Transapical Minimally Invasive Aortic Valve Implantation
Multicenter Experience

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Background—To evaluate initial multicenter results with minimally invasive transapical aortic valve implantation (TAP-AVI) for high risk patients with aortic stenosis.

Methods and Results—TAP-AVI was performed via a small anterolateral minithoracotomy with or without femoro-femoral extracorporeal circulation (ECC) on the beating heart. A pericardial xenograft fixed within a stainless steel, balloon expandable stent (Edwards SAPIEN THV, Edwards Lifesciences) was used. Fifty-nine consecutive patients (81±6 years, 44 female) were operated on from 02/06 until 10/06 at 4 centers using fluoroscopic and echocardiographic visualization. Average EuroSCORE predicted risk for mortality was 27±14%. TAP valve positioning was performed successfully in 53 patients, 4 required early conversion to sternotomy. Implantation (23-mm valves in 19 and 26-mm valves in 40 patients) was performed on the beating heart during brief periods of rapid ventricular pacing. Thirty-one patients were operated on without cardiopulmonary bypass. Neither coronary artery obstruction nor migration of the prosthesis was observed, and all valves had good hemodynamic function. Echocardiography revealed minor paravalvular leakage in 26 patients (trace in 11, mild in 12, and severe in 3). Eight patients died in-hospital (13.6%) without any valve dysfunction. Actuarial survival was 75.7±5.9% at a follow-up interval of 110±77 days (range 1 to 255 days).

Conclusions—TAP-AVI can be performed safely with good early results in high risk patients. Long-term valve performance as well as broader based applications of this promising approach will need to be studied. (Circulation. 2007;116[suppl I]:I-240–I-245.)

Key Words: valves ■ aorta ■ cardiovascular diseases ■ stent fixed xenograft ■ transcatheter techniques

Aortic valve replacement is a commonly performed operation with well-defined indications. Conventional surgical therapy, involving a median sternotomy, along with the use of cardiopulmonary bypass (CPB) and cardioplegic cardiac arrest has been performed for decades with good perioperative and long-term results. This is true even for selected octogenarians. In addition to an increasing age at operation, contemporary patients present with more comorbidities such as cerebrovascular disease, low ejection fraction, pulmonary hypertension, respiratory insufficiency, chronic renal failure, and peripheral arterial occlusive disease among others. Preoperative risk assessment is routinely performed using the EuroSCORE or the STS risk calculator for these patients. Novel therapeutic strategies, including beating heart valve implantation via an anterolateral minitho- racotomy with or without ECC, may be necessary to maintain optimal surgical outcomes in these high risk patients. Further development of transcatheter techniques may lead to the point where truly minimally invasive valve implantation becomes a common clinical reality.

Transapical transcatheter valve implantation techniques have been developed recently. Initial experimental evaluation has been successfully performed by different groups. Early clinical results, using the device on a compassionate basis for high risk patients or for patients deemed as inoperable, have been recently published. In addition, early single-center feasibility experience with the device in high risk patients for conventional surgery was recently reported. The aim of this study is to present the initial multicenter results of the first ethically approved
clinical trial for transapical minimally invasive aortic valve implantation.

Materials and Methods
The study protocol was jointly developed by an international team of cardiac surgeons and cardiologists from the participating centers and approved by the local ethics committees (Leipzig, Frankfurt, Vienna) or the local study review board (Dallas). Joint inclusion criteria were as follows: Patient age ≥75 years and presence of surgical high risk attributable significant comorbidities. Patient risk was judged by a EuroSCORE of 9 points or more, which corresponds to a predicted perioperative mortality of >11% when applying the logistic EuroSCORE risk calculation. Additional technical inclusion criteria were an echocardiographically measured aortic annulus diameter of ≤24 mm as well as symmetrically distributed calcification of the stenotic native aortic valve cusps. All patients signed informed consent before inclusion in the study.

Transcatheter Valve Implantation Technique
A tricuspid pericardial xenograft mounted in a balloon expandable low profile stainless steel stent (Edwards SAPIEN THV, formerly Cribier-Edwards, Edwards Lifesciences) was used in this clinical study. Valve diameters of 23 mm and 26 mm were available for use, depending on the size of the patients aortic annulus. The lower inflow portion of the valve was covered with polyethylene terephthalate (PET) cloth (see Figure 1). Crimping of this sutureless prosthesis onto a balloon catheter was performed under sterile conditions by a technician immediately before transcatheter implantation.

Access to the left ventricular apex was gained through a left anterolateral minithoracotomy in the fifth intercostal space, with horizontal opening of the pericardium and placement of stay sutures for exposure. Two teflon-reinforced purse-string sutures (Prolene 2-0) were then placed at the left ventricular apex lateral to the left anterior descending coronary artery. In addition a temporary epicardial pacing wire was placed on the left ventricle. The left femoral vessels were exposed as potential access for CPB. Standard peripheral cannulae for CPB were inserted in cases performed on-pump, otherwise only a venous wire was inserted. In addition a femoral arterial sheath was placed and an aortic root pigtail catheter inserted and guided into the ascending aorta. Under fluoroscopic control the apex was punctured and a soft guide wire passed antegradely across the stenotic aortic valve. A 14 French soft sheath was inserted and a superstiff guide wire passed across the aortic arch (Amplatz superstiff, 035”, 260 cm, Boston Scientific). A conventional 20-mm valvuloplasty balloon catheter was then positioned at the aortic annulus. Balloon valvuloplasty was performed during a brief episode of rapid ventricular pacing (150 to 170/min) to temporarily eliminate cardiac output from the left ventricle. Then the sheath was exchanged for the 33 French transapical valve delivery system. The balloon catheter with the crimped valve was inserted and the system carefully deaired. Exact positioning was obtained using fluoroscopic guidance such that the aortic annulus bisected the midportion of the steel stent. Aortic root angiography (20cc of contrast) was used for positional control. During a second episode of rapid ventricular pacing, rapid valve deployment was performed using standard volumetric inflation of the balloon. Prosthesis function was immediately evaluated using transesophageal echocardiography as well as aortic root angiography. Repeat dilatation of the stent was indicated in case of moderate or severe paravalvular incompetence of the prosthesis. The transapical sheath was removed and the apex closed with the purse-string sutures. The pericardium was partially adapted, precluding early extubation. The transapical valve insertion technique is illustrated in Figure 2. Device specific medication consisted of aspirin 100 mg daily only.

All procedures were performed in a completely sterile environment of a routine operative theater. This allowed for immediate conversion to conventional valve surgery and provided for optimal patient safety. For fluoroscopic imaging a monoplane angiography system (Axiom Sensis, Siemens; hybrid operative theater) or a mobile system were used.

Echocardiographic Valve Assessment and Follow-Up
Standard echocardiographic views were used for perioperative (transesophageal echocardiography=TEE) and postoperative (thoracic echocardiography=TEE) valve assessment. Left ventricular dimensions, left ventricular ejection fraction (EF), and prosthetic valve function were evaluated. Mitral valve function before and after
implantation as well as concomitant pathologies were routinely assessed. Potential aortic valve incompetence was judged as transvalvular or paravalvular and the severity was graded as none, trace, mild (1°), moderate (1 to 2°), and severe (2° or higher). All echocardiographic examinations were reviewed by an experienced and independent local examiner as well as the echocardiographic core laboratory (WF).

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

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results
A total of 59 patients with significant aortic valve stenosis at 4 centers were included in this clinical study from February 2006 until October 2006. Patients were enrolled at Leipzig (30), Vienna (24), Frankfurt (3), and Dallas (2), respectively. Patient age at implantation was 81.4±5.8 years and 74.6% were female. A total of 3 patients younger than 75 years were included because of their severe comorbidities, after additional approval by the ethics committees. Preoperative risk assessment by EuroSCORE revealed a mean of 11.2±1.8 points, corresponding to a predicted risk for mortality of 26.8±13.5% (logistic EuroSCORE). Previous cardiac surgery had been performed in 10 patients (16.9%), 8 of which had received coronary artery bypass grafting with patent grafts and 1 patient each post aortic valvuloplasty and mitral valve repair. A summary of preoperative patient characteristics is given in Table 1.

To provide a more detailed overview of the patients’ risk profile, significant comorbidities and factors not necessarily reflected by the EuroSCORE are given in Table 2. This indicates that, in addition to the high EuroSCORE predicted risk, the patients included into this study suffered severe comorbidities. All patients with concomitant mitral valve regurgitation (n=24) had mild or moderate insufficiency, not requiring additional mitral valve surgery in the presence of tight aortic stenosis.
Implantations were performed on-pump in the beginning of the study. With increasing experience, however, femoral cannulation only was performed without using CPB. Recently 18 patients received off-pump valve implantation with only a femoral venous wire in place. Repeat valve dilatation using rapid ventricular pacing was performed because of uneven stent expansion leading to moderate or severe paravalvular leak in 12 patients. Closure of the left ventricular apex was uncomplicated when using sufficiently deep bites in the presence of firm apical tissue. Additional sutures were re-quired in 12 patients, 6 of whom had to be performed during ventricular unloading using CPB. The total procedure time decreased with increasing experience throughout the study. Currently a straight forward transapical valve implantation can be routinely performed in less than 80 minutes.

Results on postoperative outcomes are given in Table 4. Despite their high-risk profile, a majority of patients were extubated early and had a short intensive care unit stay. The postoperative morbidity is acceptable in view of the high perioperative risk profile and in comparison to the results after conventional surgical valve replacement. The transapical approach proved to be safe with only 1 return to the operating room for postoperative apical bleeding. The inci-dence of stroke (n=2) was low in this series.

Echocardiographic results are given in Table 5. Good valve function with low blood flow velocities and low pressure gradients were observed in all patients. Some degree of aortic valve incompetence was diagnosed in 26 of 40 patients that were available for routine echocardiographic assessment at discharge. Aortic valve incompetence was trace, mild, or moderate in most of the patients, and none of them suffered any symptoms. In addition there were no signs of hemolysis in any of the patients. During follow-up, no increase in aortic valve incompetence occurred. At current follow up, 46 (78%) of the patients are alive. Actuarial survival for the whole patient group is 75.7±5.9% and is given in Figure 3.

**Discussion**

Minimally invasive transapical aortic valve implantation (TAP-AVI) is a novel surgical procedure developed in part to deal with an increasing preoperative risk profile of patients with aortic valve disease. The goal of this procedure is to
decrease the invasiveness of the current gold standard, conventional aortic valve replacement surgery, while maintaining excellent long-term results by taking advantage of recent technical developments in the field of transcatheter valve implantation. Primarily, good functional and hemodynamic results should be achieved when performing sutureless valve implantation. Careful assessment of patient related factors including thoughtful preoperative risk assessment is required for further evaluation of this new approach. Early feasibility trials of TAP-AVI are under way.13,14 A pivotal study is being designed at present and eventually randomized studies will follow.

The current article summarizes the first multicenter experience of TAP-AVI in a relatively large number of patients (n=59) being treated under an ethically approved protocol. The present results are good, especially when considering the overall risk profile of the patients included in this study. It is also important to note that a learning curve is associated with this new technique and that the participating centers had differing levels of experience with transcatheter techniques before beginning the study. This successful multicenter experience is an important step for further broader-based application of the promising technique of TAP-AVI. We believe that further expansion of this investigational procedure to more institutions is warranted and that randomized trials are in the foreseeable future.

Initial results in 7 patients deemed as nonoperable that received transapical aortic valve implantation on a compassionate use protocol have been recently published.15 We included similarly high risk patients in the current series, with the difference being that we often perform conventional aortic valve surgery on such patients because we seldom deem aortic stenosis patients as inoperable. Generally speaking, patient selection and inclusion criteria are a critical factor when performing studies on new devices in high risk populations. Sufficient patient survival should be achieved to be able to evaluate longer term outcomes. This may be in contradiction to the high risk profile of the patients and will definitively exclude multimorbid candidates. For better definition of inclusion criteria we used a higher EuroSCORE and a patient age of ≥75 years. Older age alone should not be the sole indicator of high surgical risk, and after the present experience we think that our inclusion criteria were appropriate. Based on our criteria, patients with a predicted risk of approximately 27% were included. We observed a mortality of approximately half of predicted (13.6%) and therefore feel our results are satisfactory. Patients with poor ejection fraction and severe respiratory insufficiency seemed to benefit the most from the minimally invasive approach. However, further long-term evaluation should be performed before including younger patients that are probably better served with conventional valve replacement. For future studies a EuroSCORE predicted risk for mortality of ≥20% and a STS risk score ≥10% may serve as uniform inclusion criteria together with a primary end point of one year survival.

The incidence of stroke was low in the current series. This low risk with TAP-AVI might be explained by the fact that all implants were performed using an antegrade technique, without excessive wire or catheter manipulation in the ascending aorta and the aortic arch. When manipulating a superstiff wire around a potentially calcified aortic arch—which is required for the retrograde transfemoral approach—particulate embolization with subsequent stroke can occur. In addition, direct antegrade passage through the native stenotic aortic valve proved to be relatively easy in this series. Complete unloading of the heart during native aortic valve dilatation and during valve implantation is important to avoid any detachment of calcium from the annulus. This can easily be achieved using rapid ventricular pacing as performed in this series.

It is informative to compare this multicenter experience to other published results. Cribier has pioneered the field of transcatheter valve implantation. Using only a 23-mm steel stent prosthesis, and therefore without consequentially using the oversizing technique, he first reported acceptable results in patients in 2002.15–17 Valves were implanted through a transfemoral arterial retrograde or a transfemoral venous antegrade transseptal approach. CoreValve, a porcine pericardial valve mounted within a Nitinol stent of 5 cm length, is another device currently under clinical investigation in the aortic position. It is designed in a way that the stent is positioned across the aortic sinuses without obstructing coronary flow. Lifelong antiplatelet therapy using aspirin and clopidogrel is required. This may be a disadvantage especially in the elderly high risk patients. Initial results after transfemoral insertion of the 25 French and the 21 French CoreValve were recently published.18 The overall in-hospital mortality of 20% is quite high when considering the EuroSCORE predicted risk was only 11% in this series.

The transapical approach used in this series is a straightforward procedure that allows for safe and reproducible transcatheter valve implantation. As proven by this series, the procedure is standardized, reproducible, and relatively simple. This will lead to longer-term successful applications. The transapical access can be safely secured when using standard purse-string sutures. For valve implantation fluoroscopic visualization is most useful, in parallel with continuous TEE monitoring. Transfemoral arterial valve implantation may be performed with similar reliability. However, retrograde passage of the stenotic aortic valve as well as the longer distance for precise manipulation of the valve, sometimes being more than 100 cm from the femoral access to the aortic annulus, have to be considered. The transapical approach provides a direct and easy access with excellent manipulation of the device. With the transapical technique no limitation in sheath diameter exists, allowing for the implantation of large and eventually cuffed prostheses to achieve a functionally optimal result for the patients.

One of the most important aspects of the current multicenter trial is the transnational team approach used by the cardiac surgeons, as well as the excellent cooperation with local cardiologists and anesthesiologists. Input from different members of the team led to a continuous refinement of the procedure toward a more and more minimally invasive approach. Catheter-based skills will undoubtedly become an increasingly important for cardiac surgeons interested in pursuing this technique for aortic valve replacement.19 Additionally, increased cooperation with interventional cardio-

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gists interested in structural valvular heart disease will be useful to promote this unique therapy. We may foresee the development of specialized “valve teams” made up of cardiac surgeons, cardiologists, anesthetists, and others, all dedicated to the optimal and potential minimally invasive treatment of the patients.

Future refinement of the sutureless devices should focus on further minimizing the risk for paravalvular leakage. In addition, smaller devices may be advantageous. Most importantly, a retrieval mechanism allowing for safe removal of a malpositioned prosthesis and redeployment of the device would be highly advantageous. Training of physicians for these procedures, possibly involving a simulator, may have to be implemented. Correct valve implantation may be further supported by image guided mechatronic assistance. This would include (1) preoperative planning including segmentation of the aortic root from computer tomography (CT) data, and virtual placement of the appropriate valve within the reconstructed root, (2) registration of the CT data with intraprocedural imaging (ie, TEE) using suitable landmarks such as the commissures, and (3) automatic positioning and placement of the valve using a mechatronic device that would be guided by a predictive algorithm that compensates for the dynamics of aortic root motion.

In summary TAP-AVI is a promising technique with proven feasibility in selected high risk patients. The early multicenter experience is encouraging, proving a reproducible technique with good perioperative results and acceptable hemodynamic function of the implanted prostheses. Coronary perfusion is well preserved when using modern imaging techniques during valve positioning and implantation. The risk of paravalvular leakage will always remain an important issue for the evaluation of sutureless devices, but may partially be solved by the oversizing technique. Future randomized and longer-term follow-up evaluations are required. Conventional aortic valve replacement surgery remains the gold standard at present.

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Disclosures
Michael Mack, Todd Dewey, Gerhard Wimmer-Greinecker, and Friedrich W. Mohr are consultants to Edwards Lifesciences, Inc.

References
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