New insights in minimally invasive valve replacement: description of a cooperative approach for the off-pump replacement of mitral valves

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Aims The aim of the present study was to evaluate whether off-pump mini-invasive mitral valve replacement is possible after prior bioprosthetic mitral valve replacement in animals.

Methods and results To validate this concept for off-pump redo mitral valve insertion, we first replaced surgically mitral valves of six sheep under extracorporeal circulation using a Mosaiq™ valve. Prior to its insertion, we added a radio-opaque ring on its base to enhance its visualization under fluoroscopy. A bovine jugular valve mounted into a stent was then inserted off-pump through an opening of the atrial wall. Mitral valves were replaced successfully in all animals. Following the surgical valve insertion, mean left atrium and left ventricular end-diastolic pressures were 38 (22–42) and 18.8 mmHg (13–22), respectively. Angiography showed perfectly functioning valves, no subaortic valve obstruction, and a mild paravalvular leak in one animal. In one animal, we were unable to control the bleeding from the atrial opening. In this case, trans-atrial valvulation was not attempted. The off-pump valvular implantation was successful in the other five sheep. Haemodynamic data did not change after the insertion of valved stents. Implanted valves were all competent. The animal with the better haemodynamics was kept alive and is still alive 3 months after implantation.

Conclusion Surgically implanted bioprosthetic valves provide excellent support for off-pump insertion of a valved stent. Further experiments are necessary, in particular with appropriate valve size, before considering this approach for percutaneous mitral valvular replacement in patients with a dysfunctional bioprosthesis.

Keywords Mitral valve implantation; Valved stents; Prosthesis; Valves; Hybrid approach

Introduction

Experience of percutaneous valve insertion is presently limited to the semilunar valves namely aortic and pulmonary valves.1–6 Extensive experimental work is undertaken to extend present indications to other cardiac valves. To date, no transcatheter technique has been described to replace atrio-ventricular valves. In surgical practice, mechanical valves are usually favoured but semi-lunar heterograft or homograft valves have been used to surgically replace the atrio-ventricular valves.7,8 The close relationships between the mitral annulus as anchoring place of the valve, the coronary artery circulation, and the aortic valve complicate any transcatheter approach to this valve.

Furthermore, the subvalvular apparatus should be controlled in such a way that this does not interfere with prosthetic valve function. Thus, direct replacement of native mitral valves is currently impossible through a transcatheter technique.

As a first approach for replacing the mitral valve mini-invasively, we imagined a procedure applicable in patients who had been previously treated by stented bioprosthetic mitral valve replacement and requiring re-operation for bioprosthetic failure. When the surgeon replaces the diseased valve initially with a stented bioprosthesis, a transcatheter replacement of the valve would become possible once it has degenerated. This might also broaden the indication for bioprosthetic valve insertion during the initial surgical procedure. The aim of the present study was to validate this concept of off-pump mitral valve insertion after earlier surgical preparation with implantation of a stented bioprosthesis.

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Methods

Development of devices for off-pump insertion of a semi-lunar valve in mitral position

For this application, we used a currently available biological valve (Mosaic, Medtronic Inc.). We sewed an additional radio-opaque ring on a basic Mosaic aortic valve to enhance its visualization under fluoroscopy (Figure 1). For transcatheter insertion, we modified the currently existing device available for human percutaneous valve replacement (NuMed Inc., Hopkinton, NY, USA). This device is very long when compared with the Mosaic valve, which has a height varying from 15 to 22 mm depending on its diameter (18–28 mm) and type (i.e. mitral/aortic). Because only 21 mm Mosaic aortic valves (model 30502101) were available for this study, the CP stent was shortened to 16 mm of length by reducing the number of rows. To avoid the creation of a tunnel after implantation, the venous wall of an 18 mm valve was dissected along the commissures as previously described. After preparation, all valved stents were preserved in a glutaraldehyde solution. The delivery system consisted of a ‘custom-made’ front-loading long sheath identical to the one used for human implantation of pulmonary values. Since the stent was made of an alloy of platinum and iridium, balloons were necessary to deploy the device. Here, 22 mm BIB balloon catheters were employed.

Study design

Six sheep weighing 35–70 kg were included in the study. We intended to replace the mitral valve surgically with a 21 mm Mosaic aortic valve sheltering an 18 mm porcine valve as a first step immediately followed by an off-pump trans-atrial implantation of a valved stent.

Surgical mitral valve replacement

The procedure was carried out under general anaesthesia. A left thoracotomy was performed. The extracorporeal circulation was then begun between the femoral artery and the right atrium, with a cannula introduced from the right jugular vein. The native mitral valve was excised through an opening of the left atrium and replaced by a 21 mm Mosaic valve with a beating heart and without any myocardial protection. After complete sewing of the heterograft, the left atrial opening was closed and the cardiopulmonary bypass stopped.

Off-pump insertion of a valved stent

After a puncture on the left atrial wall distant to the previous opening and controlled by a purse string with a 4.0 polypropylene suture material, a wire was first advanced through the previously placed heterograft and left in apex of the left ventricle. The valved stent loaded in the delivery system was then advanced over the wire under fluoroscopic guidance. The valved stent was uncovered and positioned using the radio-opaque markers present on both devices (receiver’s and donor’s valves). When in position, balloons were subsequently inflated and deflated to deploy the valved stent. After insertion, the delivery system was carefully retrieved and the purse string closed.

Figure 1 (A) A normal Mosaic valve is shown. (B) The modified Mosaic valve is shown. A radio-opaque ring was sewed on its base to increase its visualization under fluoroscopy. (C and D) In vitro views showing the valved stent placed inside the surgical implant. The valve is shown in opened (C) and closed (D) positions.
Valvular function assessment

Haemodynamic data (i.e. right and left auricular and ventricular, pulmonary artery, and aortic pressures) and angiograms (i.e. left ventriculogram and aortogram) were acquired before, after the surgery, and after the trans-atrial valve insertion. Because the implanted Mosaic valve had a diameter smaller than the native annulus, we were aware of creating an important gradient through the valve with high left atrial pressures that could potentially compromise the post-operative course. Because we did not have bigger valves available at this moment, we decided to conduct this study on an acute basis to demonstrate that the approach was feasible and relevant. Therefore, the procedure was considered successful if the following criteria were present: (i) successful delivery, (ii) appropriate position and alignment, (iii) absence of valvular regurgitation, and (iv) absence of paravalvular leakage. High mean left atrial pressure and trans-prosthetic gradient were not considered to be of value because we expected them to be high after surgically implanted valve. However, any significant additional obstruction created by the valve-implanted off-pump was considered to appreciate the rate of success. In the surviving animal, echocardiography and angiography were repeated each month until sacrifice or death.

Graft retrieval

Animals were sacrificed 1 h after off-pump valved stent implantation. Before harvesting, heparin (300 UI/kg) was given intravenously. The heart was opened from the previous atrial opening. Subaortic area was examined to determine the relationship with the aortic valve. We also inspected the position of the implanted device in relation to the surgically implanted Mosaic valve. The device was rinsed to remove excess intraluminal blood and studied. The competence of the valve was grossly tested by passing a fluid in the graft.

Results

Mitral valves were successfully replaced in all animals after a mean extracorporeal time of 65 (±10 min). Following the surgical insertion of Mosaic valves, the mean left atrium pressure was as high as 38 mmHg (range 22 to 42 mmHg) with a mean left ventricular end-diastolic pressure of 18.8 mmHg (range 13 to 22 mmHg). Angiographic control showed perfectly functioning Mosaic valves, no subaortic valve obstructions, and a mild paravalvular leak in one animal (Figure 2). In the animal with the higher atrial pressure, we were unable to control the bleeding from the atrial opening, and trans-atrial valved stent implantation was not attempted. Off-pump implantation of the valved stents was therefore attempted and successful in five out of six sheep. Implantations were performed easily in <15 min in all animals using fluoroscopic guidance only. The injection of radio-opaque dye and echocardiography were not necessary to position and deliver the valved stent correctly. Haemodynamic data did not change after the insertion of the valved stent. There was no significant gradient between the apex of the left ventricle, the subaortic region, and the aorta. Implanted valves were all competent. Aortic angiogram confirmed the absence of interference with the aortic valve (Figure 3). No migration occurred during the short follow-up. The animal with the smallest gradient and left atrial pressure (i.e. 22 mmHg) was kept alive and is still alive after 3 months of implantation with a normally functioning heterograft, no systolic gradient between the left ventricle and the aorta, and a minor to mild paravalvular regurgitation. Sequential assessments showed stable measurements with a mean left atrial pressure ~22 mmHg, a maximum gradient of <10 mmHg, a post-capillary pulmonary hypertension with a systolic pulmonary artery pressure at less than half systemic (Figure 4). After initial difficulties in growing, this animal is now gaining some weight. At autopsy (four out of five animals), all valved stents were sitting in the area of the Mosaic valves at a 'reasonable' distance from the aortic valve. As expected, the valved stents were inactivating the leaflets of the Mosaic valves. After removal, all valved stents were competent when fluid was passed through them.

Figure 2. Angiograms after surgical replacement. (A) Aortography showing no functional impairment of aortic valve. (B) Left ventricular angiogram showing good function of the surgically implanted valve.
Discussion

Minimally invasive approaches have recently been developed to avoid median sternotomy, and subsequently reduce post-operative morbidity and improve the outcome of patients undergoing mitral valve surgery. Even if they avoided conventional surgical access, none of these techniques avoids the need for cardiopulmonary bypass, which is responsible for most invasiveness of this procedure. To our knowledge, no off-pump mitral valve insertion has been described so far. We imagined a staged procedure with the aim of preparing the patient for further interventional or minimally invasive procedures. Using the frame of a surgically implanted biological valve, we were able to insert off-pump a stented valve in the mitral position in five lambs in which the procedure was attempted. For this application, both currently available surgical and transcatheter valves were modified. Stent design features of the surgical Mosaic valve include markers theoretically allowing for radiographic visualization. However, since radio-opacity was not sufficient to precisely locate the valve under fluoroscopy, we sewed additional radio-opaque markers on its base. The length of the currently available transcatheter valved stent was shortened to fit into a 21 mm Mosaic valve, and the venous wall was dissected along the commissures. Because the height of surgically implanted valves varies depending on their diameters, various lengths of valved stent could similarly be developed in the future in order to fit with the existing surgical valves.

Study limitations and unanswered questions

The major limitation to the study is the use of small Mosaic valve for the surgical replacement. Of course and as predicted, this limitation did not allow keeping the animals alive. Therefore, in five out of six animals, the study was performed acutely. The only failure of this technique was due to an uncontrolled bleeding completely related to high atrial pressure due to the size of the surgically inserted valve. The use of appropriate valve size is likely to annihilate this kind of complications.

Another concern is the use of a venous valve in a systemic circulation. In vitro testing has shown that the competency of bovine jugular valves is maintained with back pressures of ≥100 mmHg (unpublished data). Long-term studies are, however, missing at present. However, any valve substitutes (i.e. porcine, pericardial, etc.) can be used for that purpose. The only necessity is to have a valved stent not longer than the valve implanted surgically to avoid sub-aortic stenosis.
To conclude, this new approach might lead to consider biological valves as the first-line substitutes in patients where mechanical valves are usually favoured. Before human application, more animal studies with appropriate valve sizes and long-term follow-up need to be carried out. The profile of the present valved stent theoretically authorizes its insertion through a transcatheter technique. However, this still remains to be demonstrated. Finally, this concept can be applied to other cardiac valves such as aortic valves. In that location, a stented biological valve inserted surgically would give an excellent support for a valve to be inserted percutaneously. The presence of radio-opaque markers on the surgical valve would, moreover, provide at least indirectly the exact location of surrounding vulnerable structures, namely, coronary orifices and mitral valves. This is, in our opinion, the safest strategy to replace cardiac valves through transcatheter technique.

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References