (Edwards Lifesciences), with the presence of a central spacer with 2 adjacent paddles with clasps, which are utilized to grasp the mitral valve leaflets. There exists the capability for independent grasping (also present in the latest G4 MitraClip systems), and the device has a larger maximal width to aid with the potential to repair large coaptation gaps. The device can also elongate to offer a narrower profile, which can aid with subvalvular manipulation and disentanglement from the chordae. The early compassionate-use experience of PASCAL for TR demonstrated encouraging results, with moderate or less TR achieved in 82% of patients at 30 days, with

sustained results to 12 months.[40] There were functional improvements in NYHA class and 6MWT, with an acceptable safety profile (single-leaflet detachment in 2 patients; no stroke or device embolization seen throughout the totality of follow-up). The early feasibility study recently reported outcomes for 34 enrolled patients.[41] In this series, 85% of patients received device implants; of these patients, 85% achieved a reduction in TR severity of at least 1 grade with 52% achieving moderate or less TR. There were no instances of cardiovascular mortality, stroke, myocardial infarction, or reintervention during the study period, and there were again broad improvements in all function measures assessed (NYHA class, 6MWT, and KCCQ score). On the background of these encouraging initial experiences, the CLASP II TR pivotal RCT is now enrolling (NCT04097145). This trial will randomize patients with symptomatic severe TR despite medical therapy to PASCAL and medical therapy or medical therapy alone. The primary outcome is a hierarchical composite end point of all-cause mortality, heart failure hospitalization, need for surgery on the TV, and improvement of quality of life; moreover, the trial will aim to enroll 870 participants.

Transcatheter TV chordal repair devices

Currently, a single platform is under study and is described further.

Mistral

The Mistral device (Mitralix) enhances leaflet coaptation by cinching the chordae tendineae into a "flower bouquet" shape. The procedure is performed under TEE guidance using an 8.5F off-the-shelf steerable guide catheter and the 7.5F catheter Mistral delivery system. A spiral-shaped wire is deployed in the right atrium and delivered into the RV and rotated within the cords until a desired result is achieved. The 30-day data from first 7 cases were published in 2020 and showed encouraging safety and efficacy. On average, TR severity was reduced from severe to moderate with normalization of tricuspid annular plane systolic excursion and RV fractional area change. Metrics of functional status also significantly improved (NYHA class and KCCQ scores).[42] The TRIBUTE-Pivitol Study is underway (NCT05767645), with plans to finish enrollment in late 2025 and report 6-month safety data and 30-day efficacy data.

Caval valve implantation

Transcatheter caval valve implantation devices

Certain patients will not be suitable candidates for any targeted TV therapy for any combination of clinical, hemodynamic, or anatomic reasons. For these patients, it may be possible to offer procedures based around caval valve implantation, also known as heterotopic valve implantation. The rationale is to attenuate the congestive effects of severe TR by deploying valves in the caval vessels. Other procedural factors to consider are the caval anatomy, risk of valve embolization, and the low-pressure state predisposing to valve thrombosis (and, therefore, mandating oral anticoagulation).

SAPIEN valves

SAPIEN valves (Edwards Lifesciences) have been used for this indication, but a randomized trial had to be halted owing to high rates of valve embolization.[43]

TricValve

TricValve is the first dedicated device available for caval valve implantation (P&F Products + Features). The system consists of 2 self-expanding valves sequentially implanted in the SVC and then inferior vena cava via the right femoral vein. The valves need a sufficient gradient to properly function, and a v-wave cutoff of 25 mm Hg is used. The TRICUS EURO study is a nonblinded, non-randomized, prospective, multicenter, single-arm trial evaluating the TricValve system in 35 patients with severe symptomatic TR.[44] At 30 days, there was a 94% procedural success rate (defined as fall in v-wave compared with baseline). At 6 months, there were significant improvements in both quality of life and functional classification. Of note, device thrombosis was detected in 2 patients during CT scan at 3 months. The 1-year data will be presented at TCT 2023, and the US Food and Drug Administration pivitol trial (TRICAV) is slated to start late 2023.

Trillium device

Trillium device (Innoventric) features a bare metal stent with open struts in the SVC and a sealing skirt in the inferior vena cava. There is a covered atrial portion fenestrated by multiple window-shaped valves. The main benefit lies in the potential to treat patients with cava too big for TricValve. A first-in-human case report was published in late 2022,[45] and the 20-patient Innoventric Trillium Stent Graft first-in-human safety and feasibility study is currently recruiting, with primary completion expected in 2023 (NCT04289870).

Novel approaches

Beyond the above-described devices, there are ongoing significant efforts to develop novel techniques for transcatheter treatment of severe TR.

Real-world data

The data summarized in the abovementioned sections for all devices comprise early compassionate-use experience or were generated in the context of rigorously conducted early feasibility studies, with all attendant study oversight and strict inclusion and exclusion criteria. The largest contemporary data set available for transcatheter TV intervention comes from the TriValve registry from 22 European and North American centers.[46] A subsequent publication focused on data from 472 patients who underwent tricuspid interventions, compared with a propensity-matched control group comprising consecutive patients with severe TR treated medically at the Mayo Clinic (Rochester, Minnesota) and Leiden University (Leiden, the Netherlands).[47] Importantly, data were not restricted to 1 device as patients could be treated with any transcatheter device therapy. Included technologies were MitraClip, PASCAL, FORMA, Cardioband, TriCinch, Trialign, NaviGate, and caval valve implantation. The primary end point in this study was the composite of all-cause mortality or rehospitalization for heart failure. Procedural success was defined as the patient being alive at the end of the procedure with a successful device implanted and <3+ residual TR. In total, 268 propensity score–matched pairs of patients were identified. Of these, 14% had procedural failure with ≥3+ residual TR at the end of the procedure. Patients in the intervention group had a lower incidence of the primary end point (32% ± 4% vs 49% ± 3%; $P = .0003$) and both individual components (mortality: 23% ± 3% vs 36% ± 3%; $P = .001$; heart failure rehospitalization: 26% ± 3% vs 47% ± 3%; $P < .0001$). The 14% of patients in the intervention group who had an unsuccessful procedure had similar outcomes as the medical therapy group. The majority of patients in this cohort were treated with the MitraClip device (229 out of 268 patients), but there was no impact on the device choice (MitraClip vs others) on the primary end point ($P = .80$). Of note, since the wider use of the dedicated TriClip device, a report has been published from the bRIGHT postapproval study, a prospective, single-arm, open-label, multicenter, postmarket registry conducted at 26 sites in Europe.[48] It enrolled 511 subjects (mean age, 79 years) with mostly massive or torrential TR and with 80% having NYHA class III/IV symptoms. Device success (99%), 30-day rates of moderate or less TR (77%) and functional outcomes (improvements in NYHA class: 20%-79% I/II; $P < .0001$; and KCCQ score: 19 ± 23 points improvement; $P < .0001$; at 30 days) were comparable with those of previous clinical trials.

Device selection and considerations

The range of devices used in the TriValve registry highlights an important point facing clinicians offering transcatheter TV interventions: choosing from a large number of device therapies to offer the correct treatment for an individual patient. There are several factors that make device selection challenging in the TR domain (Table 2).

The first factor to acknowledge is that there are no head-to-head comparisons of different transcatheter tricuspid devices (or technical approaches), and such studies are unlikely to be conducted soon if at all. The second factor that makes this a challenging situation is that, unlike for mitral regurgitation, there is no clear surgical predicate: it is not clear whether there is a surgical gold standard for treatment of TR, and therefore, we cannot simply attempt to emulate a superior surgical approach with transcatheter therapies. The third factor is that the TRILUMINATE study is the only randomized trial for device-based therapy of TR, although there are multiple ongoing trials. Best current practice for tailoring device therapy includes consideration of the underling etiology of the TR as well as the anatomy of the leaflets, annulus, and RV, and other clinical patient factors (Figure 1).

TR mechanism and the importance of multimodal imaging

As with other structural heart procedures, multimodality imaging is critical for planning and execution of device-based therapy of TR.[49] Echocardiography is the workhorse imaging modality to define the mechanism of TR. Given the inherent difficulties with TV imaging, a structural echocardiographer with expertise in 3D TV analysis is invaluable. Annular reduction therapy can be considered for patients whose predominant mechanism is annular dilation, provided the dilation is not excessive (massive annulus size, extreme leaflet tethering, very large coaptation gaps [>10.0 mm]). Preprocedural CT is used to identify unfavorable annular features, such as shallow annular shelf depth, excessive annular calcium, or proximity to the RCA. Patients with more than or equal to moderate coaptation gaps (≥7.5 mm and not originating from the anteroseptal or posteroseptal commissure) or severe leaflet tethering are also unlikely to be good candidates for edge-to-edge repair. Additional unfavorable leaflet characteristics for edge-to-edge repair include leaflet thickening, restriction, and perforation. In general, preprocedural CT is not required to plan an edge-to-edge repair, but TEE windows must ensure accurate leaflet analysis and optimal intraprocedural guidance. In cases of poor TEE windows, ICE should be used. For patients unsuitable for annular reduction or leaflet-directed therapy, valve replacement may be the best treatment option because these

Table 2. A summary of factors affecting device choice in transcatheter treatment of severe tricuspid valve regurgitation.

Domain	Valve replacement	Coaptation device	Annular device
Etiology	Suits most etiology patterns where annular dimensions do not exceed the device's own sizing	Pure annular dilation with coaptation defect of ≤10.0 mm without excessive leaflet tethering	Pure annular dilation with coaptation defect of ≤10.0 mm without excessive leaflet tethering
RV dysfunction	Caution in severe RV dysfunction as TR completely abolished—loss of "pop-off" phenomenon	Better suited to patients with RV dysfunction	Better suited to patients with RV dysfunction
Presence of pacemaker lead	Affects implantation but can safely be jailed by some devices	Affects imaging and strategy	Affects imaging
Contraindication to anticoagulation	Avoid in this cohort	Acceptable in this cohort	Acceptable in this cohort
Damage to surrounding structures	Caution in those where coronary damage or heart block would be especially poorly tolerated	Acceptable in this cohort	Acceptable in this cohort
Need for future procedures	Limits options for reintervention but valve-in-valve approach likely possible	Limit options for reintervention but electrosurgical detachment might be possible	Least restrictive on future procedures
Durability	Untested, concern about risk of deterioration and thrombosis due to bulkiness and low flow	Untested	Untested
Safety vs efficacy	Greater efficacy but more invasive	Often only 1-2 grades TR reduction but less invasive	Often only 1-2 grades TR reduction but less invasive

RV, right ventricular; TR, tricuspid regurgitation.

platforms are generally agnostic to unfavorable annular and leaflet characteristics. The annular size, however, cannot exceed the capabilities of currently available technologies. For patients with no option for direct valve treatment, caval therapy remains the only alternative. Preprocedural CT is necessary to demonstrate favorable RA and caval anatomy.
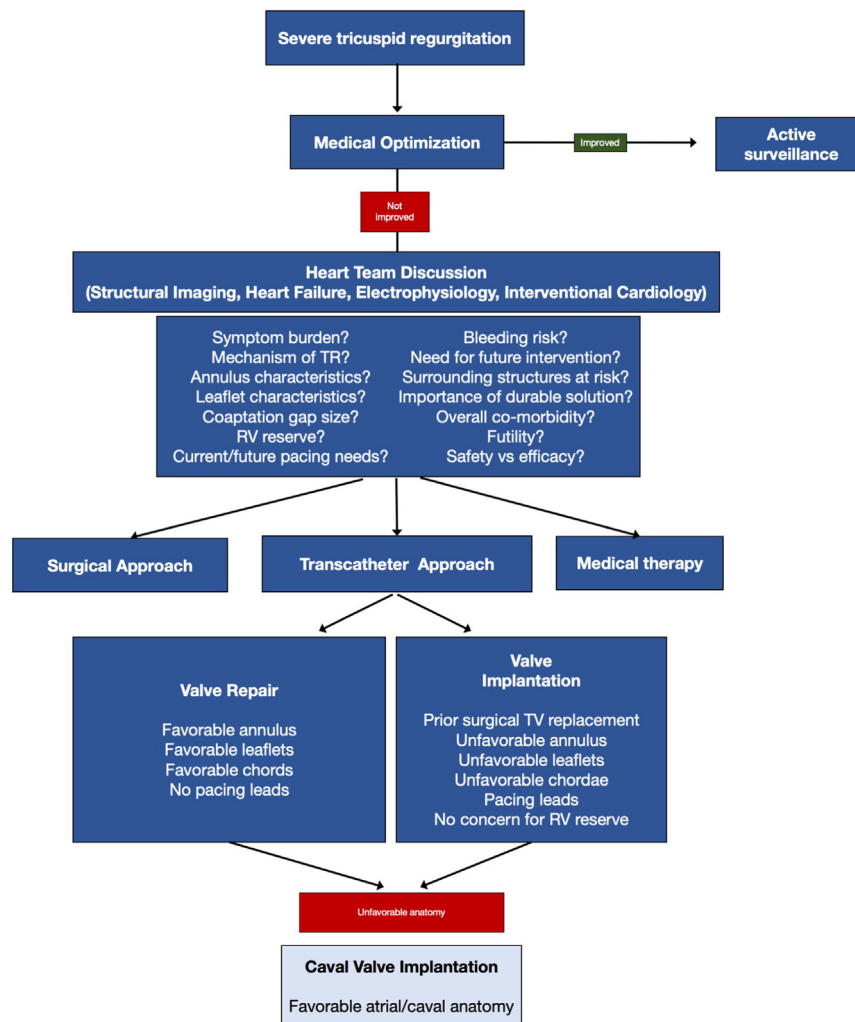

Figure 1.
A step-wise approach to assessment and device selection in patients with severe tricuspid regurgitation. RV, right ventricular; TR, tricuspid regurgitation; TV, tricuspid valve.

RV function

Reducing or eliminating TR imposes an acute increase in RV afterload. If the RV cannot compensate with increased contractility, a process known as "RV-PA uncoupling," the resultant RV failure can be fatal. This was likely the case in the patient who died postoperatively in TRISCEND EFS. A recently published retrospective analysis from the TriValve registry demonstrated that low preprocedural RV-PA coupling ratios (measured noninvasively using tricuspid annular plane systolic excursion/pulmonary artery systolic pressure) predict all-cause 1-year mortality in patients with TR undergoing TTVR.[50] RV function can usually be assessed with a combination of echocardiographic and right heart catheterization indices. In borderline or unclear cases, multimodal adjunct imaging with cardiac CT and magnetic resonance imaging can be useful.

With this concern in mind, every attempt should be made to optimize RV function before addressing severe TR with device therapy. Given the plasticity of the RV, TV, annulus, and cava, appropriate preprocedural therapy has the potential to reduce coaptation gaps and cava and annular size to the point where device therapy is no longer needed or, more realistically, unlock candidacy for the previously excluded patient. Therapeutic targets include reducing RV preload and afterload (with diuretics and pulmonary vasodilators), improving RV myocardial blood supply (with RCA revascularization), and restoring electrical synchrony (with rhythm control of atrial fibrillation and traditional cardiac resyncronization therapy, as conduction system pacing and RV-cardiac resynchronization therapy are less well studied in this population).[51,52] Invasive hemodynamics are invaluable during this process, particularly for titrating diuretics and pulmonary vasodilators and identifying cases of refractory RV failure where inotropic or mechanical circulatory support may be necessary.

While more research is needed to better predict which RV can tolerate TR device therapy, in cases of severe RV dysfunction with doubtful or questionable afterload reserve, repair techniques (which generally reduce TR by 1-2 grades and, therefore, leaves behind residual TR) may be more suitable than valve replacement (which eliminates TR completely).

Cardiac implantable electronic device-induced TR

Cardiac implantable electronic device-induced TR is broadly defined as lead-related primary TR or secondary TR. Understanding the lead position relative to the leaflet (commissural, impinging or adherent, and middle) is critical.[53] Once the lead-leaflet interaction is defined, a multidisciplinary collaboration is mandatory to determine not only the optimal plan for the valve but also the cardiac implantable electronic device lead. Lead management plans are broadly categorized as lead extraction, repositioning, or jailing—all of which can be employed via a variety of transvenous or surgical approaches. Transcatheter TV repair platforms (annular reduction and edge-to-edge repair) are generally less favorable as acoustic shadows from the leads hinder intraprocedural echocardiographic guidance and often require advanced TEE) or ICE technology. With TTVR, it is generally possible to jail the lead between the native annulus and prosthetic valve without damaging the lead, impairing valvular function, or creating significant paravalvular regurgitation around the jailed lead.

Suitability for anticoagulation

Transcatheter TV replacement necessitates a period of systemic oral anticoagulation postprocedure, although the optimal duration of anticoagulation is unknown. This is not generally required for patients undergoing any type of repair procedure. Patients referred for transcatheter TV intervention are generally elderly and may often have coexistent renal and liver disease (which may be related to the TR). This places them at high bleeding risk, and therefore, they may be less suitable for oral anticoagulants (OAC). Indeed, the most common complication seen in the TRISCEND early feasibility experience is severe bleeding, which was not related to the access site. Patients who are not eligible for at least short-term OAC are not suitable for TTVR. Some may argue this factor has been overplayed because most of the patients with severe TR have atrial fibrillation (91% in TRISCEND) and, therefore, already have another indication for OAC aside from the tricuspid intervention.

Risk for damage to surrounding structures

Both annular reduction and TTVR pose a risk for damage to surrounding structures, particularly the RCA and the conduction system. Leaflet therapies do not pose such a risk, and there is not, therefore, as great a risk for conduction disturbance requiring pacemaker implantation after such procedures. Pacemaker implantation after tricuspid intervention can be challenging, but there are various solutions beyond traditional RV pacing to include epicardial or coronary sinus leads or leadless pacemakers.

Safety vs efficacy

Transcatheter TV replacement offers superior efficacy to repair because TTVR offers the potential for abolishment of TR compared with reductions of 1-2 grade, or 50% of patients having more than or equal to moderate residual TR, with repair technologies. This is balanced against the more invasive nature of TTVR procedures, with greater potential for complications such as bleeding or damage to surrounding structures. That is to say, the choice between repair and replacement may come down to the balance of safety and efficacy and what the priority is for the individual patient being assessed for therapy.

Lifetime management

Annular reduction therapies provide arguably the greatest flexibility for future procedures. This is because annuloplasty necessarily respects and preserves the anatomy, meaning that multiple forms of future interventions could be contemplated including leaflet therapies and valve replacement. TTVR theoretically allows future valve-in-valve procedures; although these have not been described in detail, the large size of the valve frame and the designs of the valves should make this a readily applicable concept. Leaflet therapies pose the biggest challenge for future procedures (aside from adding further leaflet-based devices), which is very relevant for younger patients and as TR is only ameliorated rather than abolished; this means there can be ongoing annular dilatation and RV dysfunction, leading to progressive TR in the future. Electrosurgical detachment of leaflet devices prior to TTVR is described in one small series which may provide an option for reintervention in this group.[54]

One novel potential strategy is for patient undergoing concomitant open heart surgery for non–TV-related disorders, to undergo surgical TV intervention so that an anchoring system is in place for future TTVR. Such an approach would require dedicated systematic study before incorporating into routine clinical care. Data on transcatheter TV-in-valve procedures are relatively scarce. A 2016 registry of 156 patients suggested that treatment with commercially available nondedicated TV platforms (Melody and SAPIEN) was technically feasible and clinically successful.[55] There have been other series reporting favorable outcomes with transcatheter valve-in-valve procedures,[56] but further study is required.

Durability

The durability of all transcatheter TV interventions is unknown owing to the nascent nature of the field. There is a potential concern for structural valve deterioration of TTVR devices, particularly as they are bulky and are subjected to low flows, which may predispose them to thrombosis and consequent degeneration.

Futility

Patients with severe TR referred for consideration of transcatheter therapy tend to be elderly, frail, and comorbid. Judicious patient selection is therefore crucial to avoid medically futile procedures, whereby a technically successful intervention may be performed without a positive impact on the patient's clinical course culminating in a poor outcome. It is therefore essential that these patients are evaluated under the auspices of a multidisciplinary heart team. The goals of intervention should also be defined, as for many of these patients, the aim is to improve quality of life and reduce heart failure hospitalizations above increasing long-term survival. Shared-decision making is therefore crucial in these complex situations, and if intervention is deemed futile, then this should prompt open discussions with the patient and family about the prognosis and trigger referrals to palliative care services as appropriate.

Conclusion

Tricuspid valve regurgitation is a highly prevalent condition with multiple promising options for treatment without recourse to surgery. Patient selection is important to avoid exposing those with little to gain to unnecessary risk and identify patients most likely to benefit from procedural treatment. Device choice and technique must be tailored to the patient, taking into account the anatomy, etiology, and other patient factors. Future clinical trials will help clinicians to better understand the strengths and weaknesses of these different approaches and help clarify optimal therapeutic choices for patients.

Declaration of competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial or non-for-profit sectors.

Ethics statement and patient consent

This review article has adhered to relevant medical guidelines and no new patient data was included in anonymized or non-anonymized form that would require patient consent.

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