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Transcatheter innovations in tricuspid regurgitation: Cardioband☆

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ABSTRACT

Functional tricuspid regurgitation (FTR) has been neglected for a long time, however its prevalence and clinical relevance is not negligible. In presence of FTR, a certain quote of annular dilatation is present thus contributing to the mechanism of regurgitation. Historically, surgical annuloplasty has been the main treatment to correct FTR; however surgical repair is limited by a high risk of mortality and morbidity. For this reason, percutaneous tricuspid annuloplasty is an attractive tool for the treatment of FTR in patients at high surgical risk. A number of both direct and indirect percutaneous annuloplasty systems are currently under pre-clinical and clinical development. This review will discuss the Cardioband system, a novel direct annuloplasty device with promising result in terms of clinical safety and efficacy.

Contents

Functional tricuspid regurgitation (TR; FTR), also known as secondary TR, represents the most frequent type of TR.[1] Both in primary and secondary TR, the final common pathway is progressive tricuspid annular dilatation that occurs in the antero-posterior direction towards the right ventricular (RV) free wall.[2] In the presence of FTR, surgical correction of tricuspid annular dilation has been considered the primary target of treatment. Nevertheless, patients suffering for severe TR are frequently left untreated because of high surgical risk.[3] In this setting, emerging percutaneous tricuspid annuloplasty devices are currently under development and at early stages of clinical investigation to evaluate their potential role in addressing this unmet clinical need.

Abbreviations and acronyms: TR, tricuspid regurgitation; FTR, functional tricuspid regurgitation; RA, right ventricle or ventricular; RV, right atrial; RCA, right coronary artery; TEE, transesophageal echocardiography; 3DE, 3 dimensional echocardiography.

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Anatomical challenges for percutaneous tricuspid annuloplasty

A number of percutaneous annuloplasty systems are currently under pre-clinical and clinical development to target the tricuspid annulus, which is the principal mechanism of regurgitation in functional TR, especially in the early stages of TR, prior to significant RV remodelling and/or when associated with right atrial (RA) dilation such as in the setting of atrial fibrillation. However, several anatomical factors may challenge the development of such percutaneous annuloplasty systems[4]:

- Percutaneous tricuspid annuloplasty targets the antero-lateral part of the tricuspid annulus which is in close proximity to the right coronary artery (RCA).[5]
- Few percutaneous routes are available to achieve an ideal approach for the percutaneous treatment of the tricuspid valve. The RV has a complex shape and a thin wall, thus not allowing the transapical approach. The angulation between the tricuspid valve, the inferior and superior vena cava could also pose an added challenge; moreover, a

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prominent Eustachian valve can sometimes hamper the transfemoral approach. Access from the internal jugular vein or superior vena cava has a more favourable approach angle to the tricuspid valve, but performing transjugular procedures can be ergonomically difficult and with greater radiation exposure in the conventional cath lab setup. Also, the large number of RV trabeculations limits the possible movements below the valvular plane.

- Due to the large native tricuspid annular diameters, large bore and bulky delivery systems are needed to accommodate devices approximately twice the size of the prostheses utilized for transcatheter aortic valve replacement.
- Imaging of the tricuspid annulus has numerous challenges: transesophageal echocardiography (TEE) is limited by the anterior location of the valve. Moreover, the esophagus is not axial nor in close proximity to the tricuspid valve, so mid-esophageal images are off-axis and therefore more challenging to orientate. Tricuspid valve leaflets are thinner and can be obscured by calcification/prosthesis of left-sided structures. Three-dimensional echocardiography (3DE) gives simultaneous visualization of the three leaflets; however, poor acoustic windows in some patients and a lack of standardization of imaging views are a major limitation. Intracardiac echocardiography, especially new 3DE capable probes, could theoretically overcome these limitations since its location in the RA can provide detailed, high-quality images; however, clinical experience is still limited.
- The correct implantation of percutaneous annuloplasty systems requires good tissue quality at the hinge point and a certain distance between the tricuspid annulus and the right coronary artery. The late device detachments and tissue dehiscence that occurred after first percutaneous experiences can be a consequence of tissue fragility that limits safe and durable anchoring of the devices.[2]

Percutaneous tricuspid annuloplasty: the Cardioband system

The Cardioband Tricuspid System (Edwards Lifescience, Irvine, CA) is the first transcatheter therapy dedicated to the treatment of annular dilatation that occurs in TR. The Cardioband system consists of four main accessories:

1) **The implant**: is a polyester sleeve with radiopaque markers. The sleeve is mounted on the delivery system and the anchors are deployed from the internal part. The contraction wire that runs in the sleeve is connected to an adjustment spool that can adjust the length of the implanted device.
2) **TF Delivery system**: The Cardioband delivery system (CDS) consists of the implant delivery system (IDS) and the 24F steerable sheath (TSS). The IDS is comprised of a steerable guide catheter (GC) and an implant catheter (IC) with the Cardioband implant mounted on its distal end.
3) **Implantable metal anchors and anchor delivery shafts**: the Cardioband is attached to the native tricuspid annulus using up to 17 stainless steel anchors that are 6 mm in length. The anchors are fully repositionable and retrievable until deployed.
4) **Size adjustment tool** (**SAT**): The SAT distal tip is inserted over the implant wire, attaches to the spool and is used to control the implant adjustment spool and the implant size.

Once inserted through the transfemoral 24-Fr access sheath, up to 17 anchors can be deployed on the atrial surface of the tricuspid annulus to fix the device. The implant starts from the antero-septal commissure, progresses in a clockwise direction and ends after the postero-septal commissure and coronary sinus. Once all the anchors have been deployed, the SAT enabling bidirectional reshaping of the tricuspid annulus is advanced over the contraction wire, and the band is then cinched, allowing a reduction of the anteroposterior and septolateral tricuspid annulus diameters. The implant size can be adjusted under echocardiographic and fluoroscopic guidance using TEE real-time monitoring that evaluate the effects of progressive cinching on TR (Fig 1).

Procedural planning

Patient selection is the most critical part of the procedural planning. Similar to surgical annuloplasty, the Cardioband may have limited efficacy as a stand-alone device in patients with severe tricuspid annular dilation and severe leaflet tethering, especially when tethering height is >0.51 cm and tethering area is >0.80 cm^2.[6] Moreover, in the presence of organic TR with primary alteration of the tricuspid leaflets, percutaneous tricuspid annuloplasty can have limited impact on TR due to an extremization of the leaflet tethering (Fig 2).

Meticulous planning with computed tomography (CT) is of importance since this imaging technique provides information on the anatomical spatial relationship of the tricuspid valve apparatus and RCA as well as size of implant that echocardiography cannot provide. A larger distance between the RCA and the tricuspid leaflet hinge point is present at the insertion level of the anterior tricuspid leaflet, whereas the RCA courses more closely to the annulus at the level of the insertion of the posterior leaflet.[7] The evaluation of the anatomical relation between RCA and tricuspid annulus plays a key role for success in the procedural planning of tricuspid Cardioband in order to minimize the risk of coronary artery impingement and/or damage following the release of the anchors (Fig 3).

Cardioband on tricuspid regurgitation: early clinical results

After the first compassionate use,[8] the safety and the efficacy of the Cardioband implant for the treatment of tricuspid regurgitation has been tested in the **TRI**cuspid **R**egurgitation Re**PAI**r With Ca**R**dioband Transcatheter System (TRIREPAIR) study.[9] Thirty patients with moderate to severe TR and significant annular dilatation (>40 mm) who were deemed at prohibitive risk for cardiac surgery were enrolled in this single-arm, multicentre, prospective trial.

The Cardioband device was successfully implanted in all the patients. However, at 30-days follow-up, two deaths occurred and one of these was secondary to a device-related complication. The authors report 3 coronary complications: one patient had an occlusion of a secondary branch of the RCA which was left untreated; another patient had a worsening of a pre-existing lesion of the distal RCA which was successfully treated with the implantation of a drug-eluting stent; one patient experienced a pericardial tamponade secondary to a penetration of one anchor into the RCA. The perforation was successfully managed with prolonged balloon inflation and pericardial drainage. To avoid this complication, in the future, the use of latest echocardiography technology including innovative 3DE reconstructive modalities such as multi-planar echocardiography and echocardiography-fluoroscopic fusion may facilitate accurate and timely implantation, thus reducing the risk of RCA damage. At 30 days, 20 of 28 patients (71%) improved their functional status, as assessed by New York Heart Association functional class; at 6 months, patients had a significant improvement of their functional status assessed with The Kansas City Cardiomyopathy Questionnaire score (+24 points) and the mean 6-min walk distance increased by 60 m.

The echocardiographic results reported a significant reduction of the annular dimensions from 41.6 ± 4.9 mm to 36.2 ± 4.7 mm at discharge. The reduction remained stable at 30 days (42.2 ± 5.1 mm to 37.8 ± 3.3 mm; $p = 0.0004$) and at 6 months (41.6 ± 5.3 mm to 37.8 ± 3.4 mm; $p = 0.0014$). The effective regurgitant orifice area showed a progressive reduction from 0.78 ± 0.49 mm^2 to 41 ± 0.26 mm^2 at 6 months. At 6 months, an increase of patients with mild/moderate grades was observed (from 29% after the procedure to 73% at

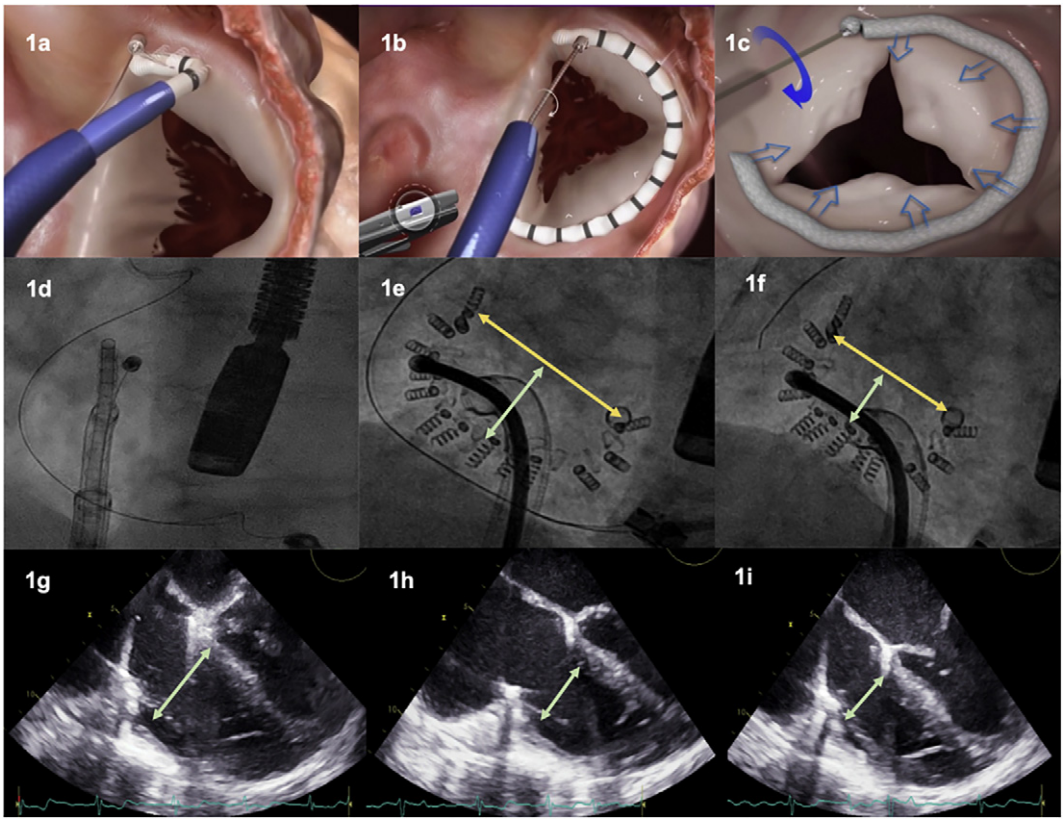

Fig 1. A case example of Cardioband implant: the first anchor is released at the level of the antero-septal commissure (panels a, d); the remaining anchors are then implanted until at least the postero-septal commissure is reached and if possible after the commissure (panels b, e). Once in site, the Cardioband is cinched (panels b, c) thus allowing a controlled reduction of the antero-posterior (yellow arrow) and septo-lateral diameters (green arrow) (panels e, f); the cinching can be controlled using live echocardiographic monitoring (panels g–i).

6 months, probably due tricuspid annular remodelling) even if 28% of patients still had a significant residual severe to torrential TR.

After the positive results of the trial, Cardioband has now received the CE mark for the treatment of functional TR and is being implanted commercially in Europe. No data are available about the use of these devices in a real-world setting. A case of staged transcatheter tricuspid valve repair via MitraClip XTR after Cardioband to treat torrential TR secondary to a large coaptation gap has also been reported.[10]

Conclusions

Percutaneous tricuspid valve annuloplasty represents a new therapeutic alternative for FTR. In this context, the Cardioband system is the first commercially available system that provides a unique solution for replicating the gold-standard of surgical tricuspid valve repair, i.e. incomplete ring annuloplasty. The initial clinical experience has confirmed the efficacy with an acceptable safety profile. In the future,

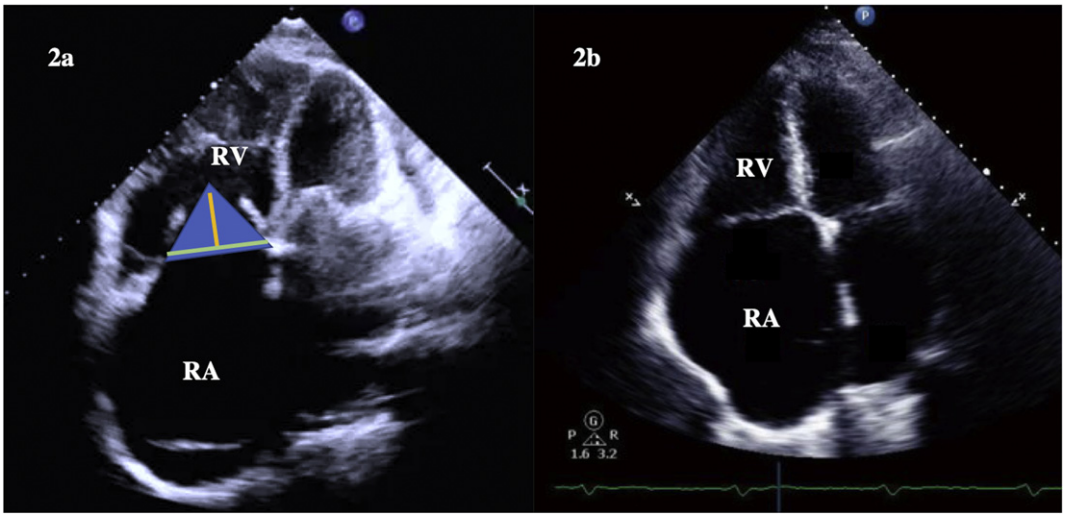

Fig 2. Differences in tricuspid valve anatomy: the panel a shows a case of tricuspid valve tethering secondary to an enlargement of the right ventricle. The panel b is representative of a tricuspid valve without significant tethering. Yellow line: tethering height; blue triangle: tenting area; green line: Antero-lateral annular diameter. Abbreviations: RA: right atrium; R: right ventricle.

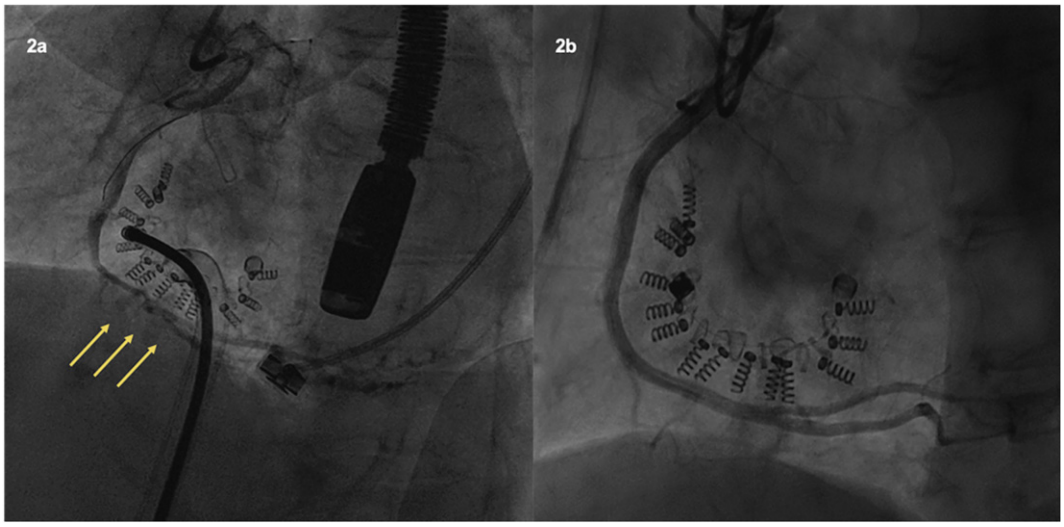

Fig 3. A case of right coronary spasm following the implant of Cardioband. Following the implant of the Cardioband, selective angiography of the right coronary artery showed diffuse spasm, more pronounced in the zone which was closer to the anchors (yellow arrow). As there was no evidence of myocardial ischemia on ECG and subsequent Troponin measurements, the mechanical spasm was managed conservatively. Repeat angiography a few days after the procedure showed complete resolution of the spasm but with continued efficacy as regards to TR reduction.

further data are needed to demonstrate the efficacy and safety of this device in a larger real-world population: the US Early Feasibility Study of the Cardioband tricuspid system is a prospective, single arm, multicenter study to evaluate the safety and device functionality of the Cardioband tricuspid system (ClinicalTrials.gov Identifier: NCT03382457). Patients with symptomatic with more than moderate FTR in medical therapy will be considered for enrolment.

Statement of conflict of interest

Dr. Latib is a consultant for Medtronic, Abbott, and Edwards Lifesciences.

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