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Tricuspid regurgitation: assessment and new frontiers

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Summary

Tricuspid regurgitation is the most frequent disease of the tricuspid valve. Of these, functional tricuspid regurgitation is the most frequent, and severe insufficiency is associated with an increasing risk of cardiovascular events and bad prognosis. The pathophysiology and assessment of tricuspid regurgitation is essential for transcatheter treatments, new treatment options. The aim of this short review is to summarise the assessment of tricuspid regurgitation and to show new transcatheter therapeutic options. Current experience with these new therapies is preliminary and further studies are needed to develop the evidence of transcatheter tricuspid valve therapy.

Introduction

Tricuspid regurgitation (TR) can result from organic (primary) and functional (secondary) pathology. Of these, functional TR is the most prevalent and is steadily increasing in frequency [1]. Functional TR is mainly due to a combination of tricuspid annular dilatation and leaflet tethering caused by further right ventricular dilatation. It develops progressively in patients with left-sided heart disease or pulmonary artery hypertension of any cause, or by remodelling with atrial fibrillation. Although functional TR responds initially to medical therapy, this may delay tricuspid valve (TV) surgery beyond the ideal period [2–4].

Since significant TR after left-sided valvular surgery is associated with poor prognosis, today a lower threshold for TR repair at the time of left-sided valve open heart surgery or intervention is recommended by international guidelines [5, 6].

At present, the ideal timing of surgery for TV disease remains controversial because of the limited data available. However, international guidelines suggest the threshold for intervention to be a tricuspid annulus dilated to ≥40 mm or >21 mm/m^2, regardless of whether the TR is moderate or severe [5, 6].

Percutaneous procedures may be an attractive alternative to surgery for patients with symptomatic functional TR and high surgical risk.

TR assessment with multi-imaging modalities

Detailed knowledge of the complex anatomy of the tricuspid valve (TV) is fundamental to understanding the several new challenges of percutaneous TR therapy. The TV is composed of three leaflets: anterior, posterior and septal.

Echocardiography is the essential imaging technique in the assessment of patients with TR (fig. 1). Two-dimensional (2D) transthoracic echocardiography (TTE) is the standard imaging techniques for to assessing the anatomy, the mechanism and severity of TR, and the haemodynamics. The European Society of Echocardiography and the American Society of Echocardiography have provided specific recommendations for grading the severity of TR on the basis of a combination of qualitative, semiquantitative and quantitative echocardiographic measures [6–9]. Three-dimensional (3D) transthoracic echocardiography may provide incremental diagnostic information, in particular regarding leaflet anatomy.

Transoesophageal echocardiography (TEE) as well as intracardiac echocardiography (ICE) play an essential role in addition to TTE, and are particularly helpful during TV intervention.

Computed tomography (CT) has become a crucial tool for defining patients' anatomy and assessing the eligibility of transcatheter TV therapies. Electrocardiogram-gated angio-CT is an essential step in the assessment of TV anatomy, and the tricuspid annular shape and dimensions, as well as semi-quantitative assessment of the tissue characteristics of tricuspid annulus and leaflets. Additionally, CT can assess the surrounding structures of TV including the coronary arteries, inferior vena cava and superior vena cava.

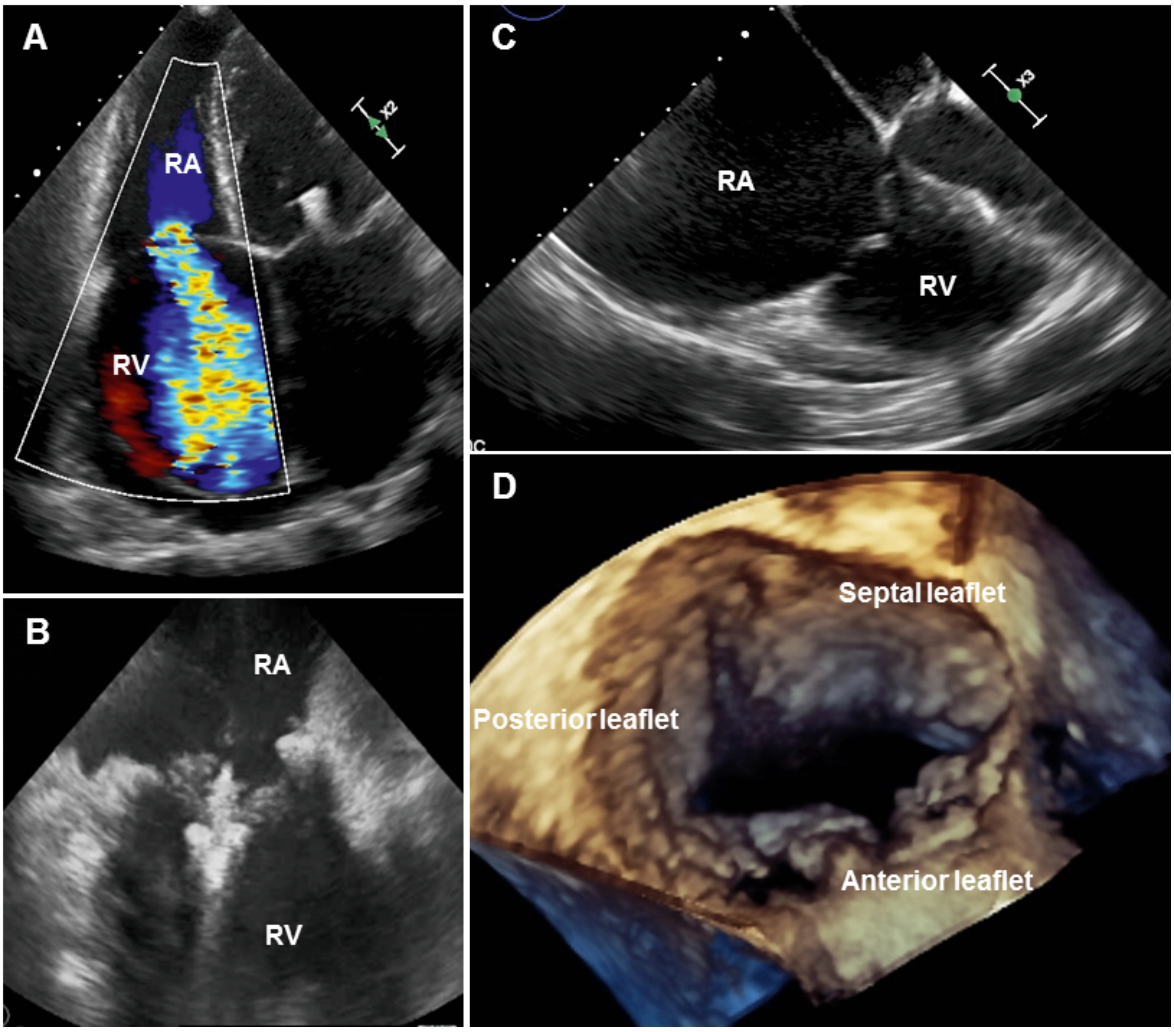


Figure 1: Echocardiographic image of tricuspid valve.
(**A**) Colour-Doppler image by use of two-dimensional (2D) transthoracic echocardiography. (**B**) Intraoperative image (MitraClip therapy) by use of intracardiac echocardiography. (**C**) 2D transoesophageal echocardiographic (TEE) image, (**D**) 3D TEE image. RA: right atrium; RV: right ventricle

Cardiac magnetic resonance imaging can provide more accurate quantification of right ventricular function and TR severity [10].

Transcatheter tricuspid valve replacement

Percutaneous valve-in-valve and valve-in-ring implantation using balloon-expandable valve systems, either for a degenerated tricuspid bioprosthesis or for ring annuloplasty failure, have been the subject of numerous case reports [11–15].

The Valve-in-Valve International Database (VIVID) Registry includes, so far, 156 patients who underwent TV-in-valve or valve-in-ring procedures [16]. This has demonstrated that this approach is technically successful and results in improved TV function. The valve-in-ring procedure has a potential difficulty generated by the rigidity of the elliptic ring, the risk of conduction disturbance and valve malpostionning, and the residual paravalvular leaks. Longer follow-up of the patients and further improvement in valve technology dedicated to tricuspid position are necessary to determine long-term valve function and to define specific risk factors for poor outcome. Figure 2 shows an example of a valve-in-valve procedure after failure of a surgical bioprosthetic valve implantation.

Transcatheter TV replacement has no risk of right ventricle outflow obstruction, and less risk of residual paravalvular leak and embolisation as a result of the low-pressure right ventricular system, compared with left-side valve disease.

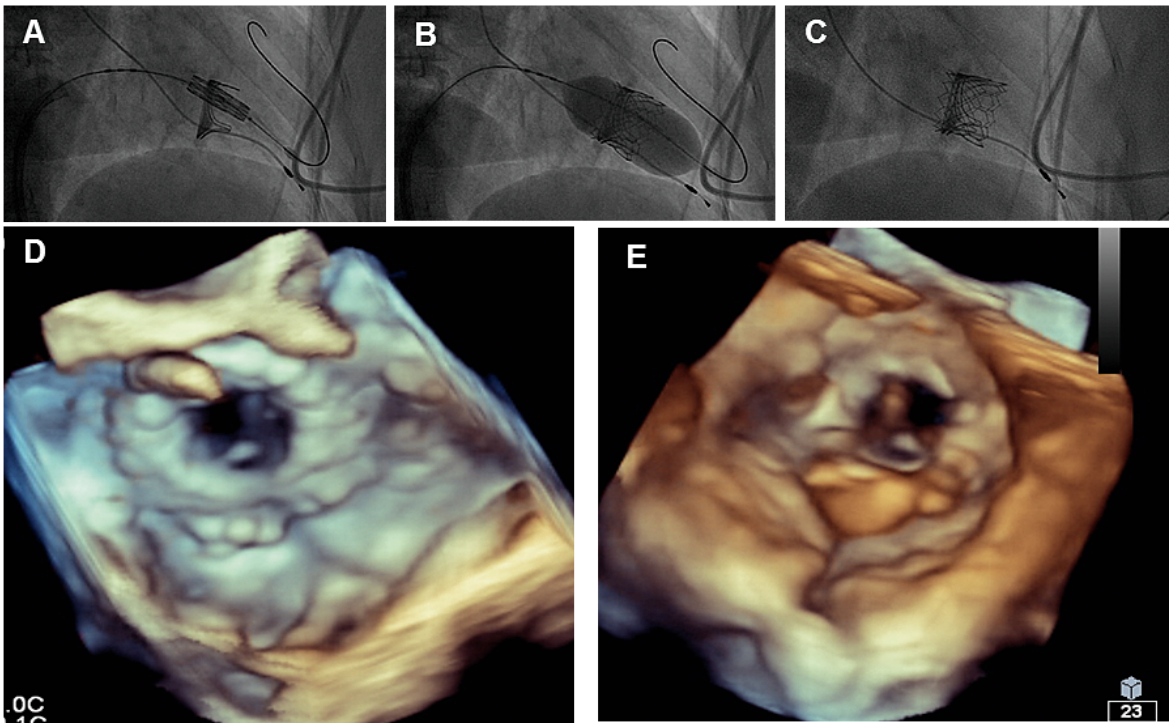


Figure 2: Valve-in-valve procedure at the tricuspid position.
(**A**) Fluoroscopic image of tricuspid valve-in-valve procedure using Edwards Sapien valve with transseptal approach. (**B**) Fluoroscopic image during deployment Edwards Sapien valve in surgical bioprosthetic valve. (**C**) Fluoroscopic image after valve-in-valve procedure using Edwards Sapien valve. (**D**,**E**) Three-dimensional transoesophageal echocardiography of patient with tricuspid valve in valve after failure of a surgical bioprosthetic valve implantation from the right atrium (**D**) and from the right ventricle (**E**).

Transcatheter replacement of a native TV was performed in Cleveland Clinic, where the world's first implantation of a GATE™ tricuspid atrioventricular valved stent (NaviGate Cardiac Structures Inc., the company licensed the stent technology from Cleveland Clinic) was successfully performed in 2016.

Transcatheter tricuspid valve repair

Transcatheter tricuspid valve repair technologies are listed in figure 3.

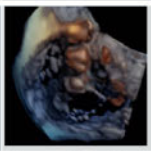
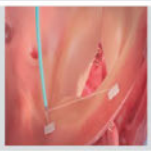
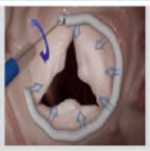
Device Name	MitraClip	Trialign	TriCinch	Cardioband	Millipede	FORMA Repair System	Caval valve implantation	TRAIPTA
Device Image								
Description	Bicuspidisation of the TV by plicating	Bicuspidisation of the TV by plicating	Bicuspidisation of the TV by cinching	direct annuloplasty device	Complete semi rigid ring	Spacer to occupy the regurgitant orifice area	caval valve implantion in vena cava	Pericardial circumferential device
Access	Transfemoral	Transjugular	Transfemoral	Transfemoral	Transfemoral	Transsubclavian	Transjugular/ transfemoral	Transjugular/ transfemoral
Status*	• About 60 patients	• About 15 patients	• About 25 patients	• About 10 patients	• About 2 patients	• About 20 patients	• About 40 patients	• Only pre-clinical data
* At the moment of reporting from recently international meeting								

Figure 3: Transcatheter tricuspid valve repair technologies.
The current status of transcatheter tricuspid valve repair technologies at the time of reporting, from a recent international meeting.

Edge-to-edge repair at the tricuspid position

Transcatheter edge-to-edge repair with the MitraClip system (Abbott Vascular Inc, Santa Clara, CA) is a validated technique for mitral position (fig. 4) [17]. This concept was initially tested in patients with severe symptomatic TR deemed at high risk for surgery [18].

Nickenig et al. described the safety and feasibility of MitraClip therapy for 64 patients with chronic severe TR [19]. The imaging guidance with TEE remains an issue, since proper visualisation of the leaflet and therefore of the grasping may be problematic [20]. A combination of TEE, TTE and/or ICE may help to overcome the difficulty in visualisation. A modified delivery system for tricuspid clipping is under development and a multicentre feasibility trial in Europe is imminent.

The Trialign system

The Trialign system (Mitralign Inc, Tewksbury, MA) is designed for percutaneous suture annuloplasty to treat functional TR that replicates the surgical Kay technique, and results in percutaneous bicuspidisation of the TV by means of plication of the posterior leaflet with a pair of percutaneously placed pledgets, via an internal jugular venous approach under fluoroscopic and TEE guidance.

Trialign is currently undergoing evaluation in a prospective multicentre US feasibility (SCOUT) (NCT02574650) and European CE-mark (SCOUT-II) study. The 30-day results of the SCOUT trial confirmed the safety of this device, which reduced annulus area and improved quality of life for 15 patients [21].

The TriCinch system

The TriCinch system (4Tech Cardio Ltd, Dublin, Ireland) is a percutaneous device for TV bicuspidisation by means of transfemoral fixation of a stainless steel corkscrew into the anteroposterior TV annulus. The ideal site for anchor implantation is defined by a careful analysis of the CT images with a 3D reconstruction, usually close to the anteroposterior commissure. The corkscrew is connected through a Dacron band to a self-expanding nitinol stent placed in the inferior vena cava under tension. The size of the stent is evaluated on pre-procedural CT. Early clinical outcomes with this technique in 24 patients were presented at an international meeting in 2016.

The PREVENT study (NCT02098200) is assessing the safety and potential efficacy of this device with the objective of obtaining a CE mark.

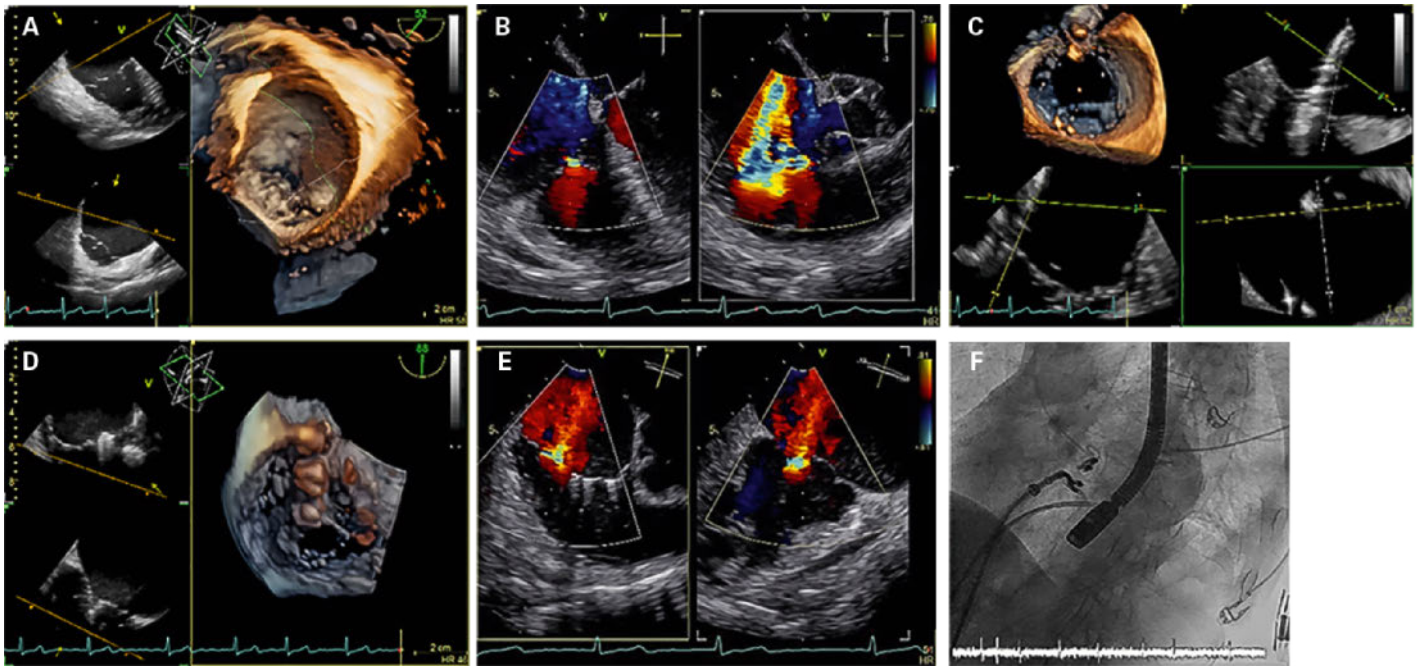


Figure 4: Edge-to-edge repair at the tricuspid position.
(**A**) 3D transoesophageal echocardiography (TEE) from right atrium with systolic gap before intervention. (**B**) Colour-Doppler X-plane TEE with severe tricuspid regurgitation before intervention. (**C**) Grasping the leaflets with the MitraClip device. (**D**) Final 3D-TEE with four clips between anteroseptal leaflets in a diastolic frame with area reduction. (**E**) Final result in colour-Doppler X-plane TEE with minimal tricuspid regurgitation. (F) Final view with four clips seen in fluoroscopy. 3D: three-dimensional

Cardioband at the tricuspid position

The Cardioband system (Edwards Lifesciences, Irvine, CA) is a transfemoral transcatheter direct annuloplasty device, which received a CE mark in 2015 for the treatment of functional mitral regurgitation (fig. 5) [22]. The same concept has been recently used to treat functional TR, since the Cardioband device closely reproduces the gold standard for surgical TR treatment, ring annuloplasty. The Cardioband is implanted on the mural part of the tricuspid annulus from anterior-septal commissure, in a clockwise direction, along the septal-posterior commissure. Under real-time, beating-heart TEE guidance, final adjustment to reshape the annulus provides a marked reduction in the diameter and therefore reduction of tricuspid regurgitation by forcing leaflet coaptation. Clinical experience with the Cardioband at the tricuspid position is still very limited, but promising [23]. Early clinical outcomes with this technique in 20 patients were presented at an international meeting in 2017.

The Millipede annular ring

The Millipede annular ring (Millipede, Santa Rosa, CA) mimics surgical annuloplasty by means of transcatheter implantation of an expandable and contractible ring that uses a novel attachment technique with many small barbed anchors to secure it in place. Clinical experience with this device is so far very limited. Early experience with this technique in two patients was presented at an international meeting in 2017.

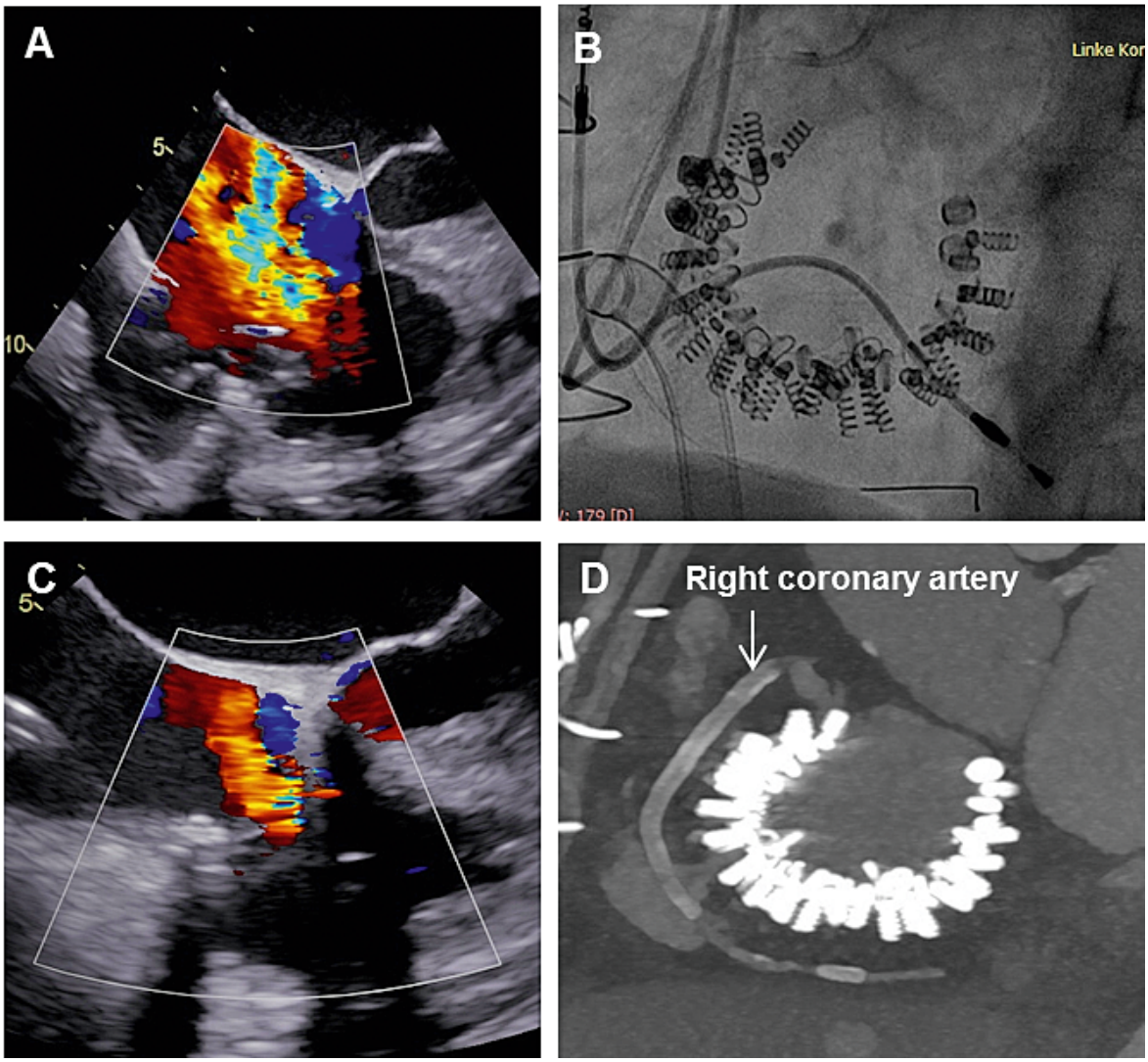


Figure 5: Cardioband at the tricuspid position.
(**A**) Preoperative colour Doppler transoesophageal echocardiography (TEE). (**B**) Fluoroscopic image of the Cardioband at the tricuspid position after cinching the device. (**C**) Postoperative colour Doppler TEE. (**D**) Postoperative computed tomography with a Cardioband at the tricuspid position and no damage to the right coronary artery.

Tricuspid valve spacer

This system consists of implantation of a device to occupy the regurgitant orifice area and provide a surface for native leaflet coaptation with the device. The FORMA Repair System (Edwards Lifesciences) consists of a spacer and a rail that is anchored at the apex of the right ventricle. The spacer is a foam-filled polymer balloon that passively expands through holes in the spacer shaft. The device is fixed at the distal end in the right ventricular myocardium. The device is locked proximally, and the excess rail length is coiled and placed in a subcutaneous pocket. Pilot studies have shown that the device can improve functional status, reduce oedema and decrease TR [24].

Further feasibility data will be provided by a prospective registry study (Early Feasibility Study of the Edwards Tricuspid Transcatheter Repair System (NCT02471807)). Early clinical outcomes with this technique in 18 patients were presented at an international meeting in 2017.

Caval valve implantation

Severe TR results in reversal of blood flow into the systemic venous circulation, including the venae cavae, leading to increased myocardial work load and worsening of right heart function associated with congestive hepatopathy and ascites [25]. This concept is based on implantation of caval valve prostheses (CAVI) in both the superior and inferior vena cava. The resulting improved haemodynamics decrease the extent of TR. Heterotopic valve implantation had a beneficial impact on New York Heart Association (NYHA) class and 6-minute walking distance of patients [26]. The procedures were performed in patients with sufficiently preserved right ventricular function, on consideration of the risk of deterioration of right ventricular function with increasing preload in patients with prior depressed right ventricular function. It was demonstrated that single valve implantation in the inferior vena cava may be safe and may effectively accomplish decongestion, and could potentially decrease the risk of valve thrombosis as well as avoiding entrapment of pacemaker leads in the superior vena cava [27].

Currently, the HOVER trial (NCT02339974), a prospective, nonrandomised study to determine the short-term safety and long-term efficacy of the valve in the inferior vena cava for the treatment of symptomatic severe TR, is ongoing [28]. The TRICAVAL randomised study is also organised by Charité University, Berlin (NCT02387697). Early clinical outcomes with this technique in 25 compassionate-use cases were presented at an international meeting in 2017.

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Transatrial intrapericardial tricuspid annuloplasty (TRAIPTA)

A circumferential device is deployed within the pericardial space to modify tricuspid annular dimension interactively and to reduce functional TR [29]. The pericardium is accessed via puncture of the right atrial appendage and the nitinol loop of the TRAIPTA system (Cardiovascular Intervention Program at the National Heart, Lung, and Blood Institute) is opened inside the pericardium to encircle the heart along the atrioventricular groove. This technique could potentially treat functional regurgitation of both atrioventricular valves, but has not yet been tested in patients.

MIA™ Minimally Invasive Annuloplasty Technology for Tricuspid

This minimally invasive annuloplasty technology is used to implant a MIA (Micro Interventional Devices, Inc., Newtown, PA) device. This is made from proprietary PolyCor™ anchors bonded to a proprietary, self-tensioning, implantable elastomer called MyoLast™. It is the low-mass polymeric implant designed specifically to comply with normal physiological valvular function. The first-in-human case was announced in 2016.

The STTAR Study, which assessed the feasibility of the procedure and the ability of the MIA implant to significantly reduce annular dimensions, was conducted in Europe.

Conclusion

Although only very limited data are available so far, transcatheter TR treatment has been dramatically evolving over several years.

It is important to point out the present stage of the development of these therapies, since clinical evidence for efficacy or safety of these various strategies and techniques are still scanty. Some of these novel devices are based on surgical techniques that evolved into less invasive approaches, whereas other techniques represent completely new concepts still awaiting validation in the clinical setting.

The complex anatomy of the TV apparatus and right heart chambers have made transcatheter treatment of the TV very challenging. Continued refinement of assessment and transcatheter techniques for TR will improve the less invasive means to treat patients with severe TR and particularly those deemed at prohibitive or high surgical risk.

Disclosure statement
No financial support and no other potential conflict of interest relevant to this article was reported.

References
The full list of references is included in the online version of the article at www.cardiovascmed.ch.