Transapical Aortic Valve Implantation
Analysis of Risk Factors and Learning Experience in 299 Patients

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Background—Transapical aortic valve implantation has evolved to a reproducible therapeutic option for high-risk patients. The aim of the present study was to evaluate our learning experience over 4 years and to analyze outcome-related risk factors.

Methods and Results—A total of 299 patients who received transapical aortic valve implantation between February 2006 and January 2010 with the Edwards SAPIEN transcatheter prosthesis were analyzed according to early experience (EE; patients 1 to 150) and recent experience (RE; patients 151 to 299). Patients consistently demonstrated high risk scores, and major perioperative parameters were comparable between the 2 groups. RE patients had a significantly higher logistic EuroSCORE (RE 33.2±17.2, EE 29.4±14; P=0.039) but a significantly lower STS (Society of Thoracic Surgeons) score (RE 11.4±7.5, EE 13.5±7.8; P=0.019). Use of contrast dye (EE 104±78 mL, RE 93±46 mL) and the need to perform a balloon redilation were significantly reduced in the RE group. Thirty-day mortality decreased from 11.3% to 6.0%, and 1-year mortality improved significantly from 30.7% (EE) to 21.5% in the RE patients (P=0.047). Multivariate logistic regression analysis revealed reduced vital capacity (<70%) and concomitant preoperative mitral regurgitation >1+ as the only independent predictors of 30-day mortality. Classic variables such as age, logistic EuroSCORE >30%, and STS score >15% failed to predict mortality.

Conclusions—Recent results with transapical aortic valve implantation indicate a progressive improvement in outcomes despite an unchanged patient risk profile, which reflects a significant learning curve that includes a better understanding of optimal patient selection. Classic surgical risk factors fail to predict outcome, which indicates the need for new transapical aortic valve implantation–specific risk scores. (Circulation. 2011;124[suppl 1]:S124–S129.)

Key Words: aortic valve ■ valves ■ surgery ■ catheters

Conventional surgical aortic valve replacement is the standard treatment for symptomatic aortic stenosis and is usually associated with a low perioperative risk and excellent patient outcome.1 Surgical risk, however, may be increased in specific patient subgroups, including those with advanced age or relevant comorbidities.2,3 Patients with an elevated predicted risk of mortality may be identified preoperatively by a logistic EuroSCORE ≥20% or an STS (Society of Thoracic Surgeons) score ≥10%4 and such patients may benefit from new, minimally invasive transcatheter aortic valve implantation. Transcatheter aortic valve implantation can be performed via a retrograde transfemoral (TF-VAI) or an antegrade transapical (TA-VAI) approach.5–11

The aim of the present study was to evaluate a potential learning experience over 4 years. In addition, multivariate logistic regression was used to identify potential independent risk factors for mortality.

Methods

From February 2006 until January 2010, a total of 299 patients received TA-VAI with the Edwards SAPIEN transcatheter xenograft (Edwards Lifesciences Inc, Irvine, CA). All patients gave written informed consent, and the study was approved by the institutional review board. The first half of the patients (patients 1 to 150) form the early experience (EE) group, and some were included in an initial feasibility study and then a pivotal study (February 2006 until April 2008). The second half of the patients (recent experience [RE] group; patients 151 to 299) were treated exclusively after CE (Conformité Européenne [European conformity]) approval of TA-VAI. Follow-up was performed in the hospital and included transthoracic echocardiography, supplemented by an interview of the patients or their family members and by information from the patients’ cardiologists or family physicians. Follow-up was 100% complete and consisted of a total of 338 patient-years.

After a team discussion between cardiologists and cardiac surgeons, patients were scheduled for TA-VAI on the basis of patient age ≥75 years and increased surgical risk, as defined by an additive EuroSCORE ≥9 points or an STS score >10%. Additional inclusion
patients had a significantly higher logistic EuroSCORE but a tentatively high-risk profile throughout the study; however, RE TA-AVI was performed in those patients who were referred to our department with symptomatic aortic stenosis who fulfilled these criteria were screened for potential TA-AVI with transesophageal echocardiography to measure the aortic annulus diameter. Oversizing of 10% to 20% of the implanted aortic annulus diameter. Oversizing of 10% to 20% of the implanted valve size was performed to improve tissue purchase and to minimize the risk of paravalvular leak. A coronary angiogram was performed in all patients and cardiac computed tomography in those in whom a short coronary-to-annulus distance was suspected. Patients with relevant coronary artery disease who were poor candidates for conventional aortic valve surgery underwent prior percutaneous coronary intervention, if feasible. TA-AVI was performed in a standard fashion, as described previously.12

### Statistical Analysis

Continuous variables are expressed as mean±SD for those variables with a gaussian distribution. Categorical data are expressed as proportions. Categorical variables between the first (EE) and second (RE) halves of the patient population were compared with Pearson χ² test, whereas independent continuous variables were compared by 2-tailed Student’s t test or Mann-Whitney U test as appropriate. Univariate and stepwise multivariate logistic regression analysis of predictors of 30-day mortality were examined via 81 preoperative cardiovascular risk factors and 41 preoperative and intraoperative dichotomous variables and 41 preoperative and intraoperative numeric variables (see Appendix in the online-only Data Supplement). Those variables that had a probability value of <0.1 by univariate analysis were included in the multivariable model, and corresponding odds ratios and 95% confidence intervals were determined. Cumulative survival was calculated by Kaplan-Meier methods with 95% confidence limits, and comparisons were made between the first and second halves of the patient population with the log-rank test. P <0.05 was considered significant. Statistical calculations were performed with the SPSS 17.0 and Microsoft Excel 2007 software packages.

### Results

TA-AVI was performed by the same team in the hybrid operative theater with full intubation (n=292) or with thoracic epidural anesthesia (n=7). Preoperative patient variables are shown in Table 1. Patients demonstrated a consistently high-risk profile throughout the study; however, RE patients had a significantly higher logistic EuroSCORE but a significantly lower STS score. Preoperative cardiovascular risk factors are shown in Table 2. Despite a significantly lower STS score, RE patients still presented with a truly high-risk profile, which explains the significantly higher logistic EuroSCORE, because the RE patients were more likely to present with previous surgery, coronary artery disease, or peripheral vascular disease. In conclusion, the 2 patient groups were not fully comparable in regard to the individual risk variables, but as indicated by the paradoxical development of the STS score versus the logistic EuroSCORE, both groups demonstrated a consistently high-risk profile. To adjust for the observed minor differences in the risk profile, a multivariate analysis of the individual risk factors was performed.

Postoperative outcomes are shown in Table 3. Major stroke occurred in only 2 patients. Overall, RE patients demonstrated a trend toward a lower 30-day mortality (EE 11.3% versus RE 6.0%) and a significant improvement in 1-year survival despite comparable risk profiles. The Kaplan-Meier curve (Figure) demonstrates the survival of the 2 patient groups.

As demonstrated in Table 4, RE patients required significantly shorter fluoroscopy time, less contrast dye, less frequent postimplantation balloon redilation, and less frequent cardiopulmonary bypass support; in addition, there was a trend toward shorter total procedure times. The statistical analysis also revealed a slightly less aggressive oversizing...
concept during the second half of the series. In addition, in our recent experience, residual bleeding that necessitated extra stitches at the apical access site occurred significantly less frequently.

Postoperative echocardiographic results (at hospital discharge) are shown in Table 5. Despite apical access, the left ventricular ejection fraction remained stable. The SAPIEN prosthesis demonstrated excellent antegrade performance, with mean gradients in the single digits; however, statistically, RE patients demonstrated significantly higher gradients. Compared with the EE patients, the rate and the severity of paravalvular leaks that resulted in aortic insufficiency were decreased significantly in the second half of the series.

Univariate analysis (Table 6) revealed a nonsignificant trend toward a higher risk for 30-day mortality for patients treated within our early experience (odds ratio 2.0). Of all preoperative and intraoperative factors analyzed (see Appendix in the online-only Data Supplement), only a reduced vital capacity of less than 70% and concomitant mitral regurgitation of more than 1+ could be identified as independent risk factors for 30-day mortality by stepwise multivariate regression. In contrast, an elevated classic risk score (logistic EuroSCORE >30% or STS score >15%) failed to predict 30-day mortality.

Discussion

The present series comprises the very early experience (since February 2006) and the largest single-center cohort of patients treated with TA-AVI worldwide. The first half included
eral vascular disease, which is a well-recognized risk factor for poor clinical outcomes. Thus, this specific patient subgroup should be assessed very carefully and might not benefit from isolated T-AVI. Therefore, the need to develop and validate new scoring tools for T-AVI patients.

Concomitant mitral regurgitation (MR) >1+ was identified as the other independent risk factor for mortality. Patients presenting with mitral regurgitation >1+ who received TA-AVI demonstrated a 30-day mortality as high as 23.9%. Thus, this specific patient subgroup should be assessed very carefully and might not benefit from isolated T-AVI.

Both of the classic risk-scoring algorithms (STS score >15%, logistic EuroSCORE >30%) failed to predict mortality. The shortcomings of the currently available scoring systems have been demonstrated recently.15,16 This indicates the strong need to develop and validate new scoring tools suitable for assessment of the risk of T-AVI patients.

### Table 5. Postoperative Echocardiographic Results

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients 1–150</th>
<th>Patients 151–299</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF, %</td>
<td>55±13</td>
<td>56±11</td>
<td>NS</td>
</tr>
<tr>
<td>Δ Preoperative LVEF, %</td>
<td>1.0</td>
<td>0.1</td>
<td>NS</td>
</tr>
<tr>
<td>AV Pmax, mm Hg*</td>
<td>15±6</td>
<td>17±6</td>
<td>0.004</td>
</tr>
<tr>
<td>AV Pmean, mm Hg*</td>
<td>7.9±4</td>
<td>9.2±3</td>
<td>0.04</td>
</tr>
<tr>
<td>AI, n (%)</td>
<td>0.024</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

None (trace) 72 (48) 102 (68) 1+ 74 (49) 38 (25) 2+ 4 (3) 9 (6) 3+ ... ... ... 

LVEF indicates left ventricular ejection fraction; NS, not significant; Δ Preoperative LVEF, difference between preoperative and postoperative LVEF; AV, aortic valve; Pmax, maximum transvalvular (aortic) pressure gradient; Pmean, mean transvalvular (aortic) pressure gradient; and AI, aortic insufficiency (paravalvular leaks).

*Complete Bernoulli equation.

The initial feasibility study, and the second half exclusively represents routine clinical use after CE approval was granted. There was neither a change in inclusion or exclusion criteria throughout this study: The indication for TA-AVI at our institution remains for patients older than 75 years of age with an increased risk profile or documented clinical findings that make conventional surgery technically challenging (eg, porcelain aorta, mediastinal radiation).4,8

We can ascertain 3 major conclusions from the present study. First, TA-AVI is feasible and can be consistently performed as a reproducible procedure, having been performed 299 times in our institution over a 4-year period. Second, we have observed strong evidence of a learning curve when comparing our initial clinical experience to the more recent post–CE mark approval period, with shorter procedure times, less fluoroscopy, and less contrast dye exposure. Third, we were able to demonstrate that the anastomode and direct transapical approach leads to excellent outcomes in high-risk patients with aortic stenosis. Our results herein are at least as good as other currently reported series of TF-AVI.6,10,11,13 Many transcatheter aortic valve studies that have been published to date have been performed with a clear “transfemoral first” protocol. This implies that patients with suitable femoral vessels are being treated with a retrograde transfemoral approach, whereas those with peripheral vascular disease, which is a well-recognized risk factor for adverse outcomes in patients undergoing conventional aortic valve surgery, receive a transapical approach. The US PARTNER trial (Placement of Aortic Transcatheter Valve Trial), for example, followed such a “transfemoral-first” strategy. However, there is no clinical evidence at present for the superiority or inferiority of one (transfemoral) or the other (transapical) approach.

The present data can be considered closer to an “all-comers study” than the previously published TA-AVI studies. Patients referred to our cardiac surgery department for TA-AVI received that procedure after a team discussion, even if femoral vessels would have been suitable for TF-AVI. Patients from our cardiology department were referred to our surgical team for TA-AVI if they had documented femoral artery disease. A similar number of patients received TF-AVI by use of other devices during the present study period at our institution. The transfemoral patients were those who were referred directly to our cardiology department for a transcatheter aortic valve procedure or those patients who were referred to our surgical department but with an aortic annulus that was too large to receive an Edwards SAPIEN valve. Even in the presence of such an “all-comers” TA strategy, it is interesting to note that 39% (EE) and 56% (RE) of the TA-AVI patients had documented peripheral vascular disease (Table 2), a rate that is comparable to other published series.6,11,14

Poor respiratory function, defined as vital capacity <70%, was identified as an independent risk factor for perioperative mortality in the present study. The combination of older age, frailty, and poor respiratory reserve may result in an excessive risk of respiratory failure and reintubation in these patients. The exact quantification of preoperative respiratory dysfunction and the differentiation from effects of aortic stenosis represent a challenging area in need of further clinical evaluation.

### Table 6. Multivariate Logistic Regression Predictors of 30-d Mortality

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30-d Mortality, %</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>First 150 patients (EE)</td>
<td>11.3</td>
<td>2.00 (0.86–4.62)</td>
</tr>
<tr>
<td>Vital capacity (&lt;70%)</td>
<td>14.8</td>
<td>3.86 (1.61–9.22)</td>
</tr>
<tr>
<td>MR &gt;1</td>
<td>23.9</td>
<td>5.59 (2.49–12.58)</td>
</tr>
<tr>
<td>LogES &gt;30%</td>
<td>10.6</td>
<td>1.52 (0.67–3.31)</td>
</tr>
<tr>
<td>STS &gt;15%</td>
<td>12.9</td>
<td>1.72 (0.77–3.85)</td>
</tr>
</tbody>
</table>

OR (95% CI) indicates odds ratio (95% confidence interval); EE, early experience; MR, mitral regurgitation; LogES, logistic EuroSCORE; and STS, Society of Thoracic Surgeons.
We observed differences between the 2 groups, with a higher logistic EuroSCORE and a lower STS score in the RE group. These results may be within the normal variations. Overall, both patient groups comprised a high-risk cohort with a significantly higher rate of redo procedures, a higher rate of peripheral vascular disease, and a higher percentage of concomitant coronary artery disease among the RE patients. Overall indications did not change throughout the study after the position paper was published.4

Despite problems with determining the actual risk of conventional surgery in the present patient population, we can consider the overall results as excellent. In the first half of our experience, with a completely new procedure that involved a completely different approach to the aortic valve, we were able to match the STS score–predicted 30-day mortality. In the second half of our experience, we were able to obtain a mortality rate that was half of what the STS score predicted. We can conclude that TA-AVI results in mortality rates that are at least as good as conventional aortic valve replacement in high-risk aortic stenosis patients and that results appear to improve with increasing clinical experience.

Learning aspects that are particular to TA-AVI include specific knowledge as to optimal preoperative and perioperative sizing of the annulus, where to access the apex, how to minimize the risk of ventricular complications, how to improve the precision of valve positioning by use of fluoroscopic and transesophageal echocardiographic guidance, stepwise valve implantation by gradual balloon dilation with the capability for minor position adjustments, and specialized postoperative intensive care.12 In addition, we were able to immediately transition from the investigational stage to the post–market approval stage without an interruption in implantations, which is in contrast to the experience from other centers with a lower number of implants and a greater number of interruptions.14

Regarding apical access, residual bleeding that required extra stitches at the left ventricular apex was less frequently encountered in the RE patients. Overall, apical access must be considered to be safe, with bleeding complications in only 1% to 2% of patients and with the majority of patients extubated within 24 hours after surgery.

We believe that ideal conditions for T-AVI include performance of all procedures by a specialized team, use of a hybrid operative theater, and use of high-quality fluoroscopic imaging. New improvements in imaging, such as 3-dimensional reconstruction with a DynaCT (Siemens Inc, Erlangen, Germany) with use of specific anatomic landmarks, may lead to further standardization of TA-AVI and eventually further improved outcomes.17

Interestingly, during the second half of the present study experience, a less aggressive oversizing concept (difference between implanted valve size and measured annular diameter) was used, which might explain the slightly higher RE gradients observed. However, echocardiographic results with regard to the frequency and severity of aortic insufficiency (paravalvular leaks) improved significantly. In addition, the need to perform postimplantation balloon redilation decreased significantly. These results might indicate a learning curve with regard to better positioning and sizing of the transcatheter valve prosthesis over time.

In summary, TA-AVI leads to excellent clinical outcomes in high-risk patients with aortic stenosis and compares favorably to published series of TF-AVI and to estimated risk profiles for conventional aortic valve surgery. However, the study also indicates the urgent need to develop new T-AVI–specific risk models, because both the STS score and logistic EuroSCORE that are most commonly used failed to predict mortality. Evidence of a learning effect for this new procedure could be demonstrated clearly. With a rapidly increasing clinical experience in many centers around the world, this promising technique may become even more prevalent in the near future.

Acknowledgments

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Disclosures

None.

References


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SUPPLEMENTAL MATERIAL

Appendix:
Parameters tested as possible predictors of 30-day mortality using univariate and multivariate logistic regression:

**Preoperative general:** Age; gender; body weight; height; body mass index; body surface area; length of preoperative hospital stay; NYHA functional status; STS score; Additive EuroSCORE; Logistic EuroSCORE; first 150 patients.

**Preoperative extracardiac:** Chronic obstructive pulmonary disease; peripheral vascular disease; neurological dysfunction; serum creatinine >200 mmol; pulmonary hypertension; arterial hypertension; diabetes; history of smoking; carotid artery disease >70%; hyperlipidemia; chronic dialysis; vital capacity, forced expiratory volume in one second.

**Preoperative cardiac:** Previous syncope; atrial fibrillation; porcelain aorta; previous pacemaker/ICD; previous cardiac surgery; critical preoperative status; recent myocardial infarction; concomitant coronary artery disease.

**Preoperative cardiac catheterization:** Aortic regurgitation >I+; maximum aortic valve pressure gradient; mean aortic valve pressure gradient; aortic valve orifice area; left ventricular end diastolic pressure; left ventricular ejection fraction; pulmonary artery pressure; concomitant coronary artery disease; mitral regurgitation.

**Intraoperative variables:** Implanted valve size; intraoperative annulus diameter; amount of contrast dye; fluoroscopy time; additional apical suture; procedural time; conversion to sternotomy; CPB use; conversion to CPB; CPB time; cross clamp time; coronary ischemia; coronary intervention; coronary artery bypass graft; too low valve positioning; aortic annular injury; Valve in a valve implantation (SAPIEN in SAPIEN); post-implant valve dilatation; new high grade AV block; transfer to recovery room.