Valve-in-a-Valve Concept for Transcatheter Minimally Invasive Repeat Xenograft Implantation

Objectives
This study sought to evaluate the feasibility of minimally invasive transapical repeat valve-in-a-valve (VinV) implantation.

Background
Reoperative heart valve replacement for degenerated xenografts is associated with an increased surgical risk.

Methods
Conventional Carpentier Edwards porcine aortic (n = 5) and mitral (n = 2) valve prostheses were implanted in 7 pigs. Transapical VinV implantation of a pericardial xenograft fixed within a 23-mm stainless steel, balloon expandable stent (Cribier Edwards, Edwards Lifesciences, Irvine, California) was then performed under fluoroscopic and echocardiographic visualization on the beating heart with ventricular unloading via cardiopulmonary bypass and rapid ventricular pacing.

Results
Valve deployment was successfully performed in all cases. The radiopaque marking within the stent of the conventional aortic or mitral xenograft allowed for optimal positioning of the stent-delivered valve. All valves were firmly positioned without any migration. There were neither paravalvular nor transvalvular leaks, and good hemodynamic function was observed in all cases. All coronary arteries remained patent. Positioning and function were confirmed by autopsy in all animals.

Conclusions
The VinV concept is promising for minimally invasive beating heart repeat aortic or mitral valve replacement, using a stent-fixed sutureless prosthesis. (J Am Coll Cardiol 2007;50:56–60) © 2007 by the American College of Cardiology Foundation

Heart valve replacement is routinely performed using xenografts in elderly patients, leading to good hemodynamic and functional outcome. Individual patients may suffer xenograft degeneration with subsequent repeat stenosis or incompetence requiring reoperation. The risk of reoperative surgery may be significantly increased, up to 6% to 15%, mostly because of advanced age, additional risk factors, and an increased technical difficulty caused by adhesions (1–3).

The goal of this study was to evaluate the feasibility of transcatheter implantation of a sutureless stent-fixed xenograft into a conventional bioprosthesis (valve-in-a-valve [VinV]) on the beating heart using a minimally invasive transapical approach in an acute experimental model.

Methods
The VinV technique was evaluated in 7 pigs in an experimental hybrid operative theater (including a monoplane fluoroscopic angiography system) under routine hemodynamic monitoring and support as used in clinical cardiac surgical practice. Approval was obtained from the governmental offices before beginning this study, and all animals received humane care in compliance with standard guidelines (4). Standard general anesthesia and endotracheal intubation were applied for all surgical interventions.

At the beginning of the study, conventional aortic (AVR, n = 5) or mitral valve replacement (MVR, n = 2) using a Carpentier Edwards porcine xenograft (Edwards Lifesciences Inc., Irvine, California) was performed. Median sternotomy (AVR) or left lateral thoracotomy (MVR) was used. The ascending aorta and the right atrial appendage (AVR) or the descending aorta and the right atrial appendage (MVR) were cannulated for cardiopulmonary bypass (CPB). Valve implantation was performed during cardioplegic cardiac arrest (AVR) or under ventricular fibrillation and topical cooling (MVR). Horizontal Teflon-
reinforced mattress sutures (Tevdek, Ethicon, Hamburg, Germany) were used to anchor the valve to the corresponding annulus. After reperfusion of the heart, the cannulas for CPB were left in place and the incision was temporarily closed. Access to the left ventricular apex was then gained through an inferior partial sternotomy (as opposed to a lateral minithoracotomy in humans) because of the anterior position of the heart and the specific chest wall anatomy in pigs. The apical access site was secured using 2 Teflon-reinforced purse-string sutures (Prolene 3-0). In addition, an epicardial pacing wire was positioned.

A 23-mm Edwards Sapien transcatheter heart valve equine pericardial xenograft (model 9000, Edwards Lifesciences) mounted on a stainless steel stent (Fig. 1) was used together with a 24-F delivery sheath, as previously described (5). Transapical VinV placement was performed on the beating heart using several steps: 1) apical puncture and antegrade (aortic position) or retrograde (mitral position) insertion of a flexible guidewire and sheath through the conventional xenograft; 2) insertion of a superstiff guidewire (Amplatz superstiff, 035 inch, 260 cm; Boston Scientific, Natick, Massachusetts) through the conventional xenograft, anchored in the descending aorta (aortic position) or in the pulmonary veins (mitral position); 3) insertion of a 14-F transapical sheath, followed by balloon valvuloplasty of the conventional xenograft during rapid ventricular pacing (170 beats/min) using a 20-mm balloon; 4) exchange of the 24-F transapical application system and insertion of the crimped prosthesis and positioning within the conventional xenograft under fluoroscopic and echocardiographic imaging; 5) transapical valve deployment under repeat rapid ventricular pacing; and 6) functional assessment using routine hemodynamic monitoring, transesophageal echocardiography, and angiography. All animals were killed after final measurements, the hearts were excised, and pathological examinations were performed to confirm VinV position and fixation.

Results are given in a standard fashion expressed as mean ± SD throughout this article.

Results

Induction and conduct of anesthesia was uneventful in all animals, and all procedures were completed as planned. Seven pigs (5 female) with a body weight of 73 ± 5.6 kg were used. Five animals underwent conventional AVR with a 23-mm prosthesis, and 2 animals received MVR with a 25-mm prosthesis. After conventional valve replacement surgery, 5 animals were easily weaned off CPB and 2 remained on CPB because of hemodynamic instability. Hemodynamic results, including mean arterial pressure and central venous pressure, were stable throughout the procedures as indicated in Table 1.

The VinV implantation was performed using a 23-mm steel stent-fixed xenograft (Edwards Sapien transcatheter heart valve) in all cases. This valve size selection was based on previous measurements at Edwards laboratories indicating good function of the 23-mm xenograft within a 23- or 25-mm conventional Carpentier Edwards porcine prosthesis. At implantation the top of the conventional stent wireform was aligned with the top of the steel stent valve frame. Transapical valve implantation took 13 ± 2 min.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Hemodynamic Function During the Procedures</th>
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<tr>
<td></td>
<td>MAP (mm Hg)</td>
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<tr>
<td>CPB start</td>
<td>49 ± 7</td>
</tr>
<tr>
<td>Aortic crossclamp/cardiac fibrillation</td>
<td>46 ± 7</td>
</tr>
<tr>
<td>Release crossclamp/defibrillation</td>
<td>47 ± 5</td>
</tr>
<tr>
<td>End of reperfusion</td>
<td>51 ± 8</td>
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<tr>
<td>After transapical valve implantation</td>
<td>49 ± 6</td>
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CPB = cardiopulmonary bypass; CVP = central venous pressure; MAP = mean arterial blood pressure.
without any complications. Closure of the apex after removal of the introduction sheath was performed without any problems using purse-string sutures.

Hemodynamic function was stable after VinV implantation (Table 1). Functional evaluation using transesophageal and epicardial echocardiography together with angiography showed good valve function with neither transvalvular nor paravalvular leaks in all cases. Transvalvular pressure gradients were low with a maximum gradient of 14 ± 2 mm Hg and a mean gradient of 4 ± 1 mm Hg, respectively.

Typical fluoroscopic and angiographic findings during aortic VinV implantation are shown in Figure 2 and during mitral VinV implantation in Figure 3. At postmortem examination, macroscopic examination revealed that all Edwards Sapien xenografts were fully deployed and expanded within the conventional prostheses. There was no obstruction of coronary flow in any of the cases. The sutureless valves showed precise positioning in all cases with good alignment of the conventional stent wireform and the upper edge of the steel stent. Fixation was stable with higher forces and during oblique tension required to pull the steel stent out of the conventional xenograft. Typical illustrations of how the steel stent is located in the conventional prosthesis are shown in Figure 4, together with radiographic images confirming proper alignment.

**Discussion**

Transcatheter heart valve implantation techniques recently have been developed. The basic principle is based on fixation of a pericardial xenograft in a low-profile nitinol or steel stent that can be crimped onto a catheter. Because of the low profile of the stent, excellent hemodynamic function of these devices may be achieved. Access to the heart is gained by using a transfemoral or a transapical approach. Experimental studies on different approaches have been performed (5,6), and clinical feasibility studies in selected high-risk patients have been conducted (7–9). Recently the concept of transcatheter transapical aortic valve implantation has been proven clinically (10).

All of these nonconventional approaches aim at treating high-risk patients with degenerative valve disease. To min-
**Figure 3** VinV Implantation in the Mitral Position Within a Conventional 25-mm Carpentier Edwards Porcine Prosthesis

(A) Valve positioning within the conventional mitral valve prosthesis. The superstiff guidewire is passed from the apex retrogradely through the mitral prosthesis, curves in the left atrium, and is anchored in a pulmonary vein. (B) Mitral valve-in-a-valve (VinV) in position.

**Figure 4** Macroscopic and Radiological View of a 23-mm Edwards Sapien Xenograft Within a 23-mm Conventional Carpentier Edwards Porcine Prosthesis After Explantation

(A) Macroscopic inflow view. (B) Macroscopic lateral view. (C) Radiological inflow view. (D) Radiological lateral view.
imize the reoperative risk for failed xenografts, the VinV concept was developed. This VinV concept takes advantage of recently developed transcatheter valve implantation techniques as well as clinical experience with the transapical approach. For the mitral position, feasibility has been proven using transcatheter insertion of a bovine jugular vein xenograft within a conventional xenograft (11). To the best of our knowledge, the present study is the first systematic experimental evaluation of the potentially advantageous VinV technique using a pericardial xenograft in the aortic and mitral position.

There were several important findings from the present study: VinV implantation is technically feasible with good alignment using a transapical approach. Valve fixation within a conventional xenograft is stable after adequate balloon dilatation, with no evidence of device migration. Suitable sizes for VinV implantation can be delineated from in vivo and in vitro testing. Hemodynamic function after VinV implantation is good, probably because of the low profile with good opening area of the stent-based xenograft. The transapical approach is safe and allows for direct and antegrade VinV implantation with excellent ability for exact positioning and implantation.

A particularly important finding of our study was that no paravalvular leaks were observed. This result is probably because of the excellent alignment and fixation and strong purchase of the steel stent-based xenograft within the stents of the conventional prosthesis, a finding that was confirmed at postmortem examination. It also is important to note that we did not observe any obstruction of coronary blood flow in the current study. We believe the risk of coronary obstruction also will be minimal in human studies because the new xenograft remains completely inside the stent of the conventional prosthesis.

The new VinV procedure may lead to a significantly decreased risk for reoperative valve replacement surgery. Based on the current findings and the early clinical experience with transapical valve implantation (10), the current approach may evolve into a truly minimally invasive procedure with off-pump beating-heart valve implantation.

In summary, the VinV concept was developed to potentially decrease the reoperative risk for high-risk patients with failed xenografts. Experimental results indicate the safety and feasibility of this approach. Similar to the experience with minimally invasive transapical aortic valve implantation, we believe that the VinV concept will be the first truly minimally invasive repeat procedure performed off-pump on the beating heart through a small anterolateral thoracotomy.

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REFERENCES