

An Update on Transcatheter Tricuspid Valve Therapies

A review of the current state of transcatheter tricuspid valve therapies and where they are headed next.

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The tricuspid valve has traditionally been considered the “forgotten” valve and is often neglected by clinicians. However, the incidence of tricuspid regurgitation (TR) associated with left valvular disease is significant, ranging from 8% to 35% of cases.¹ Despite the association of increased mortality with significant TR, this valvular disease remains under-recognized and relatively untreated. The high in-hospital mortality and recurrence rate with current surgical replacement or repair techniques is well recognized. For this reason, significant TR is undertreated, opening the door to the development of new transcatheter therapies.² This article provides an update of the current transcatheter therapies developed in the past few years.

PERCUTANEOUS TRICUSPID VALVE DEVICES

The current transcatheter devices for the treatment of TR are shown in Figure 1, and the results of the main studies are reported in Table 1.³⁻⁸ A number of transcatheter technologies are at different stages of development and clinical use. A glimpse of current practice can be obtained from the Transcatheter Tricuspid Valve Therapies registry, which collected data on 135 patients treated with new percutaneous tricuspid valve technologies, showing a 65% rate of procedural success and a 30-day mortality of 3.7%.⁹

Percutaneous annuloplasty systems address the annular dilation that is the main pathophysiologic mechanism of TR. The annular-based devices require sufficient annular tissue for anchoring, have a small risk of right coronary artery injury, and do not preclude possible further interventions on the leaflet. However, these tech-

nologies may be less effective in patients with excessive leaflet tethering. To ensure sustained long-term results, complete annuloplasty should theoretically be preferred. The current annuloplasty and annular reshaping systems include those discussed here.

TriCinch Device

The TriCinch system (4Tech Cardio Ltd.) was designed to reduce functional TR (FTR) by decreasing the septo-lateral distance, thus mimicking the Kay procedure by cinching at the anteroposterior commissure and preserving native anatomy. The first-generation TriCinch device was previously described.¹⁰ Data from the PREVENT trial show a successful procedure in 18 (85%) patients with a significant acute reduction of TR obtained in 94% of the patients. However, due to the high complication rate (two procedures were aborted for hemopericardium and a late anchor detachment was reported in four cases without any serious adverse event), a second-generation device has been developed. The current device adopts a nitinol coil anchor that is deployed in the pericardial space at the level of the anteroposterior commissure and has a sealing device to prevent hemopericardium. After successful preclinical testing in 65 acute and chronic animals, the first-in-human case with the second-generation TriCinch device was performed without procedural complications, and 30-day improvement in TR severity and quality of life were reported.¹¹

Cardioband Annuloplasty System

The Cardioband system (Edwards Lifesciences) is a direct surgical-like annuloplasty device inserted

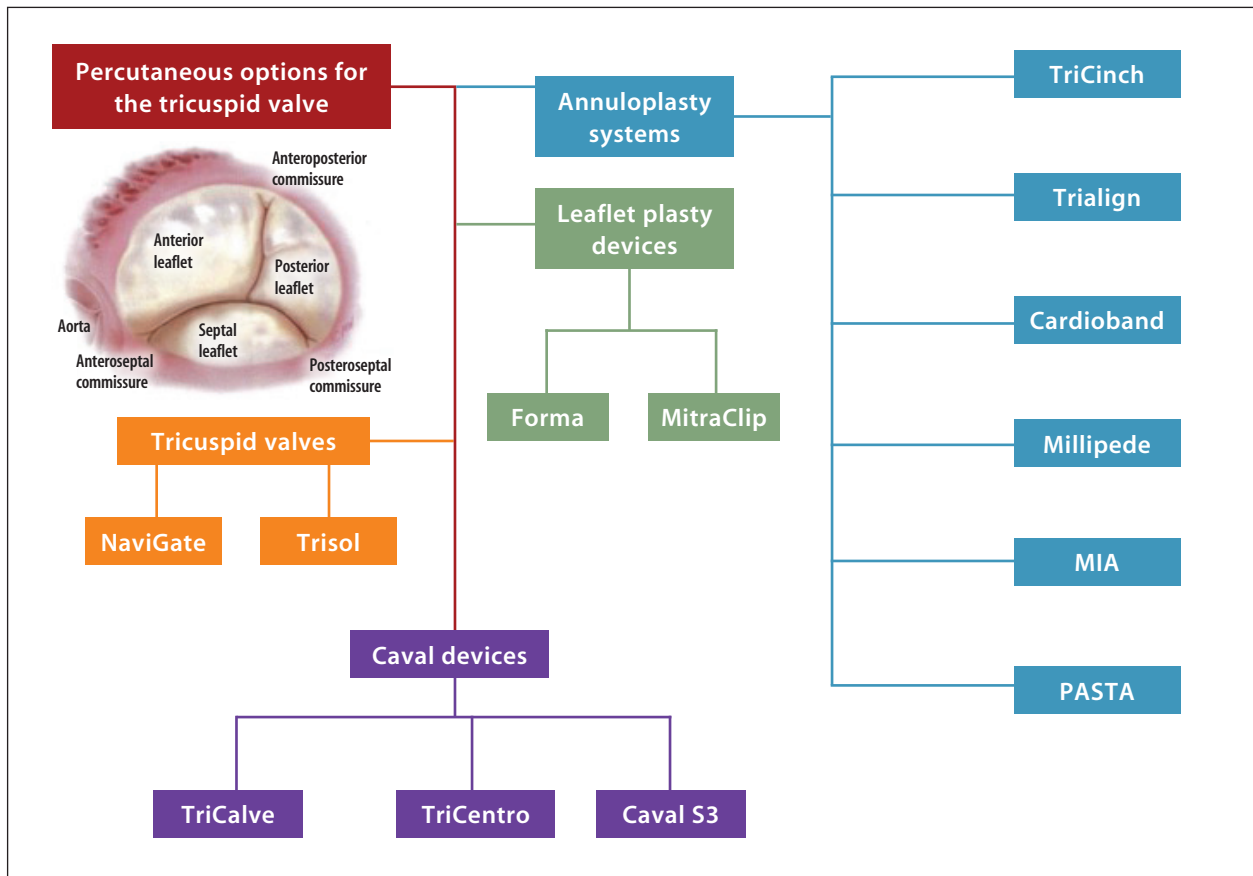


Figure 1. An overview of the current technologies for the treatment of TR.

through a 24-F delivery system via the femoral vein. The flexible implant is delivered through a steerable catheter and attached to the annulus using multiple anchors from the level of the anteroseptal commissure to the mid-part of the septal leaflet. Once the Cardioband has been fully implanted on the annulus, contraction of the band is applied to reduce annular diameters and TR. The European CE Mark TRI-REPAIR study enrolled 40 patients with FTR and an annular diameter > 40 mm. Procedural success was achieved in all patients with a 17% average reduction in septolateral diameter. Significant TR and annular reduction postcinching were maintained at 6-month follow-up.³ In May 2018, the Cardioband received CE Mark approval for the treatment of FTR.

Trialign System

The Trialign system (Mitralign,) is a percutaneous tricuspid valve annuloplasty system designed to mimic the Kay surgical procedure. The system consists of an articulating 8-F wire catheter inserted through the jugular vein, a pledget catheter, and a plication lock

device. Two pledgets are fixed at the anteroposterior and posteroseptal commissures and then sutured together using the dedicated plication lock device, thus plicating the posterior leaflet.¹²

In the SCOUT trial, an early feasibility study conducted with 15 patients with at least moderate FTR, successful implantation was achieved in all patients with 93% procedural success and 80% technical success at 30 days (three patients had single-pledget dehiscence without reintervention).⁴ The ongoing SCOUT II trial is a prospective, single-arm, multicenter study enrolling symptomatic patients with chronic FTR and is planned to include up to 60 patients.

Minimally Invasive Annuloplasty Device

The minimally invasive annuloplasty (MIA) device (Micro Interventional Devices, Inc.) is composed of low-profile PolyCor anchors (Micro Interventional Devices, Inc.) and a suture and is designed to reduce annular dimensions and regurgitation after being deployed in the patient's native annulus. The 17-F steerable delivery system has an end effector that allows for the deploy-

TABLE 1. BASELINE CHARACTERISTICS AND CLINICAL AND PROCEDURAL DETAILS FOR THE PERCUTANEOUS DEVICES WITH THE LARGEST TRIAL EXPERIENCES

	CardioBand ³	Trialign ⁴	Forma ⁵	TriCinch ⁶	MitraClip ⁷	CAVI ⁸
Total patients (N)	20	15	18	24	64	25
Mean age (y)	75	74	76	71	77	74
Women (%)	75	87	72	–	55	52
Secondary TR (%)	100	100	100	100	88	96
Atrial fibrillation (%)	61	67	89	–	84	–
Ejection fraction (%)	54	60	59	–	47	51
Logistic EuroSCORE (%)	5	–	9	12	28	18
Previous left-sided heart surgery	45	–	72	–	40	76
30-day mortality (%)	10	0	0	0	7	12
30-day technical success (%)	100	80	89	75	97	92
Dislocation/dehiscence (%)	0	20	6	17	0	6
Residual moderate-to-severe TR (%)	20	–	64	45	72	–
Reduction in regurgitation volume (mL)	38	23	–	–	26	–
EROA (mm ²)	–	51	103	–	90	–
Annular diameter (mm)	–	40	46	–	42	51
Annular reduction (%)	27	5	8	–	13	1
NYHA class I–II (%)	73	100	93	75	31	53
Change in 6MWT	+58 m	+53 m	+84 m	+58%	+16 m	–
Abbreviations: 6MWT, 6-minute walk test; CAVI, caval aortic valve implantation; EROA, effective regurgitant orifice area; NYHA, New York Heart Association; TR, tricuspid regurgitation.						

ment of the device in a 270° partial ring pattern. The STTAR trial will recruit patients to address the feasibility and the performance of the MIA device in FTR. The first three open surgical implantations have been successful with no device-related complications and a 38% reduction of annular dimensions.¹³ However, no transcatheter procedures have been performed in humans.

Millipede Iris Device

The Iris transcatheter annuloplasty ring (Millipede, Inc.) is an adjustable, complete annuloplasty ring that has been used both in the mitral and tricuspid position. In the initial human experience, nine surgical patients were treated with the Iris device in an initial temporary placement series followed by a series of permanent implants. Two of these patients received the Iris device in both the mitral and tricuspid position, with a reported mitral regurgitation and TR grade at 30 days of 0 to 1 and with a reduction in tricuspid diameter of 42% to 45% and resolution of TR in both cases.¹⁴ However, the company is currently focused on transeptal transcatheter implantation for the mitral device.

PASTA

Pledget-assisted suture tricuspid valve annuloplasty (PASTA) is a novel technique using marketed equipment to deliver percutaneous transannular sutures to create a double-orifice tricuspid valve to reproduce the Hetzer technique. In 22 pigs, PASTA significantly reduces annular dimensions and TR.¹⁵ Preliminary first-in-human compassionate use of the device was associated with technical success but there was postprocedural dehiscence of the sutures.

LEAFLET REPAIR DEVICES

Leaflet repair devices target the tricuspid leaflets using different concepts. The Forma transcatheter tricuspid repair system (Edwards Lifesciences) improves the leaflet coaptation using a spacer placed in the middle of the valve. Conversely, the MitraClip transcatheter mitral valve repair system (Abbott Vascular) is used to grasp two adjacent leaflets (anteroseptal and/or posteroseptal) to obtain either a bicuspidization or a clover plasty. The leaflet devices could be considered in case of excessive valve remodeling with apical

tethering, primitive pathology of the leaflets (prolapse, catheter-related TR), or in advanced anatomies not suitable for annuloplasty.

MitraClip System for TR

The MitraClip system is a well-known percutaneous option for patients with severe mitral regurgitation. The off-label use of the MitraClip has been the most utilized approach for the treatment of FTR with more than 1,000 procedures already performed worldwide. However, the conventional edge-to-edge repair technique used on the mitral valve faces several technical issues when applied to the tricuspid position. The miskey technique, done by inserting the clip delivery system 90° counterclockwise from its typical insertion position, has been shown to facilitate the MitraClip system orientation. The aim is to target the anteroposterior and posteroseptal leaflets guided by transgastric view of the tricuspid valve and the result after the first clip. Ideal cases should have a coaptation gap < 7 mm. Cases with larger coaptation gaps may require a “zip-ping” technique of multiple clips starting in the commissure and moving centrally. In the future, the new-generation MitraClip XTR system with larger clip arms will probably become standard of care for tricuspid clipping. Anteroposterior clips are usually avoided as they tend to cause tricuspid valve distortion and do not treat annular dilatation.

The feasibility of tricuspid clipping was first shown in a multicenter European registry that collected a series of 64 patients treated with MitraClip in FTR. At 9-month follow-up, a significant reduction in TR grade, effective regurgitant orifice area, regurgitant volume, septolateral diameter, and improved 6-minute walk test were found both for patients treated with the tricuspid valve alone (n = 42) and for those treated in combination with the mitral valve (n = 22).⁷ Small TR coaptation gap size and a central/antroposterior TR jet location independently predicted procedural success on multivariate analysis in a recent multicenter experience.¹⁶

The currently enrolling TRILUMINATE trial is recruiting a minimum of 85 patients with at least moderate TR and scheduled for tricuspid plasty using a dedicated tricuspid delivery system.

The Forma System

The Forma repair system is a retrievable device that reduces TR by occupying the regurgitant orifice area and providing a platform to enable the coaptation of the native valve leaflets. The device consists of the “spacer,” a foam-filled polymer balloon, and a

rail that is anchored at the right ventricular (RV) apex using a 24-F sheath introducer. Twenty-nine patients have been enrolled in the Forma early feasibility study. RV perforation occurred in two patients, and nine patients experienced at least one adverse 30-day event, including three patients who required device-related surgery (one RV perforation, one device migration, and one device infection).¹⁷ The clinical experience of 18 patients treated under a compassionate clinical use program have been reported, with 15 patients having completed 1-year clinical follow-up. Successful device implantation was achieved in 16 (89%) patients, with a reduction from 94% severe TR to 46% moderate to severe or less TR observed at 1 year.¹⁸

CAVAL AORTIC VALVE IMPLANTATION

The aim of the caval aortic valve implantation (CAVI) option is predominantly to reduce the symptoms of right-sided heart failure by decreasing caval backflow. Two different devices have been used for CAVI: balloon-expandable devices used for transcatheter aortic valve replacement and dedicated self-expandable CAVI devices (TricValve, P&F Products Features GmbH). A multicenter registry including 25 patients treated by compassionate use with either the Sapien 3 or XT valves (Edwards Lifesciences) or the TricValve reported a procedural success rate of 96%, with 30-day mortality at 8%. Patients experienced an improvement in their New York Heart Association class as well as a reduction in body weight and creatinine values.⁸ Two ongoing trials, HOVER and TRIVALVE, are currently evaluating the feasibility of CAVI with the balloon-expandable Sapien valve for treating TR.

TRANSCATHETER TRICUSPID VALVE IMPLANTATION

The NaviGate bioprosthesis (NaviGate Cardiac Structures) is currently the only available dedicated device allowing fully orthotopic transcatheter tricuspid valve replacement in humans. The valve is a cone-shaped, nitinol, tapered stent with three xenogeneic pericardial leaflets with a low-height profile and annular winglets for secure anchoring of the leaflets. The valve is deployed through a 42-F introducer sheath via the transjugular vein. After the first-in-human experience, 27 compassionate-use cases have been performed worldwide with good results in terms of improvements in TR severity (no postoperative paravalvular leak in six patients, trivial TR in three patients, and mild TR in two patients). Three patients died during follow-up as a consequence of their advanced clinical condition.¹⁹

CONCLUSION

Surgery is still the gold standard for the correction of TR, but most patients with severe TR are left untreated because of the prohibitive operative mortality. The emerging percutaneous technologies for TR are an attractive alternative with the initial clinical experience reporting excellent procedural safety. However, more procedural data and long-term follow-up are required to identify the best candidates and better understand device efficacy and durability. ■

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