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Percutaneous repair of tricuspid regurgitation

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Tricuspid regurgitation (TR) is common both in patients with left side valvular heart disease and in patients with permanent atrial fibrillation and is associated with increased mortality, morbidity, and an increased risk of hospitalization. Surgery for isolated tricuspid repair is a viable option but burdened by a high-operative risk and a post-operative course characterized by high morbidity. Recently, percutaneous interventional techniques have emerged as a viable option in selected high-risk patients who may clinically benefit from tricuspid valve repair. The purpose of this article is to provide an overview of the current state of transcatheter restorative treatment of TR by providing an overview of new devices in clinical development.

Introduction

Tricuspid regurgitation (TR) has often been considered a benign valvular disease with an indolent course, so much so that for years it was treated with medical therapy alone. Recent evidence has demonstrated an independent prognostic impact of tricuspid valve disease both in terms of survival and hospitalizations for heart failure.[1] Isolated surgical correction of TR is a feasible approach but burdened by a mortality of approximately 8% and with a subsequent post-surgical course with a complication rate of approximately 20%. The rationale for the development of percutaneous repair techniques arises from the need to guarantee a restoration of the tricuspid valve function to improve the prognosis of patients without burdening them with complications usually observed with surgery.

Surgical experience

Current percutaneous restorative technologies for TR seek to replicate currently used surgical techniques. In surgery, the most used repair technique is annuloplasty with positioning of a prosthetic annular ring by suture.[2] The rationale for using this technique is derived from the presence of annular dilatation in 80% of TR cases; the objective is therefore to restore the original dimensions of the valvular annulus with an increase in the coaptation of the leaflets.

Most suture-only annuloplasty techniques are modified versions of the technique popularized by Kay and colleagues or the De Vega annuloplasty. Other repair techniques with sutures are Kay's valvuloplasty, which involves plication of the posterior leaflet generating a functionally bicuspid valve, and clover technique, a surgical procedure for suturing the leaflets which allows the generation of an 'edge-to-edge'. Prosthetic annuloplasties, on the other hand, allow a reduction in the size of the annulus by positioning an undersized prosthetic ring with different degrees of rigidity. The implanted prosthetic ring is incomplete to avoid damaging the conduction system by generating an atrio-ventricular block. Most published studies, both randomized and observational, have demonstrated that annuloplasty and prosthetic repairs are more durable than suture annuloplasty, particularly in patients with severe tricuspid annular dilatation or pulmonary hypertension. In addition to being more durable, the use of prosthetic rings is associated with improved long-term survival and event-free survival for up to 15 years after surgery compared with suture annuloplasty.[3]

Percutaneous repair

In percutaneous intervention, the objective is to perform a repair of the tricuspid valve, obtaining effective, long-lasting results and minimizing the risk of complications compared to surgery. However, the

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development of percutaneous technologies for the treatment of TR is challenging due to the anatomical characteristics of the valve.[4]

First, the anatomical target for the treatment of TR is the annulus, which is located in proximity to the right coronary artery on the anterolateral side of the valve; in some cases, the proximity of the coronary artery to the ring contraindicates the use of percutaneous approaches in relation to the possible risk of iatrogenic damage. The lesson learned from previous experience with percutaneous mitral valve annuloplasty is that meticulous pre-procedural planning, using cardiac tomography, is critical to plan the procedure and minimize the risk of iatrogenic damage.[1]

Second, the transcatheter ring is made up of a less robust tissue component which can hinder the permanent anchoring of the device.

Third, the tricuspid annulus can reach high degrees of dilation, making it difficult to create devices capable of treating such anatomies.[5]

Fourth, the trans-apical route is relatively contraindicated due to the thin wall of the right ventricle and the rich sub-valvular chordal apparatus. The trans-jugular route and the trans-femoral route appear to be the only viable ones in addition to the trans-pericardial access, which is however impractical.[6]

Main devices for tricuspid valve repair.

EC (European Community)-marked devices currently used are: the TriClip (Abbott Vascular, Temecula, CA, USA), the PASCAL system (Edwards Lifesciences, Irvine, CA, USA), and the Cardioband (Edwards Lifesciences, Irvine, CA, USA). While the first two systems target the plasty of the leaflets, obtaining a bicuspidalization or mimicking a surgical 'clover' procedure, the third device targets the annulus.[6]

TriClip

The TriClip presents itself as a revisitation of the well-known MitraClip with a dedicated delivery system to reach the tricuspid valve. There are four sizes of the device available but the XTW model with an arm width of 6 mm and a grasping area of 9 mm is the most used to date. The TriClip provides the abolition of regurgitation by approximating the leaflets which allows the coaptation gap to be corrected; an indirect traction action on the leaflets also allows the size of the ring to be reduced while performing an indirect annuloplasty. Numerous multi-centre studies and experiences validated its use. In the 6-month feasibility study, TriClip reduced the rate of severe or more than severe TR from 94 to 42%.[7] At 2 years, TR was reduced to moderate or less than moderate in 60% of patients and the reduction of at least one degree of regurgitation was achieved in 85.4% of patients. The randomized study comparing treatment with TriClip against medical therapy, however, failed to demonstrate a reduction in the rate of hospitalization for heart failure with the invasive approach; furthermore, no differences were highlighted in mortality with a benefit of the interventional arm in terms of quality of life and reduction in the degree of TR.[8]

PASCAL

The PASCAL device (PAddles Spacer Clasp ALfieri) is conceptually similar to the MitraClip however with some differences. In fact, it features a central 'spacer (bulking element)' in its IP10 version and is made of nitinol which allows the device to be delicately anchored to the edges, minimizing the risk of iatrogenic damage. The device is available in two models: the IP10, wider (10 mm) and with a central 'spacer' and the PASCAL ACE which has a similar length of the arms (14 mm) to the other model but narrower (6 mm); furthermore, it is not equipped with a 'spacer'. The first study that validated its use on the tricuspid valve included 28 patients in 6 centres. Patients with coaptation gaps >15 mm, severe leaflet tethering, and TR caused by pacemaker leads were excluded. A total of 40 PASCAL devices were implanted (1.4 ± 0.6 per patient), 28 between the anterior and septal leaflet and 12 between the posterior and septal leaflet. Of note, independent leaflet grasping was used in 36 of 40 (90%) PASCAL devices. Procedural success (implantation of at least one device with post-procedural TR <2 + without the need for surgery) was 86%. In one patient, implantation was not possible due to poor quality of echocardiographic images. The implant failed due to large coaptation gap in another patient who died of terminal heart failure a week later. Two patients had leaflet detachment and were managed conservatively. The 30-day mortality was 7.1% (2 of 28 patients). One patient with leaflet detachment died 29 days after the procedure from a presumed cardiac cause. Another patient was hospitalized for heart failure despite persistent TR reduction.[9] The American study Edwards PASCAL TrAnS-catheter Valve RePair System in Tricuspid Regurgitation, (CLASP-TR EFS) enrolled 34 patients with implantation of the device obtained in 85% of cases; in treated patients, 85% reduced TR by at least one degree and 52% of patients had a reduction in regurgitation to moderate or less at the end.[10]

Cardioband

The Cardioband system (Edwards Lifesciences, Irvine, CA, USA) for tricuspid valve repair is the first EC-approved transcatheter therapy for TR and is a variant of its mitral counterpart. It consists of a sutureless contraction band covered by a polyester sleeve secured to the annulus using a series of helical anchors implanted under imaging guidance along the anterior, lateral, and posterior segments of the tricuspid annulus.

After the first experiences with the device for compassionate use, the safety and efficacy of the Cardioband implant for the treatment of TR were evaluated in the TRIcuspid Regurgitation RePAIr With CaRdioband Transcatheter System (TRI-REPAIR) study.[11] Thirty patients with moderate to massive TR and significant septo-lateral annular dilatation (>40 mm) considered prohibitive risk for cardiac surgery. The Cardioband device was successfully implanted in all patients. Echocardiographic results reported a significant reduction in septo-lateral annular dimensions from 41.6 + 4.9 to 36.2 + 4.7 mm ($P < 0.01$) at discharge. The reduction remained stable at 30 days (from 42.2 + 5.1 to 37.8 + 3.3 mm; $P = 0.0004$) and at 6 months (from 41.6 + 5.3 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 at baseline to 0.41 ± 0.26 mm^2 at 6 months. The study's 2-year follow-up data were recently published. The annular diameter was significantly reduced upon discharge and this reduction was maintained for up to 2 years. The septo-lateral annular diameter went from 41.9 ± 4.6 mm ($n = 26$) at baseline to 36.5 ± 3.3 mm ($n = 19$) at 1 year ($P < 0.001$) and at 35.2 ± 4.6 mm ($n = 14$) at 2 years. In parallel with the annular reduction, the severity of TR improved significantly. While at baseline, 24% of patients had ≤ moderate TR, at 2 years the percentage with moderate TR rose to 72%.[12]

New systems not EC approved yet

There are numerous systems being developed. The main ones are listed below:

- K-Clip: K-Clip™ is a new system that features a clipping system with an anchor in the centre. Once implanted at the level of the commissures and in the annular area, the anchored clip is subsequently closed. This allows for a solid anchoring, minimizing the risk of detachment, and at the same time significantly reducing the size of the ring. The system has been tested for compassionate use in 15 patients. A reduction of at least two or three degrees of regurgitation was observed in 60 and 26% of patients, respectively; 10 out of 15 patients achieved a reduction in regurgitation to moderate.
- DragonFly: The DragonFly-T (Valgen MedTech, Hangzhou, Zhejiang, China) is a new system for edge-to-edge tricuspid valve plasty. It has a clip shape with a central spacer and 4 sizes (thickness from 4 to 6 mm and length from 9 to 12 mm) which allow to customize the system. After the implant for compassionate use, a first study for 'early feasibility' is being launched (NCT05671640).
- DragonRing: The DragonRing system (Valgen MedTech, Hangzhou, Zhejiang, China) is a new annuloplasty system that consists of an anchor release system currently being tested for mitral valve implantation. Implants of the tricuspid ring are planned.
- Cardiac implant: the system consists of the implantation of a two-stage annuloplasty system through a transjugular approach. In the first procedure, a 'primer' is implanted which is subsequently processed in a second procedure carried out 90 days after the first. The first human implantation was successfully performed in September 2022 and enrolment in the 'early feasibility' study is underway.

Conclusions

The repair of the tricuspid valve appears difficult due to appropriate patient selection, often presenting at an advanced stage, and due to procedural limitations such as sub-optimal imaging, difficulties to reach the tricuspid valve plane in a perpendicular fashion, and difficult navigation in the right ventricle. The initial results with edge-to-edge and annuloplasty systems appear encouraging but require improvement and should be directed towards selected candidates in whom the TR has a suitable anatomy for the use of such devices and in which an optimal result can truly change the patient's prognosis.

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Data availability

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