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Percutaneous treatment of tricuspid valve in refractory right heart failure

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KEYWORDS
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The renewed interest in tricuspid valve pathology is a consequence of the high mortality rate associated with this valve dysfunction, mostly functional, and secondary to left ventricular impairment, or pulmonary hypertension. Despite the clear relationship between tricuspid insufficiency and mortality, surgical treatment is offered to a small group of patients, due to the significant in-hospital mortality secondary also to the multiple comorbidities and the advanced stage of left ventricular dysfunction. During the last few years, new therapeutic options have been developed for the percutaneous treatment of tricuspid insufficiency which, albeit still in the experimental phase, provides an alternative to surgery in patients at very high-risk or frankly inoperable. We will describe the various percutaneous therapeutic options available today, and their potential application to clinical practice.

Introduction

Functional tricuspid incompetence (TI), ordinarily secondary to left heart disorders or pulmonary hypertension, in absence of organic structural valvular disease, is the most frequent condition affecting the tricuspid valve in the western countries.[1,2] The notion, held for many years, that tricuspid valve dysfunction would correct itself once the left heart problem had been addressed, has restrained surgical repair or replacement in the past.[3] Although several studies demonstrated the advantages of a more aggressive surgical approach to correction of functional TI,[4] only a small portion of patients actually receive treatment,[3,5] due to their very high in-hospital mortality.[6,7] During the last few years, several new therapeutic options have been developed for the percutaneous treatment of tricuspid insufficiency to provide a less invasive alternative to surgery in patients at very high-risk or frankly inoperable. Notwithstanding the complex anatomy of the tricuspid valve apparatus, which objectively render the percutaneous approach difficult,[8] initial evidences provided encouraging results in terms of feasibility and efficacy.[9,10]

Percutaneous treatment of tricuspid incompetence

Several percutaneous treatment have been developed (*Table 1*) with the purpose of reducing the back-flow in the vena cava, characteristic of severe TI, or to decrease the size of the severely dilated tricuspid valvular annulus, or to enhance coaptation of the valvular leaflets.

Transcatheter implant of bicaval valves

The purpose of implanting bioprostheses in the superior and inferior vena cava is to preclude the back-flow of blood, which frequently occurs in patients with severe TI, and significant dilation, and dysfunction of the right ventricle, so as to avert congestive impairment of the liver and other organs.

Following the initial experience with balloon-expandable prostheses conceived for treatment of aortic valve stenosis, a specific device for this procedure has been designed: the TricValve (P&F Products & Features Vertriebs GmbH, Vienna, Austria, in cooperation with Brazil Biomedica, Sao José do Rio Petro, Brazil). This device is made up of two biological valve prostheses, both with

Table 1 Techniques for percutaneous repair/replacement of tricuspid incompetence

Devices	Category	Procedure and device description	Clinical experience
TriCinch	Annuloplasty system	The system consists of a corkscrew anchor, a self-expanding stent (27–43 mm), and a Dacron band connecting the two. Once anchored to the anteroposterior annulus, the stent is released in the IVC and tension is applied through the Dacron band.	PREVENT trial: 24 patients • Procedural success in 85% patients • Two cases of haemoperitoneum • Four late anchor detachment • One right coronary artery damage
Trialign	Annuloplasty system	The rationale behind replicates Kay surgical procedure: by delivering polyester pledgets onto the tricuspid annulus, on both sides of the posterior valvular leaflet, the system allows annulus plication, and valve bicuspidalization. Access via jugular vein.	SCOUT I Trial: 15 patients • 100% procedural success • Reduced annular size, area, and EROA • Three late pledget detachment and one coronary damage SCOUT II Trial: 60 patients - recruiting
Millipede	Annuloplasty system	A repositionable and retrievable complete ring with individually-controlled collars, attached to tricuspid annulus via corkscrew-shaped anchors. The implant is then contracted, reducing the annulus to a physiological size. Risk of complete AV block	Two patients (surgical implant) • Immediate reduction in valve diameter • TR abolishment • Positive remodelling of both RV and LV
Cardioband	Annuloplasty system	A flexible implant is delivered through a flexible catheter. Multiple anchors are attached to the annulus, and once they are all fixed, tensions can be applied reducing the dilated annulus to a physiological size.	20 patients (compassionate use) • Reduction in TR grade and annulus diameter • Reduction in EROA, PISA radius and VC TRI-REPAIR Trial: 30 patients - recruiting
MitraClip	Coaptation device	It consists of 4-mm wide cobalt-chromium polyester-covered implant with two arms that can grasp two leaflets. Multiple clips can be positioned to maximize results. Delivery via both transjugular and transfemoral access.	64 patients (compassionate use) • Significant reduction in TR grade, EROA, regurgitant volume, septo-lateral diameter • Improvement of clinical outcomes at 9-month follow-up
FORMA	Coaptation device	The device consists of a rail anchored to RV apex and a foam-filled polymer balloon that acts as a coaptation device. FORMA device is advanced via left subclavian/axillary vein access, and it is fully retrievable.	Cohort of 18 patients • Procedural success rate 89% • No operative mortality. • $\leq$severe TR in 71% patients at 6 months • NYHA class and clinical outcomes improvement at 1 year
Tric Valve and balloon-expandable prosthesis	Transcatheter caval valve prosthesis	Tric Valve Device consists of two self-expandable bioprosthetic valves with nitinol frames, to be deployed into superior and inferior vena cava at cavoatrial inflow. Tric valves do not require a pre-stenting of caval veins. Available sizes from 28 mm to 43 mm.	24 patients (compassionate use) • Procedural success in all the cases • Clinical improvements observed during follow-up
Sapien Caval Valve	Transcatheter caval valve prosthesis	29-mm Edwards-Sapien XT or Sapien 3 valves can be deployed in the IVC and SVC via femoral vein access. Pre-stenting of caval veins is required for anchoring and structural support.	Published outcomes limited to 10 patients: • 100% acute success; • 90% patients improved $\geq$1 NYHA functional class at 9 months. HOVER Trial: 15 patients—ongoingTRICAVAL Trial: 40 patients—ongoing
NAVIGATE Valve	Transcatheter valve prosthesis	The low-height profile allows easier advancement through the vessels. Winglets engage the annulus from both atrial and ventricular sides. The device does not protrude significantly into adjacent chambers.	First compassionate implantation was a procedural success, with no events in the short-term follow-up.Now reached almost 10 implants.

IVC, inferior vena cava; SVC, superior vena cava.

three cusps of bovine pericardium mounted over a Nitinol stent. Results from a multicentre registry, including 23 patients treated with balloon or self-expandable prostheses (Lauten A. Caval Interventional treatment Option for Valve Implantation [CAVI] as interventional treatment option for severe TR. Presentation EuroPCR 2017, Paris, France), have recently been reported. In this series, 19 patients received double valvular prosthesis in the superior and inferior vena cava and four in the inferior vena cava only. The procedure was successful in all patients, and their 30 days survival was 82.6%. The treatment provided improvement of heart failure symptoms and a better quality of life. Despite the relative technical ease of the treatment, its impact on survival was negligible, with most of the patients dying during the mid-term follow-up, limiting significantly the validity of the procedure.

The FORMA system

The FORMA device (Edwards Lifesciences, Irvine, CA, USA) is designed to indirectly reduce severe TI secondary to tricuspid annular dilation, without valve cusps coaptation. The device consists of a balloon 'spacer' and a rail that is anchored at the right ventricular apex. The system is designed to reduce tricuspid regurgitation by occupying the regurgitant orifice area and providing a surface for the coaptation of the valve's native leaflets. Eighteen patients received the device for 'compassionate' use, and the procedure was successful in 89% of the cases without periprocedural deaths. The procedure was complicated by cardiac tamponade requiring surgery ($n = 1$), device migration ($n = 1$), ventricular arrhythmias ($n = 1$), and device thrombosis ($n = 1$) resolved after anticoagulant therapy optimization. After 1-year follow-up, patients had a significant improvement of TI and NYHA (New York Heart Association) functional class (Perlman G. Transcatheter Tricuspid Valve Repair with a New Transcatheter Coaption Device for the Treatment of severe Tricuspid Regurgitation—One-Year Clinical and Echocardiographic Results, Presentation EuroPCR 2017, Paris, France). The multicentre feasibility study (NCT02471807) and the Canadian-European study CE SPACER (Repair of Tricuspid Valve Regurgitation Using the Edwards Tricuspid Transcatheter Repair System; NCT02787408), enrolled so far 78 patients.

Mitralign

The Mitralign device (Mitralign, Tewksbury, MA, USA), is a percutaneous annuloplasty system reproducing the key technique of surgical valvuloplasty,[11] based on the conversion of an incompetent tricuspid valve into a bicuspid valve, by plicating the anterior and posterior portion of the tricuspid valve annulus. Through a trans-jugular approach, and with fluoroscopy and transoesophageal echocardiography guidance, a set of anchors are positioned in proximity of the antero-posterior and posterior commissure at the annular level, which are held together by a suture system, thus plicating the annulus and decreasing its circumference. Should that be necessary a second set of anchors could be implanted to optimize the final result. In the SCOUT I (Symptomatic Chronic Functional Tricuspid Regurgitation) study, the procedure was successfully carried out in all the 15 patients enrolled (only one periprocedural complication, right coronary artery stenosis treated with coronary stenting), and afforded a reduction of the size of the tricuspid valve annulus, as well as an increase in the left ventricular stroke volume while improving quality of life and NYHA functional class.[12] In three patients detachment of one anchor was documented at 30 days. The multicentre SCOUT II study is underway to evaluate the efficacy of the device in 30 patients with functional TI.

TriCinch

The TriCinch (4Tech Cardio Ltd, Galway, Ireland) is an annuloplasty device with an anchoring system (a steel screw), a Nitinol self-expandable stent release system (stent available in several sizes: 27, 32, 37, and 43 mm), and a connecting Dacron sheet. The anchor element is implanted in the tricuspid annulus, near the anteroposterior commissure through a flexible catheter via a femoral venous approach. Annular plication is performed by tensioning the anchor, in order to reduce the valve area and improve leaflets coaptation. Finally, a self-expanding stent, which is connected to the anchor element, is deployed in the inferior vena cava in order to maintain the tension applied on the tricuspid annulus. The Prevent (Percutaneous Treatment of Tricuspid Valve Regurgitation with the TriCinch System; ClinicalTrials.gov identifier: NCT02098200) study was design to evaluate the safety and efficacy (decrease of at least one grade of TI) of the TriCinch system in patients with TI. Among the 24 patients treated, the procedure was successful in 18 (85%), providing an acute significant reduction of TI in 94% of them. Among the causes of unsuccessful procedures, two were interrupted for haemopericardium, and in four cases a late detachment of the anchor was documented.

Cardioband

The Cardioband (Edwards Lifesciences) system is an annuloplasty device originally designed for the mitral valve. The system consists in the positioning of 16–18 anchors in the posterior and anterior portion of the tricuspid valve annulus. After the positioning of the anchors traction tread connected to them is pulled under tension, as to reduce the distance among them, thus reducing the size of the annulus and decreasing the grade of valvular incompetence. Preliminary data from the feasibility study have been recently reported (Kuck KH. Tricuspid Repair with the Edwards Cardioband System. Early Results of the TRI-Repair Study. Presentation EuroPCR 2017, Paris, France). Among the 20 patients treated to this day, there was a 27% reduction of the tricuspid valve ring and improvement of quality of life. Two patients died for causes unrelated to the device during the 30-day follow-up period. Presently is underway a study to evaluate the efficacy of the device in a large number of patients. Among the devices presented so far, Cardioband is probably the one with the best chance of success in the mid-long term.

Millipede

The Millipede (Millipede Inc., Santa Rosa, CA, USA) system is a complete semi-rigid ring, utilized clinically both in the mitral and tricuspid position, and designed to allow complete repositioning. The device has been used for treatment of mitral incompetence in nine patients, two of whom had both mitral and tricuspid annuloplasty, affording a reduction of the tricuspid valve diameter of 42–45% and complete correction of TI in both cases (Rogers J. Transcatheter tricuspid valve therapies: Millipede. Presentation TCT 2016; Washington, DC, USA).

MitraClip

Presently more than 500 patients received, for 'compassionate' use, MitraClip (Abbott, Abbott Park, IL, USA) implant in tricuspid position. The main difficulties associated with this procedure stem from the problematic acquisition of high resolution echocardiographic images of the tricuspid valve, as well as the lack of versatility of the MitraClip system in the right atrium, due to the limited distance between the inferior vena cava and the tricuspid valvular plane. Furthermore, at variance from the mitral valve incompetence, where the therapeutic target is the origin of the regurgitant jet, in IT the target is the centre of the valve, with the typical large leaflets coaptation defect. Accordingly, the goal of the procedure is to capture two adjacent cusps so as to replicate the bicuspidalization procedure or the 'clover' valvuloplasty. In the vast majority of the cases, the procedure consists in the obliteration of the antero-septal commissure, which is the easier target due to the more favourable angle between inferior vena cava and valvular plane. More the one clip is usually necessary to achieve satisfactory result. A recent multicentre study on 64 patients treated with MitraClip for functional IT reported 97% procedural success, and a very low periprocedural complication rate (30 days mortality 5%).[13] In over than 50% of the cases more than one clip was necessary, and the antero-septal commissure was the chosen target in 80% of the patients. The procedure affords a significant reduction of IT and improves functional capacity and quality of life.

Percutaneous valve replacement

Implant of percutaneous prosthetic valve in the contest of surgical bioprosthes degeneration (valve-in-valve) or after surgical annuloplasty (valve-in-ring) has been accomplished with various devices.[14,15] The Gate™ (NaviGate Cardiac Structures Inc., Laguna Hills, CA, USA) prosthesis is, currently, the only available percutaneous device. Presently only a limited number of implants have been done for 'compassionate' use, through a trans-atrial or trans-jugular approach, with promising results.

The problem of permanent pacemaker leads

The presence of a permanent pacemaker lead through the tricuspid valve, could cause TI, and impair the efficacy of various systems designed for TI control. Among the systems described, percutaneous valve replacement, the MitraClip and Cardioband systems are the ones less affected by the presence of the pacemaker lead.

Patient's selection and future perspectives

Although the initial clinical experience with various devices has been promising, it is still to be determined the patient who could benefit the most from this treatment. In the current experimental phase, most of the patients receiving the treatment have advanced heart failure and several comorbidities, and are offered percutaneous treatment for 'compassionate' use, or for excessive surgical risk. In these settings it is very difficult to assess the potential benefits of percutaneous treatment of the tricuspid valve. At variance from the percutaneous treatment of the aortic and mitral valve (percutaneous aortic valve replacement and percutaneous repair of degenerative mitral incompetence), where the procedure has a curative intent, the percutaneous repair/replacement for severe IT, instead, represent a further potential attempt at improving the complex management of patients with advanced heart failure, with the main goal of relieving the patients symptoms. Severe IT, is often the sign of an advance cardiac condition, and albeit the relationship between severe IT and increased mortality is well known, the correction of tricuspid regurgitation, in this setting, could hardly provide a prognostic benefit, which is inevitably dependent from the advanced stage of the cardiac condition and the associated comorbidities of these patients.

The need to recognize an 'optimal timing' for percutaneous treatment of the tricuspid valve is vital in order to avoid unnecessary procedures. In this regard, right ventricular dysfunction and severe pulmonary hypertension should be regarded as major contraindication to the procedure. Furthermore, when surgical treatment is not recommended for the many comorbidities limiting the patient life expectancy, percutaneous treatment should be considered only as palliative measure. On the other hand, for patients with a reasonable life expectancy and an elevated surgical risk, the percutaneous option is clearly appealing. Structural interventional cardiology has advanced substantially in the treatment of valvular heart diseases with many percutaneous treatments for the repair/replacement of mitral valve presently in the experimental stage. It is possible that in the future percutaneous treatment options for the mitral valve will achieve the same results of the surgical treatment, when that will occur, a reliable percutaneous treatment of IT would become necessary to guarantee the patients the same treatment achieved with surgery of the mitral valve and initial stages of tricuspid valve involvement (annular dilation and limited-moderate regurgitation). Accordingly, the successful percutaneous treatment of mitral valve pathology could constitute the trigger for the development of effective percutaneous treatment of the tricuspid valve. It is likely that because of the progressive nature of functional IT, the greater advantage offered by these devices will be achieved during the early stages of the process, before the right ventricular dysfunction and massive annular dilation. The history of interventional

cardiology demonstrates that simplicity and reproducibility are essential to ensure the success of these procedures.

Conclusions

Tricuspid valve incompetence, mostly functional, is a condition with a significant impact on survival. Unfortunately only a small number of patients receive treatment for the high mortality rate associated with surgical repair/replacement procedures, in patients already operated on for left heart valvular problems. The development of percutaneous techniques is of the outmost interest, as an alternative in patients at high surgical risk, and is comforted by promising efficacy and safety results. There still is the need to recognize the optimal patient and the 'optimal timing' for percutaneous treatment of the tricuspid valve.

Conflict of interest: none declared.

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