Aortic stenosis (AS) is characterized by left ventricular (LV) pressure overload leading to LV hypertrophy and concentric remodeling, and it may lead to reduced LV systolic function that is uncommonly asymptomatic. According to American College of Cardiology/American Heart Association guidelines and European Society of Cardiology guidelines, LV systolic dysfunction, defined as LV ejection fraction (LVEF) of <50%, is a class I indication for aortic valve replacement (AVR) in asymptomatic severe AS, whereas asymptomatic severe AS with preserved LVEF (≥50%) has no AVR indication unless critical (very severe) AS is present.

Methods

Study Patients

This study was approved by the Mayo Clinic Institutional Review Board. This retrospective study included all patients aged >18 years who underwent surgical AVR from January 1995 to June 2009 at Mayo Clinic, Rochester, MN, for severe AS defined as a mean aortic valve gradient ≥ 40 mm Hg, aortic valve area (AVA) < 1 cm², or indexed A VA < 0.6 cm²/m², as well as leaflet calcification with severe restriction of opening. Only patients who had undergone a trans-thoracic echocardiography (TTE) at Mayo Clinic within 3 months before AVR and agreed to allow access to their medical records for research were included. Patients with concomitant moderate-severe
Echocardiography

Two-dimensional and Doppler TTE studies were performed on commercially available ultrasound equipment (Acuson Sequoia, Siemens Medical, Mountain View, CA; Vivid-7, GE Healthcare, Milwaukee, WI; and iE33, Philips Healthcare, Andover, MA) in accordance with the American Society of Echocardiography guidelines with interpretation performed by an experienced cardiologist with level III training in echocardiography. Doppler values were calculated as the average of 3 cardiac cycles for patients with sinus rhythm and 10 for atrial fibrillation. LV outflow tract diameter was measured in the parasternal long-axis view in early systole from the point of aortic cusp insertion into the interventricular septum to the point of aortic cusp insertion into the interventricular fibrosa. AVA was estimated by quantitative Doppler ultrasound using the continuity equation. Peak and mean flow velocity across the valve were determined in the window where the highest velocity could be recorded using continuous wave Doppler with the cursor as parallel as possible with the flow across the valve. Peak and mean transvalvular gradients were estimated using the modified Bernoulli equation. LVEF was determined by the modified method of Quinones or Simpson biplane method; the final reported LVEF method was at the discretion of the expert echocardiographer. LV stroke volume was calculated using pulsed-wave Doppler as the product of the LV outflow area and LV outflow tract time velocity integral and indexed for body surface area (stroke volume index [SVi]). LV mass index was estimated using Devereux formula. In men, LV mass index >116 g/m² and in women, >104 g/m² were considered indicative of LV hypertrophy. Increased relative wall thickness was present when this ratio was >0.42. Valvuloaortic impalement (Zva) was calculated using the formula (systolic blood pressure+mean aortic valve pressure gradient)/SVi.

Analysis

Data are presented as mean±SD or number and percentages. Differences in values between groups were tested by 1-way ANOVA; categorical variables were tested by the χ² exact test or Fisher exact test when the expected value in any of the cells of a contingency table was below 5. Creatinine and E/e’ were presented as a median and interquartile range, and differences were tested using the Kruskal–Wallis test because of a non-Gaussian distribution for these variables. In the case of significant differences between groups, paired comparisons were performed and significance was set using the Bonferroni correction (0.05/6=0.008). Correlations were obtained using Spearman rank test. For overall tests, a P value of <0.05 was considered significant and 2-sided tests were used. Mortality rates were calculated and plotted using the product limit method; rates were compared using the log-rank test. Further estimation of risk was performed using Cox proportional hazard models. All significant variables in the univariate analysis were inserted in the multivariable analysis, except Zva because of significant collinearity with SVi. Sex was not significant in the univariate analysis, but it was included as it is known to affect long-term outcome in the general population. As symptomatic status is known to be an important factor among patients with AS undergoing AVR, we also tested LVEF stratified according to the presence of symptoms. Because patients over a long-time period were included, we adjusted for the effect of time period, dividing the patients into 3 groups of similar size (1995–1999, 2000–2004, and 2005–2009). To further study the importance of LVEF, we tested the multivariable model in patients without another indication for AVR, such as very severe AS defined as AVa<25 m/s or aortic valve mean gradient≥60 mm Hg, symptoms or positive stress test, LVEF<50%, or concomitant coronary revascularization indicated to improve survival. The overall differences between models were tested by calculating the difference in log likelihood χ² between models that were based on the same set of patients. The assumptions (proportional hazard assumption, linearity of continuous variables, and lack of interaction) were tested and found valid. Statistical analysis was performed with STATA/SE 12.0 (StataCorp LP; TX) software.

Results

Patients

From 2606 patients with severe AS undergoing AVR, excluded were 295 with no TTE <3 months before AVR, 154 with moderate-severe or severe valve condition other than AS, 52 with missing values for LVEF, 32 with concomitant aortic root replacement, 30 previous AVR, 18 previous mitral valve surgery, and 8 endocarditis leading to the final study population of 2017 patients.

LVEF was <50% in 300 (15%) patients, 50% to 59% in 331 (16%), 60% to 69% in 908 (45%), and ≥70% in 478 (24%). Clinical characteristics at the time of TTE are presented in Table 1. Symptomatic status was obtainable in 1983 (98.3%) patients. Of these, 1467 (74%) were symptomatic. Patients with lower LVEF, particularly those with LVEF<50%, presented more often with symptoms and with worse New York Heart Association functional class (NYHA-FC; 2.1±0.6 versus 1.9±0.7 versus 1.9±0.7 versus 1.8±0.7 in patients with LVEF<50%, 50% to 59%, 60% to 69%, ≥70% respectively; P<0.001). Comparing patients with LVEF<50% to those with LVEF between 50% and 59%, the first group were more likely to be men, more often treated with diuretics and angiotensin-converting enzyme inhibitors, had a higher NYHA-FC, and were less likely treated with calcium-channel blockers (P<0.05 for each).

Echocardiographic Data

Both end-systolic and end-diastolic LV diameters correlated inversely with LVEF (r²=−0.83; P<0.0001 and r²=−0.52; P<0.00001, respectively). Clinically small, but statistically significant differences in AVA, indexed AVA, and transvalvular gradients were observed between groups (Table 2). Eccentric hypertrophy (higher LV mass index and lower relative wall thickness) was a common geometry pattern in patients with LVEF<50%.

Operative Data

Operative data are summarized in Table 3. The overall median time from TTE to AVR was 12 days (interquartile range, 4–29
days); however, there were significant differences between groups ($P=0.0001$). Patients with LVEF<50% had a shorter time from TTE to AVR with a median of 7 days (3–18) compared with 14 days (5–31) in patients with LVEF≥50%. There was no significant difference in TTE to AVR time between the 3 groups with LVEF≥50%. Concomitant coronary

<table>
<thead>
<tr>
<th>Table 1. Patient Characteristics</th>
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<tbody>
<tr>
<td>LVEF&lt;50%, n=300</td>
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<td>-----------------</td>
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<tr>
<td>Age, y</td>
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<tr>
<td>Sex, male</td>
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<tr>
<td>Atrial fibrillation</td>
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<td>Hypertension</td>
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<td>Diabetes mellitus</td>
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<td>Body surface area, m²</td>
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<td>Symptoms</td>
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<td>NYHA-FC, no. 1/2/3/4</td>
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<td>Treatment</td>
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<td>Beta-blockers</td>
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<tr>
<td>CCB</td>
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<tr>
<td>ACE inhibitors</td>
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<td>Nitritates</td>
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<tr>
<td>Creatinine, mg/dL</td>
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</table>

Data are represented as number and percentage or for continuous variables, as mean±SD. A total of 426 patients had missing values for COPD (83 in LVEF<50%, 73 in LVEF 50%–59%, 175 in LVEF 60%–69%, and 95 in LVEF≥70%). Forty-eight patients had missing values at NYHA-FC (10 in LVEF<50%, 6 in LVEF 50%–59%, 19 in LVEF 60%–69%, and 13 in LVEF≥70%). ACE indicates angiotensin-converting enzyme; CCB, calcium-channel blocker; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; and NYHA-FC, New York Heart Association functional class.

*P<0.008 vs. LVEF=50%.

<table>
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<tr>
<th>Table 2. Echocardiographic Data</th>
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<tr>
<td>LVEF&lt;50%, n=300</td>
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<tr>
<td>LV ejection fraction, %</td>
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<tr>
<td>Aortic valve area, cm²</td>
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<tr>
<td>AV, cm²/m²</td>
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<tr>
<td>AV maximum velocity, m/s</td>
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<td>AV mean gradient, mmHg</td>
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<tr>
<td>Zva, mmHg mL⁻¹ m⁻²</td>
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<td>LV EDD, mm</td>
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<td>LV ESD, mm</td>
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<td>Concentric remodeling</td>
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<tr>
<td>Eccentric hypertrophy</td>
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<tr>
<td>Concentric hypertrophy</td>
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<tr>
<td>Stroke volume index, mL/m²</td>
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</tbody>
</table>

AV indicates aortic valve; AVAi, aortic valve area index; EDD, end-diastolic diameter; ESD, end-systolic diameter; LVEF, left ventricular ejection fraction; and Zva, valvuloarterial impedance.

*P<0.008 vs. LVEF<50%.
†P<0.008 vs. LVEF 50%–59%.
‡P<0.008 vs. LVEF 60%–69%.
revascularization surgery was performed in 42% of patients (n=850) with no differences between groups. Larger prostheses were used in patients with LVEF<60% (23.6±2.2 versus 23.3±2.1, 22.9±2.0, and 22.6±1.9 mm in the LVEF<50%, LVEF 50% to 59%, LVEF 60% to 69%, and LVEF ≥70% groups, respectively; P=0.0004). However, when indexed for body surface area, only patients with LVEF<50% had larger prostheses.

Clinical Outcomes
During follow-up of 5.3±4.4 years, 1056 (52%) patients died. A significant decrease in all-cause mortality during follow-up was observed with increasing LVEF, P<0.0001. Five-year all-cause mortality estimates (95% confidence interval) were 0.41 (0.35–0.47), LVEF<50%; 0.35 (0.29–0.41), LVEF 50% to 59%; LVEF 60% to 69%; 0.26 (0.23–0.29), LVEF 60% to 69%; 0.22 (0.18–0.26; Figure 1).

In the subset of patients with LVEF≥50%, mortality was increased among those with LVEF<60% (hazard ratio [HR], 1.58; P<0.001), with a similar risk increase in both symptomatic (HR, 1.56; P<0.001) and asymptomatic patients (HR, 1.58; P=0.006). Finally, the 5-year event rates increased with decreasing LVEF in a linear relationship.

Predictors of Outcome
In a univariable Cox regression analysis, age, NYHA-FC, concomitant concomitant coronary revascularization surgery, a history of hypertension, atrial fibrillation, diabetes mellitus, coronary heart disease, chronic obstructive pulmonary disease, AVA, Zva, SVi, LV mass index, time period 1995 to 1999, and LVEF were univariate predictors of mortality (Table 4). When adjusting for the aforementioned variables except Zva (because of significant colinearity with SVi), LVEF, age, sex, history of atrial fibrillation, diabetes mellitus, chronic obstructive pulmonary disease, SVi, and NYHA-FC remained associated with mortality. These findings were comparable when Zva was substituted for SVi.

Comparing the overall log likelihood χ² of the predictive power of the multivariable models, the model including clinical variables (age, sex, concomitant concomitant coronary revascularization surgery, history of hypertension, chronic obstructive pulmonary disease, diabetes mellitus, coronary heart disease, atrial fibrillation, and NYHA-FC) was significantly improved by addition of TTE data (LV mass index, AVA, and stroke volume index), P=0.005. Further improvement was achieved by addition of LVEF<60% to the combined clinical and TTE model, P<0.0001.

The relationship between mortality and LVEF adjusted for the presence of symptoms is shown in Figure 2; in this model, the coexistence of symptoms and LVEF<60% was associated with the highest mortality rate (5-year mortality of 0.39; n=172). The isolated presence of LVEF<60% was associated with a 5-year survival rate of 0.27 (n=214) and the isolated presence of symptoms with a 5-year survival rate of 0.34 (n=29). Patients with LVEF≥60% and no symptoms had the lowest mortality rate (0.19; n=66). Interaction terms were

Table 3. Operative Data

<table>
<thead>
<tr>
<th>LVEF&lt;50%, n=300</th>
<th>LVEF 50%–59%, n=331</th>
<th>LVEF 60%–69%, n=908</th>
<th>LVEF≥70%, n=478</th>
<th>P Value</th>
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<tr>
<td>CABG surgery</td>
<td>141 (47)</td>
<td>150 (45)</td>
<td>367 (41)</td>
<td>192 (40)</td>
</tr>
<tr>
<td>Mitral valve surgery</td>
<td>6 (2)</td>
<td>11 (3)</td>
<td>24 (3)</td>
<td>23 (5)</td>
</tr>
<tr>
<td>Tricuspid surgery</td>
<td>2 (1)</td>
<td>3 (1)</td>
<td>7 (1)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Septal myectomy</td>
<td>3 (1)</td>
<td>2 (1)</td>
<td>22 (2)</td>
<td>32 (6)</td>
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<td>Prosthesis type</td>
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<tr>
<td>Biological</td>
<td>236</td>
<td>251</td>
<td>687</td>
<td>359</td>
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<tr>
<td>Mechanical</td>
<td>64</td>
<td>80</td>
<td>219</td>
<td>118</td>
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<tr>
<td>Ross procedure</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Prosthesis size, mm</td>
<td>23.6±2.2</td>
<td>23.3±2.1</td>
<td>22.9±2.0*</td>
<td>22.6±1.9†</td>
</tr>
<tr>
<td>Prosthesis size/BSA, mm/m²</td>
<td>12.2±1.7</td>
<td>12.0±1.4</td>
<td>11.8±1.2*</td>
<td>11.9±1.2</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>8 (2.7)</td>
<td>7 (2.1)</td>
<td>4 (0.4)</td>
<td>4 (0.8)</td>
</tr>
</tbody>
</table>

BSA indicates body surface area; CABG, coronary artery bypass graft; and LVEF, left ventricular ejection fraction.

*P<0.008 vs. LVEF<50%.
†P<0.008 vs. LVEF 50%–59%.

Figure 1. Overall survival as a function of left ventricular ejection fraction (LVEF). The expected survival is based on mortality rates of the Minnesota white population with a similar age and sex.
analyzed for interdependence between LVEF and date of AVR and were nonsignificant.

Testing the multivariable models in 1333 patients without history of coronary heart disease, LVEF remained associated with mortality (HR, 0.90 per 10%; P = 0.008, for the model including age, sex, LV mass index, SVi, AVA, NYHA-FC, history of hypertension, atrial fibrillation, chronic obstructive pulmonary disease, and diabetes mellitus, and HR = 0.89 per 10%, P = 0.002, when Zva was substituted for SVi).

In the subset of patients with very severe AS (n=756), LVEF of 60% to 69% and LVEF ≥ 70% but not LVEF 50% to 59% were associated with lower mortality compared with LVEF <50% (LVEF 50%–59%, HR=0.87, P=0.42; LVEF 60%–69%, HR=0.62, P=0.003; and LVEF ≥70%, HR=0.54, P<0.001).

Finally, we tested the effect of LVEF in 255 patients without any other indication for AVR; LVEF ≥60% was associated with reduced mortality compared with patients with LVEF of 50% to 59% (LVEF 60%–69%; HR, 0.48; P=0.003 and LVEF ≥70%; HR, 0.52; P=0.02). This association persisted when adjusting for the same variables in the aforementioned models (LVEF 60%–69%; HR, 0.28; P<0.001 and LVEF ≥70%; HR, 0.45; P = 0.03 for both models).

### Discussion

The primary finding of this study in a large population of patients with severe AS was that preoperative LVEF was a strong predictor of survival during long-term follow-up after AVR. This was true in both symptomatic and asymptomatic patients, in patients with very severe AS, and in patients without a history of coronary heart disease.

Although there is evidence that LVEF is an indicator of the outcome of patients undergoing cardiac surgery, the definition of reduced LVEF is less clear. In one of the first articles

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**Table 4. Cox Regression Analysis Predictors of Mortality**

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<tr>
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<th>Univariable</th>
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<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P Value</td>
<td>HR (95% CI)</td>
<td>P Value</td>
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<tr>
<td>Age, y</td>
<td>1.06 (1.05–1.07)</td>
<td>&lt;0.001</td>
<td>1.05 (1.04–1.06)</td>
<td>&lt;0.001</td>
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<tr>
<td>Sex, male</td>
<td>0.91 (0.80–1.03)</td>
<td>0.13</td>
<td>0.83 (0.69–0.98)</td>
<td>0.03</td>
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<tr>
<td>Hypertension</td>
<td>1.44 (1.27–1.64)</td>
<td>&lt;0.001</td>
<td>1.00 (0.83–1.21)</td>
<td>0.99</td>
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<td>Coronary heart disease</td>
<td>1.44 (1.25–1.65)</td>
<td>&lt;0.001</td>
<td>1.17 (0.96–1.42)</td>
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<td>Atrial fibrillation</td>
<td>1.61 (1.37–1.90)</td>
<td>&lt;0.001</td>
<td>1.43 (1.13–1.80)</td>
<td>0.003</td>
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<td>COPD</td>
<td>1.90 (1.57–2.30)</td>
<td>&lt;0.001</td>
<td>1.31 (1.06–1.62)</td>
<td>0.01</td>
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<td>Diabetes mellitus</td>
<td>1.60 (1.40–1.84)</td>
<td>&lt;0.001</td>
<td>1.27 (1.06–1.52)</td>
<td>0.009</td>
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<td>NYHA-FC</td>
<td>1.31 (1.20–1.44)</td>
<td>&lt;0.001</td>
<td>1.31 (1.15–1.49)</td>
<td>&lt;0.001</td>
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<td>NYHA-FC 1</td>
<td>1.43 (1.23–1.66)</td>
<td>&lt;0.001</td>
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<tr>
<td>NYHA-FC 2</td>
<td>1.64 (1.34–2.02)</td>
<td>&lt;0.001</td>
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<tr>
<td>Concomitant CABG</td>
<td>1.15 (1.02–1.30)</td>
<td>0.02</td>
<td>0.97 (0.82–1.15)</td>
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<td>LVEF (per 10%)</td>
<td>0.83 (0.80–0.87)</td>
<td>&lt;0.001</td>
<td>0.88 (0.83–0.94)</td>
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<td>LVEF&lt;50%</td>
<td>0.81 (0.67–0.98)</td>
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<td>LVEF 50%–59%</td>
<td>0.53 (0.45–0.62)</td>
<td>&lt;0.001</td>
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<tr>
<td>LVEF 60%–69%</td>
<td>0.48 (0.40–0.58)</td>
<td>&lt;0.001</td>
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<td>LVEF≥70%</td>
<td>0.98 (0.97–0.98)</td>
<td>&lt;0.001</td>
<td>0.99 (0.98–1.00)</td>
<td>0.02</td>
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<td>SVi, mL/m²</td>
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<td>&lt;0.001</td>
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<tr>
<td>AV maximum velocity, m/s</td>
<td>0.92 (0.83–1.03)</td>
<td>0.14</td>
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<tr>
<td>AV mean gradient, mmHg</td>
<td>1.00 (0.99–1.00)</td>
<td>0.07</td>
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<tr>
<td>LV mass index, per 10 g/m²</td>
<td>1.03 (1.01–1.05)</td>
<td>0.002</td>
<td>1.00 (0.99–1.04)</td>
<td>0.33</td>
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<tr>
<td>Relative wall thickness</td>
<td>1.63 (0.90–2.98)</td>
<td>0.11</td>
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<tr>
<td>Zva, mmHg mL⁻¹ m⁻²</td>
<td>1.04 (1.02–1.06)</td>
<td>&lt;0.001</td>
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<td>Time period</td>
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<td>1995–1999</td>
<td>0.72 (0.63–0.90)</td>
<td>0.002</td>
<td>0.71 (0.49–1.03)</td>
<td>0.07</td>
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<td>2000–2004</td>
<td>0.94 (0.79–1.11)</td>
<td>0.44</td>
<td>0.95 (0.77–1.17)</td>
<td>0.65</td>
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<td>2005–2009</td>
<td>1.15 (1.02–1.30)</td>
<td>0.02</td>
<td>0.97 (0.82–1.15)</td>
<td>0.74</td>
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AV indicates aortic valve; CABG, concomitant coronary revascularization; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; LVEF, left ventricular ejection fraction; NYHA-FC, New York Heart Association functional class; SVi, stroke volume index; and Zva, valvuloarterial impedance.
describing the effect of LVEF after AVR, O’Toole et al12 gath-
ered a cohort of 93 patients with AS, aortic regurgitation, and
mixed AS/aortic regurgitation who had LVEF estimated by
ventriculography. Although not significant, there was a trend
toward increased mortality in the subset of patients with AS
and LVEF<50%, and the authors concluded that depressed
LVEF might cause a moderate increase in postoperative
mortality. Current guidelines2,3 propose that AVR should
be recommended in patients with LVEF<50% and provide
2 supporting references. In the first article, Connolly et al13
studied the prognosis of 154 patients with severe AS and
with LVEF≤35% undergoing AVR. Improvement in symp-
toms and LVEF occurred in most patients. In the article by
Tribouilloy et al,14 the outcome after AVR in 81 patients with
severe AS and with LVEF≤40%, aortic valve mean gradient
<40 mm Hg, and no contractile reserve on dobutamine stress
echocardiography was noted to be better with AVR than with
medical management. Although both studies were well con-
ducted, their interpretations were restricted to patients with
severe AS and reduced LVEF. To our knowledge, no clinical
outcome data support the selection of LVEF<50% as the cut
point for referral to AVR.

The paucity of available data on the effect of LVEF on
outcome of AVR in patients with severe AS and preserved
LVEF led us to examine a large cohort of patients undergo-
ing AVR for AS in an attempt to determine the effect of LVEF
on survival after AVR. We found that although the traditionally
accepted cutoff for LV systolic dysfunction at LVEF<50%
was associated with the highest 5-year mortality rate, LVEF
50% to 59% was also associated with increased mortality at
5 years compared with the higher LVEF groups. In a recent
publication, we demonstrated that reduced longitudinal LV
function was associated with a poor postoperative outcome
in patients with AS and LVEF≥40% undergoing AVR.15 Similar
findings have since been demonstrated in asymptomatic
patients with AS16 and AS patients with LVEF≥50%.17 The
findings from these small cohort studies have been attrib-
uted to the improved ability of global longitudinal strain in
detecting early stages of LV systolic impairment, as reduced
longitudinal function is known to precede reduced circumfer-
tential function. However, it is also possible that these findings
reflect that the threshold for preserved LVEF was set too low, as our findings suggest.

Our study suggests that not only patients with LVEF<50%
but also those with LVEF<50% to 59% had a less favorable
postoperative outcome. This supranormal threshold probably
reflects that patients with severe AS have smaller cavities as a
consequence of LV remodeling, requiring higher LVEF to pre-
sure stroke volume. Indeed, Dumesnil et al18 demonstrated
an independent relationship between LVEF and relative wall
thickness; thus, for a similar extent of intrinsic myocardial
shortening, the LVEF will tend to increase in relation to the
extent of LV concentric remodeling. In addition, impaired
LV systolic deformation has been demonstrated to be pres-
ent despite preserved LVEF, as a consequence of concentric
remodeling.19

In our study, the higher LVEF threshold is further sup-
ported by the findings that 69% of patients had LVEF≥60%
and that most of these patients had concentric geometry
either concentric remodeling or concentric hypertrophy).
Although relative wall thickness was markedly higher in
patients with LVEF 50% to 59% compared with those with
LVEF<50%, it was lower than in the LVEF≥60% group, sug-
gesting adaption with eccentric remodeling to preserve
stroke volume in this subgroup. A recent study in hyperten-
sive patients has shown that nondilated eccentric LV remod-
eling is associated with better outcome compared with other
types of remodeling.20 Further supporting this, LV end-di-
stolic diameter increased across groups as LVEF decreased.
Despite larger LV size, SVi was lower in patients with LVEF
50% to 59% compared with patients with LVEF≥60%, sug-
gesting that LV systolic function is impaired in this subgroup
of patients.

The triad of severe AS, reduced stroke volume, and pre-
served LVEF has lately received great attention, and several
studies have demonstrated that a reduced stroke volume in
this setting is associated with a poor outcome.21,22 Compared
with patients with normal stroke volume, this paradoxical
low-flow condition is associated with concentric remodel-
ing, smaller LV chamber size, and, although within the
normal range, lower LVEF.23 The increased mortality in
patients with paradoxical low-flow AS could thus be attrib-
uted to reduced LV function not detected when defining this
as LVEF<50%. This finding is supported by several studies
demonstrating that these patients indeed have reduced lon-
gitudinal LV function, re-emphasizing the need to choose a
different LVEF cutoff.24,25

This study has several limitations. It was a retrospec-
tive review of prospectively gathered data, and its accuracy
depended on the availability of information within the medi-
cal records. LVEF was prospectively measured using multiple
echocardiographic methods. Strain rate information was not
available. Most of the patients had indications for AVR other
than LVEF. As this was not a randomized trial, we can only
speculate on the ideal cutoff for referring patients to AVR.
Addition of LVEF to the model of clinical and TTE variables
resulted in only a small increase in area under the curve. The
numerous statistical tests may have resulted in a type I error.
Information on the cause of death was not available, although
it has been suggested that all-cause mortality is a more robust

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**Figure 2.** Overall survival as a function of left ventricular ejection fraction (LVEF) and symptomatic status.

![Survival Curve](image-url)
parameter than cause-specific death.26 Our study concerned patients undergoing surgical AVR; patients undergoing transcatheter AVR were not included.

In summary, in patients with severe AS undergoing AVR, LVEF provides important prognostic information beyond standard risk factors. Although the traditionally accepted cutoff or LV systolic dysfunction at LVEF<50% is associated with the highest mortality, patients with LVEF 50% to 59% also have increased mortality compared with patients with LVEF≥60%, regardless of symptomatic status.

Sources of Funding

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Disclosures

None.

References


**CLINICAL PERSPECTIVE**

Although the management of symptomatic patients with severe aortic stenosis (AS) may seem straightforward, asymptomatic patients with severe AS present important challenges. In the latter group, current guidelines specify that aortic valve replacement is recommended when left ventricular ejection fraction (LVEF) is <50%. The optimal cutoff to define normal systolic function is unknown in the setting of AS-associated remodeling. We examined 2017 consecutive patients with severe AS (aortic valve area<1 cm², indexed valve area<0.6 cm²/m², or aortic valve mean gradient≥40 mm Hg) undergoing aortic valve replacement and followed them for a median of 5 years. Preoperative LVEF was a strong predictor of survival during long-term follow-up after aortic valve replacement. This was true in both symptomatic and asymptomatic patients, in patients with very severe AS, and in patients without a history of coronary heart disease. Preoperative LVEF provided important prognostic information beyond standard risk factors and echocardiographic variables. Patients with LVEF<50% had the highest all-cause mortality rate; in addition, compared with those with LVEF≥60%, patients with LVEF 50% to 59% also experienced increased mortality. These findings should be corroborated in prospective studies, as they may indicate that the LVEF cut point recommended in the current guidelines is too low.
Effect of Left Ventricular Ejection Fraction on Postoperative Outcome in Patients With Severe Aortic Stenosis Undergoing Aortic Valve Replacement
Jordi S. Dahl, Mackram F. Eleid, Hector I. Michelena, Christopher G. Scott, Rakesh M. Suri, Hartzell V. Schaff and Patricia A. Pellikka

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