Valvular Heart Disease

Transcatheter Aortic Valve Implantation
Durability of Clinical and Hemodynamic Outcomes Beyond 3 Years in a Large Patient Cohort

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Background—Although short- and medium-term outcomes after transcatheter aortic valve implantation are encouraging, long-term data on valve function and clinical outcomes are limited.

Methods and Results—Consecutive high-risk patients who had been declined as surgical candidates because of comorbidities but who underwent successful transcatheter aortic valve implantation with a balloon-expandable valve between January 2005 and December 2006 and survived past 30 days were assessed. Clinical, echocardiographic, and computed tomographic follow-up examinations were performed. Seventy patients who underwent successful procedures and survived longer than 30 days were evaluated at a minimum follow-up of 3 years. At a median follow-up of 3.7 years (interquartile range 3.4 to 4.3 years), survival was 57%. Survival at 1, 2, and 3 years was 81%, 74%, and 61%, respectively. Freedom from reoperation was 98.5% (1 patient with endocarditis). During this early procedural experience, 11 patients died within 30 days, and 8 procedures were unsuccessful. When these patients were included, overall survival was 51%. Transaortic pressure gradients increased from 10.0 mm Hg (interquartile range 8.0 to 12.0 mm Hg) immediately after the procedure to 12.1 mm Hg (interquartile range 8.6 to 16.0 mm Hg) after 3 years ($P<0.03$). Bioprosthetic valve area decreased from a mean of 1.7 ± 0.4 cm$^2$ after the procedure to 1.4 ± 0.3 cm$^2$ after 3 years ($P<0.01$). Aortic incompetence after implantation was trivial or mild in 84% of cases and remained unchanged or improved over time. There were no cases of structural valvular deterioration, stent fracture, deformation, or valve migration.

Conclusions—Transcatheter aortic valve implantation demonstrates good medium- to long-term durability and preserved hemodynamic function, with no evidence of structural failure. The procedure appears to offer an adequate and lasting resolution of aortic stenosis in selected patients. (Circulation. 2010;122:1319-1327.)

Key Words: heart valves ■ aortic stenosis ■ heart valve prosthesis

Transcatheter aortic valve implantation (TAVI) with a balloon-expandable valve is a promising technique for patients with severe aortic stenosis. More than 5000 procedures have been performed to date worldwide, mostly confined to patients at high surgical risk. Thus far, short- and medium-term outcomes have been encouraging; however, data on long-term clinical outcomes, valve durability, and structural integrity are lacking.

Clinical Perspective on p 1327

Surgically implanted stented bioprostheses in the aortic position have shown 10-year freedom from valvular failure in the range of 60% to 90%, with younger patients predisposed toward premature deterioration. At 5 years, freedom from structural failure is generally >95%, and although early failure requiring reoperation or leading to mortality has been reported, freedom from reoperation at 5 years is also generally >95%. Whether TAVI can achieve similar outcomes is still unknown.

Data on clinical outcomes from TAVI have largely been limited to 30 days or, rarely, 1 year, showing both sustained reductions in transvalvular gradients and increases in transvalvular areas. Cribier et al reported on 2 patients up to 2 years after TAVI, and our group has previously described clinical outcomes to 2 years, with hemodynamic performance to 1 year. In the present series, we report on long-term clinical outcomes, valvular structural integrity, and hemodynamic changes in a large patient cohort evaluated a median of 3.7 years after TAVI (interquartile range [IQR] 3.4 to 4.3 years).

Methods

Patients

The present analysis included patients undergoing TAVI in our institution between January 2005 and December 2006, including the first-in-human transarterial and off-pump transapical series. Given our aim to study long-term outcomes and durability, patients with unsuccessful procedures or early (<30 days) mortality were excluded from the present analysis, because these cases typically reflected procedural
difficulties encountered during implantation and the initial learning curve rather than issues with the transcatheter valve per se. All patients were evaluated at a minimum of 3 years after the procedure.

All patients had severe symptomatic aortic stenosis and were assessed to be unsuitable for surgery because of excessive or prohibitive surgical risk by a team of senior cardiologists and cardiac surgeons. All patients were approved on a compassionate-use basis and gave written informed consent.

Initial cases were performed by the transfemoral approach, with availability of the transapical approach from October 2005. Patients were initially assessed for the procedure with echocardiography, cardiac catheterization, and angiography of the aortic root and iliofemoral arterial system. The transapical approach was used if the iliofemoral arterial system was of small caliber or severely tortuous and calcified. Patients were excluded from the procedure if they were candidates for conventional open heart surgery, if the aortic annulus diameter was <18 or >26 mm, or if a reasonable quality or duration of life after the procedure was unlikely.

Procedures

The techniques for transfemoral and transapical aortic valve implantation have been described previously.2-4,11,12 Transfemoral procedures were performed in the cardiac catheterization laboratory, and transapical procedures were performed in the operating room with mobile image intensifiers used for fluoroscopic guidance. Patients were preloaded with aspirin (325 mg) and clopidogrel (300 to 600 mg) and continued to take clopidogrel (75 mg) for 6 months and aspirin (81 mg) indefinitely. In patients requiring anticoagulation (eg, those with atrial fibrillation), clopidogrel therapy was discontinued when the international normalized ratio reached ≥2.0.

From January 2005 to June 2006, the balloon-expandable Cribier-Edwards (Edwards Lifesciences, Irvine, Calif) equine valve was implanted. After June 2006, the Edwards SAPIEN bovine valve (Edwards Lifesciences) was used. Initial transfemoral and transapical procedures were performed with the RetroFlex delivery catheter.13 Subsequent procedures used the RetroFlex-II delivery system (Edwards Lifesciences) for transfemoral procedures and the Ascendra transapical catheter (Edwards Lifesciences) for transapical procedures.2

Data Collection and Definitions

Patients were enrolled in a prospective registry, with clinical evaluations at 1, 6, and 12 months after TAVI. Subsequent annual follow-up was performed either by the implantation team or by the local physician. In all cases, patients underwent a verbal interview with the implantation team either in person or by telephone.

Transthoracic echocardiography was performed before hospital discharge and then at similar intervals at the implantation center. Aortic valve area was calculated with the continuity equation (velocity-time integral method) from data derived before and after device implantation. Measurement of the left ventricular outflow tract for calculations of aortic valve area was performed with 2-dimensional imaging in a zoomed-up parasternal long-axis view. For patients located geographically far from Vancouver, Canada (eg, Toronto, Canada, or Houston, Tex) and unable to return to the implantation center for further studies, these measurements were undertaken by an experienced local service, and detailed echocardiography reports were used. Aortic incompetence (AI) was classified as follows: None, trivial, mild, moderate, or severe.14,15

Structural valve deterioration was defined as dysfunction or deterioration of the implanted valve (excluding that caused by infection or thrombosis) as determined by clinical investigation, reoperation, or autopsy and referred to changes intrinsic to the valve, including wear, fracture, calcification, leaflet retraction/disruption, or overlap in the struts of the stent or between adjacent cells.

Functional class was assessed with New York Heart Association (NYHA) definitions. Myocardial infarction was defined as ischemic symptoms associated with ECG changes or a 3-fold rise in cardiac biomarkers. A neurological event was defined as any new neurological deficit, whether temporary or permanent and whether global or focal. Postprocedural bleeding was defined as any episode of major internal or external bleeding that occurred after hospital discharge that caused death, hospitalization, or permanent injury or necessitated transfusion of >3 U of blood. Frailty was defined according to the criteria of Fried et al.17 Renal function was assessed by the glomerular filtration rate with the Modification of Diet in Renal Disease equation.18 Stent fracture was defined as visible separation or overlap in the struts of the stent or between adjacent cells.

Computed Tomography

To help assess structural integrity, stent fracture, and potential migration of implanted valves, focused cardiac/aortic computed tomography (CT) evaluation was performed. All patients with glomerular filtration rate >45 mL/min were requested to return for CT evaluation. Studies were performed at a minimum of 3 years after the procedure. CT examinations were performed with 64-slice scanners. Retrospective gating was used to enable measurements of the transcatheter aortic valve stent during systolic phases of the cardiac cycle to allow measurements to be taken in a similar fashion to preprocedural annular assessments, as described previously.19 Studies were read with AW 4.3-4.4 Advantage Workstations (GE Healthcare, Milwaukee, Wis). Axial data sets, maximum-intensity projections, curved multplanar reformats, and other postprocessing tools were all used for image analysis. By convention, orthogonal views of the stents were reconstructed with a double-oblique technique, and then measurements were made in the sagittal and coronal directions.20 The internal diameters of the stents were measured at the base and distal aspect. The positions are described as “annular” (representing the base inflow ventricular end) and “aortic”;

Figure 1. A, Three-dimensional volume-rendered reconstruction of the ascending aorta with an Edwards SAPIEN valve in situ. Orthogonal projections of the valve at the level of the annulus (B) and distal aortic end of the stent (C; coronal diameter, white line; sagittal diameter, black line). D, Curved multplanar reformat of the left main coronary artery and the ascending aorta showing the relationship of the left main ostium and the distal end of the valve. The distance measured is represented by the black arrowhead.
Table 1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Patients (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean±SD</td>
<td>84.7±7.6</td>
</tr>
<tr>
<td>Age ≥90 y, n (%)</td>
<td>10 (14.2)</td>
</tr>
<tr>
<td>Logistic EuroSCORE, mean±SD</td>
<td>31.7±16</td>
</tr>
<tr>
<td>STS score, %, mean±SD</td>
<td>9.6±3.5</td>
</tr>
<tr>
<td>STS &gt;10% and/or logistic EuroSCORE &gt;20, n (%)</td>
<td>57 (81.4)</td>
</tr>
<tr>
<td>Transfemoral procedure, n (%)</td>
<td>55 (78.6)</td>
</tr>
<tr>
<td>Transapical procedure, n (%)</td>
<td>15 (21.4)</td>
</tr>
<tr>
<td>Cribier-Edwards THV, n (%)</td>
<td>49 (70)</td>
</tr>
<tr>
<td>Edwards SAPIEN THV, n (%)</td>
<td>21 (30)</td>
</tr>
<tr>
<td>Prior thoracotomy, n (%)</td>
<td>26 (37.1)</td>
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<tr>
<td>Porcelain aorta, n (%)</td>
<td>19 (27.1)</td>
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<td>Chronic lung disease, n (%)</td>
<td>24 (34.3)</td>
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<td>Pulmonary hypertension, n (%)</td>
<td>18 (25.7)</td>
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<tr>
<td>Cerebral vascular disease, n (%)</td>
<td>17 (24.3)</td>
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<td>Cerebral ischemic event, n (%)</td>
<td>11 (15.7)</td>
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<tr>
<td>Peripheral vascular disease, n (%)</td>
<td>22 (31.4)</td>
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<tr>
<td>Prior myocardial infarction, n (%)</td>
<td>55 (78.6)</td>
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<tr>
<td>Frailty,17 n (%)</td>
<td>16 (22.9)</td>
</tr>
<tr>
<td>Glomerular filtration rate ≥60 mL/min, n (%)</td>
<td>39 (55.7)</td>
</tr>
<tr>
<td>Glomerular filtration rate &lt;30 mL/min, n (%)</td>
<td>7 (10)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction ≤35%, n (%)</td>
<td>12 (17.1)</td>
</tr>
<tr>
<td>Mitral regurgitation more than moderate, n (%)</td>
<td>30 (42.9)</td>
</tr>
<tr>
<td>Obesity, n (%)</td>
<td>25 (35.7)</td>
</tr>
<tr>
<td>Morbid obesity, n (%)</td>
<td>10 (14.2)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>17 (24.3)</td>
</tr>
</tbody>
</table>

STS indicates Society of Thoracic Surgeons; THV, transcatheter heart valve.

Statistical Analysis
Continuous variables are described as mean±SD when normally distributed or as medians with IQRs when not. Normality was tested with the Shapiro-Wilks goodness-of-fit test. Categorical variables are described by frequencies and percentages. For the end points of aortic valve area and transaortic mean gradient, a mixed-effects model with generalized estimating equations was used, and adjustment for the baseline value was performed to test for a trend over time from immediately after the procedure to 3 years later. Because of the skewed distribution of the transaortic mean gradient, a log transformation was applied before analysis. For the outcome of NYHA class, a logistic regression with generalized estimating equation was used to test for changes from year 1 to year 3 in NYHA III/IV compared with NYHA I/II. All models used an unstructured covariance structure in the generalized estimating equation modeling. The estimate of the regression coefficient for time and the associated 95% confidence limits are provided. Testing was based on a significance level of 0.05. Survival, major adverse cardiovascular and cerebrovascular events, and major adverse valve-related events were expressed with a Kaplan-Meier time-to-event analysis. Analyses were conducted with SAS 9.2 (SAS Institute, Inc).

Results
Baseline Characteristics
Seventy patients formed the study cohort, of whom 55 had a transfemoral procedure and 15 had a transapical procedure (Table 1). During the study period, an additional 8 patients had failed procedures, and 11 patients died within 30 days (2 patients were in both groups) and were excluded from the main analysis. Baseline estimated surgical risk was high (mean logistic EuroSCORE [European System for Cardiac Operative Risk Evaluation] 31.7±16, Society of Thoracic Surgeons score 9.6±3.5). Median follow-up was 3.7 years (IQR 3.4 to 4.3 years), with a minimum duration from implantation of 3 years and a maximum of 5 years. Mean age was 84.7±7.6 years. Significant comorbidities were common and included frailty (22.9%), age ≥90 years (14.2%), obesity (35.7%), morbid obesity (14.2%), glomerular filtration rate <60 mL/min (55.7%), porcelain aorta (27.1%), chronic lung disease...
Survival
The 70 patients with successful procedures who survived past 30 days had an overall survival rate of 57% at a median of 3.7 years. Survival at 1, 2, and 3 years was 81%, 74%, and 61%, respectively (Figure 2). Overall survival free from reoperation was 98.5% (1 patient with endocarditis). When all patients with attempted procedures were included (including those with <30-day mortality), the overall survival was 51%

Valve-related mortality occurred in 3 cases. Two deaths were secondary to intracerebral hemorrhage, both of which were in the setting of supratherapeutic anticoagulation with coumadin (international normalized ratios of 13 and 4, respectively). The remaining death was sudden and occurred in a 99-year-old woman 2.8 years after the procedure who had a well-functioning valve on echocardiogram 8 months before her death. Postmortem evaluation revealed a structurally intact prosthesis with no evidence of deformation (Figure 3). It appeared circular and well expanded, with no identifiable perivalvular probe patent defect. The leaflets were freely mobile, with no evidence of thrombosis, perforation, or vegetations. There were small amounts of fibrous connective tissue in the vicinity of the commissural regions and extending in and around the metallic mesh. No deaths were directly related to valvular dysfunction. The most common cause of mortality was respiratory problems (8 deaths, 26.7%; Table 2).

Morbidity
The overall rate of major adverse cardiovascular and cerebrovascular events at 3 years was 48.6%, and the overall rate of major adverse valve-related events was 21.4% (Figure 2). Major adverse cardiovascular and cerebrovascular events were primarily contributed to by mortality (Table 3). Post-procedural bleeding events were uncommon and generally occurred in the setting of combination therapy with antiplatelet agents and anticoagulants or supratherapeutic anticoagulation. The overall neurological event rate at 3 years was 8.6%, of which more than two thirds occurred more than 6 months after valve implantation. Only 1 patient required percutaneous coronary intervention, more than 2 years after TAVI. Coronary vessels were successfully engaged in all patients who underwent subsequent coronary angiography after TAVI (Figure 4).

The single case of valve endocarditis occurred 5 months after implantation and required high-risk reoperation. The patient had a prolonged in-hospital course and a transient ischemic attack but survived.

Functional Class
At baseline, 1%, 3%, 69%, and 17% of patients were in NYHA class I, II, III, and IV, respectively (Figure 5). At
1-year follow-up, 93% of surviving patients were in NYHA class I/II. In surviving patients who were in NYHA class III or IV at baseline, 85% and 100% had improved by at least 1 functional class, respectively. Throughout the follow-up period, ≥90% of surviving patients remained in NYHA class I/II. There was no significant difference in the likelihood of being in NYHA class III/IV versus NYHA I/II from year 1 to year 3 (odds ratio 1.26, 95% confidence limits 0.74 to 2.16, P=0.40).

Echocardiographic Findings
Echocardiographic follow-up was available for 37 of 43 patients who were alive at 3 years. The transaortic gradient decreased from 45.0 mm Hg (IQR 33.5 to 55 mm Hg) at baseline to 10.0 mm Hg (IQR 8.0 to 12.0 mm Hg) after the procedure (P<0.01). Subsequently, there was a small increase in the transaortic gradient at 3 years to 12.1 mm Hg (IQR 8.6 to 16.0 mm Hg), which corresponded to an average annualized increase of 3.8% (95% confidence limits 0.3% to 7.3%, P=0.03; Figure 6).

The calculated aortic valve area increased from 0.6±0.2 cm² at baseline to 1.7±0.4 cm² after the procedure (P<0.01). Subsequently, there were reductions in the mean area at 12 months (1.5±0.3 cm²) and 36 months (1.4±0.3 cm²; Figure 7). This represents an annualized decrease by −0.06 cm² (95% confidence limits −0.09 to −0.02) per year (P<0.01).

AI was a common finding after the procedure and was trivial in severity in 40%, mild in 44%, and moderate in 6%. There were no cases of severe AI. One patient progressed from mild to moderate AI. This was paravalvular, noted at 6 months, and remained unchanged at 12 months. The patient died 3 months before his next scheduled echocardiogram. Of the 4 patients with moderate AI, 2 cases improved to mild AI by 6 months and 2 remained unchanged.

Of the total cohort, 30 patients had serial echocardiograms 3 years after the procedure that were of sufficient quality to quantify the degree of AI at both time points. All patients with mild postprocedural AI were either unchanged or improved over time. There were no cases of progression to moderate or severe AI (Table 4).

CT Findings
CT scans were performed in 21 patients at a minimum of 3 years after implantation. There were no cases of stent fracture, visible leaflet thickening, calcification, or fusion and no evidence of thrombus. There were no significant differences between sagittal and coronal measurements at the annular or aortic ends, which suggests that valves were circular (Table 4).

Eight patients had CT scans immediately after the procedure and after a minimum of 3 years of follow-up that allowed for serial comparisons. In these, no evidence of stent migration was detected as measured by the distance from the top of the stent to the origin of the left main coronary artery ostium (mean distance after procedure 3.0±3.6 mm; mean distance at follow-up 1.9±3.7 mm; P=0.24). With regard to valve size after the procedure, the diameter at the annular end was slightly smaller than at the aortic end (sagittal annular diameter 19.9 mm versus aortic diameter 21.3 mm, P=0.02; coronal annular diameter 20.8 mm versus aortic diameter 21.9 mm, P=0.29). At long-term follow-up, this difference was no longer apparent (sagittal annular diameter 20.0 mm versus aortic diameter 20.1 mm, P=0.74), and similar results were noted in the coronal projection (annular diameter 20.3 mm versus aortic diameter 20.6 mm, P=0.52). Although there was no significant change at the annular end with time, there was a small decrease in diameter at the aortic end (Table 5).

Valve Structural Integrity
There were no cases of structural or nonstructural valvular deterioration. There were no cases of valve thrombosis or late valve embolization. No patients required valvuloplasty, repeat procedures, or surgery on the implanted valve to treat stenosis or regurgitation.

Discussion
The present study reports the outcomes of a cohort of TAVI patients with the longest follow-up currently available. The balloon-expandable valve appears durable to a median of 3.7 years.

Table 3. Major Adverse Outcomes at 3 Years

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients (n=70)</th>
</tr>
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<tbody>
<tr>
<td>Death</td>
<td>27 (38.6)</td>
</tr>
<tr>
<td>MACCE</td>
<td>34 (48.6)</td>
</tr>
<tr>
<td>MAVRE</td>
<td>15 (21.4)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>6 (8.6)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>6 (8.6)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Postprocedural bleeding</td>
<td>5 (7.1)</td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>New permanent pacemaker</td>
<td>5 (7.1)</td>
</tr>
<tr>
<td>Structural valve deterioration</td>
<td>0</td>
</tr>
<tr>
<td>Nonstructural valve deterioration</td>
<td>0</td>
</tr>
<tr>
<td>Late valve embolization</td>
<td>0</td>
</tr>
<tr>
<td>Valve thrombosis</td>
<td>0</td>
</tr>
</tbody>
</table>

MACCE indicates major adverse cardiac and cerebrovascular events; MAVRE, major adverse valve-related events.

Values are n (%) or n.
years and as long as 5 years, with no evidence of structural valvular deterioration and no requirements for reintervention for valve stenosis or regurgitation.

Clinical Outcomes

The present study cohort represents one of the earliest experiences of TAVI, at a time when the procedural learning curve was high, equipment evolution was rapid, and various techniques and equipment were often used on a first-in-human basis. For the present analysis to focus primarily on long-term durability and outcomes, we excluded patients with procedural failures and those who had early (≤30 days) mortality. The survival rate of 57% at a median of 3.7 years is not unexpected in the extremely high-risk patients evaluated during the early phase of TAVI and compares favorably with studies assessing survival in elderly patients with severe aortic stenosis who do not undergo valve replacement. Such patients, when left untreated, quickly succumb to the disease; Kojodjojo et al reported a 1-year survival rate of only 51% in patients who were not surgical candidates and 66% in those who declined surgery. Similarly, Bach et al reported a 1-year survival rate of only 62% in unoperated patients.

The baseline risk level of the study population was extremely high, and significant comorbidities were common. Subsequently, patients died either because of their comorbidities or secondary to conditions associated with advanced age. This poses an obvious challenge for longer-term follow-up of transcatheter valve implantation in elderly high-risk patients. In current practice, the procedure is generally only performed in patients with prohibitive or elevated risk due to comorbidities or advanced age, and in these populations, the valve appears to outlast the patient. Although the relief of otherwise terminal and untreatable aortic stenosis is welcome, the future challenge is to select patients who would both benefit from the procedure and have a reasonable quality of life not limited by severe comorbidities. Longer follow-up of this elderly high-risk population will be difficult to achieve. It appears likely, however, that a lower-risk population would have higher long-term survival and would allow longer evaluation of clinical outcomes, as well as valvular function and hemodynamics.

Valve-related mortality occurred in 3 patients. Although we used accepted definitions for reporting such events after surgical valve replacement, it appears unlikely that any of the
deaths in the present cohort occurred as a direct result of the transcatheter valves. In a patient who died suddenly, postmortem examination found no significant structural valvular abnormality. The overall neurological event rate in the present study cohort (8.6%) appears low given previously reported1,3 periprocedural event rates of 4.2% to 5.5%; however, given that most periprocedural strokes are terminal events,1 such patients would have been excluded from the present analysis. The residual neurological event rates more likely reflect late neurological events in a high-risk population, as evidenced by the majority of such events occurring more than 6 months after valve implantation.

All postprocedural bleeding events occurred in the setting of anticoagulation with warfarin. Two patients had intracerebral hemorrhage, with the remainder being of gastrointestinal origin. The indication for anticoagulation was atrial fibrillation in all cases (patients did not undergo anticoagulation on the basis of valve implantation). This highlights the elevated risk of anticoagulant therapy in this elderly high-risk population. There is a currently a paucity of data on the optimal antithrombotic regimen after TAVI. During the study period, dual-antiplatelet therapy was prescribed for 6 months, followed by aspirin alone. For patients requiring warfarin, clopidogrel was discontinued when warfarin reached therapeutic levels. However, it may be reasonable to omit antiplatelet agents entirely or shorten their treatment duration in patients who are undergoing concomitant anticoagulation. Further trials are required to evaluate the best and safest approach that balances the risk of bleeding with potential thromboembolic complications.

Valvular Function
The present study demonstrated excellent valve durability, with no evidence of structural valve deterioration or need for reoperation for stenosis or regurgitation at a median of 3.7 years. A small decrease in the calculated valve area and a small increase in the transvalvular gradient were observed. These changes are unlikely to be clinically significant given their small magnitude and the sustained functional improvements. Surgically implanted bioprostheses tend to fail 10 to 15 years after implantation because of factors such as leaflet calcification or tearing, which lead to either stenosis or

Table 4. Valve Dimensions Measured by CT

<table>
<thead>
<tr>
<th></th>
<th>Aortic Valve Diameter Immediately After Implantation</th>
<th>Aortic Valve Diameter &gt;3* Years After Implantation</th>
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<tbody>
<tr>
<td></td>
<td>Annular, mm</td>
<td>Aortic, mm</td>
</tr>
<tr>
<td>Entire cohort (n=21)</td>
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<tr>
<td>Sagittal</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Coronal</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Matched cohort (n=8)</td>
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<tr>
<td>Sagittal</td>
<td>19.9</td>
<td>21.3</td>
</tr>
<tr>
<td>Coronal</td>
<td>20.8</td>
<td>21.9</td>
</tr>
</tbody>
</table>

Annular indicates the inflow/ventricular end of the valve; aortic, the outflow/upper end of the valve; and N/A, not available.
Changes in valve dimensions in the coronal and sagittal planes were measured with CT. Eight patients had scans immediately and >3 years after implantation, which allowed for serial comparison (bottom row).
Changes in dimensions in each plane and position are represented. There were no significant differences between sagittal vs coronal dimensions at each level at a given time point (all $P>$0.20).
*Follow-up CT was performed at a median of 3.4 years (IQR 3.2–3.6 years).
† $P=0.20$ vs immediately after implantation.
‡ $P=0.01$ vs immediately after implantation.
§ $P=0.29$ vs immediately after implantation.
‖ $P=0.05$ vs immediately after implantation.
regurgitation.6,7,24 We noted an annualized aortic valve area reduction of 0.06 cm² and a gradient progression of 3.8%, which compares well with a recent series that evaluated surgically implanted bioprosthetic aortic valves and showed an annualized rate of mean gradient progression of 0.6 mm Hg per year.25

**Aortic Incompetence**

Previous studies have demonstrated that AI is a common finding after TAVI, with the majority of cases being of mild severity and paraavalvular in nature.1,26 In the present study, postprocedural AI was also common and generally mild. Although we attempted to determine the origin of incompetence in all follow-up echocardiograms, this was not possible in a substantial number. No other studies have assessed the natural history or progression of AI after implantation of the Edwards balloon-expandable valve. Rajani et al.27 recently reported on 13 patients treated with the Medtronic CoreValve (Medtronic, Minneapolis, Minn) bioprosthesis, in whom incompetence was noted in 86%, was generally mild, and remained stable in 70% of patients up to 12 months of follow-up. The present study demonstrates that most AI either remains unchanged or improves. In cases in which deterioration was noted, this was by less than 1 regurgitant grade.

**CT Evaluation**

We found no evidence of late stent fracture, valve movement, aortic erosion from the stent frame, thrombus, leaflet thickening, fusion, or calcification. It has been established that the native aortic annulus is an oval rather than a circular structure.19,20,28,29 Recent data suggest the aortic annulus becomes less elliptical after TAVI.29 Our late CT evaluation suggests the balloon-expandable valve remains circular, with no differences between sagittal and coronal measurements. Implanted valves were mildly but significantly smaller at the annular end than at the aortic end, consistent with some degree of underexpansion within the restraining native annulus. Although we noted a small, statistically significant decrease in the diameter of the stent at the aortic end, this was within the margin of error of CT measurements,30 and given the small serial follow-up cohort size, it should be corroborated by larger studies. It is reassuring that there was no late recoil at the annular end given the constraints of the annulus.

**Study Limitations**

The present study has a number of limitations. First, the patient population represents the earliest experience with TAVI, when knowledge about valve sizing and position was limited, which may have had a negative effect on valve deterioration rates. Current practices in which valves are frequently oversized may result in improved hemodynamics. Second, echocardiographic follow-up of bioprostheses is often difficult, with variability in reporting by different laboratories. Evaluation by a core laboratory was not performed as part of the present study. A proportion of the present cohort was unable to return to the implantation center for follow-up, largely owing to geographical constraints; however, because the same experienced peripheral center usually performed serial echocardiograms for a given patient, this allowed for consistency and assessment of change. Third, given the contrast load required for CT evaluation, patients were often excluded if renal function was poor. Such patients may in turn have more aggressive disease progression or calcification, although this was not noted on echocardiography.

**Conclusions**

Transcatheter valve implantation is a relatively new and promising technique for treatment of aortic valve disease. Medium- to long-term results after TAVI are reassuring, with excellent valve durability, no evidence of structural valvular failure, and preserved hemodynamics resulting in favorable clinical outcomes. When used in patients who are deemed a poor surgical risk, the procedure offers an adequate and lasting resolution of aortic stenosis.

**Disclosures**

Drs Cheung, Webb, and Ye are consultants to Edwards Lifesciences. Dr Leipsic is on the speaker’s bureau for Edwards Lifesciences. The remaining authors report no conflicts.

**References**


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**CLINICAL PERSPECTIVE**

Transcatheter aortic valve implantation is rapidly gaining acceptance as a viable therapy for high-risk patients with severe symptomatic aortic stenosis. Thus far, short-term outcomes have been encouraging, with limited data beyond 1 year. The present study evaluated the medium- to long-term outcomes of an early cohort undergoing transcatheter aortic valve implantation, with all patients evaluated by follow-up at a minimum of 3 years from the procedure. The study demonstrated excellent durability, with no evidence of structural valvular failure, and preserved hemodynamics. Small changes in valve area and transvalvular gradients were documented for the first time, which were generally similar to those in previously published surgical series that reported on bioprosthetic valves in the aortic position. Patients showed significant improvement in functional state, which appeared to be preserved over time. Postprocedural aortic regurgitation was generally mild and did not appear to worsen over time. Detailed computed tomographic imaging demonstrated no evidence of valve fracture, deformation, or valve migration. At a median of 3.7 years, patients surviving more than 30 days after a successful procedure had a survival rate of 57%. The bulk of late mortality in this high-risk cohort was due to significant comorbidities and was generally unrelated to aortic valve disease. Overall, when used in patients who are deemed to be poor surgical candidates, transcatheter aortic valve implantation appears to offer an adequate and lasting resolution of symptomatic aortic stenosis.
Transcatheter Aortic Valve Implantation: Durability of Clinical and Hemodynamic Outcomes Beyond 3 Years in a Large Patient Cohort

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