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A new approach to the interventional therapy of tricuspid regurgitation

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1. ABSTRACT

Currently, there are no fully developed interventional approaches for the treatment of tricuspid regurgitation (TR). The aim of this study was to evaluate the feasibility of orthotopic interventional placement of a biological prosthetic valve in the tricuspid position by inserting, with a transvenous approach, a self-expandable valve-bearing stent into the right atrium. Based on findings of computerized tomography (CT), a model of the porcine right heart was obtained. A self-expanding vascular endoprosthesis, carrying a prosthetic heart valve, was reshaped to fit the superior vena cava and the tricuspid annulus. Fenestrations were created to allow blood flow from the inferior vena cava and coronary sinus. This new device ("tricuspid endoprosthesis": TE) was implanted operatively into the superior vena cava, right atrium, and tricuspid annulus in six pigs. CT demonstrated proper fitting of the device, and echocardiography demonstrated correct positioning and function of the TE. Five animals were successfully weaned from cardiopulmonary bypass. Autopsy confirmed correct positioning of the TE without major trauma to surrounding tissues. These findings demonstrate a complete interventional approach for treating TR.

2. INTRODUCTION

Nowadays, effective and relatively safe completely interventional and hybrid techniques are available for the treatment of aortic, pulmonary, and mitral valve diseases. Nevertheless, little attention has been paid to the development of an interventional therapy for tricuspid valve (TV) disease (1, 2). Placement of prosthetic valves in the vena cava inferior (VCI) only relieves the symptoms due to venous stasis, which is only one aspect of the pathophysiology of tricuspid regurgitation (TR), and does not affect the modifications in cardiac architecture caused by this condition. Therefore, we aimed to achieve orthotopic placement of a prosthetic valve in the tricuspid position. On the other hand, the simple placement of a stent-valve in the tricuspid annulus seems unfeasible due to the lack of suitable anchoring structures. We aimed to develop a self-expandable valved stent-graft that would mostly be anchored in the vena cava superior (VCS) and would fit the right atrium down into the TV. The prosthetic valve in this stent-graft was intended to be placed in the tricuspid position (thus orthotopic) in order to correct TR. In principle, this approach should divide the anchoring mechanism of the prosthetic valve into two parts: a longitudinal part, which is carried by the stent-graft and

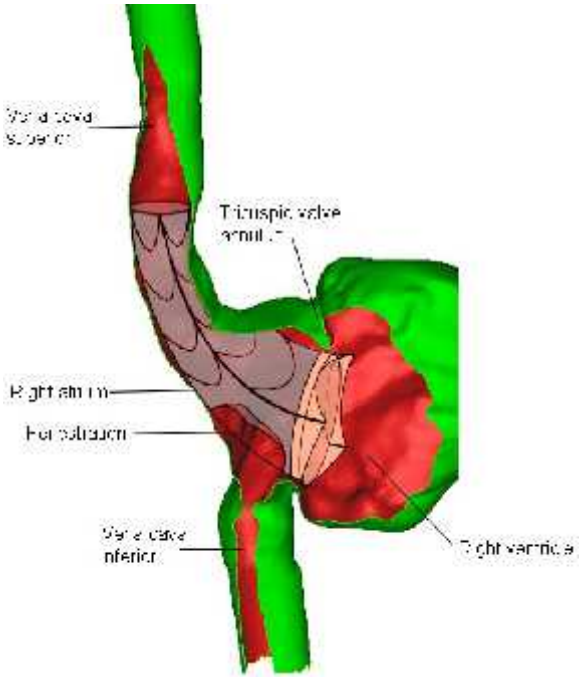

Figure 1. Tridimensional model of the right heart including a graphic representation demonstrating the principle of the tricuspid-endoprosthesis.

Figure 2. Tricuspid–endoprosthesis: Note the curved character and fenestrations.

thereby mainly by the VCS, and a radial part, which can be easily supported by the tricuspid annulus. A fixed angle orthotopic position of the prosthetic valve should thereby be achieved with minimal load on TV structures. This intended new device, which was named a "tricuspid endoprosthesis" (TE), was designed, built, and evaluated in an animal model.

3. MATERIALS AND METHODS

3.1. Right heart model

In order to properly shape the intended TE, a "representative" computerized tomography (CT) scan of a pig (65 kg in weight) was obtained. This scan included the VCS, VCI, and coronary sinus. The diameters as well as the angles of each structure were measured. Finally, a three-dimensional model of the right heart including the VCS, VCI, and coronary sinus was generated using the software Mimics-Materialise® (Figure 1).

3.2. Tricuspid endoprosthesis

We intended that the endoprosthesis should first allow orthotopic placement of a biological heart valve in the tricuspid position. In addition, the endoprosthesis should be compressible in order to be introduced via the internal jugular vein. After releasing the endoprosthesis in the correct position, the biological heart valve in the prosthesis should work, allowing unimpaired blood flow to the TV and anchoring the endoprosthesis. This was all intended to be achieved by the re-expansion of a previously compressed endoprosthesis. To build this device, we chose a polyester-covered nitinol stent-graft (Jotec®, Hechingen, Germany) that was 30 mm in diameter and 15 cm in length. Two 29-mm aortic valves (Medtronic-Freestyle® and Edwards-Prima®) were used and tailored as biological heart valves. Based on the models and previous measurements of the right heart, two additional elastic metal struts (V2a steel) were integrated (sewn) into the stent-graft structure. Thus, it was possible to confer a curved shape to the originally straight stent-graft, allowing the endoprosthesis to fit the course of the VCS, right atrium, and TV. A covered stent was used to better allow self-made design changes by sewing. In order to allow an inflow of blood from the VCI, also based on the right heart models, wide fenestrations (two of 1.0 cm^2 each) were cut into the covering of the distal third of the stent-graft (Figure 2).

3.3. Animal model

Six pigs (65 kg in weight) were used for evaluation of the TE. Permission was obtained from the local authorities (TSG Nr 8.87-51.04.02.09.396). The experimental animals were cared for in accordance with the applicable NIH publication (No. 86-23, revised 1985).

3.4. Surgical procedures

Routine monitoring and catheterization were performed for cardiothoracic surgery. After premedication, general anesthesia was induced. Double peripheral venous cannulation (internal jugular vein and femoral vein) was performed; after sternotomy, the ascending aorta was cannulated. Normothermic full cardiopulmonary bypass (CPB) was established (no heat exchanger) with full anticoagulation. All the following procedures were performed with the heart beating. The right atrium was longitudinally incised, and the crimped endoprosthesis was inserted under direct vision. First, the distal endoprosthesis with the valve was placed in the tricuspid position and released. Then, the proximal part of the prosthesis was released in the right atrium and VCS. After de-airing, the right atrium was closed, and animals were weaned from CPB. Coagulation was reconstituted with protamine, and the sternum was closed. Clinical observation as well as hemodynamic monitoring was carried out for a further two hours. Thirty minutes after stopping CPB, a dose of 0.5 mg epinephrine was administered in order to maximize the load on the valve. After completion of the investigations, all animals were euthanized and autopsies were performed.

3.5. Hemodynamic monitoring

Intraoperative and postoperative hemodynamics were assessed with routine monitoring (central venous line) and pulse contour analysis (Picco®, Pulsion, Germany). Additional pressure lines were inserted into the VCS, VCI, and right ventricle. Diuresis was quantified with urethral catheterization

Figure 3. Echocardiographic assessment of the implanted tricuspid-endoprosthesis from an apical view: note the closed and open prosthetic valve in tricuspid position.

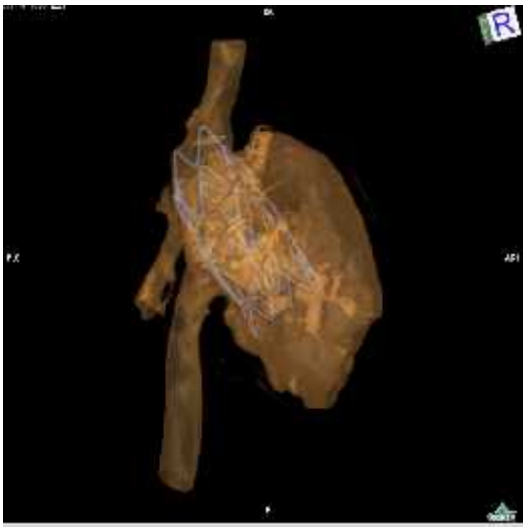

Figure 4. Tridimensional reconstruction of the right heart cavities with the endoprosthesis "in situ" demonstrating the relationship between the device and unaffected surrounding structures.

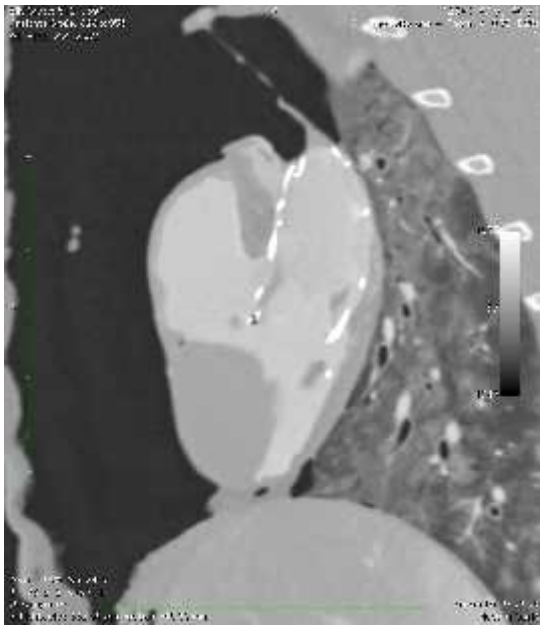

Figure 5. Hemodynamic effectiveness of the Tricuspid-endoprosthesis: note the slight difference in contrast density between the atrium and the ventricle.

3.6. Imaging

Echocardiography (GE-I-Vivid®) was used for visualization. A satisfactory visualization of the tricuspid region could be achieved by a transdiaphragmatic apical approach. Other unconventional epicardial views were also obtained. In the last two of the six animals, contrasted CT (Siemens®) of the chest was performed in order to obtain a three-dimensional display of the whole heart with the TE in place. Additional computer processing of the data was performed (OsiriX®).

4. RESULTS

4.1. Surgery

Weaning from CPB was successful in five of the six animals that underwent implantation of our device. One animal suffered ventricular fibrillation, probably due to hypothermia because a heat exchanger was not available. The duration of the open implantation procedure consisted of about one minute to release the TE and ten minutes to open and close the right atrium. Besides single supraventricular extrasystoles, no other arrhythmia occurred.

4.2. Hemodynamic monitoring

After weaning from extracorporeal circulation and removal of the cannulas, there were no significant changes in central venous pressure except for those referable to loss of blood volume and successive volume substitution. Arterial pressure showed no critical drops, and cardiac output remained roughly the same. There was no pressure gradient across the VCS, the prosthesis, and the biological valve in evidence. Also, no pressure gradient was detectable from the VCS to the VCI. Diuresis was present during the whole observation period.

4.3. Echocardiography

Ultrasound imaging showed proper positioning of the device into the tricuspid annulus and a correct opening and closing dynamic of the prosthetic valve (Figure 3). No relevant depression of right ventricular function could be seen. No relevant displacement of the whole TE could be seen over the observation period of two hours, especially during the "epinephrine load test."

4.4. Computed tomography

The two-dimensional and three-dimensional images obtained by performing contrasted CT scanning in two animals showed a satisfactory fitting of the stent to the VCS and right atrial cavity, as well as the absence of critical deformation of the right cardiac structures due to the expanded stent (Figure 4). The difference in contrast density between the right atrium and the right ventricle demonstrated an effective hemodynamic atrioventricular separation by the valve prostheses (Figure 5).

4.5. Post-mortem examination

Autopsy showed no significant gross lesions caused by contact of the stent with the surrounding cardiac structures; the leaflets of the native TV appeared to be gently displaced by the distal portion of the stent without causing obstruction to the right outflow tract of the right

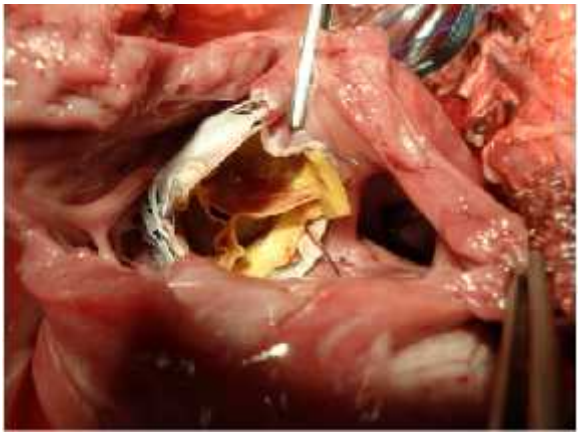

Figure 6. Autopsy: Apical view showing the endoprosthesis "in situ": the valve is positioned in orthotopic tricuspid position without obstruction of the RVOT.

Figure 7. Autopsy: View to the lateral right atrium. Correct position of the fenestrations with no obstruction of the blood flow from VCI (blue probe inserted through the VCI).

ventricle (Figure 6). Also, the fenestrations in the TE were found to be properly placed in order to allow blood inflow from the VCI and the coronary sinus into the TE (Figure 7).

5. DISCUSSION

Isolated primary TR is a rare condition. In contrast, secondary or functional TR, which occurs mainly as a consequence of left-sided heart disease, is a common condition. Tricuspid annular dilatation is a result of right ventricular volume and pressure overload (2). Secondary TR, if untreated, greatly affects the outcome of patients undergoing mitral or aortic valve surgery, despite adequate correction of the associated left-sided disease (3, 4). Some series show progression of TR in operated patients and even "ex novo" arising TR, months or years after the previous mitral procedure (5). Since reoperations for worsening or newly appeared TR show high mortality rates, only a few patients are referred to surgery for repeat tricuspid repair or replacement (2). A good interventional approach to correct TR would probably improve results in these patients. However, despite the easy accessibility of the right atrium for trans-catheter procedures through the jugular vein, only a few reports describing percutaneous approaches to TV disease have been published. In 2005, Boudjemline first described a percutaneous TV mounted on a self-expanding nitinol frame, but this was not explored further (6). Recently, Lauten proposed a therapeutic approach for TR consisting of the implantation of valved bi-caval stents in order to reduce venous regurgitation and its adverse consequences (7). Although relief of some TR related symptoms may be achieved, this procedure seems to be a more palliative approach because TR and its consequences are not basically addressed. In 2011, Roberts reported the cases of 15 patients worldwide in whom TR after pervious TV surgery was interventionally treated (8). With overall good results, he could clearly demonstrate the feasibility of orthotopic interventional valve placement. In previous reports, almost all of the valve placements (Melody® by Medtronic) were performed by way of the jugular vein. Unfortunately, for this kind of interventional therapy, some previously surgically implanted device like a degenerated biological valve prosthesis is necessary, which is very rare. Other procedures, such as percutaneous "edge to edge" techniques, are not suited for the treatment of TR due to the special anatomic features of the valve itself (2). Our approach takes into account two major issues. First, orthotopic valve placement can be performed into a native TV and is therefore not dependent on previous tricuspid surgery. Next, despite the difficulties associated with placing a valved stent in a delicate nontubular structure (the TV), orthotopic placement of the valve inside the TV is made possible. This is achieved by displacement of the anchoring mechanism of the valve, which was previously reported by our group (9). Consideration of these issues leads to a more physiological solution, in contrast to previously published approaches, especially because the right atrium is protected and orthotopic placement of a valve best prevents volume overload in the right ventricle. A relatively large prosthesis inside the right atrium might raise the risk for thrombotic events; however, the majority of patients with TR are already on anticoagulation therapy. In our experiments, we chose to study the pig because its anatomy is very similar to that of humans. Open access to the right atrium was chosen because initially it seemed important to observe the behavior of such a new device inside the heart. A more elaborate prosthesis can be inserted easily via the internal jugular vein under fluoroscopy. Taken together, our results demonstrate the feasibility of our approach. Individual design and tailoring of such prostheses from imaging results is an emerging concept. Because the experiments were performed with a custom-made device and the observation period only covered the acute period of the first 2 hours after surgery, a more professional prosthesis will be investigated in a larger experimental project in the future.

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Abbreviations: CPB: cardiopulmonary bypass; CT: Computerized tomography; RVOT: right ventricular outflow tract; TR:tricuspid-regurgitation; TE: Tricuspid-endoprosthesis; TV: tricuspid valve; VCS: Vena cava superior; VCI: Vena cava inferior

Key Words: Tricuspid valve, interventional therapy, endovascular procedure, right atrium, atrial stent, load displacement, vena cava; coronary sinus

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