

## Minimally invasive transapical beating heart aortic valve implantation – proof of concept

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Received 13 October 2006; received in revised form 29 October 2006; accepted 30 October 2006; Available online 9 November 2006

### Abstract

**Objective:** To evaluate the feasibility of minimally invasive transapical beating heart aortic valve implantation (TAP-AVI) for high-risk patients with aortic stenosis. **Methods:** TAP-AVI was performed via a small anterolateral minithoracotomy with or without femoral extracorporeal circulation (ECC) on the beating heart. A pericardial xenograft fixed within a stainless steel, balloon expandable stent (Cribier-Edwards, Edwards Lifesciences, Irvine, CA, USA) was used. Thirty consecutive patients ( $82 \pm 5.1$  years, 21 (70%) female) were operated from 02/06 until 09/06 at one center using fluoroscopic and echocardiographic visualization. Average EuroSCORE predicted risk for mortality was  $27 \pm 12\%$ . **Results:** Valve positioning was successful in 29 patients and one required early conversion to full sternotomy. Implantation ( $8 \text{ mm} \times 23 \text{ mm}$  and  $22 \text{ mm} \times 26 \text{ mm}$  valves) was performed on the beating heart during brief periods of rapid ventricular pacing. ECC was applied in 13 patients. Neither coronary artery obstruction nor migration of the prosthesis was observed and all valves displayed good hemodynamic function. Echocardiography revealed minor paravalvular leakage in 14 patients (trace in three, mild in nine and moderate in two). Three patients (10%) died, one on postoperative day (POD) three secondary to preoperative global myocardial failure and two on POD 18 and 86 due to abdominal complications. **Conclusions:** Minimally invasive beating heart TAP-AVI is feasible. Initial results are encouraging in view of the high-risk profile of the patients. Long-term studies as well as randomized protocols are required.

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**Keywords:** Aortic valve replacement; Transapical aortic valve implantation; Minimally invasive cardiac surgery; Beating heart cardiac surgery; Transcatheter valve implantation

### 1. Introduction

Aortic valve replacement is a standard procedure performed for more than five decades with excellent short and long-term outcomes. More than 50,000 patients are being operated in the USA and more than 11,000 patients in Germany annually [1,2]. Surgical valve replacement is the only definitive therapeutic strategy, indicated in presence of severe symptomatic disease with a valve orifice area of  $\leq 1 \text{ cm}^2$  [3]. Current conventional surgical techniques consist of partial or complete sternotomy with extracorporeal circulation (ECC) and cardioplegic cardiac arrest.

In parallel with an overall increasing life expectancy more and more elderly patients are being diagnosed with AS. Besides older age additional perioperative risk factors may be

present such as low ejection fraction, pulmonary hypertension, respiratory dysfunction, renal failure or peripheral arterial occlusive disease. Such co-morbidities are associated with an increased perioperative risk, particularly for mortality. Truly minimally invasive strategies may be an important treatment option for such high-risk patients. Important areas of development include minimizing the overall surgical trauma by potentially avoiding a sternotomy, avoiding the use of ECC and implanting the prostheses on the beating heart thereby avoiding cardiac arrest.

The aim of our study was to evaluate the feasibility of minimally invasive transapical aortic valve implantation (TAP-AVI) on the beating heart in high-risk patients.

### 2. Methods

Before performing a clinical study, extensive experimental evaluation of the transapical approach as well as transcatheter valve implantation techniques was performed

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[4,5]. The clinical study protocol was approved by the local ethical committee and the study was registered at the federal governmental offices.

### 2.1. Patient selection

Patient selection was performed on the basis of an increased perioperative risk profile according to the EuroSCORE scale [6]. Patients with  $\geq 9$  points indicating a risk for mortality of  $>11\%$  according to the logistic EuroSCORE were considered suitable for inclusion into the study. Detailed echocardiographic analysis was then performed in order to delineate the diameter of the aortic annulus as well as the distribution of cusp calcification, presence of fused commissures, tricuspid or bicuspid pathology as well as presence of severe eccentric calcification. Patients with an aortic annulus  $\leq 24$  mm and equally distributed calcification were considered suitable for inclusion in the study. The therapeutic option of TAP-AVI was discussed extensively with the patients and family members. This discussion focused on the overall risk profile of the individual patient, on the preoperative activities of daily living and the motivation of the individual patient, and on the ongoing results of the new technique. All patients considered suitable for inclusion into the study gave informed consent; no one opted for a conventional surgical approach.

### 2.2. Cribier-Edwards prosthesis

The Cribier-Edwards prosthesis is a pericardial xenograft mounted on a stainless steel stent and is available in two sizes—23 mm and 26 mm (Edwards Lifesciences, Irvine, CA, USA). Comparable to other pericardial xenografts, the valve has three cusps and three commissures. The stainless steel stent has a very low profile when fully expanded. The lower inflow portion of the valve is covered with polyethylene terephthalate (PET) cloth. The prosthesis is the same device as used in recent clinical percutaneous approaches [7–9] (see Fig. 1). The sutureless stent-fixed aortic valve was prepared for transapical antegrade delivery under sterile conditions in the operating room by a technician just prior to implantation. The delivery catheter was flushed with a heparinized saline solution. The deployment balloon was primed with a mixture of saline and contrast that was free of air. The valve was crimped onto the deployment balloon so that it was equidistant between two radiopaque markers and was able to be passed through the 33F transapical delivery sheath. All valve deployments were performed using standard volumetric inflation of the balloon.

### 2.3. Technical equipment: operating theatre

All operations were performed in a hybrid operation theatre. This is a standard operating room with an additional angiography system equivalent to any standard catheterization laboratory. A monoplane fluoroscopic angiography system (Axiom Sensis, Siemens, Munich, Germany) was used. Fluoroscopy is important for providing a perpendicular view of the aortic root. This allows for optimal delineation of the level of the aortic annulus in relation to the aortic sinuses, along with imaging of the coronary ostia. Optimal visualization of the

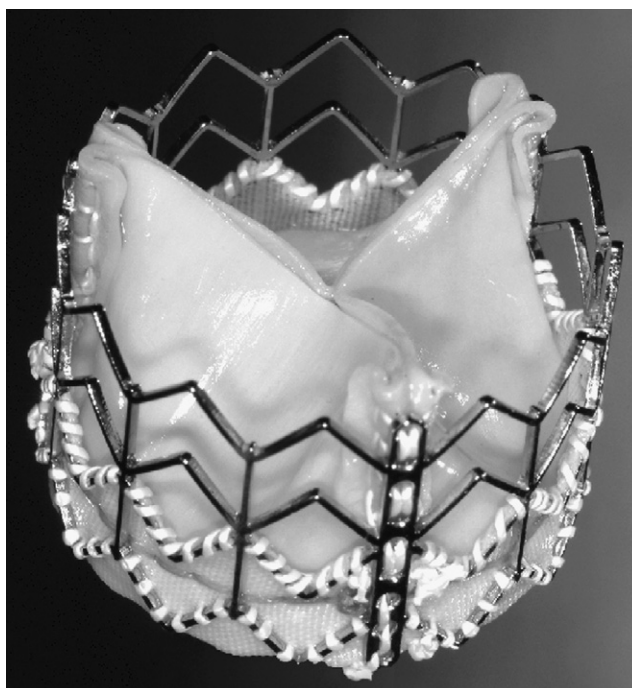


Fig. 1. Cribier-Edwards prosthesis: Balloon expandable pericardial xenograft fixed on a low-profile steel stent for transcatheter delivery.

aortic root was usually achieved at a left anterior oblique  $25^\circ$  and cranial  $10^\circ$  position. Besides standard hemodynamic monitoring, transesophageal echocardiography and extracorporeal circulation (ECC) were routinely available. Transesophageal echocardiography was used for repeated measurements of aortic annular diameters. We chose a valve

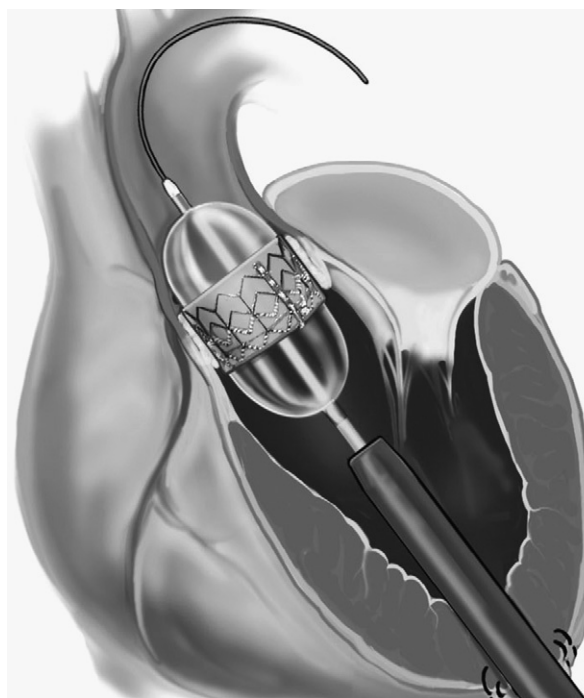


Fig. 2. Schematic illustration of transapical aortic valve implantation. The prosthesis is being dilated at the annular level within the native aortic valve cusps. Transapical sheath insertion is secured with a purse-string suture.

size that was 2–3 mm larger than the echocardiographic annular measurements in order to achieve good contact with the aortic annulus and to minimize the risk of paravalvular leaks (oversizing technique).

#### 2.4. Transapical aortic valve implantation (TAP-AVI): operative technique

The patients were placed in a supine position with the left chest slightly elevated. The left sided femoral vessels were dissected, either for cannulation for ECC (on pump procedure) or to place a venous guidewire (off pump procedure) for safety reasons in order to be prepared for fast cannulation. In addition a femoral arterial sheath (6F) was inserted and an aortic root pigtail catheter for angiographic visualization was placed. High dose heparin (300 IU/kg) was given for on-pump cases, and low dose heparin (5000 IU) was used for off-pump procedures with a target activated clotting time of 180–200 s. An anterolateral minithoracotomy (5–7 cm) was then performed in the fifth intercostal space to access the apex of the heart. The pericardium was incised longitudinally and fixed with stay sutures allowing persistent ventilation of the lungs. A bipolar epicardial pacing wire was placed and tested. Two apical purse-string sutures with Teflon felt pledgets were placed with an inner diameter of approximately 2–3 cm. The left ventricular apex was punctured and a soft guidewire passed antegradely across the stenotic aortic valve under fluoroscopic and echocardiographic monitoring. A 14F soft sheath was introduced and positioned across the aortic valve. A 035" super-stiff guide-wire (Amplatz super-stiff; 260 cm, Boston Scientific) was then positioned across the aortic arch and 'anchored' into the descending aorta. The sheath was partially withdrawn and a 20 mm balloon valvuloplasty catheter positioned under fluoroscopic and echocardiographic guidance. Balloon valvuloplasty was performed once during a brief episode of rapid ventricular pacing (150/min.). The balloon catheter and apical sheath were withdrawn and a 33F transapical delivery sheath inserted bluntly. The valve was then inserted using the specific application system. After careful de-airing of the sheath the valve was positioned so that the annulus bisects the stent. Fluoroscopic and echocardiographic imaging was used to position the valve and single shot aortic root angiography was used to confirm the intraannular position below the coronary ostia. During a second brief episode of rapid ventricular pacing, the valve was near instantaneously implanted using rapid balloon inflation. Rapid pacing was then stopped and hemodynamic function allowed to recover. Repeat dilatation was indicated in the presence of moderate paravalvular leakage. Valve function was immediately assessed by using angiographic and echocardiographic visualization. The transapical sheath was removed and the apex securely closed with the purse-string sutures. ECC was weaned, if necessary, and the cannulas removed and protamine administered. Intercostal blockade was performed using Ropivacaine. The pericardium was partially closed over the apex and a left lateral chest tube inserted. The incision was closed in a standard fashion. A schematic illustration of TAP-AVI is displayed in Fig. 2, and perioperative images are displayed in Fig. 3a–c.

Postoperative device specific medical therapy consisted only of aspirin 100 mg daily.

#### 2.5. Statistical evaluation

Results are given in a standard fashion throughout the manuscript. Continuous variables are expressed as mean  $\pm$  SEM or as median when appropriate, and categorical variables are expressed as proportions.

### 3. Results

#### 3.1. Patient characteristics

Thirty consecutive patients underwent TAP-AVI between February and September 2006, and all patients are included in this study. All patients suffered severe symptomatic aortic stenosis (aortic valve area  $< 0.9$  cm<sup>2</sup>) and their preoperative characteristics are displayed in Table 1. Additional comorbidities that were not reflected in the EuroSCORE risk assessment are displayed in Table 2.

#### 3.2. Perioperative results

All patients were operated on using an anterolateral minithoracotomy. Exposure of the left ventricular apex was good in all patients, even in re-operations. For proper valve

Table 1  
Preoperative patient characteristics

Patient number (n)	30
Age (years)	82 $\pm$ 5
Female gender (n)	21
NYHA	3.5 $\pm$ 0.6
Body weight (kg)	70 $\pm$ 14
EuroSCORE (points)	11.3 $\pm$ 1.7
Logistic EuroSCORE <sup>a</sup> (%)	27.1 $\pm$ 12.2
Previous cardiac surgery <sup>b</sup> (n)	5
Cardiac index (l/min/m <sup>2</sup> )	1.8 $\pm$ 0.4
LVEDP (mmHg)	20 $\pm$ 9
AOA (cm <sup>2</sup> )	0.5 $\pm$ 0.2 (range 0.3–0.9)

NYHA: New York Heart Association; LVEDP: left ventricular enddiastolic pressure; AOA: aortic valve opening area.

<sup>a</sup> Predicted risk for mortality.

<sup>b</sup> All re-operative patients had previous coronary bypass graft surgery with patent grafts.

Table 2  
Presence of additional comorbidities not necessarily reflected in the EuroSCORE risk assessment (n = 30 total)

Coronary artery disease	7
Recent myocardial infarction	4
Mild to moderate mitral valve incompetence	6
Recent cardiac decompensation	4
Previous stroke	5
Pulmonary disease/COPD	7
Hypertension	23
Diabetes	12
Leukemia	3
Renal failure	13
On dialysis	3

COPD: Chronic obstructive pulmonary disease.



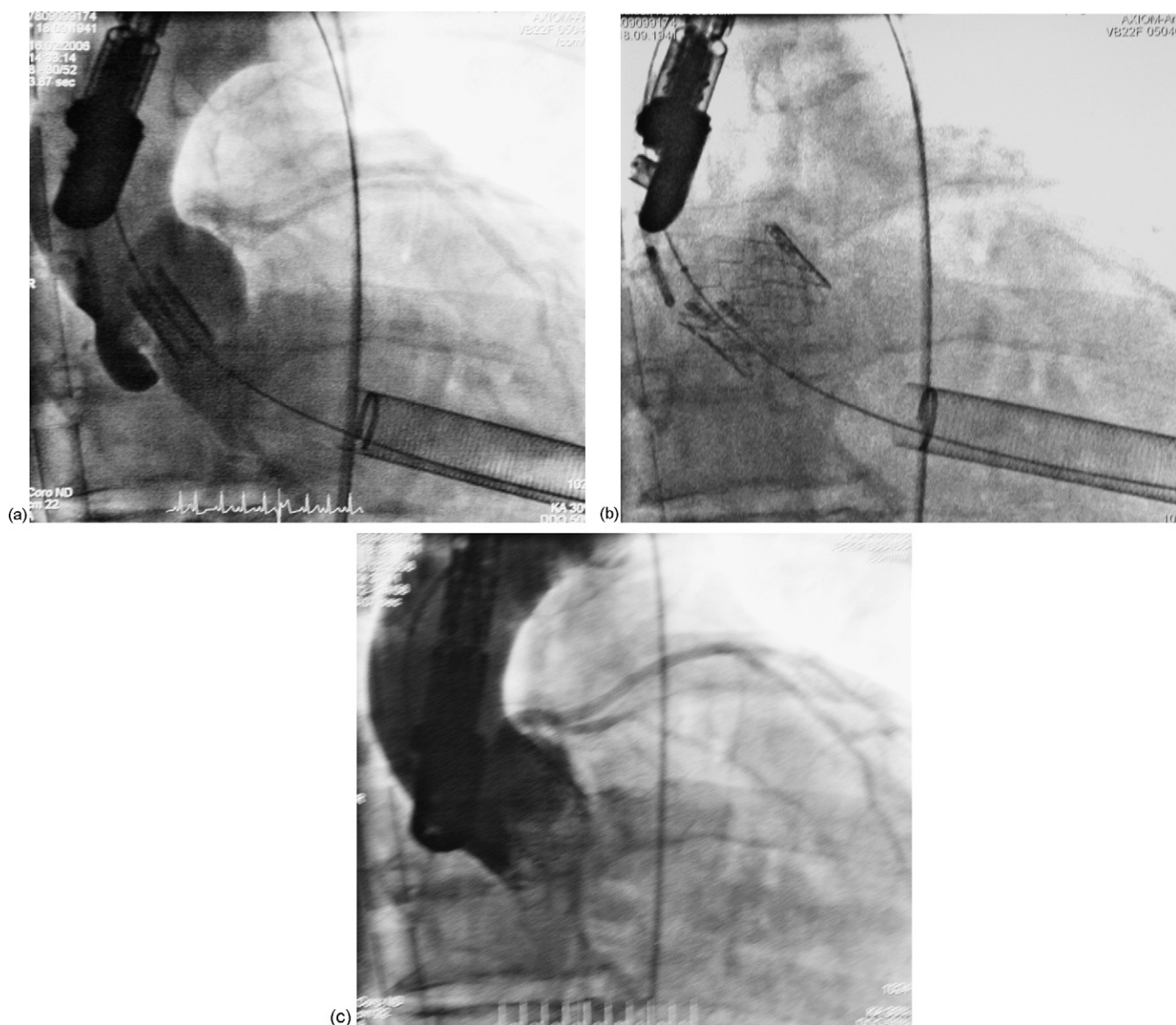


Fig. 3. Stepwise illustration of transapical aortic valve implantation: (a) valve positioning at the annulus. (b) Dilated valve in situ. (c) Aortic root angiography displaying good valve function and patent coronary arteries.

positioning, fluoroscopic and angiographic visualization was most reliable. Transesophageal echocardiography was useful for valvular morphologic and hemodynamic assessment, but was not adequate for precise valve positioning during deployment due to shadowing caused by the crimped steel stent and balloon catheter. Rapid ventricular pacing at 150/min was sufficient in all patients to unload the left ventricle during valve deployment. Regular cardiac rhythm was recaptured after cessation of pacing in all patients. Valve implantation was performed using ECC in 13 patients and without ECC support in 17 patients. Nine patients underwent femoral cannulation for possible ECC support, but ECC was subsequently not required. More recently, eight patients underwent surgery completely off pump with only a venous wire inserted in the femoral vein.

Valve implantation was successful in 29 of 30 patients (96.7%). One patient with severe eccentric calcification of

one of the native aortic valve cusps required early conversion to full sternotomy: In this patient balloon dilatation was more gradual rather than instantaneous. The valve slipped downwards due to the eccentric calcification, resulting in a fixed position in the left ventricular outflow tract and subsequent severe mitral valve incompetence. Conversion to conventional valve replacement was successfully performed.

There was no neurological event and no stroke in any of the patients. Perioperative laboratory examination did not reveal any relevant increase in myocardial enzymes despite performing apical puncture and applying apical purse-string sutures. Further perioperative results and early postoperative outcomes are summarized in Table 3.

Cardiac rhythm was stable throughout the study in all patients. Preoperatively, 18 patients were in sinus rhythm, 10 in atrial fibrillation and two had a pacemaker. Postoperatively,

Table 3  
Perioperative results ( $n = 30$ )

Aortic valve annulus as measured by intraoperative TEE (mm)	22.8 ± 1.5
Implanted valve size 23 mm	8
Implanted valve size 26 mm	22
Oversizing technique	All patients
Contrast given (ml)	79 ± 35 (range 20–150)
Fluoroscopy (min)	8 ± 4.5
Additional sutures at the apex	8
Requiring ECC support	2
Median duration of intubation (h)	6.5
Same day extubation ( $n$ )	25
Median ICU stay (h)	20
Median hospital stay (days)	14
Mean follow-up <sup>a</sup> (days)	127 ± 63

TEE: transesophageal echocardiography; ECC: extracorporeal circulation; ICU: intensive care unit.

<sup>a</sup> Effective from October 27, 2006.

two additional patients required pacemaker implantation, 17 were in sinus rhythm and nine in atrial fibrillation.

### 3.3. Morbidity and mortality

In-hospital morbidity is summarized in Table 4. A total of seven patients had a completely uneventful postoperative course without any complications. Three patients (10%) died in-hospital, all due to non-valvular causes. One patient died on postoperative day (POD) 86 and one on POD 18 due to an acute abdomen followed by multiorgan failure. The third patient suffered severe biventricular myocardial failure preoperatively during induction of anesthesia. Valve implantation was performed during resuscitation as salvage procedure. Despite good valve function the patient subsequently died on postoperative day 3 due to low cardiac output syndrome. Autopsy confirmed correct valve positioning and patent coronary arteries in all three patients who died.

Rethoracotomy for diffuse chest wall bleeding was performed in one patient who was receiving Clopidogrel™ preoperatively. One other patient required surgical removal of an intrapleural hematoma several days after a thoracentesis was performed. Postoperative cardiopulmonary resuscitation was performed successfully in two patients due to AV block (1) and respiratory dysfunction.

### 3.4. Echocardiographic results

Echocardiographic results for the 29 patients who successfully underwent valve implantation are shown in Table 5. Preoperative and early postoperative (pre-discharge) transthoracic echocardiographic measurements are displayed.

Table 4  
In-hospital morbidity ( $n = 30$ )

None	7
Pleural effusion	11
Postoperative episode of supraventricular tachyarrhythmia	9
Transient hemofiltration	4
Tracheostomy for weaning off ventilation	3
Cardiopulmonary resuscitation <sup>a</sup>	2
Pericardial effusion (medical therapy)	2
Others	14

<sup>a</sup> Both successful, no valve dysfunction on echocardiography.

Table 5  
Echocardiographic results

$n = 29$	Preoperative	Postoperative <sup>a</sup>
$V_{max}$ (m/s)	4.2 ± 0.6	1.9 ± 0.5
$P_{max}$ (mmHg)	76 ± 23	15.8 ± 8.2
$P_{mean}$ (mmHg)	43 ± 14	7.5 ± 4.7
LVPWd (mm)	15 ± 4	15 ± 3
EF (%)	52 ± 13	55 ± 12
Aortic incompetence	Any	14
	Trace	3
	Minimal (1°)	9
	Moderate (1°–2°)	2

$V_{max}$ : maximum transvalvular blood flow velocity;  $P_{max}$ : maximum transvalvular pressure gradient; (simplified Bernoulli equation);  $P_{mean}$ : mean transvalvular pressure gradient; LVPWd: left ventricular posterior wall enddiastolic diameter; EF: ejection fraction.

<sup>a</sup> Transthoracic measurements prior to discharge.

A small amount of aortic incompetence was diagnosed in 14 patients prior to discharge. Incompetence was transvalvular in five (all mild) and paravalvular in nine of these patients, respectively. None of these patients had any signs of hemolysis or clinically or hemodynamically important insufficiency.

### 3.5. Follow-up

Patients are being followed on a routine basis at 6 months, 1 year and annually thereafter. One patient with a porcelain aorta was readmitted and required re-operation on postoperative day 37 due to new onset severe aortic valve incompetence. During successful re-operation, an annular dehiscence close to the left-right coronary commissure was found. As of the beginning of October 2006, transapically implanted aortic valve prostheses have been in situ without further complication for a mean of 108 days (range 27–230 days). Due to the relatively short period of experience with this technique, meaningful follow-up data are not yet available.

## 4. Discussion

Transapical aortic valve implantation (TAP-AVI) has become a clinical reality for selected patients at some specialized centers. Recently, results from seven patients considered to have an excessive operative risk and treated as compassionate use were published [10]. At present research groups in Dallas, Frankfurt, Vancouver, Vienna and Leipzig are working together on the transapical approach using the Cribier-Edwards prosthesis, also known as the Ascendra™ investigators. Others will soon join these efforts. To the best of our knowledge the present series is the first ethically approved study on minimally invasive beating heart transapical aortic valve implantation (TAP-AVI). The initial results of this study are excellent, especially in view of the high-risk profile of our patient population. Thus the clinical feasibility of minimally invasive beating heart TAP-AVI is proven.

### 4.1. Concept of TAP-AVI

We believe the concept of transapical aortic valve implantation (TAP-AVI) is logical and feasible due to several

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