Risk Prediction in Aortic Valve Replacement: Incremental Value of the Preoperative Echocardiogram

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Background—Risk prediction is a critical step in patient selection for aortic valve replacement (AVR), yet existing risk scores incorporate very few echocardiographic parameters. We sought to evaluate the incremental predictive value of a complete echocardiogram to identify high-risk surgical candidates before AVR.

Methods and Results—A cohort of patients with severe aortic stenosis undergoing surgical AVR with or without coronary bypass was assembled at 2 tertiary centers. Preoperative echocardiograms were reviewed by independent observers to quantify chamber size/function and valve function. Patient databases were queried to extract clinical data. The cohort consisted of 432 patients with a mean age of 73.5 years and 38.7% females. Multivariable logistic regression revealed 3 echocardiographic predictors of in-hospital mortality or major morbidity: E/e' ratio reflective of elevated left ventricular (LV) filling pressure; myocardial performance index reflective of right ventricular (RV) dysfunction; and small LV end-diastolic cavity size. Addition of these echocardiographic parameters to the STS risk score led to an integrated discrimination improvement of 4.1% (*P*<0.0001). After a median follow-up of 2 years, Cox regression revealed 5 echocardiographic predictors of all-cause mortality: small LV end-diastolic cavity size; LV mass index; mitral regurgitation grade; right atrial area index; and mean aortic gradient <40 mm Hg.

Conclusions—Echocardiographic measures of LV diastolic dysfunction and RV performance add incremental value to the STS risk score and should be integrated in prediction when evaluating the risk of AVR. In addition, findings of small hypertrophied LV cavities and/or low mean aortic gradients confer a higher risk of 2-year mortality. (***J Am Heart Assoc***. 2015;4:e002129 doi: 10.1161/JAHA.115.002129)

Aortic stenosis (AS) is one of the most common valvular heart diseases with a pooled prevalence of 12.4% in older adults.[1] Severe AS has been identified as a major cause of morbidity and mortality and, if untreated, can result in debilitating clinical symptoms, progressive heart failure, and sudden cardiac death. The economic impact of AS on the

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health care system is substantial.[2] Traditionally, surgical aortic valve replacement (SAVR) has been the mainstay of treatment for severe AS, but has been associated with 3.2% to 5.6% perioperative mortality when performed without and with concomitant coronary artery bypass graft surgery (CABG), respectively.[3,4] In high-risk elderly patients, the risk of mortality approaches 10%, and 1 of 3 of these patients' experiences a major morbidity.[3,4] A contributing factor to the adverse outcomes observed is that many of the elderly patients considered for SAVR are frail and have multiple chronic conditions.[5]

The emergence of therapeutic alternatives to surgery, such as transcatheter aortic valve replacement (TAVR), has provided a treatment alternative for a significant number of patients with severe AS and high surgical risk, usually defined as a predicted risk of mortality >8% to 10%.[6] Approximately 290 000 elderly patients at high surgical risk could potentially be treated with TAVR in Europe and North America.[1] Hence, the significance of operative risk prediction has increased dramatically owing to its importance in guiding therapeutic decision making in patients with severe AS. Clinicians and researchers rely on risk scores such as The Society of

Thoracic Surgeons (STS) Predicted Risk and the European System for Cardiac Operative Risk Evaluation (EuroSCORE) to estimate risk, although it is recognized that these scores do not capture a number of important variables.

At the present time, risk scores integrate very few echocardiographic variables in their calculations, typically limited to left ventricular (LV) ejection fraction (LVEF), mitral regurgitation (MR) grade, and pulmonary artery systolic pressure (PASP). This represents a missed opportunity to enhance risk prediction given the wealth of hemodynamic, functional, and structural data available in routinely performed preoperative echocardiograms. Recently, our group demonstrated the incremental prognostic value of preoperative echocardiograms in patients undergoing isolated CABG.[7] Thus, we expanded this hypothesis to patients undergoing SAVR to determine the incremental prognostic value of the echocardiogram in addition to the STS risk score to predict short- and long-term mortality and major morbidity.

Methods

Study Design

A cohort of consecutive patients undergoing SAVR with or without CABG at 2 tertiary referral hospitals in the United States and Canada was assembled. Preoperative echocardiograms were analyzed by 2 independent observers who were blinded to the outcomes. A comprehensive echocardiographic protocol was quantitatively measured, reflecting right- and left-sided chamber size and geometry, systolic and diastolic function of the right and left ventricles, and valvular hemodynamics. Clinical variables were extracted from patient databases and vital status from the Social Security Registry. The study was approved by the institutional review board before commencement, and the manuscript was prepared in accord with the Strengthening of Reporting of Observational Studies in Epidemiology guidelines.[8]

Setting

The cohort consisted of consecutive patients who underwent isolated SAVR or combined SAVR+CABG at the Massachusetts General Hospital between 2008 and 2010 (Harvard University, Boston, MA) and at the Jewish General Hospital between 2010 and 2012 (McGill University, Montreal, Quebec, Canada). Both hospitals are academic centers with access to TAVR (although TAVR was in its early stages of adoption and limited to research protocols during the time frame of this study). Patients were followed from the time of their index admission to hospital discharge and subsequently followed forward for vital status up to February 2013.

Participants

The inclusion criteria were: (1) severe AS defined as a peak velocity ≥4 m/s, mean gradient ≥40 mm Hg, aortic valve area (AVA) <1.0 cm^2, or indexed AVA <0.6 cm^2/m^2 by Doppler echocardiography in combination with 2-dimensional echocardiographic appearance of severe valvular AS; (2) SAVR performed with or without CABG; (3) preoperative transthoracic echocardiogram (TTE) performed at the study center ≤3 months before surgery. Patients who had concomitant mitral or tricuspid valve surgery, greater than moderate aortic regurgitation, previous valvuloplasty or valve replacement, or complex congenital heart disease were excluded. Patient who had surgical intervention on the aorta were not excluded. Because echocardiographic images were reanalyzed for the purpose of this study, patients were excluded if their digital echocardiographic images could not be retrieved or were uninterpretable.

Predictor Variables

A comprehensive list of quantitative parameters of left- and right-sided chamber size, geometry, systolic and diastolic function, and valvular function was established a priori and then measured from the preoperative echocardiograms. The acquisitions, measurements, and normal reference limits adhered to the guidelines of the American Society of Echocardiography (ASE).[9–13] Right and left atrial areas were measured at end-systole in the apical 4-chamber view; left atrial height was also measured to calculate left atrial volume using the single-plane area-length method. Right ventricular (RV) area was measured at end-diastole and end-systole in the apical 4-chamber view to calculate fractional area change (FAC) as: [RV end-diastolic area—RV end-systolic area]/[RV end-diastolic area]. Tricuspid valve closure to opening time was measured by continuous-wave Doppler of the tricuspid regurgitation and/or pulsed Doppler of the tricuspid inflow. Pulmonic ejection time was measured from pulsed Doppler profiles obtained at the distal RV outflow tract. RV myocardial performance index (MPI), an index of RV efficiency reflecting both systolic and diastolic function, was calculated as: [Tricuspid valve closure opening time—Pulmonic ejection time]/[Pulmonic ejection time]. PASP was measured by continuous-wave Doppler of the tricuspid regurgitation with 10 mm Hg added for right atrial pressure. The choice of parameters was confined to those that could be measured from the routine echocardiography protocol at both institutions; for example, tricuspid annular plane systolic excursion and/or velocity were not included in our panel because they were not routinely acquired in all patients.

LVEF and LV volumes were measured using the biplane Simpson's method. LV mass was measured using the Devereux method. LV diastolic function was graded as normal, impaired relaxation, pseudonormal filling, or restrictive filling according to the ASE's recommended multiparametric approach that integrates pulsed Doppler of the mitral and pulmonary vein inflow, tissue Doppler of the medial and lateral annulus, and left atrial volume. Valvular regurgitation was graded as normal, mild, moderate, or severe according to the ASE's recommended cutoffs for color Doppler jet area, vena contracta diameter, and proximal isovelocity shell area, where applicable. Measures of AS severity included peak velocity, peak and mean gradients, dimensionless index calculated as [LV outflow tract (LVOT) velocity/Peak velocity], AVA using velocity time integrals rather than velocities, and AVA indexed to body surface area.

Measurements were performed in duplicate by 2 independent echocardiography readers and arbitrated by a third senior reader. All readers were cardiologists trained in echocardiography. To ensure accuracy and consistency of measurement techniques, readers participated in focused training sessions and quality audits throughout the study. Readers were blinded to the clinical data and outcomes when interpreting the echocardiograms.

Outcome Variables

The primary outcome was a composite of in-hospital mortality or major morbidity defined according to the STS as any one of the following: all-cause death, stroke, renal failure (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease [RIFLE] classification $\geq$3), prolonged ventilation $\geq$48 hours, or need for reoperation.[14] The secondary outcome was long-term all-cause mortality defined as death from any cause occurring from the time of cardiac surgery to the end of follow-up. There were no patients lost to follow-up for the primary or secondary outcomes.

Data Sources

Echocardiograms were acquired with the Philips IE33, Sonos 7500, or GE Vivid 7 machines and analyzed on the Xcelera workstation (Philips Medical Systems, Andover, MA) at the Massachusetts General Hospital; and with the GE Vivid 7 machine and EchoPAC workstation (GE, Milwaukee, WI) at the Jewish General Hospital. Clinical data, including in-hospital outcomes, were extracted from the STS Adult Cardiac Surgery Database and vital status was extracted from the Social Security Death Index by way of the Research Patient Data Registry (Partners Healthcare, Boston, MA) at the Massachusetts General Hospitals; and from the ChartMaxx electronic medical record at the Jewish General Hospital.

Statistical Analyses

Echocardiography variables were preserved in their continuous form[15] and standardized such that the resulting odds ratios (ORs) represented the increase in odds per SD in that variable. To test the appropriateness of entering a continuous variable in a logistic regression model, each echocardiographic variable (*x*-axis) was plotted against the logit of the primary outcome (*y*-axis) and the resulting graphical plot was inspected for linearity. When a nonlinear relationship was observed, the variable was transformed into ordinal form.

For the primary outcome, multivariable logistic regression with Akaike information criterion (AIC)-based model selection was used to identify the optimal echocardiographic parameters to predict in-hospital mortality or major morbidity after adjusting for the STS predicted risk of mortality or major morbidity (STS-PROMM). For the secondary outcome, multivariable Cox regression with AIC-based model selection was used to identify the optimal echocardiographic parameters to predict all-cause mortality after adjusting for the Society of Thoracic Surgeons predicted risk of mortality (STS-PROM). The AIC model selection procedure approximates a backward-forward selection procedure with a *P*-value cutoff of $\approx$0.15, hence the optimal predictors may have confidence intervals (CIs) that cross unity.

Model performance statistics were calculated for STS-PROM (or STS-PROMM) alone, and then for STS-PROM (or STS-PROMM) plus the echocardiographic variables. These statistics included the c-statistic and integrated discrimination improvement (IDI).[16] All analyses were performed with the STATA 13 statistical software package (StataCorp LP, College Station, TX).

Results

A total of 1144 patients underwent SAVR at both sites during the study period, of which 432 were eligible and included in the cohort (Figure). The main exclusion criterion was not having an available echocardiogram $\leq$3 months before surgery; excluded patients who did not have an available echocardiogram were similar to included patients in terms of mean age (73.9 vs. 73.5 years), proportion of females (41.1% vs. 38.7%), STS-PROM (5.5% vs. 5.3%), and observed in-hospital mortality (3.2% vs. 3.2%). The median time from echocardiography to surgery was 13 days (interquartile range [IQR], 6–43). The median time from surgery to end of follow-up was 728 days (IQR, 354–1063).

Baseline clinical characteristics are shown in Table 1 and in-hospital outcomes are shown in Table 2. The mean age of the cohort was 73.5$\pm$10.3 years, with 38.7% females. The surgical procedure was isolated SAVR in 49.3% and combined
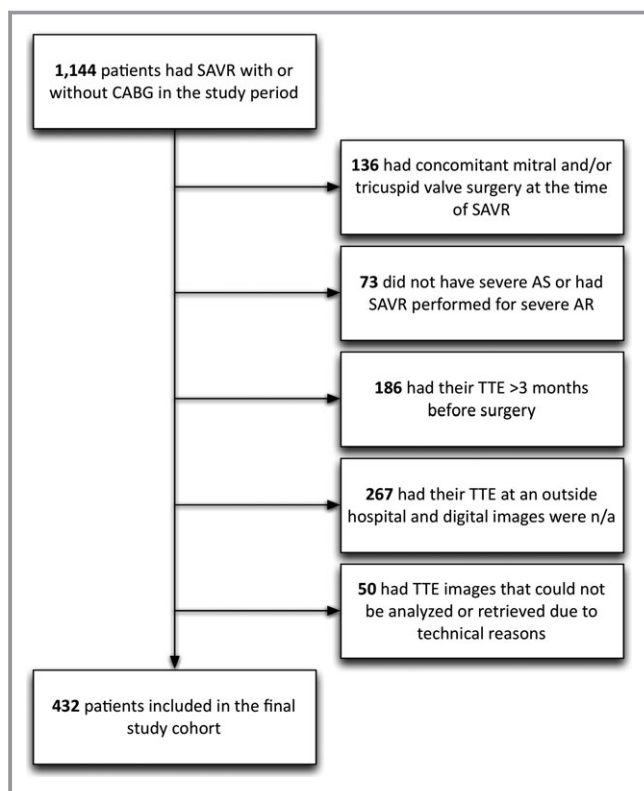
Figure. Flow diagram. Of 1144 patients that underwent SAVR with or without CABG, 432 met the selection criteria and were included in the cohort. Excluded patients who did not have an available echocardiogram were similar to included patients in terms of mean age (73.9 vs. 73.5 years), proportion of females (41.1% vs. 38.7%), STS-PROM (5.5% vs. 5.3%), and observed in-hospital mortality (3.2% vs. 3.2%). AR indicates aortic regurgitation; AS, aortic stenosis; CABG, coronary artery bypass graft surgery; SAVR, surgical aortic valve replacement; STS-PROM, Society of Thoracic Surgeons predicted risk of mortality; TTE, transthoracic echocardiography.

SAVR/CABG in 50.7%. The mean STS-PROM was 5.3±5.1%, and STS-PROMM was 25.7±14.1%. There were 45 deaths and 88 composite adverse events observed (20.4% in-hospital mortality or major morbidity). Adverse event rates were similar at both study centers. Those who had an adverse event were more likely to have advanced age, female sex, chronic kidney disease, and recently decompensated heart failure.

Preoperative echocardiographic parameters are shown in Table 3. AS severity was reflected by AVA 0.75±0.22 cm^2, indexed AVA 0.39±0.11 cm^2/m^2, and peak and mean gradients of 79.6 and 52.7 mm Hg, respectively. One hundred ten patients had severe AS with low mean gradient <40 mm Hg, of which 10.2% had low LVEF <35%. The prevalence of RV systolic dysfunction (abnormal FAC) was 14.4%, whereas subclinical RV dysfunction (abnormal RV MPI with normal RV FAC) was 45.2%. The prevalence of LV

hypertrophy was 52.3% and small LV end-diastolic volume index (LVEDV$_i$) was 9.3%.

In the logistic regression model to predict in-hospital mortality or major morbidity, 3 echocardiographic parameters were independently predictive after adjusting for STS-PROMM (Table 4): E/e' (standardized OR, 1.40; 95% CI, 1.03, 1.78), RV MPI (OR, 1.25; 95% CI, 0.94, 1.65), and LVEDV$_i$ (OR, 0.82; 95% CI, 0.54, 1.00). Model performance was significantly improved by addition of these 3 echocardiographic parameters to the STS-PROMM, resulting in an IDI of 4.1% (*P*<0.001) and an increase in c-statistic from 0.70 for STS-PROMM alone to 0.74 for STS-PROMM plus echocardiographic parameters. The IDI was driven mainly by the new model predicting a higher risk in patients that experienced an adverse event.

A Cox model was then used to predict long-term all-cause mortality at the median follow-up of 2 years (maximum of 4.2 years), and 5 echocardiographic parameters were independently predictive after adjusting for STS-PROM (Table 5): LV mass index (standardized hazard ratio [HR], 1.38; 95% CI, 1.03, 1.91), RA area index (HR, 1.28; 95% CI, 0.94, 1.70), mean aortic gradient <40 mm Hg (HR, 2.23; 95% CI, 1.04, 4.76), mitral regurgitation grade (HR, 1.45; 95% CI, 0.97, 2.16), and LVEDV$_i$ (HR, 0.54; 95% CI, 0.35, 0.82). Addition of these echocardiographic parameters led to an increase in Harrell's c-statistic from 0.82 for STS-PROM alone to 0.85 for STS-PROM plus echocardiographic parameters.

In sensitivity analyses, regression models were rerun with bootstrapping (1000 repetitions); these models identified the same echocardiographic optimal predictors and yielded similar effect sizes for each predictor. The intervariable correlation between the echocardiographic parameters included in the adjusted multivariable models was low (R, 0.02–0.31).

Discussion

Our 2-center study has shown that the preoperative echocardiogram contributes incremental value to identify high-risk candidates for SAVR. In particular, small LV cavity size, LV diastolic dysfunction (high E/e' ratio), and RV dysfunction (high RV MPI) were identified as powerful predictors of in-hospital mortality and major morbidity after SAVR. Enlarged RA cavity size, small LV cavity size, LV hypertrophy, MR, and low mean aortic gradient <40 mm Hg were predictive of long-term mortality over a median follow-up period of 2 years. None of these echocardiographic parameters are currently considered in risk scores for patient selection in AVR.

The magnitude of the incremental value provided by the echocardiogram is important, comparable to other well-

Table 1. Clinical Characteristics

| | Overall (n=432) | In-Hospital Mortality or Major Morbidity | |
		Yes (n=88)	No (n=344)
Age, y	73.5±10.3	75.5±10.5	73.0±10.2
Female, %	167 (38.7)	41 (46.6)	126 (36.6)
BMI, kg/m^2	28.8±6.0	28.7±6.7	28.8±5.8
Diabetes, %	157 (36.3)	35 (39.8)	122 (35.5)
Chronic renal disease, %	185 (42.8)	51 (58.0)	134 (39.0)
Chronic lung disease, %	77 (17.8)	21 (23.9)	56 (16.3)
Peripheral vascular disease, %	72 (16.7)	13 (14.8)	59 (17.2)
Cerebrovascular disease, %	74 (17.1)	16 (18.2)	58 (16.9)
Previous myocardial infarction, %	143 (33.1)	36 (40.9)	107 (31.1)
Atrial fibrillation, %	104 (24.1)	24 (27.3)	80 (23.3)
Prior cardiac surgery, %	56 (13.0)	11 (12.5)	45 (13.1)
Heart failure within 2 weeks, %	205 (47.5)	54 (61.4)	151 (33.9)
Charlson comorbidity index	2.2±1.5	2.6±1.5	2.0±1.5
STS-PROM	5.3±5.1	8.0±6.9	4.6±4.3
Aortic prosthesis size, mm	22.4±2.1	22.3±2.2	22.4±2.1
Concomitant coronary bypass, %	219 (50.7)	54 (61.4)	165 (48.0)
Cardiopulmonary bypass time, min	140.6±59.6	160.4±74.2	135.5±54.2

BMI indicates body mass index; STS-PROM, Society of Thoracic Surgeons predicted risk of mortality.

Table 2. In-Hospital Outcomes

	Overall (n=432)
Mortality or major morbidity, %	88 (20.4)
Mortality, %	14 (3.2)
Stroke, %	18 (4.2)
Acute kidney injury (RIFLE ≥3), %	25 (5.8)
Prolonged intubation (≥48 hours), %	32 (7.7)
Reoperation, %	47 (10.9)

RIFLE indicates Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease.

accepted cardiovascular prognostic tests, such as the coronary artery calcium scan in primary prevention (increase in c-statistic, +0.04; IDI, 1.5%).[17,18] In the current study, as in our previous study of patients undergoing isolated CABG,[7] measures of LV diastolic dysfunction and RV dysfunction emerged as the main incremental predictors of postoperative outcomes. Moreover, measures of LV remodeling and low mean aortic gradient emerged as strong predictors of postoperative outcomes in the setting of SAVR, reflecting the deleterious effect of this phenotypic response to chronic pressure overload.

Consistent with our findings, Boldt et al. found that patients with AS often have elevated RV filling pressures indicative of subclinical RV dysfunction,[19] and Haddad et al. found that RV MPI assessed by intraoperative transesophageal echocardiography was associated with a higher incidence of circulatory failure after aortic and mitral valve surgery.[20] Maslow et al. found that RV FAC was associated with a greater requirement for inotropic or mechanical support and longer length of stay after CABG.[21] The RV MPI and FAC are recommended by the Guidelines for the Echocardiographic Assessment of the Right Heart from the American Society for Echocardiography[12] and have the advantage of (1) being readily measurable from most routine echocardiography acquisition protocols and (2) being validated by prognostic data. Right atrial (RA) dilation was also shown to be predictive, which is not surprising given that RA size is reflective of the chronicity of underlying RV dysfunction.[22]

Elevated LV mass is an established predictor of adverse cardiovascular events,[23] which has garnered interest in the past 5 years as a risk factor in the setting of SAVR. LV mass reflects the severity and chronicity of the pressure overload caused by AS, as well as adaptive or maladaptive efforts to remodel in response. Our findings are consistent with work from the Cleveland Clinic showing that LV mass was predictive of late mortality,[24] whereas concentric geometry and small LV cavity size were predictive of early mortality and prolonged intubation.[25] The negative impact of a small LV cavity size is supported by anecdotal accounts of surgeons

Table 3. Preoperative Echocardiographic Parameters

	Overall (n=432)	In-Hospital Mortality or Major Morbidity	
		Yes (n=88)	No (n=344)
LVOT diameter, cm	2.1±0.2	2.1±0.2	2.1±0.2
LVOT velocity, cm/s	93.4±21.8	91.8±22.1	93.8±21.8
Peak velocity, cm/s	439.3±47.3	426.7±84.7	442.5±74.7
Peak gradient, mm Hg	79.6±27.0	75.7±29.3	80.6±26.3
Mean gradient, mm Hg	52.7±18.6	50.0±20.2	53.4±18.2
Mean gradient			
<40 mm Hg, %	110 (25.5)	26 (29.6)	84 (24.5)
40 to 69 mm Hg, %	246 (57.1)	49 (55.7)	197 (57.4)
≥70 mm Hg, %	75 (17.4)	13 (14.8)	62 (18.1)
Dimensionless index	0.22±0.07	0.22±0.07	0.22±0.06
Aortic valve area, cm^2	0.75±0.22	0.76±0.24	0.74±0.21
Aortic valve area index, cm^2/m^2	0.39±0.11	0.41±0.12	0.39±0.11
Ascending aorta diameter, cm	3.2±0.5	3.2±0.5	3.2±0.5
Bicuspid aortic valve, %	43 (10.5)	6 (7.2)	37 (11.3)
LA volume index, mL/m^2	44.0±17.7	43.2±17.8	44.2±17.7
LV end-diastolic volume index, mL/m^2	59.5±20.2	57.4±20.7	60.0±20.1
LVEF, %	57.8±14.3	56.1±14.9	58.3±14.1
LVEF			
<35%, %	44 (10.2)	10 (11.4)	34 (9.9)
35% to 54%, %	94 (21.9)	27 (30.7)	67 (19.6)
55% to 74%, %	261 (60.7)	45 (51.1)	216 (63.2)
≥75%, %	31 (7.2)	6 (6.8)	57 (7.3)
LV MPI	0.27±0.16	0.29±0.16	0.27±0.16
LV mass index, g/m^2	114.7±32.7	113.1±35.3	115.1±32.1
Mean e'	6.0±2.0	5.5±1.7	6.2±2.0
Mean E/e'	18.1±8.5	21.2±9.9	17.3±8.0
RA area index, cm/m^2	9.4±2.9	9.7±2.9	9.4±2.8
RV end-diastolic area index, cm/m^2	8.5±2.2	8.7±2.2	8.5±2.2
RV fractional area change, %	47.0±11.6	46.8±13.8	47.1±11.0
RV MPI	0.41±0.22	0.48±0.23	0.39±0.21
Pulmonary arterial systolic pressure, mm Hg	42.1±13.3	44.3±13.7	41.5±13.1
Mitral regurgitation			
None or trivial, %	158 (36.9)	32 (36.4)	126 (37.1)
Mild, %	203 (47.4)	39 (44.3)	164 (48.2)
Moderate, %	65 (15.2)	16 (18.2)	49 (14.4)
Severe, %	2 (0.5)	1 (1.1)	1 (0.3)
Tricuspid regurgitation			
None or trivial, %	227 (53.1)	38 (43.2)	178 (54.1)
Mild, %	164 (38.3)	39 (44.3)	125 (38.0)
Moderate, %	34 (7.9)	10 (11.4)	24 (7.3)
Severe, %	3 (0.7)	1 (1.1)	2 (0.6)

LA indicates left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; MPI, myocardial performance index; RA, right atrium; RV, right ventricle.

Table 4. Optimal Echocardiographic Predictors for In-Hospital Mortality/Morbidity

	Unadjusted	Adjusted
	Odds Ratio (95% CI)	Odds Ratio (95% CI)
STS-PROMM	1.003 (1.002, 1.003)	1.003 (1.002, 1.004)
LVEF		
<35%	1.41 (0.65, 3.06)	
35% to 55%	1.93 (1.12, 3.35)	
55% to 75%	Referent	
>75%	1.15 (0.45, 2.97)	
LV end-diastolic volume index	0.82 (0.98, 1.01)	0.82 (0.54, 1.00)
E/e'	1.51 (1.18, 1.92)	1.40 (1.03, 1.78)
LV mass index	1.00 (0.72, 1.38)	
MR grade	1.10 (0.84, 1.45)	
LA volume index	1.00 (0.70, 1.19)	
RV FAC	0.97 (0.77, 1.23)	
RV end-diastolic area index	1.16 (0.91, 1.47)	
RV MPI	1.44 (1.14, 1.82)	1.25 (0.94, 1.65)
PASP	1.30 (0.87, 1.68)	
TR grade	1.32 (0.99, 1.75)	
RA area index	1.12 (0.89, 1.43)	
Mean aortic gradient		
<40 mm Hg	1.24 (0.73, 2.13)	
40 to 70 mm Hg	Referent	
>70 mm Hg	0.84 (0.43, 1.66)	

The unadjusted column represents results from individual logistic regressions, whereas the adjusted column represents results from one multivariable logistic regression. FAC indicates fractional area change; LA, left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; MPI, myocardial performance index; MR, mitral regurgitation; PASP, pulmonary artery systolic pressure; RA, right atrium; RV, right ventricle; STS-PROMM, Society of Thoracic Surgeons predicted risk of mortality or major morbidity; TR, tricuspid regurgitant.

Table 5. Optimal Echocardiographic Predictors of 2-Year Mortality

	Unadjusted	Adjusted
	Odds Ratio (95% CI)	Odds Ratio (95% CI)
STS-PROM	1.005 (1.004, 1.007)	1.005 (1.004, 1.007)
LVEF		
<35%	2.18 (0.92, 5.20)	
35% to 55%	2.08 (1.03, 4.21)	
55% to 75%	Referent	
>75%	2.26 (0.85, 6.07)	
LV end-diastolic volume index	0.66 (0.54, 0.98)	0.54 (0.35, 0.82)
E/e'	1.51 (1.18, 1.92)	
LV mass index	1.00 (0.72, 1.38)	1.38 (1.03, 1.91)
MR grade	1.72 (1.18, 2.52)	1.45 (0.97. 2.16)
LA volume index	1.19 (1.00, 1.69)	
RV FAC	0.93 (0.69, 1.25)	
RV end-diastolic area index	1.16 (0.87, 1.55)	
RV MPI	1.37 (1.11, 1.68)	
PASP	1.48 (1.14, 1.91)	
TR grade	1.87 (1.31, 2.66)	
RA area index	1.70 (1.32, 2.19)	1.28 (0.94, 1.70)
Mean aortic gradient		
<40 mm Hg	1.64 (0.85, 3.14)	2.23 (1.04, 4.76)
40 to 70 mm Hg	Referent	
>70 mm Hg	0.13 (0.48, 2.66)	

The unadjusted column represents results from individual logistic regressions, whereas the adjusted column represents results from one multivariable logistic regression. FAC indicates fractional area change; LA, left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; MPI, myocardial performance index; MR, mitral regurgitation; PASP, pulmonary artery systolic pressure; RA, right atrium; RV, right ventricle; STS-PROM, Society of Thoracic Surgeons predicted risk of mortality; TR, tricuspid regurgitant.

and cardiologists who recall such patients to be "difficult to manage" and prone to perioperative complications. One advantage of our study is that we used Simpson's biplane method in all patients to measure LV volumes with greater precision than a single linear dimension.[10]

The constellation of low mean aortic gradient, small LV cavity size, and concentric hypertrophy were identified as predictors of adverse events; these features are associated with the phenotype of paradoxical low-gradient severe AS, which has received considerable attention.[26] This phenotype is often misleading for clinicians because establishing the diagnosis can be challenging and the prognosis falsely reassuring given a heart that is not dilated or hypokinetic (to the contrary, the LV often appears hyperdynamic). However, studies have convincingly shown, and our data

reaffirm, that paradoxical low-gradient AS constitutes a particularly high-risk group with operative risk of 6% to 33% and medically treated survival <50% at 3 years.[27–30] Patients with paradoxical low-gradient AS are particularly vulnerable to the deleterious effects of patient-prosthesis mismatch and, accordingly, may be good candidates for TAVR.

The evidence for (unrepaired) MR as a risk factor for mortality after SAVR, as shown in our Cox multivariable model, is consistent with an analysis from the Johns Hopkins cardiac surgery database showing that moderate MR was an independent predictor of long-term mortality after SAVR, especially when the etiology was organic and the degree of MR was less likely to improve.[31] An analysis from the PARTNER trial similarly showed that significant MR was associated with an HR of 1.77 for 2-year mortality post-SAVR.[32]

Despite the impact of MR on mortality, the optimal management of such patients with moderate MR undergoing SAVR is not clear, given that the operative risk of double-valve surgery continues to be markedly greater than single-valve surgery.[33,34]

This study had a number of limitations. First, approximately one half of patients were excluded because they did not have a digitally available echocardiogram performed at the study hospitals within the 3-month time frame. The likelihood of selection bias is low given that included and excluded patients had nearly identical age, sex, and predicted and observed mortality. Second, our findings cannot be directly extrapolated to patients undergoing TAVR given that these patients were not included in our cohort. Third, although this is one of the largest series of SAVR with echocardiographic data, statistical power to assess short-term mortality remains limited given the rarity of this occurrence. Fourth, although most of our echocardiographic predictors are routinely measured during a standard complete exam (mean aortic gradient, LV mass, MR grade, RA area, and E/e'), some may not be and thus could lengthen the exam interpretation time by a few minutes (LVEDV, RV MPI). Fifth, the results remain to be validated in an external cohort of AVR patients, although it is reassuring to note that the echocardiographic predictors identified in this study are consistent with those identified in a separate cohort of CABG patients.[7]

In conclusion, the preoperative echocardiogram is readily available and contributes incremental—yet underutilized—prognostic information than can be added to existing risk scores. The growing body of evidence from our studies in CABG and AVR, as well as studies from other groups, suggests that findings of LV diastolic dysfunction and RV function should be incorporated in cardiac surgery risk prediction models. Furthermore, findings of elevated LV mass, small LV cavity size, and low mean aortic gradient reflect the clinical entity of paradoxical low-gradient AS that confers a high risk of adverse events. Incorporating such parameters will lead to refined estimates of risk, which, in turn, will assist clinicians in guiding patients toward the most appropriate therapeutic pathway.

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Disclosures

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