Structural Heart Disease

Self-Expanding Transcatheter Aortic Valve Replacement Versus Surgical Valve Replacement in Patients at High Risk for Surgery

A Study of Echocardiographic Change and Risk Prediction

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Background—The CoreValve US High-Risk Clinical Study compared clinical outcomes and serial echocardiographic findings in patients with severe aortic valve stenosis after transcatheter aortic valve replacement (TAVR) with a self-expanding bioprosthesis or surgical aortic valve replacement (SAVR).

Methods and Results—Eligible patients were randomly assigned 1:1 to TAVR with a self-expanding bioprosthesis or SAVR (N=747). Echocardiograms were obtained at baseline, discharge, 30 days, 6 months, and 1 year after the procedure and were analyzed at a central core laboratory. Compared with SAVR patients (N=357), TAVR patients (N=390) had a lower mean aortic valve gradient, larger valve area, and less patient–prosthesis mismatch (all P<0.001), but more paravalvular regurgitation at discharge, which decreased at 1 year. SAVR patients experienced significant right ventricular systolic dysfunction at discharge and 1 month with normal right ventricular function at 1 year. One-year all-cause mortality was 14.2% for TAVR and 19.1% for SAVR patients. Preimplantation aortic regurgitation ≥mild was associated with reduced mortality hazard for both the TAVR (hazard ratio 0.48, 95% confidence interval 0.27–0.85; P=0.01) and the SAVR groups (hazard ratio 0.53, 95% confidence interval 0.32–0.87; P=0.01). Aortic regurgitation ≥mild after TAVR was associated with increased risk for all-cause mortality (hazard ratio 1.95, 95% confidence interval 1.08–3.53; P=0.03).

Conclusions—in patients with severe aortic stenosis at increased surgical risk, TAVR was associated with better systolic valve performance, similar left ventricular remodeling, more paravalvular regurgitation, and less right ventricular systolic dysfunction compared with SAVR. Despite an overall mortality reduction for the TAVR group, ≥mild aortic valve regurgitation after TAVR was associated with an increased mortality hazard.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01240902.

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Key Words: aortic stenosis ■ echocardiography ■ mortality ■ paravalvular regurgitation ■ surgical aortic valve replacement ■ transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) has emerged as an alternative to surgical aortic valve replacement (SAVR) in patients with severe symptomatic aortic stenosis at extreme1,2 or high3 surgical risk. We have previously reported that TAVR with a self-expanding aortic valve bioprosthesis in patients at increased risk for surgery was associated with better 1-year and 2-year survival compared with surgery.4 Several studies have demonstrated sustained and even continuous reductions in aortic valve gradients and improvements in aortic valve area (AVA) after TAVR.5–8 One randomized study in high-risk patients showed that compared with SAVR, balloon-expandable TAVR resulted in larger indexed effective orifice area (EOA) and less patient–prosthesis mismatch (PPM), albeit with more paravalvular aortic regurgitation (AR); these opposing prognostic factors may have led to the similar 2-year survival rates in the 2 groups.9–11

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WHAT IS KNOWN

- Transcatheter aortic valve replacement with a self-expanding bioprosthesis compared with surgical aortic valve replacement has been shown to result in sustained reductions in aortic valve gradients and improvements in aortic valve area but higher rates of paravalvular aortic regurgitation.
- The impact of changes, as well as right ventricular and left ventricular function on outcome, has not been studied.

WHAT THE STUDY ADDS

- After transcatheter aortic valve replacement with a self-expanding bioprosthesis in high-risk patients, paravalvular regurgitation improves over time but nonetheless is associated with an increased risk of all-cause mortality at 1 year when mild or greater aortic regurgitation remains.
- These data confirm a low prevalence (6.2%) of severe patient-prosthesis mismatch with the self-expanding bioprosthesis.
- Both the transcatheter aortic valve replacement and surgical aortic valve replacement cohorts demonstrated significant reduction of left ventricular mass, left ventricular mass index, and relative wall thickness after 1 year.
- The transcatheter aortic valve replacement cohort demonstrated significant improvement in concentric left ventricular remodeling at 1 year and less right ventricular systolic dysfunction than surgical aortic valve replacement.

We previously reported greater reductions in aortic valve gradients and larger EOA in patients undergoing self-expanding TAVR versus SAVR. An improved functional and hemodynamic result after TAVR may have been one factor that contributed to the lower observed mortality in our study, but better systolic hemodynamic performance and lower-rate of PPM may be offset by a higher rate of AR with TAVR compared with surgery. This hypothesis has not been studied in patients undergoing self-expanding TAVR.

We performed a comprehensive echocardiographic analysis of patients undergoing TAVR and SAVR that included assessments of valve hemodynamics, left and right ventricular (RV) function, mitral and aortic valvular regurgitation, and left ventricular (LV) remodeling. The purpose of this report was to compare the 1-year echocardiographic findings in patients at increased risk for surgery who were treated with TAVR or SAVR in a large randomized clinical study and to evaluate these changes in the context of a potential survival benefit in patients undergoing TAVR.

Methods

Study Design

This study was a multicenter, randomized, noninferiority trial performed at 45 clinical sites in the United States. Medtronic funded the trial and developed the protocol in collaboration with the Study Steering Committee. The institutional review board of each site approved the protocol. The first draft of this article was prepared by the first author and coprincipal investigators and was then reviewed by all coauthors, who have approved its content for publication.

Patient Selection

Patient inclusion and exclusion criteria for the CoreValve US High-Risk Clinical Study have been reported in detail. Patients with severe aortic stenosis and heart failure symptoms of New York Heart Association class II or higher were eligible for inclusion in this study if they were considered to be at increased risk for SAVR. Severe aortic stenosis was defined as an AVA of ≤0.8 cm² or an indexed AVA of ≤0.5 cm²/m² and either a mean aortic valve gradient of >40 mm Hg or a peak aortic jet velocity of >4.0 m/s. Patients were considered by 2 clinical site cardi surgeons to have a >15% estimated surgical mortality rate at 30 days. Patients were assigned to TAVR through the iliofemoral artery or an alternate access route.

Study Procedure

All patients were randomly assigned in a 1:1 ratio to treatment with TAVR or SAVR. The patients assigned to SAVR were treated by means of conventional surgery with the use of cardiopulmonary bypass. The choice and size of the surgical bioprosthetic valve were left to the discretion of the surgeon. Transcatheter valve size was determined by analysis of multidetector computed tomography obtained before enrollment, which provided perimeter-based annular dimensions. Follow-up assessments were performed at discharge and at 1 month, 6 months, and 1 year after the procedure.

Echocardiographic Analysis

An independent Echo Core Laboratory (Mayo Clinic, Rochester, MN) reviewed all echocardiograms and was blinded to the clinical outcomes of patients. Echocardiography core laboratory methods and inter- and intraobserver variability for echocardiography study analyses have been recently published. Specifically, measurements were made from 3 cardiac cycles when cardiac rhythm was sinus and from 5 cycles when atrial fibrillation was present. Independent observers measured aortic valve mean gradients and peak gradients and velocities at each time point. All measurements were performed by a sonographer and approved by a level 3–trained physician echocardiographer. Aortic pressure gradient was calculated as [4×(peak aortic valve velocity²–LV outflow tract velocity²)]. The LV outflow tract diameter of the native aortic valve was measured within 5 mm of the aortic annulus and after TAVR was measured from the outer to the outer aspect of the prosthesis from the parasternal long-axis view. The EOA of the aortic valve was calculated from the continuity equation (the LV outflow tract Doppler stroke volume divided by the aortic valve velocity time integral). The LV outflow tract diameter was measured within 5 mm of the aortic annulus at baseline and after SAVR, avoiding the basal septal bulge. The outer to outer edge diameter of the ventricular end of the CoreValve bioprosthesis was used to measure Doppler stroke volume in TAVR patients.

Cardiac size, ventricular function, and valvular function were measured according to published guidelines. RV systolic function was assessed qualitatively according to published guidelines and described as being normal; mildly, moderately, or severely impaired; or indeterminate. Both qualitative and quantitative (modified Simpson’s method) approaches were used to evaluate LV ejection fraction. When LV volume could not be measured, the LV ejection fraction was measured using LV dimensions and visually assessed by a physician echocardiographer. An integrative semiquantitative approach was used to assess severity of valvular regurgitation.

As previously published, the grading of AR severity was based on regurgitation color jet density and width, circumferential extent of turbulent regurgitation color jet around the aortic annulus for paravalvular regurgitation, and diastolic flow reversal in the descending aorta. When the color flow aliasing velocity was low (<50 cm/s), the severity of valvular regurgitation was not assessed. Paravalvular
regurgitation after valve intervention was graded using all available parameters, including the circumferential extent of AR from multiple parasternal short-axis views, in accordance with the Valve Academic Research Consortium recommendations: none/trace, no or a brief duration of color jet; mild, a circumferential extent <10% (<56° in clock face) with turbulent regurgitation jet; moderate, a circumferential extent of 10% to 20% (36°–72°); and severe, a circumferential extent >20% (>72°). When there was >1 jet, the values of all regurgitation jets of 2 mild were added. Because the circumferential extent could not be seen in some patients, a multiparametric interpretation of AR was used to determine the final severity grading.

Left ventricular (LV) mass was determined by the following formula:

\[
\text{LVM} = 0.83 \times [(\text{LVEDD} + \text{LVPW} + \text{IVS})^3 - \text{LVEDD}^3] + 0.6
\]

where LVM is the LV mass, LVEDD is the LV end-diastolic diameter in cm, LVPW is the LV posterior wall thickness at end diastole in cm, and IVS is the interventricular wall thickness at end diastole in cm. LV concentric remodeling was present if the relative wall thickness (RWT) was >0.42 cm and the LV mass index remained normal (≤95 g/m² for women; ≤115 g/m² for men).14 Inter- and intraobserver variability for the echocardiography measurements were assessed in a selected cohort of the patients using the interclass correlation coefficients and have been reported.8

PPM was graded using EOA indexed to body surface area with absent PPM defined as EOA index >0.85 cm²/m², moderate PPM as EOA index ≥0.65 cm²/m² and ≤0.85 cm²/m², and severe PPM as EOA index ≤0.65 cm²/m².

Clinical Events

Patients were followed for at least 1 year after the procedure. This analysis included those patients in the implanted cohort, defined as patients who had either a transcatheter or a surgical valve implanted. Standardized Valve Academic Research Consortium criteria were used by an independent clinical events committee to assess clinical events.17 Univariate predictors of all-cause mortality were assessed based on echocardiographic findings at baseline (preimplantation) and echocardiographic findings from the first available study after valve intervention (discharge or 1 month).

Statistical Methods

Categorical variables were compared between treatment groups using the Fisher exact test or Chi-square test if there are no expected cell counts <5. Continuous variables were presented as means (±SD) and compared with the use of the 2-sample t test. The Cox proportional hazard model was used to estimate the association between echocardiographic parameters and mortality. All statistical analyses were performed with the use of SAS software, version 9.2 (SAS Institute, Cary, NC). The analysis sample was the implanted cohort, including all patients with at least one aortic valve implanted. A 2-sided test with a \( P \) value <0.05 was considered significant.

Results

Patients

A total of 795 patients underwent randomized treatment assignment. The as-treated sample included 747 patients, of whom 390 were treated with TAVR and 357 were treated with SAVR. The implanted cohort included 389 patients treated with TAVR and 353 patients treated with SAVR. The demographic and clinical characteristics of the patients at baseline according to treatment group are provided in Table 1.

Baseline Echocardiographic Findings

Baseline echocardiographic findings are found in Table 2. There were no differences between the 2 groups in baseline hemodynamics, including peak velocity and gradient, mean aortic valve gradient, or AVA or indexed AVA. Baseline LV dimensions and volumes, stroke volumes, mass, and ejection fraction were also similar in the 2 groups. Few patients (5%–6%) had moderate or severe AR at baseline with no difference in prevalence between groups.

### Table 1. Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TAVR, N=389</th>
<th>SAVR, N=353</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body surface area, m²</td>
<td>1.8±0.2</td>
<td>1.9±0.2</td>
</tr>
<tr>
<td>Age, y</td>
<td>83.2±7.1</td>
<td>83.3±6.4</td>
</tr>
<tr>
<td>STS PROM score, %</td>
<td>7.3±3.0</td>
<td>7.5±3.4</td>
</tr>
<tr>
<td>Logistic EuroSCORE, %</td>
<td>17.7±13.1</td>
<td>18.7±13.0</td>
</tr>
<tr>
<td>Male sex</td>
<td>53.0 (206)</td>
<td>51.8 (183)</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>14.4 (56)</td>
<td>13.0 (46)</td>
</tr>
<tr>
<td>III</td>
<td>65.6 (255)</td>
<td>69.4 (245)</td>
</tr>
<tr>
<td>IV</td>
<td>20.1 (78)</td>
<td>17.6 (62)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>75.3 (293)</td>
<td>75.6 (267)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>25.4 (99)</td>
<td>25.5 (90)</td>
</tr>
<tr>
<td>Prior balloon valvuloplasty</td>
<td>5.9 (23)</td>
<td>6.2 (22)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>40.9 (158)</td>
<td>41.0 (144)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>44.7 (174)</td>
<td>44.2 (156)</td>
</tr>
<tr>
<td>Home oxygen</td>
<td>12.9 (50)</td>
<td>11.3 (40)</td>
</tr>
<tr>
<td>Creatinine &gt;2 mg/dL</td>
<td>3.1 (12)</td>
<td>4.8 (17)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>40.7 (158)</td>
<td>45.6 (161)</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or % (no). There were no significant between-group differences in baseline characteristics. NYHA indicates New York Heart Association; SAVR, surgical aortic valve replacement; STS PROM, Society for Thoracic Surgery Predicted Risk of Mortality; and TAVR, transcatheter aortic valve replacement.
Table 2. Baseline Echocardiographic Findings

<table>
<thead>
<tr>
<th>Echocardiographic Parameter</th>
<th>TAVR, N=389</th>
<th>SAVR, N=353</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak velocity, m/s</td>
<td>4.4±0.6</td>
<td>4.4±0.6</td>
</tr>
<tr>
<td>Peak gradient, mm Hg</td>
<td>78.8±23.1</td>
<td>77.8±20.4</td>
</tr>
<tr>
<td>Mean gradient, mm Hg</td>
<td>48.3±15.3</td>
<td>47.7±13.9</td>
</tr>
<tr>
<td>Area, cm²</td>
<td>0.7±0.2</td>
<td>0.7±0.2</td>
</tr>
<tr>
<td>Area index, cm²/m²</td>
<td>0.4±0.1</td>
<td>0.4±0.1</td>
</tr>
<tr>
<td>Aortic annulus diameter, cm</td>
<td>2.2±0.2</td>
<td>2.2±0.2</td>
</tr>
<tr>
<td>Left ventricle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End diastolic dimension, cm</td>
<td>5.0±0.6</td>
<td>5.0±0.6</td>
</tr>
<tr>
<td>End systolic dimension, cm</td>
<td>3.2±0.8</td>
<td>3.3±0.7</td>
</tr>
<tr>
<td>End diastolic volume, mL</td>
<td>132.2±49.9</td>
<td>136.8±54.5</td>
</tr>
<tr>
<td>End systolic volume, mL</td>
<td>61.8±34.4</td>
<td>64.2±39.9</td>
</tr>
<tr>
<td>2D stroke volume, mL</td>
<td>70.4±27.2</td>
<td>72.6±27.0</td>
</tr>
<tr>
<td>Doppler stroke volume, mL</td>
<td>75.8±23.5</td>
<td>75.0±20.2</td>
</tr>
<tr>
<td>Mass, g</td>
<td>226.1±72.5</td>
<td>227.5±65.0</td>
</tr>
<tr>
<td>Mass index, g/m²</td>
<td>122.5±35.7</td>
<td>123.5±33.6</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>58.0±11.4</td>
<td>57.6±11.9</td>
</tr>
<tr>
<td>Concentric remodeling, RWTm</td>
<td>0.5±0.1</td>
<td>0.5±0.1</td>
</tr>
<tr>
<td>Concentric remodeling, RWTp</td>
<td>0.5±0.1</td>
<td>0.5±0.1</td>
</tr>
<tr>
<td>Mitral regurgitation, %</td>
<td>N=382</td>
<td>N=343</td>
</tr>
<tr>
<td>None</td>
<td>5.0 (19)</td>
<td>4.1 (14)</td>
</tr>
<tr>
<td>Trace</td>
<td>37.4 (143)</td>
<td>41.4 (142)</td>
</tr>
<tr>
<td>Mild</td>
<td>47.6 (182)</td>
<td>43.4 (149)</td>
</tr>
<tr>
<td>Moderate</td>
<td>9.7 (37)</td>
<td>10.2 (35)</td>
</tr>
<tr>
<td>Severe</td>
<td>0.3 (1)</td>
<td>0.9 (3)</td>
</tr>
<tr>
<td>Aortic regurgitation, %</td>
<td>N=385</td>
<td>N=346</td>
</tr>
<tr>
<td>None</td>
<td>15.1 (58)</td>
<td>14.7 (51)</td>
</tr>
<tr>
<td>Trace</td>
<td>37.9 (146)</td>
<td>33.2 (115)</td>
</tr>
<tr>
<td>Mild</td>
<td>41.8 (161)</td>
<td>46.0 (159)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5.2 (20)</td>
<td>5.5 (19)</td>
</tr>
<tr>
<td>Severe</td>
<td>0.0 (0)</td>
<td>0.6 (2)</td>
</tr>
</tbody>
</table>

Continuous data are presented as mean±SD; ordinal data are presented as % (no). There were no significant between-group differences in baseline echocardiographic findings. 2D indicates 2-dimensional; RWTm, mean relative wall thickness; RWTp, posterior relative wall thickness; SAVR, surgical aortic valve replacement; and TAVR, transcatheter aortic valve replacement.

volumes, and Doppler stroke volume (−12.0 mL; P<0.0001) at discharge versus baseline (Table 3). Although LV ejection fraction was not changed at discharge, it was significantly improved by 1 year (+2.6%; P<0.001).

Compared with patients undergoing TAVR, the LV ejection fraction (P<0.05) and stroke volume by 2-dimensional (2D) echocardiography (P<0.0001) and Doppler methods (P<0.0001) were significantly lower at discharge in patients undergoing SAVR. These early differences were no longer significant at 1 year, although stroke volume was significantly lower in the SAVR group compared with the TAVR group at 1 year (P<0.0001).

Postprocedural Valvular Regurgitation

The frequencies of mitral regurgitation after the procedure are found in Table I in the Data Supplement. There was improvement in the degree of mitral regurgitation at 1 year in patients undergoing TAVR (P=0.0009) and at discharge and 1 year in patients undergoing SAVR (P<0.0001 for both time points). At baseline, the frequency of AR was similar between the TAVR and SAVR treatment groups. The degree of total AR did not change at discharge; however, it was significantly lower (P=0.0004) in patients at 1 year after TAVR. In contrast, the degree of total AR was significantly improved at discharge (P<0.0001) and 1 year (P<0.0001) in patients undergoing SAVR. In addition, the degree of total AR was lower at both time points (all P<0.0001) in patients undergoing SAVR compared with those undergoing TAVR.

Left Ventricular Remodeling

A paired analysis of the parameters of LV remodeling is found in Table II in the Data Supplement. In patients undergoing TAVR, there were significant reductions in LV mass (P<0.0001), LV mass index (P<0.0001), and interventricular and posterior wall thickness (P=0.0001) at 1 year compared with baseline. In patients undergoing SAVR, there were also significant reductions in LV mass (P<0.0001), LV mass index (P<0.0001), and interventricular and posterior wall thickness at 1 year compared with baseline (P=0.0002). Concentric LV remodeling was significantly reduced at 1 year (P<0.01 for RWTm and RWTp) compared with baseline in patients undergoing TAVR but not in patients undergoing SAVR.

Right Ventricular Function

A comparison of RV function over time between TAVR and SAVR groups is shown in Figure 1. Although there were no significant differences in RV systolic function at baseline (P=0.24), RV systolic function was significantly reduced in the SAVR group (P<0.001) compared with the TAVR group at discharge and at 1 month. RV function was not significantly different between treatment groups at 6-month (P=0.83) or 1-year (P=0.14) follow-up.

Patient-Prosthesis Mismatch

The relative incidence of none, moderate, or severe PPM did not change within patient groups over time, but there was a consistent difference between treatment groups at each follow-up interval (P<0.001; Figure 2). The incidence of any PPM in the SAVR group at 1 year was 56.3% (25.7% severe) versus 27.0% (6.2% severe) in the TAVR group (P<0.001). At 1 year, no PPM was present in 73.0% of TAVR patients and 43.7% of SAVR patients.

Paravalvular Regurgitation

The incidence of mild, moderate, or severe paravalvular AR was greater in the TAVR group for each follow-up interval (P<0.001; Figure 3). Comparing paired echocardiograms at discharge and 1 year for TAVR patients with moderate to severe paravalvular regurgitation at discharge, 76% experienced an improvement of at least 1 grade (Figure 4).

Compared with baseline, the SAVR cohort had a significant reduction of AR at discharge, 1 month, and 1 year.
There was no significant change in the severity of AR from discharge to 1-year follow-up for the SAVR cohort. In addition, we explored the potential interaction between LV remodeling and paravalvular regurgitation severity by stratification of the patients with potentially significant paravalvular regurgitation (moderate and severe) at 30 days or those without paravalvular regurgitation (none or trace) and observed no difference in LV dimension, LV mass index, or LV intraventricular wall thickness at 1-year follow up (Table III in the Data Supplement).

### Echocardiographic Predictors of Mortality

One-year all-cause mortality was 14.2% for TAVR patients and 19.1% for SAVR patients ($P<0.04$ for superiority). Univariate echocardiographic parameters associated with a statistically significant risk of mortality were identified (Figure 5).

- At baseline, an LVEDV index above normal was associated with reduced mortality hazard for SAVR ($P<0.05$) but not for TAVR. RV systolic dysfunction ≥mild and mitral regurgitation ≥mild were both associated with increased mortality hazard for TAVR ($P<0.05$) but not for SAVR. The presence of AR ≥mild at baseline was associated with reduced mortality hazard for both TAVR and SAVR treatment groups ($P<0.05$ for both).

After treatment, a normal Doppler stroke volume index was associated with reduced hazard for TAVR ($P<0.05$) but did not reach statistical significance for SAVR. RV systolic dysfunction ≥mild was associated with increased hazard for TAVR and SAVR groups ($P<0.05$ for both). AR ≥mild at discharge was associated with increased hazard for TAVR ($P<0.05$) but not for SAVR.

### Discussion

The current analysis provides insight into the relative effects of TAVR and SAVR on LV and RV performance up to 1 year after intervention for patients with severe aortic valve stenosis. In addition, we provide an analysis of the echocardiographic features at baseline and after valve intervention that are associated with mortality. This study is unique because it describes the largest patient cohort to date randomized to either TAVR or SAVR; we used an echocardiographic core laboratory with reproducibility analysis; and we relied on centrally adjudicated assessment of clinical outcomes.

Our principal findings are as follows: (1) TAVR with a self-expanding prosthesis was associated with superior systolic valve performance and a substantially lower incidence of PPM during all follow-up intervals; (2) TAVR was associated
with a greater incidence of paravalvular regurgitation that improved over time but nonetheless conferred a mortality hazard; (3) SAVR was associated with a higher incidence of RV systolic dysfunction at discharge and 1 month but normal RV systolic function at 1 year; and (4) both treatment groups demonstrated significant LV reverse remodeling at 1 year.

**Valve Performance**

Similar to prior reports, we found that 1-year aortic valve hemodynamics were more favorable in patients undergoing TAVR than SAVR. Our study restricted the inclusion of patients to those with annular diameters between 18 and 29 mm based on multidetector computed tomography imaging, and we recommended that SAVR be performed with the largest surgical valve possible at the time of surgery. The hemodynamic beneficial effects of TAVR over SAVR were identified at hospital discharge and were sustained at every follow-up interval in the TAVR group. In particular, the frequency of PPM was substantially lower in patients treated with TAVR than with SAVR. In our analysis, the self-expanding valve was associated with a 6.2% prevalence of severe PPM at 1 year. This is considerably lower than the 20.2% prevalence of severe PPM reported for balloon-expandable TAVR, although the method for calculating stroke volume is different for balloon-expandable and self-expandable bioprostheses. Another explanation is that the lower profile of the frame and the supra-annular position of the self-expanding bioprosthesis used for this study likely contributed to the lower mean and

**Figure 1.** Right ventricular (RV) systolic function over time by treatment group. SAVR indicates surgical aortic valve replacement; and TAVR, transcatheter aortic valve replacement.

**Figure 2.** Incidence of patient–prosthesis mismatch (PPM) over time by treatment group. SAVR indicates surgical aortic valve replacement; and TAVR, transcatheter aortic valve replacement.
peak gradients and larger EOAs observed in this study. We think that long-term outcomes may relate, in part, to the superior valve hemodynamic performance of TAVR versus SAVR.

Paravalvular Aortic Regurgitation

We report an improvement in both mitral regurgitation and AR after both TAVR and SAVR, but note that our entry criteria precluded study enrollment of moderate–severe and severe aortic or mitral valve regurgitation. Similar to our prior report in extreme-risk patients,2 a paired analysis found that 76% of patients with moderate or severe paravalvular AR at discharge had an improvement in the severity of regurgitation at 1 year. This continued improvement in paravalvular AR severity over time compares favorably to similarly designed studies of balloon-expandable TAVR, which reported a lower rate of paravalvular AR improvement (31.9%) at 1 year.7

Taken together, these findings support the recent report that the self-expanding valve frame may contribute to paravalvular regurgitation improvement over time.8 Nonetheless, the echocardiographic finding of $\geq$ mild paravalvular regurgitation early after TAVR was associated with a significant mortality hazard at 1 year (hazard ratio 1.95), which is similar to the hazard ratio (2.1) reported for $\geq$ mild paravalvular regurgitation in the balloon-expandable TAVR trial.7 Interestingly,
Figure 5. Relationship between baseline (A) and discharge (B) echocardiographic parameters and all-cause mortality at 1 year. CI indicates confidence interval; LVEDV, left ventricular end diastolic volume; RV, right ventricle; SAVR, surgical aortic valve replacement; and TAVR, transcatheter aortic valve replacement.
we also observed a significantly reduced risk for 1-year mortality in both TAVR and SAVR patients with ≥mild paravalvular regurgitation at baseline, which suggests a protective effect of preprocedure AR. The possible effect of baseline AR on clinical outcomes in patients with discharge AR requires further investigation.

**Ventricular Remodeling and Systolic Function**

Both the TAVR and SAVR cohorts demonstrated significant reduction of LV mass, LV mass index, and RWT after 1 year; however, only the TAVR cohort also demonstrated significant improvement in concentric LV remodeling at 1 year. The magnitude of LV mass regression was larger in the SAVR cohort. This finding seems paradoxical given the improved systolic hemodynamic performance associated with TAVR. We hypothesize that the apparent improvement in LV mass after SAVR may be overestimated using echocardiographic methods. Because LVEDD is a principal component of the echocardiographic calculation of LV mass, it follows that the magnitude of LV mass reduction within the SAVR treatment group may reflect a primary reduction in the LV end-diastolic dimension only. Compared with baseline, we observed a significant reduction in LV end-diastolic diameter and LV end-diastolic volume early after SAVR without significant change in septal or posterior LV wall thickness at discharge or at 30-day follow-up. It is important to note that Hahn et al also reported greater early LV mass regression for SAVR compared with balloon-expandable TAVR. A plausible explanation for this consistent finding is that the LV diastolic dimension after SAVR decreased in response to diminished LV preload resulting from reduced RV systolic function.

An alternative explanation for the small observed difference in LV mass regression between treatment groups could be the effect of a higher incidence of paravalvular regurgitation within the TAVR treatment group; however, we found no significant relationship between the severity of paravalvular regurgitation and any parameter of LV remodeling.

The SAVR cohort experienced significantly more RV systolic dysfunction at discharge and 1 month, which returned to normal at 1 year. This finding is consistent with recent published reports of acute reduction of RV systolic function after SAVR, but not TAVR, with recovery of RV function at 6-month follow-up.

**Limitations**

There are important limitations to this study. The calculations of LV mass were made using ventricular dimensions, and these may have been reduced because of relatively lower preload and stroke volume in the SAVR patient group. Cardiac magnetic resonance imaging may be a more effective method to assess LV mass regression. The follow-up period in this study is limited to 1 year. Multiple potential associations of echocardiographic variables with mortality were tested, which leads to the possibility of proliferated type 1 error. However, this is a post hoc exploratory analysis. Longer term studies will determine the long-term durability of transcatheter and surgical aortic valves and may reveal additional echocardiographic parameters associated with mortality hazard that were not significant at 1 year.

**Conclusions**

We present the largest patient cohort to date randomized to either TAVR or SAVR using an echocardiographic core laboratory and centrally adjudicated clinical outcomes. In patients with severe aortic stenosis who are at increased surgical risk, TAVR with a self-expanding prosthesis was associated with better systolic valve performance, similar LV remodeling, more paravalvular regurgitation, and less RV systolic dysfunction compared with SAVR. Despite an overall mortality reduction for the TAVR group, ≥mild aortic valve regurgitation after TAVR was associated with an increased mortality hazard at 1 year.

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Self-Expanding Transcatheter Aortic Valve Replacement Versus Surgical Valve Replacement in Patients at High Risk for Surgery: A Study of Echocardiographic Change and Risk Prediction


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