A personalized approach to interventional treatment of tricuspid regurgitation: experiences from an acute animal study

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Abstract

OBJECTIVES: Interventional treatment of tricuspid valve disease has so far received little attention due to the anatomical challenges in a thrombogenic surrounding. In the present study, we present an imaging-based, personalized interventional approach to the therapy of tricuspid regurgitation.

METHODS: In our porcine model, we used rapid prototyping to build a matrix reproducing the geometry of the right atrium that was previously derived from computer tomography (CT) scans. Over this matrix, a braided nitinol device fitting almost completely the right atrium was crafted. An additional tubular stent component was developed to carry a tissue valve prosthesis. This part was designed to be connectable to the annular portion of the main device. In our feasibility study, the crimped device was implanted via jugular access into the right atrium of 12 pigs and expanded subsequently. Following isolated implantation of the device without the valve-carrying component, further procedures included implantation of the whole composite device, including the mentioned tissue valve. Representing a only feasibility study, all implantations were performed under full bypass and direct sight. On-site visualization was performed by both echocardiography and fluoroscopy. Additional imaging was realized by postoperative CT scans.

RESULTS: Following implantation, 9 of 12 animals were weaned from cardiopulmonary bypass. Correct positioning of the device and orthodromic blood flow as maintained by the valve prosthesis were demonstrated by echocardiography and fluoroscopy. Postoperative contrast CT evaluation demonstrated proper fitting of the device into the right-sided heart cavities without obstruction of the outflow tract. Autopsy additionally confirmed its correct positioning without major trauma to surrounding structures.

CONCLUSIONS: We demonstrated the feasibility in principle of a personalized interventional treatment for tricuspid regurgitation using a braided stent, based on individual cardiac imaging, with anchoring forces mainly exerted on the venae cavae and on the inner surface of the right atrium. The design process of this device is a good indicator of the growing potential of an imaging-based personalized simulation and production approach for the treatment of tricuspid valve disease.

Keywords: Heart valve prosthesis • Tricuspid valve

BACKGROUND

Effective interventional and minimally invasive techniques are clinically available for the treatment of aortic, pulmonary and mitral valve disease. Little attention has been given to the possibility of an interventional therapy for tricuspid valve disease.

Atrioventricular valves have a challenging anatomical configuration [1, 2]. For a prosthetic device, both force distribution and fixation are crucial.

In the present study the problem of even distribution of force was met by a new device that was custom designed to fit the right atrial cavity, displacing the anchoring radial forces from the tricuspid annulus to the venae cavae and the whole surface of the right atrium. Due to the variation in dimension, optimized anchoring of a hollow body within the atrium requires a ‘custom-tailored’ approach, based on a tridimensional model of the right-sided heart cavities. Such a model is obtainable by means of rapid prototyping, based on processed computer tomography (CT) scans.

Our aim was to demonstrate the conceptual feasibility of the described design approach in an animal model.

MATERIALS AND METHODS

Animal care

Twelve adult female pigs of approximately 65 kg were included in the study. All experiments were approved by the local authority...
Rapid prototyping

In a preparatory study, we obtained an in silico tridimensional reconstruction of the right-sided cardiac cavities of a female pig of 65 kg, including the superior and inferior venae cavae and the sinus coronarius. By rapid prototyping, we derived a solid alumide® mould (Fig. 1), reproducing the inner volume of the right atrium except for the auricle.

Braided atrial stent and introduction device

Based on the primitive form of the alumide® model, we designed a matching compressible nitinol stent. Based on its material and structure, it was able to grant stability to the carried biological valve prostheses by force transmission from the annulus to the atrial wall and the adjacent venae cavae.

Several prototypes were developed and refined in an iterative design process. The first prototype (P1) reproduced the entire outline of the right atrium, including both venae cavae, and therefore, was named the ‘bicaval hollow body’. The annular portion of P1 was coated with a thin silicon layer to secure a sealing mechanism with the surrounding structures. An additional tubular stent was equipped with a custom-tailored valve, hand crafted from porcine pericardium on a commonly available nitinol stent. The valve leaflets were manufactured by use of porcine pericardium on a custom-tailored scaffold that was previously developed as part of another project. External valve size was ~30 mm.

This component was easily connectable to the annular portion of the main structure (Fig. 2). Both P1 and the valve-carrying component were crimpable to a diameter of 8 mm (24 Fr).

Following primary testings of both device parts in a 2-step procedure, a second prototype P2 was developed. Having noticed that excellent stability was granted also with a modified stent shape, the inferior caval component was eliminated and the device was termed a ‘monocaval hollow body’. The 2 aforementioned device parts were connected prior to implantation (Fig. 3), and the procedure subsequently shortened to a single-step insertion, elaborated in the next paragraph.

Surgical procedure

After routine fasting and premedication, anaesthesia was induced and maintained by continuous venous administration of propofol and fentanyl. Intraoperative and postoperative haemodynamics were assessed with routine monitoring (central venous line) and pulse contour analysis (Picco®, Pulsion, Germany). Additional pressure lines were inserted into the vena cava superior, vena cava inferior and right ventricle. Diuresis was quantified with urethral catheterization. In deep anaesthesia, the right jugular vein and the right femoral vein were surgically exposed. A weight-adapted amount of heparin was administered and a venous cannula was inserted into the femoral vein. Median sternotomy and cannulation of the aorta ascendens were then performed and cardiopulmonary bypass established. The insertion procedure was then stepwise modified in an iterative improvement process.

Insertion procedure P1: bicaval hollow-body (n = 5)

After inserting a guidewire from the right jugular vein into the inferior vena cava, the 24-F delivery catheter was inserted into the cardiac cavity carrying the crimped main stent. In the first 2 cases, a right atriotomy was performed and the superior vena cava was snared around the delivery catheter to establish total cardiopulmonary bypass. Positioning of the stent in this way could be observed by direct vision. In the following 2 cases, insertion and placement were fluoroscopy guided. In the last case using P1, the atrium was opened after insertion of the main device and the valve-carrying component was connected to its annular portion under direct vision. The atriotomy was then sutured and bypass performance was progressively reduced. To grant effective anticoagulation, heparin was only partially antagonized after decannulation. The chest of each animal was finally closed by approximation of the presternal soft tissues with rough sutures. Clinical observation was continued for a mean period of approximately 2 h after stopping cardiopulmonary bypass.

Figure 1: Rapid prototyping-based approach to customized stent production. Following computer tomography (CT)-based primary data generation (A), a 3D hollow body was shaped (B) and main structural parts identified as vascular stent, valve-bearing area and atrial hollow body. The model was then produced from alumide® (C) and a personalized stent was subsequently produced that fitted this alumide® mould (D).
Insertion procedure P2: monocaval hollow-body ($n = 7$)

As mentioned above, the stent P2 was already equipped with its valve-carrying component prior to implantation. The crimped stent was immediately advanced towards the annulus. Again, the first 2 procedures were performed with an open atrium under direct sight. In the remaining cases, the heart cavities were not opened, although sternotomy and exposure of the heart allowed direct observation of the procedure. Further steps were identical to those described above.

Intraoperative and postoperative imaging

**Echocardiography.** Satisfactory imaging through echocardiography was challenging. Sufficient visualization and functional evaluation of the implanted valve prostheses was achieved by pointing the echo probe on the apex of the heart using a transdiaphragmatic approach. Although standardized echocardiography sections were unachievable, visualization of the right ventricular inlet was feasible, and it was possible to visualize the position and function of the valve prostheses after cessation of cardiopulmonary bypass.
Computerized tomography. In 6 of the 12 animals, we were able to perform a postoperative contrasted CT scan of the chest. The images were post-processed to create 3D reconstructions (OsiriX® Imaging Software, Pixmeo, Switzerland).

Autopsy

Postoperative autopsy was performed in all cases. Particular attention was dedicated to the detection of gross lesions caused by the stent to the surrounding structures, as well as to the presence of obstruction of the venae cave or of the right outflow tract caused by radial forces applied by the implanted device.

RESULTS

Weaning from cardiopulmonary bypass was successful in 10 of the 12 animals that underwent implantation of our device. One animal suffered ventricular fibrillation, probably due to hypothermia after open implantation of the bicaval hollow body, whereas another animal had severe right ventricular distention followed by hypotension and finally cardiac arrest after an incorrect interventional placement of the monocaval device. However, in all successful cases, haemodynamic monitoring showed no significant changes in central venous pressure after ending extracorporeal circulation. Arterial pressure showed no critical drops and diuresis was present during the whole observation period. Cardiac rhythm remained preserved except for single beat ventricular and supraventricular extrasystoles during the insertion procedures. Following insertion, no atrio-ventricular (AV) blocks and no malignant ventricular tachycardia occurred.

Echocardiographic imaging showed proper positioning of the device into the tricuspid annulus and a correct opening and closing dynamics of the prosthetic valve when 1 was present. Postoperative contrasted CT scans showed a satisfactory fitting of the stent to the venae cavae and to the right atrial cavity as well as no critical deformation of the right cardiac structures due to the expanded stent. Post-mortem examinations showed no significant gross lesions caused by the stent. The distal portion of the stent displaced the leaflets of the native tricuspid valve without causing obstruction to the right outflow tract of the right ventricle (Fig. 4).

DISCUSSION

Despite the easy transcatheter accessibility of the right atrium via the jugular or femoral veins, only a few percutaneous approaches to tricuspid valve disease have been published. Over the past 10 years, to our knowledge, only 3 experimental designs have described a percutaneous orthotopic tricuspid prosthesis mounted to a self-expanding nitinol frame but so far, no devices have found clinical translation [2–4]. Recently, Lauten et al. proposed a therapeutic approach to tricuspid regurgitation by implantation of caval stents to reduce venous regurgitation and its adverse consequences [5]. Although relief of systemic symptoms related to tricuspid regurgitation is achieved, the procedure offers no solution for adverse effects on cardiac mechanics and right atrial dilatation. In 2011, Roberts et al. described a series of 15 patients in whom tricuspid regurgitation was treated by implanting the percutaneous Melody® pulmonary valve prostheses (Medtronic®) in right atrioventricular position [6]. Other reports of single experiences with the Melody® valve have been published over the past year [7–9]. Although the results described by Roberts and other authors seem to be promising, the tricuspidal insertion of the Melody® pulmonary prostheses requires the presence of a degenerated biological prostheses. The structural weakness of the surrounding structures offers, in its native condition, no ‘solid ground’ for the anchoring of a permanent intracardiac device. By contrast, long-time exertion of focal radial forces, such as required to fixate a valve-carrying stent into the
tricuspid annulus, can lead to damage of structures, such as the AV node, with consequent disorders.

Individualized prototyping offers a sophisticated method to overcome these restrictions. Apart from the perfect fitting of a custom-tailored stent, in silico modelling of force distribution offers a systematic approach to identify potential fracture sites and points of extreme strain for both material and tissue.

The device that we designed and tested presents a new therapeutic approach to tricuspid regurgitation. The lining of the inner surface of the right atrium and one or both venae cavae by our stent structure allows widespread distribution of forces emerging from the prosthetic valve, as we similarly showed for the mitral position [1]. Especially in patients with chronic tricuspid regurgitation, atrial dilatation is often in a progressed state of disease and atrial function consequently low. For the same reason, a standardized sizing approach of an inner lining is not feasible. Only a personalized and custom-tailored stent structure will allow even distribution of forces.

CONCLUSION

We demonstrated the feasibility in principle of a personalized interventional treatment of tricuspid regurgitation using a braided stent, based on individual cardiac imaging, with anchoring forces mainly exerted on the venae cavae and on the inner surface of the right atrium. The design process of the device is a good indicator of the growing potential of imaging-based personalized simulation and production of treatments for tricuspid regurgitation.

Limitations of study

The present study suffers the typical limitations of a feasibility study: in the animals, no disease was present. Anatomical consequences, such as severely dilatated atria, might still prove challenging in terms of even force distribution. In our opinion, in silico modelling of force and pressure distribution is mandatory in diseased patients, but was not carried out in our case. The acute setting that we chose poses additional limitations, because structural damage in particular might only occur in long-term use of our device. Both designed prototypes represent relatively large foreign bodies within the circulation. Although atrial function is often minimal in patients with tricuspid disease, the placement of such large foreign bodies in a moving, contractile surrounding especially challenges the structural integrity of our devices. Continuous anticoagulation by phenprocoumon or similar will be mandatory due to the large foreign contact surface within the circulatory system to reduce the risk of thrombosis. Long-term in vitro studies will have to prove the stability of the design and its positioning.

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REFERENCES