Comparison Between Transcatheter and Surgical Prosthetic Valve Implantation in Patients With Severe Aortic Stenosis and Reduced Left Ventricular Ejection Fraction

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Background—Patients with severe aortic stenosis and reduced left ventricular ejection fraction (LVEF) have a poor prognosis with conservative therapy but a high operative mortality when treated surgically. Recently, transcatheter aortic valve implantation (TAVI) has emerged as an alternative to surgical aortic valve replacement (SAVR) for patients considered at high or prohibitive operative risk. The objective of this study was to compare TAVI and SAVR with respect to postoperative recovery of LVEF in patients with severe aortic stenosis and reduced LV systolic function.

Methods and Results—Echocardiographic data were prospectively collected before and after the procedure in 200 patients undergoing SAVR and 83 patients undergoing TAVI for severe aortic stenosis (aortic valve area ≤1 cm²) with reduced LV systolic function (LVEF ≤50%). TAVI patients were significantly older (81±8 versus 70±10 years; P<0.0001) and had more comorbidities compared with SAVR patients. Despite similar baseline LVEF (34±11% versus 34±10%), TAVI patients had better recovery of LVEF compared with SAVR patients (ΔLVEF, 14±15% versus 7±11%; P=0.005). At the 1-year follow-up, 58% of TAVI patients had a normalization of LVEF (>50%) as opposed to 20% in the SAVR group. On multivariable analysis, female gender (P=0.004), lower LVEF at baseline (P=0.005), absence of atrial fibrillation (P=0.01), TAVI (P=0.007), and larger increase in aortic valve area after the procedure (P=0.01) were independently associated with better recovery of LVEF.

Conclusion—In patients with severe aortic stenosis and depressed LV systolic function, TAVI is associated with better LVEF recovery compared with SAVR. TAVI may provide an interesting alternative to SAVR in patients with depressed LV systolic function considered at high surgical risk. (Circulation. 2010;122:1928-1936.)

Key Words: aortic stenosis ■ echocardiography ■ prosthesis ■ stenosis ■ valves

Patients with severe aortic stenosis (AS) and reduced left ventricular (LV) ejection fraction (LVEF) have a dismal prognosis when treated conservatively. Accordingly, the guidelines recommend performing aortic valve replacement (AVR) in patients with severe AS presenting with LVEF <50% (Class I indication).1 The improvement in LVEF after AVR varies extensively from one patient to another, and LVEF often remains abnormal. Moreover, AVR is associated with markedly increased operative mortality in patients with severe AS and reduced LVEF.2–6

Clinical Perspective on p 1936

In recent years, transcatheter aortic valve implantation (TAVI) has emerged as an alternative to surgical AVR (SAVR) in patients considered at high or prohibitive surgical risk.7–10 We recently reported that TAVI is associated with better hemodynamic performance and thereby less incidence of prosthesis-patient mismatch compared with SAVR with stented or stentless bioprostheses.11 In this regard, previous studies have shown that patients with depressed LV systolic function are extremely sensitive to the residual pressure overload imposed by prosthesis-patient mismatch.12–14 Moreover, the ischemic, oxidative stress, and inflamatory injuries associated with open heart surgery induce apoptosis of a significant proportion of cardiomyocytes, which may compromise postoperative recovery of myocardial function.15,16 We thus hypothesized that TAVI would be associated with...
better recovery of LVEF compared with SAVR. The primary objective of the study was to compare TAVI and SAVR with respect to postprocedural change in LVEF in patients with severe AS and reduced LV systolic function. The secondary objective was to compare these 2 procedures with regard to periprocedural mortality in this high-risk group of patients.

Methods

We analyzed the clinical and echocardiographic data of 200 patients who underwent SAVR with or without coronary artery bypass grafting (CABG) between 2006 and 2008 and 83 patients who underwent TAVI with or without preemptive percutaneous coronary intervention between 2005 and 2009 at Quebec Heart and Lung Institute (formerly Laval Hospital, Quebec, Canada), St Paul Hospital (Vancouver, Canada), Adult Congenital and Valvular Heart Disease Center (Muenster, Germany), Vienna General Hospital (Vienna, Austria), or University of Ottawa Heart Institute (Ottawa, Canada). Inclusion criteria were an aortic valve area (AVA) ≤1 cm², indexed AVA ≤0.6 cm²/m², and LVEF ≤50%. We excluded from this study patients who did not have LVEF measured by echocardiography at the participating centers within 1 month before the procedure and patients living long distances from the participating centers who planned to have their postdischarge clinical and echocardiographic follow-up performed at another hospital. Clinical, Doppler echocardiographic, operative, and outcome data were collected prospectively at each participating center. The study protocol was performed in accordance with the institutional ethics committees of each participating center, and all patients gave informed written consent for the procedures. The need for consent to participate in this research study was waived in view of its observational and anonymous nature.

SAVR Procedure

The SAVR interventions were performed through a standard midline sternotomy with cardiopulmonary bypass and mild systemic hypothermia. Patients undergoing aortic root enlargement, the Bentall procedure, or a concomitant procedure on another valve (eg, mitral or tricuspid valve repair or replacement) were excluded. A stented bioprosthesis was implanted in 142 patients (71%) and a mechanical valve in 58 patients (29%). The prosthesis size was selected according to the size of the aortic annulus, as determined by the manufacturer’s size. The distribution of the models and sizes of prostheses implanted in the SAVR group are shown in the online-only Data Supplement. The distribution of prosthesis size in the SAVR group was as follows: 3% for 19 mm, 17.5% for 21 mm, 38.5% for 23 mm, 31% for 25 mm, and 10% for 27 mm. Concomitant CABG was performed in 117 patients (59%). In those patients, the mean number of grafted vessels was 2.2 ± 1.2 (range, 1 to 5).

TAVI Procedure

TAVI was performed with the use of the Cribier-Edwards or Edwards SAPIEN (Edwards Lifesciences Inc, Irvine, Calif) balloon-expandable prostheses. Two valve sizes of 23- and 26-mm expanded diameter were available. The 23-mm valve was selected if aortic annulus diameter was between 16 and 21 mm by transesophageal echocardiography, and the 26-mm valve was selected if the diameter was between 22 and 25 mm. Forty-eight percent of patients received a 23-mm valve, and 52% received a 26-mm valve (online-only Data Supplement). Patients included in the Placement of Aortic Transcatheter Valve (PARTNER) trial were excluded from this analysis. TAVI was approved for compassionate use by the Canadian Department of Health and Welfare (Ottawa, Canada) in patients with symptomatic severe AS considered either nonoperative or very-high-risk surgical candidates. The procedures were performed by transfemoral approach in 44 patients (53%) and by transapical approach in 39 patients (47%) using techniques described in detail in previous reports.8,10 Preemptive percutaneous coronary intervention was performed at the discretion of the surgeon within the 60 days preceding TAVI in 42 patients (51%) in whom the mean number of stents was 1.5 ± 0.5 (range, 1 to 2).

Assessment of Coronary Artery Disease Severity and Completeness of Revascularization

The severity of coronary artery disease was assessed by the angiographic Duke Myocardial Jeopardy Score, which expresses how many of the 6 coronary arterial segments are jeopardized by significant (>70% estimated luminal area reduction) stenoses; 2 points are added to the score for each jeopardized segment. Complete revascularization was defined as the insertion of at least 1 stent or graft in each diseased territory (right coronary artery, left anterior descending artery, and circumflex system).18

Doppler Echocardiography

Patients underwent Doppler echocardiographic examination at baseline, hospital discharge, and 1-year (12±3 months) follow-up. Acquisition and collection of the Doppler echocardiographic data were standardized in the 5 centers11,19,20 and echocardiographic data were analyzed in each center by the same experienced echocardiographers. The Doppler echocardiographic measurements included LV end-diastolic volume, LVEF calculated with the Simpson method, transvalvular pressure gradient determined by the Bernoulli formula, and AVA calculated by the continuity equation. The AVA was indexed for body surface area, and the occurrence of severe prosthesis-patient mismatch was defined as an indexed AVA ≤0.65 cm²/m². Twenty-five echocardiographic exams were randomly selected, and measurements of gradient, AVA, and LVEF were repeated by 2 independent observers. The values of intraobserver and interobserver variability were 2.1% and 4.1% for mean gradient, 4.7% and 8.5% for AVA, and 5.5% and 8.2% for LVEF.

The degree of aortic and mitral regurgitation (MR) was classified as mild, moderate, and severe.22 Seventy-one patients included in this series underwent a low-dose (up to 20 μg/kg·min−1) dobutamine stress echocardiography to assess myocardial contractile reserve and to corroborate stenosis severity.19

Statistical Analysis

Results are expressed as mean±SD or percentages unless otherwise specified. Continuous variables were tested for distribution normality with the Shapiro-Wilk test. Differences between patient groups were analyzed with the use of the 2-sided Student t test for continuous variables, Wilcoxon rank-sum test for ordinal variables, and the χ² test or Fisher exact test for categorical variables as appropriate. The association between periprocedural (30-day) mortality and the risk factors was examined by logistic regression analysis. A 2-way ANOVA or ANCOVA for repeated measures, followed by a Tukey posthoc test, was used to evaluate the effects of time (baseline versus discharge versus 1 year) and treatment (SAVR versus TAVI) on Doppler echocardiographic variables. Multivariable linear regression analysis was used to identify the independent predictors of postprocedural LVEF recovery. Clinically relevant variables with a value of P<0.05 on individual analysis were included in the multivariable models.

To eliminate covariate differences that may lead to biased estimates of treatment effect, a propensity score adjustment was also used. A propensity score representing the probability of having TAVI as opposed to SAVR was calculated for each patient by using a logistic regression analysis that identified variables independently associated with the type of procedure. The calculated propensity score was then incorporated into subsequent ANCOVA and multivariable regression models. The effect of the clinical and Doppler echocardiographic variables on survival was assessed with Cox proportional-hazard models. Clinically relevant variables with a value of P<0.05 on individual analysis were incorporated into the multivariable models.

A value of P<0.05 was considered statistically significant. Statistical analyses were performed with JMP 7.0.2 and STATISTICA 9.0 software.
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

Patients treated by TAVI were older, were more frequently women, had a smaller body surface area, and had more comorbidities compared with patients treated by SAVR (Table 1). Accordingly, the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgeon (STS) scores were 2-fold higher in TAVI than in SAVR group. Baseline AVA was significantly (P = 0.003) smaller in the TAVI group. After AVA was indexed for body surface area, the difference remained statistically significant (P = 0.04) but was not clinically relevant (0.36 versus 0.38 cm²/m²). Furthermore, there was no significant difference between the 2 groups with regard to baseline transvalvular pressure gradient. TAVI patients also had a higher prevalence of MR, whereas baseline indexed LV end-diastolic volume and LVEF were similar in both groups. The Duke Myocardial Jeopardy Score before the revascularization procedure (ie, preemptive percutaneous coronary intervention or concomitant CABG) was also similar in both groups. One hundred eighty SAVR patients (90%) had complete revascularization or did not need any revascularization compared with 36 of the TAVI patients (43%; P < 0.0001). Although patients undergoing TAVI had a smaller LV outflow tract diameter compared with SAVR patients (Table 1), the median prosthesis size was larger (23 mm [interquartile range, 23 to 25 mm] versus 26 mm [interquartile range, 23 to 26 mm]; P < 0.001). This is related to the facts that with TAVI the operator generally uses a prosthesis size that is larger than the patient’s annulus and that the prosthesis is not necessarily expanded at its maximum size. Age, gender, body surface area, body mass index, New York Heart Association (NYHA) functional class, coronary artery disease, chronic kidney failure, previous myocardial infarction, previous stroke, previous open heart surgery, previous percutaneous coronary intervention, native AVA, and severity of MR at baseline were independently associated with the type of procedure and were used to calculate propensity score.

Periprocedural Mortality

During the first 30 days after the procedure, 24 patients in the SAVR group (12%) and 16 in the TAVI group (19%) died (P = 0.12 on individual analysis, P = 0.51 after adjustment for age, and P = 0.99 after adjustment for age and propensity score). The individual predictors of 30-day mortality were older age (odds ratio [OR] per 1-year increase, 1.05; 95% confidence interval [CI], 1.01 to 1.10; P = 0.01), history of myocardial infarction (OR, 2.24; 95% CI, 1.03 to 5.31; P = 0.04), previous open heart surgery (OR, 2.08; 95% CI, 1.00 to 4.39; P = 0.05), presence of MR (OR, 1.61; 95% CI, 1.12 to 2.34; P = 0.01), logistic EuroSCORE (OR per 1-point increase, 1.04; 95% CI, 1.02 to 1.06; P = 0.001), and STS score (OR per 1-point increase, 1.08; 95% CI, 1.02 to 1.14; P = 0.007).

We compared the predicted (by logistic EuroSCORE or STS score) and observed 30-day mortality rates in the first 50% and last 50% of patients treated in each center to assess the effect of learning curve on periprocedural mortality (Figure 1). As expected in the SAVR group, there was no evidence of a learning-curve effect; both the predicted and observed mortality rates decreased slightly (by 2%) in the
second half of patients compared with the first half, and the ratio of predicted (logistic EuroSCORE) to observed mortality remained unchanged at 1.5. In this group, the logistic EuroSCORE overestimated 30-day mortality by an average of 6% (absolute), whereas the STS score underestimated mortality by an average of −6%. In the TAVI group, the observed 30-day mortality decreased by 6%, the predicted mortality by logistic EuroSCORE increased by 5%, and the ratio of predicted to observed mortality increased from 1.3 to 2.1 in the second versus first half of patients, suggesting the presence of a learning-curve effect.

Postprocedural Changes in Doppler Echocardiographic Variables

Among the 283 patients enrolled in the study, 161 (120 SAVR and 41 TAVI) had a Doppler echocardiographic follow-up in the participating centers at 12 ± 3 months after the procedure. TAVI was associated with better improvement in AVA and transvalvular gradient compared with SAVR (Table 2). The postprocedural increase in AVA (absolute, 0.82 ± 0.07 versus 0.63 ± 0.05 cm²; P = 0.003; percent: 145 ± 13% versus 90 ± 10%, P = 0.002) and reduction in gradient (absolute, −27 ± 13 versus −18 ± 15 mm Hg, P = 0.003; percent: −71 ± 15% versus −51 ± 28%, P < 0.001) were significantly larger in TAVI than in SAVR patients. Accordingly, TAVI patients had a lower incidence of severe prosthesis-patient mismatch (16%) compared with SAVR patients (29%).

Aortic regurgitation (transvalvular or paravalvular) was more frequent at discharge and at the 1-year follow-up in the TAVI group than in the SAVR group. Prevalence of mild and moderate aortic regurgitation was 26% and 6% in the TAVI group, respectively, versus 4% and 0% in the SAVR group at discharge and 31% and 6% in the TAVI group versus 5% and 0% in the SAVR group at the 1-year follow-up (P = 0.002).

TAVI patients had more frequent and more severe MR at baseline, and the extent of postprocedural reduction in MR was similar in both groups (P = 0.73). Consequently, the prevalence and severity of MR remained significantly higher (P = 0.006) in the TAVI group than in the SAVR group 1 year after the procedure (TAVI: mild, 43%; moderate, 25%; and severe, 3%; SAVR: 23%, 7%, and 0%, respectively).

TAVI patients had faster and better recovery of LVEF after the procedure compared with SAVR patients (Figure 2A). They also had better regression of LV dilation (reduction in indexed LV end-diastolic volume at 1 year, −15 ± 22 versus

![Table 2. Postprocedural Changes in AVA and Gradient](attachment:image)

![Figure 1.](attachment:image)

![Figure 2.](attachment:image)

Tukey posthoc test: *P < 0.05 versus SAVR; †P < 0.05 versus baseline.
had better late cardiovascular survival (Cox proportional-hazard ratio, 0.29; \( P = 0.04 \)) and tended to have better overall survival (hazard ratio, 0.53; \( P = 0.09 \)) after adjustment for age, previous myocardial infarction, chronic kidney failure, NYHA functional class, atrial fibrillation, mean gradient at baseline, severity of MR at baseline, and propensity score. Moreover, in a subset of 39 patients (13 TAVI and 26 SAVR) in whom the functional status had been documented objectively with the use of 6-minute walk test performed before and 1 year after procedure, the postprocedural change in LVEF correlated well (\( r = 0.65, P = 0.0008 \)) with the change in walked distance.

### Predictors of Postprocedural LVEF Recovery

On individual analysis, female gender (\( P = 0.03 \)), worse NYHA functional class (\( P = 0.03 \)), absence of atrial fibrillation (\( P = 0.03 \)), lower baseline LVEF (\( P = 0.03 \)), smaller baseline AVA (\( P = 0.003 \)), TAVI procedure (\( P = 0.005 \)), post-procedural change in AVA (\( \Delta \text{AVA} = 1 \text{-year AVA} - \text{baseline AVA}; P = 0.01 \)), and complete or no need for coronary revascularization (\( P = 0.05 \)) were significant predictors of better LVEF recovery (Table 3). Patients with a low baseline transvalvular gradient (mean gradient <30 mm Hg) had similar (\( P = 0.44 \)) recovery of LVEF (9±13%) compared with those with a high gradient (11±12%). Among the 71 patients with low-flow, low-gradient AS who underwent dobutamine stress echocardiography before the procedure, myocardial contractile reserve defined by a relative increase in stroke volume >20% was not a predictor of LVEF recovery (\( \Delta \text{LVEF}, 6 \pm 13 \% \) versus 5±11% in patients with and without contractile reserve respectively; \( P = 0.85 \)).

On multivariable analysis, the predictors of absolute change in LVEF after the procedure were female gender (\( P = 0.004 \)), absence of atrial fibrillation (\( P = 0.01 \)), baseline LVEF (\( P = 0.005 \)), TAVI (\( P = 0.007 \)), \( \Delta \text{AVA} \) (\( P = 0.01 \)), and complete or no need for coronary revascularization (\( P = 0.01 \)) (Table 3). After further adjustment for propensity score, TAVI (\( P = 0.02 \)) and \( \Delta \text{AVA} \) (\( P = 0.03 \)) remained independently associated with better recovery of LVEF.

After the exclusion of the 15 TAVI patients with severe MR at baseline (none of the SAVR patients had severe MR),

### Table 3. Individual and Multivariable Determinants of the Absolute Change in LVEF Between Baseline and 1-Year Follow-Up

<table>
<thead>
<tr>
<th>Variables</th>
<th>Individual Analysis</th>
<th>Multivariable Analysis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Estimate ± SD</td>
<td>( R^2 )</td>
</tr>
<tr>
<td>NYHA functional class III or higher</td>
<td>-2.8 ± 1.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>3.1 ± 1.4</td>
<td>0.05</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>-3.2 ± 1.5</td>
<td>0.05</td>
</tr>
<tr>
<td>LVEF at baseline, %</td>
<td>-0.3 ± 0.1</td>
<td>0.05</td>
</tr>
<tr>
<td>AVA at baseline, cm²</td>
<td>-20.7 ± 6.9</td>
<td>0.09</td>
</tr>
<tr>
<td>( \Delta \text{AVA}, \text{cm²} )</td>
<td>7.6 ± 2.9</td>
<td>0.07</td>
</tr>
<tr>
<td>Complete or no need for revascularization</td>
<td>2.6 ± 1.4</td>
<td>0.04</td>
</tr>
<tr>
<td>Treatment group (TAVI)</td>
<td>7.1 ± 2.4</td>
<td>0.08</td>
</tr>
<tr>
<td>Propensity score</td>
<td>0.7 ± 0.3</td>
<td>0.05</td>
</tr>
</tbody>
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Model 1 included the variables that were significant (\( P < 0.05 \)) on individual analysis. Model 2 is also adjusted for propensity score.
the predictors of postprocedural LVEF increase were baseline LVEF (P = 0.01), ΔAVA (P = 0.02), and TAVI (P = 0.02) on multivariable analysis. Moreover, in subsets of 25 TAVI patients and 75 SAVR patients matched (with a 1:3 ratio) for baseline LVEF (33 ± 9 versus 34 ± 9%; P = 0.74) and presence and severity of MR (MR grade, 1.44 ± 0.82 versus 1.47 ± 0.82; P = 0.86), the absolute increase in LVEF was significantly higher in the TAVI group than in the SAVR group (14 ± 10% versus 6 ± 12%; P = 0.01).

Among patients undergoing TAVI, there was a trend (P = 0.08) for a better recovery in LVEF in patients treated by the transfemoral approach (18 ± 14%) compared with those treated by the transapical approach (10 ± 12%; Figure 4). Patients with the transapical approach, however, had a significantly higher LVEF at baseline compared with patients with the transfemoral approach, and the average LVEFs were similar in both subgroups 1 year after the procedure. There was no significant difference between SAVR patients undergoing concomitant CABG and those without CABG with regard to baseline LVEF and postprocedural improvement in LVEF (Figure 5). The postoperative change in LVEF was not significantly different (P = 0.26) in SAVR patients with a small prosthesis (≤ 21 mm; 5 ± 7%) versus those with a larger prosthesis (> 21 mm; 10 ± 8%).

Discussion

The most important finding of this study is that, despite a much worse risk profile at baseline, TAVI was associated with better recovery of LVEF compared with SAVR. At 1 year after the procedure, 58% of the TAVI survivors had an LVEF > 50% as opposed to only 20% in the SAVR group. There was a nonsignificant trend for higher 30-day mortality in the TAVI group, but after adjustment for covariate differences, early mortality risk was found to be equivalent in both groups.

Effect of Type of Procedure on LVEF Recovery

Few studies have documented the improvement in LVEF after TAVI.8,11,23 However, these studies generally included a small number of patients with short-term follow-up, pooled patients with LVEF ≤ 50% and those with LVEF > 50%, and/or did not include a comparison with a group of patients with SAVR.

Previous studies have reported that improvement in LVEF after AVR is positively related to female gender, presence of syncope, and preoperative mean gradient and inversely related to preoperative LVEF and AVA, previous myocardial infarction, and presence of hypertension and coronary artery disease.2,4,24 Preprocedural LVEF and AVA were also found to be associated with postprocedural recovery of LVEF in the present study. Moreover, the improvement in LVEF was more important in the TAVI group even though the baseline risk profile a priori favored the SAVR group.

As highlighted in Table 3, several factors contribute to postprocedural recovery of LVEF. The larger increase in LVEF observed in the TAVI group may be due, at least in part, to the better improvement in aortic valve hemodynamics (ie, AVA and gradient) achieved by TAVI. TAVI indeed yielded to a more complete relief of the valvular obstruction and thereby of the pressure overload imposed on the left ventricle compared with SAVR. In this regard, it is important to emphasize that a ventricle with depressed systolic function is highly sensitive to an increase in afterload, especially during the periprocedural period during which the myocardial function is more vulnerable.12–14 The difference in postprocedural gradient between the 2 groups nonetheless appears smaller than one would expect from the observed difference in indexed AVA and from the average value of indexed AVA of the SAVR group, which is located on the steep portion of the gradient-indexed AVA curve (Table 2). The relationship between indexed AVA and gradient indeed follows an inverse exponential function.23 Consequently, small differences in indexed AVA have a much bigger effect on gradient and LV workload at the lower end of the scale (ie, when indexed AVA is < 0.8 to 0.9 cm²/m²) than small differences at the larger end of the scale. This discrepancy may be explained by the facts that the gradient is highly flow dependent and that SAVR patients had lower LVEF and thus lower transvalvular flow rate compared with TAVI patients. Hence, the differ-
ence in gradient would likely have been much higher had the level flow rate been similar in both groups. This discrepancy may also be due, at least in part, to technical difficulties in the measurement of AVA in patients with prosthetic heart valves.\textsuperscript{23} It should also be emphasized that Doppler echocardiographic evaluation at rest does not necessarily reflect the valve hemodynamics during a patient’s daily activities, and the smaller the indexed AVA is at rest, the larger the increase in gradient is for a given increase in flow rate during exercise.\textsuperscript{26} Hence, it is likely that the difference in gradient between the 2 groups would be magnified under exercise conditions. Furthermore, the results of this study suggest that postprocedural recovery of LVEF depends more heavily on the magnitude of improvement in valve hemodynamics achieved by the procedure rather than on the preprocedural or postprocedural values of AVA or gradient.

Rajappan et al\textsuperscript{27} have reported that, in patients with severe AS and normal coronary angiogram, the postoperative recovery of coronary flow reserve is directly related to the increase in AVA achieved by AVR. Consistent with these findings, Bakhtiary et al\textsuperscript{28} have shown that AVR with a stentless bioprosthesis is associated with better improvement in coronary reserve compared with AVR with a stented bioprosthesis.\textsuperscript{28} Hence, the better valvular hemodynamics and lower residual afterload associated with TAVI may have contributed to the better recovery of coronary flow reserve and LVEF in high-risk patients with severe AS and depressed LV systolic function.

Importantly, the type of procedure remained a strong independent predictor of LVEF recovery after adjustment for the postprocedural increase in AVA, which suggests that, besides valvular hemodynamics, other important factors contributed to the better improvement in LVEF observed in TAVI patients. Several myocardial injuries associated with open heart surgery, including ischemia, ischemia/reperfusion, inflammatory response, cardioplegia, surgical trauma, and oxidative stress, may lead to apoptosis of cardiomocytes and contractile dysfunction of surviving myocytes.\textsuperscript{15} These factors may affect the recovery of LV function of patients undergoing SAVR, and the patients with preexisting LV systolic dysfunction are the most vulnerable in this regard. By avoiding these factors or by minimizing their impact, TAVI may allow better protection and recovery of myocardial function in these high-risk patients. The trend for better recovery of LVEF in transfemoral versus transapical TAVI is most likely related to the higher baseline LVEF in the transapical group (Figure 4). A greater degree of myocardial damage with the transapical approach during either catheter insertion/manipulation or apical repair approach may also potentially have contributed to limit the postprocedural recovery of LVEF. Future improvements in catheter size and apical repair technique should reduce the myocardial damage associated with this approach.

LVEF is a powerful predictor of clinical outcome in patients with cardiovascular diseases, including AS.\textsuperscript{24} Consistently, in the present study, better postprocedural recovery of LVEF was associated with better improvement in functional status and better late survival. Although the results of LVEF recovery obtained with TAVI in patients with severe AS and depressed LV systolic function are encouraging, further randomized studies are needed to determine whether this new therapeutic modality will improve survival in this specific population. The PARTNER trial may provide important new insights in this regard.

**Clinical Implications**

In patients with severe AS and depressed LV systolic function, the surgeon should ideally implant a prosthetic valve with superior hemodynamic performance to avoid any residual pressure gradient. Persistent afterload excess after SAVR may indeed have a highly detrimental impact on postoperative hemodynamic and clinical outcomes in these high-risk patients.\textsuperscript{12–14} In some patients, optimal relief of valvular obstruction can be achieved by implantation of a new generation of stented bioprosthetic or bileaflet mechanical valves implanted in the supra-annular position. In other patients, however, the surgeon may have to perform more invasive procedures such as implantation of a stentless bioprosthesis or enlargement of the aortic root to achieve optimal hemodynamics and to avoid prosthesis-patient mismatch.\textsuperscript{25} These procedures may, on the other hand, increase the duration of aortic cross-clamp time and the risk of perioperative bleeding. This is an important limitation, especially in the context of patients with vulnerable myocardial function, in whom the surgeon should attempt to minimize, as much as possible, the complexity and duration of the procedure. Therefore, these patients with severe AS and depressed LV systolic function pose an important challenge with regard to therapeutic management because they require a valve replacement procedure that ensures optimal valve hemodynamics with complete relief of LV outflow obstruction while minimizing the operative risk. The results of the present study suggest that TAVI may achieve both of these goals and thus may provide a potential alternative to SAVR in these patients.

The operative risk associated with SAVR may vary extensively among patients with severe AS and depressed LV systolic function. It thus appears judicious to individualize the therapeutic strategy according to the patient’s baseline risk profile and to refer only patients who have a high or prohibitive surgical risk to TAVI. Some previous studies reported that the logistic EuroSCORE markedly overestimates the risk of operative mortality after SAVR.\textsuperscript{29,30} However, these studies did not specifically analyze the performance of this score in the subset of patients with severe AS and depressed LV systolic function. The results of the present study suggest that the logistic EuroSCORE overestimates operative mortality, whereas the STS score underestimates the operative risk in this subset of patients after SAVR (Table 1 and Figure 1). Moreover, besides the logistic EuroSCORE or STS score, other factors not included in these scores should be taken into account in the selection of the most appropriate treatment in patients with severe AS and reduced LVEF. In particular, patients with a lack of myocardial contractile reserve on dobutamine stress echocardiography or with low preoperative transvalvular gradient display a markedly increased operative risk with SAVR\textsuperscript{3,24} and may thus be oriented to TAVI. In addition, TAVI may be contemplated in patients with a small calcified aortic root, given that these
patients have increased risk for operative mortality and morbidity and for the occurrence of severe prosthesis-patient mismatch after SAVR.\(^{11,12}\)

**Study Limitations**

This was a posthoc nonprespecified analysis, and we cannot rule out the possibility that other potential confounding variables not included in the models might have affected the results. Echocardiographic data were not analyzed in a core laboratory. However, the protocol for acquisition and analysis of Doppler echocardiographic images was standardized among the participating centers, and the measurements were performed by the same experienced echocardiographers in each center. Furthermore, given that the primary outcome variable for this study was the postprocedural change in LVEF, each patient served as his or her own control.

Assessment of myocardial contractile reserve has been shown to be useful to determine operative risk in patients with low-LVEF, low-gradient AS undergoing SAVR.\(^{5,24}\) In the present study, dobutamine stress echocardiographic data were not available in 60% of patients. Indeed, this series included a large number of patients with high gradient in whom dobutamine stress echocardiography was not indicated. This limitation, however, is unlikely to have affected the results of the analyses of postprocedural LVEF recovery given that it has previously been demonstrated that the extent of preoperative contractile reserve does not predict the improvement in LVEF after SAVR in patients with low-LVEF, low-gradient AS.\(^{24}\) Accordingly, in the subset of patients who underwent dobutamine stress echocardiography in the present series, there was no significant association between contractile reserve and postprocedural LVEF recovery. This finding is most likely related to the fact that contractile reserve is influenced not only by intrinsic myocardial function but also by the presence of afterload mismatch, which may not be corrected by dobutamine stimulation.

TAVI patients had a higher prevalence of concomitant MR at baseline. LVEF may underestimate the extent of myocardial systolic dysfunction in the presence of MR. However, the prevalence of MR decreased to a similar extent in both groups after the procedure, and the presence or severity of MR at baseline or at follow-up was not a significant predictor of LVEF recovery. Moreover, an additional analysis in subsets of TAVI and SAVR patients matched for the presence and severity of MR provided results similar to those obtained in the whole cohort. Hence, it is unlikely that the difference in prevalence of MR between the 2 groups may have affected the results with regard to LVEF recovery.

The duration of follow-up was short. Further studies are necessary to assess the durability of prosthetic valves implanted by TAVI. Valve durability is indeed an important consideration in the selection of the most appropriate valve procedure, especially in the younger population.

**Conclusions**

In patients with severe AS and depressed LV systolic function, TAVI is associated with faster and better recovery of LVEF compared with SAVR. These findings support the need for the realization of a randomized clinical trial comparing these 2 modalities of treatment with regard to recovery of LV function and survival in this specific population. Pending the results of these trials, TAVI may provide a good alternative to SAVR in patients with severe AS and depressed LV systolic function considered at high or prohibitive surgical risk.

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**Disclosures**

Drs Rodés-Cabau, Webb, Dumont, Doyle, De Larochellière, and Pibarot hold consultancies with and/or are on the speakers’ bureau of Edwards Life Sciences and/or have received research grants from this company. The other authors report no conflicts.

**References**


Patients with severe aortic stenosis and reduced left ventricular ejection fraction have a poor prognosis with medical treatment but a high operative mortality when treated surgically. These patients pose an important challenge with regard to therapeutic management because they require a valve replacement procedure that ensures optimal valve hemodynamics with complete relief of left ventricular outflow obstruction while minimizing the operative risk. The results of the present study suggest that transcatheter aortic valve implantation may achieve both of these goals. The most important finding of the multicenter TOPAS Study is that transcatheter aortic valve implantation may provide a good alternative to surgical aortic valve replacement in patients with severe aortic stenosis.

CLINICAL PERSPECTIVE


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Comparison Between Transcatheter and Surgical Prosthetic Valve Implantation in Patients With Severe Aortic Stenosis and Reduced Left Ventricular Ejection Fraction


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# SUPPLEMENTAL TABLE

**Table** Distribution of the models and sizes of prostheses

<table>
<thead>
<tr>
<th>Prosthesis Type</th>
<th>Prosthesis Size</th>
<th>Prosthesis Type</th>
<th>Prosthesis Size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19 n (%)</td>
<td>21 n (%)</td>
<td>23 n (%)</td>
</tr>
<tr>
<td>Surgical prostheses</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical Valves</td>
<td>Mechanical Valves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>St Jude Mechanical</td>
<td>2 (1)</td>
<td>4 (2)</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Hancock II</td>
<td>-</td>
<td>4 (2)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Carbomedic Top-Hat</td>
<td>-</td>
<td>2 (1)</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>MCRI On-X</td>
<td>-</td>
<td>3 (1.5)</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Biosprostheses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St Jude Epic</td>
<td>-</td>
<td>-</td>
<td>2 (1)</td>
</tr>
<tr>
<td>CEP Magna</td>
<td>3 (1.5)</td>
<td>18 (9)</td>
<td>38 (19)</td>
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<tr>
<td>Medtronic Mosaic</td>
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<td>3 (1.5)</td>
<td>7 (3.5)</td>
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<tr>
<td>Medtronic Advantage</td>
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<td>1 (0.5)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Mitroflow</td>
<td>1 (0.5)</td>
<td>4 (2)</td>
<td>7 (3.5)</td>
</tr>
<tr>
<td>Transcatheter Bioprostheses</td>
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<td></td>
</tr>
<tr>
<td>Edwards-SAPIEN/Cribier-Edwards</td>
<td>-</td>
<td>40 (48)</td>
<td>-</td>
</tr>
</tbody>
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