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Inclusion of Functional Status Measures in the Risk Adjustment of 30-Day Mortality After Transcatheter Aortic Valve Replacement

A Report From the Society of Thoracic Surgeons/American College of Cardiology TVT Registry

Suzanne V. Arnold, MD, MHA,[a] Sean M. O'Brien, PhD,[b] Sreekanth Vemulapalli, MD,[b] David J. Cohen, MD, MSc,[a] Amanda Stebbins, MS,[b] J. Matthew Brennan, MD, MPH,[b] David M. Shahian, MD,[c] Fred L. Grover, MD,[d] David R. Holmes, MD,[e] Vinod H. Thourani, MD,[f] Eric D. Peterson, MD, MPH,[b] Fred H. Edwards, MD,[g] for the STS/ACC TVT Registry

ABSTRACT

OBJECTIVES The aim of this study was to develop and validate a risk adjustment model for 30-day mortality after transcatheter aortic valve replacement (TAVR) that accounted for both standard clinical factors and pre-procedural health status and frailty.

BACKGROUND Assessment of risk for TAVR is important both for patient selection and provider comparisons. Prior efforts for risk adjustment have focused on in-hospital mortality, which is easily obtainable but can be biased because of early discharge of ill patients.

METHODS Using data from patients who underwent TAVR as part of the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry (June 2013 to May 2016), a hierarchical logistic regression model to estimate risk for 30-day mortality after TAVR based only on pre-procedural factors and access site was developed and internally validated. The model included factors from the original TVT Registry in-hospital mortality model but added the Kansas City Cardiomyopathy Questionnaire (health status) and gait speed (5-m walk test).

RESULTS Among 21,661 TAVR patients at 188 sites, 1,025 (4.7%) died within 30 days. Independent predictors of 30-day death included older age, low body weight, worse renal function, peripheral artery disease, home oxygen, prior myocardial infarction, left main coronary artery disease, tricuspid regurgitation, nonfemoral access, worse baseline health status, and inability to walk. The predicted 30-day mortality risk ranged from 1.1% (lowest decile of risk) to 13.8% (highest decile of risk). The model was able to stratify risk on the basis of patient factors with good discrimination (C = 0.71 [derivation], C = 0.70 [split-sample validation]) and excellent calibration, both overall and in key patient subgroups.

CONCLUSIONS A clinical risk model was developed for 30-day death after TAVR that included clinical data as well as health status and frailty. This model will facilitate tracking outcomes over time as TAVR expands to lower risk patients and to less experienced sites and will allow an objective comparison of short-term mortality rates across centers. (J Am Coll Cardiol Intv 2018;11:581–9) © 2018 by the American College of Cardiology Foundation.

From the [a]Saint Luke's Mid America Heart Institute and the University of Missouri-Kansas City, Kansas City, Missouri; [b]Duke University, Durham, North Carolina; [c]Lahey Hospital and Medical Center and Harvard Clinical Research Institute, Boston, Massachusetts; [d]University of Colorado School of Medicine, Aurora, Colorado; [e]Mayo Clinic, Rochester, Minnesota; [f]Medstar Washington Hospital Center/Georgetown University, Washington, District of Columbia; and the [g]University of Florida College of Medicine-Jacksonville, Jacksonville, Florida. The STS/ACC TVT Registry is an initiative of the Society of Thoracic Surgeons and the American College of Cardiology. This research was supported by the American College of Cardiology's National Cardiovascular Data Registry. The views expressed in this report represent those of the authors and do not necessarily represent the official views of the

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ABBREVIATIONS AND ACRONYMS

AIC = Akaike information criterion

CI = confidence interval

KCCQ = Kansas City Cardiomyopathy Questionnaire

NYHA = New York Heart Association

STS = Society for Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

Since 2011, patients in the United States who have severe aortic stenosis and are at increased risk for morbidity and mortality with cardiac surgery have been increasingly treated with transcatheter aortic valve replacement (TAVR). A less invasive means of valve replacement, TAVR has been shown in clinical trials to have outcomes that are at least equivalent to surgical aortic valve replacement with respect to short- and long-term survival (1-4). Furthermore, TAVR, at least via the transfemoral route, offers patients quicker recovery of functional status and quality of life and shorter length of stay compared with surgical valve replacement (5-7). As a result, the number of patients who seek treatment of their aortic valve disease with TAVR and the number of hospitals that perform TAVR have grown rapidly throughout the United States.

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To monitor the outcomes of patients undergoing TAVR as the procedure moved from clinical trials to commercial use, the American College of Cardiology and the Society of Thoracic Surgeons (STS) jointly created the TVT (Transcatheter Valve Therapy) Registry. Initial efforts from the TVT Registry to provide benchmarked, risk-adjusted outcome reports to hospitals to support quality improvement have focused on in-hospital mortality, as this is easily and accurately collected. However, the American Heart Association (8) and the STS (9) have advocated for reporting mortality within a standardized time frame (most commonly 30 days), as this is less influenced by differences in local post-acute care facilities and also mitigates the potential for gaming through postoperative transfer of critically ill patients to other facilities. As such, the primary goal of this study was to develop and validate a risk adjustment model for 30-day mortality after TAVR. In addition to standard clinical factors, we sought to incorporate 2 additional markers of patient risk: patient-reported health status and gait speed. As both of these factors have been previously shown to be associated with poor outcomes after TAVR (10,11), their inclusion in the model is likely to provide better risk adjustment beyond models based on clinical factors alone. Finally, as a secondary goal, we also re-estimated the existing in-hospital mortality risk adjustment model (12) with health status and gait speed, because of the importance of these factors for risk adjustment and to provide consistency between the models.

METHODS

STUDY SAMPLE AND PROTOCOL. Details of the design, structure, and data elements for the TVT Registry have been published previously (13,14). Launched in 2011 as a joint initiative of the STS and the American College of Cardiology, the TVT Registry now includes more than 450 clinical sites across the United States. Hospitals are required to participate in the registry by Medicare to obtain reimbursement for the procedure, such that data on nearly all TAVR procedures performed outside of clinical trials in the United States are captured in the registry. To promote quality improvement efforts both locally and nationally, participating centers receive quarterly reports comparing each center's case mix, practice patterns, and outcomes to the national experience. Registry activities have been approved by a central Institutional Review Board, and the Duke University School of Medicine Institutional Review Board granted a waiver of informed consent for this study. Sites collect baseline and follow-up data on patient demographics, comorbidities, hemodynamic status, functional status, patient-reported health status, and outcomes.

OUTCOMES DEFINITION. The primary outcome for our analysis was all-cause mortality at 30 days after TAVR. To reduce bias due to missing outcomes data, we limited our analysis to sites with ≥90% complete data for 30-day survival status. The secondary outcome was in-hospital all-cause mortality. Because reporting of this outcome was complete, no sites were

National Cardiovascular Data Registry or its associated professional societies, identified at https://cvquality.acc.org/NCDR-Home. The study sponsors were not involved in the design and conduct of the study; analysis and interpretation of the data; preparation of the manuscript; or decision to submit the manuscript for publication. Dr. Arnold is supported by a Career Development Grant Award (K23 HL116799) from the National Heart, Lung, and Blood Institute. Dr. Brennan is supported by a grant from the Patient-Centered Outcomes Research Institute (CER-1306-04350). Dr. Cohen has received research grant support from Edwards Lifesciences, Medtronic, and Boston Scientific; and consulting fees from Medtronic and Edwards Lifesciences. Dr. Thourani has served as an adviser for Edwards Lifesciences, Abbott Vascular, Boston Scientific, and Gore Vascular. Dr. Peterson has received grants and personal fees from Janssen and Eli Lilly; and personal fees from Boehringer Ingelheim, Bayer, and AstraZeneca. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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excluded because of missing data for this secondary analysis.

HEALTH STATUS AND GAIT SPEED. The principal health status instrument for the TVT Registry is the 12-item version of the Kansas City Cardiomyopathy Questionnaire (KCCQ) (15), a patient-reported disease-specific health status survey developed to describe and monitor symptoms, functional status, and quality of life in patients with heart failure (16,17). It has undergone psychometric testing in patients with severe aortic stenosis (18), and worse baseline KCCQ-12 scores have been associated with higher risk for mortality after TAVR (10). Scores range from 0 to 100, with higher scores indicating less symptom burden and better quality of life. Linguistically and culturally validated translations of the KCCQ were provided to non-English speakers.

Gait speed was measured pre-procedurally using the 5-m walk test, which was measured in meters per second as the average of 3 patient trials. Patients unable to walk were indicated as such. Slow gait speed, which is an important marker of frailty, has been associated with increased risk for mortality after both surgical aortic valve replacement and TAVR (11,19).

MODEL DEVELOPMENT AND VALIDATION. The purpose of these analyses was to develop models that could be used to risk-adjust outcomes after TAVR by accounting for differences in patient risk across sites. These models are intended to be used for site reporting and feedback as well as to examine site-level variability in outcomes. The model coefficients will be regularly updated over time, as there are changes in patient mix, sites and operators, and technology. As such, previously used methods for risk adjustment that cannot be easily updated over time (e.g., Bayesian statistical framework [12]) were not used. Instead, hierarchical logistic regression with site-specific random intercepts was used to estimate risk-adjusted mortality rates for 30-day and in-hospital mortality for each site. P values for the covariates in the model were Wald-type p values that were calculated by dividing each estimated regression coefficient by its asymptotic standard error and comparing it with a normal distribution. Of note, we excluded procedures before June 2013 (the early experience) in order to analyze a more contemporary time frame.

Covariates for the models included all factors from the original TAVR in-hospital mortality model, which were selected on the basis of clinical judgement (12). In addition, baseline KCCQ-12 scores and gait speed were included. Because of conceptual overlap with these measures and to minimize potential for gaming, New York Heart Association (NYHA) functional class IV was removed as a covariate. Although both KCCQ-12 and gait speed have been associated with TAVR outcomes, these factors have not been included in prior risk adjustment models, because of a high level of missingness. In our cohort, 11.7% of patients were missing baseline KCCQ-12 scores, and 17.7% were missing gait speed. Because patients missing these data tend to be sicker and have lower KCCQ-12 scores and slower gait speeds, we used 2 approaches to limit bias due to missing data. First, we limited our analyses to sites with ≥90% complete data for both KCCQ-12 and gait speed. Second, among included sites, we imputed missing KCCQ-12 and gait speed data to the median. As patients with missing data tend to be slightly sicker than those with collected data (with lower KCCQ-12 scores and slower gait speeds, on average), imputing missing data to the median essentially inserted a slight negative bias by making the missing patients appear less sick than they actual are. This will essentially slightly penalize sites with missing data, as they will not benefit from full risk adjustment (thereby encouraging more complete data collection). We elected not to use multiple imputation for this purpose, because of: 1) a lack of standard formulas to calculate hospital-specific risk-adjusted mortality rates and 95% confidence intervals (CIs) when combining multiple imputation with hierarchical modeling; 2) the computational burden of using multiple imputation in future production runs of the TVT Registry feedback report; and 3) the intended slight negative bias to encourage complete data collection, as described earlier. To assess for selection bias, we compared site-level factors, patient-level characteristics, and outcomes between included and excluded sites using 2-sided Wilcoxon rank-sum tests for median values and standardized differences (a >10% difference is considered clinically relevant) for categorical variables.

Because the purpose of these models is for risk adjustment of outcomes for site reporting, all covariates deemed clinically relevant were retained in these nonparsimonious models. Linearity for all continuous variables was tested using restricted cubic splines, and variables with nonlinear relationships with the outcome were categorized, as appropriate. Validation was performed using a split-sample technique (70/30 split), and calibration was also tested in multiple key patient subgroups. Finally, we compared the models including gait speed and KCCQ versus NYHA functional class IV (previous model) to assess the improvement in risk adjustment with inclusion of these variables and compared the models using Akaike information criterion (AIC), where

smaller AIC values indicate a better fit of the model to the data. All analyses were performed with SAS version 9.4 (SAS Institute, Cary, North Carolina), and statistical significance was defined as a 2-sided p value of <0.05.

RESULTS

PATIENT POPULATION. After excluding 225 sites with <90% complete data on baseline KCCQ and baseline 5-m walk test, the analytic cohort for the in-hospital analysis consisted of 26,867 patients from 225 sites who underwent TAVR between June 1, 2013, and May 31, 2016 (Online Table 1). For the 30-day analysis, we excluded an additional 37 sites with <90% complete data on 30-day survival status and, among these sites, an additional 845 patients without 30-day survival status. Our final analytic sample for the 30-day analysis therefore included 21,661 patients from 188 sites who underwent TAVR between June 1, 2013, and May 31, 2016. There were no significant differences in teaching status, bed size, or annual TAVR procedural volume between included and excluded sites (Online Table 2). There were few meaningful differences between patients from included and excluded sites, with patients from included sites being less likely to be of nonwhite race or Hispanic ethnicity (6.4% vs. 11.1%, standardized difference 17%) and more likely to have a tricuspid aortic valve (94.7% vs. 87.6%, standardized difference 25%). The rate of death at 30 days was also similar between included and excluded sites (4.7% vs. 5.1%, standardized difference 2%).

Demographic and clinical characteristics of the 30-day (primary) analytic population are shown in **Table 1**. As expected, the treated population was most often very elderly and white and had a high burden of both cardiac and noncardiac comorbidities. Only 10.9% of procedures were nonelective, and 21.5% used nonfemoral access. Overall, 11.8% of patients were unable to perform the 5-m walk test, and gait speeds were generally very slow (normal walk speed is ≥0.83 m/s). More than one-half of patients had KCCQ scores <45 at baseline, which is roughly equivalent to NYHA functional class IV status.

DEVELOPMENT AND VALIDATION OF 30-DAY MODEL. Among 21,661 patients in the 30-day cohort, 1,025 patients (4.7%) died in the 30 days after the procedure. The demographic and clinical factors of patients who survived and those who died are shown in **Table 1**, and the multivariate-adjusted odds ratios with 95% CIs are shown in **Table 2**. Factors that were independently associated with greater odds of 30-day death after TAVR included older age, lower body surface area, home oxygen, worse renal function and current dialysis, moderate or severe tricuspid insufficiency, peripheral artery disease, left main coronary artery disease, and prior myocardial infarction. Platelet count was nonlinearly associated with mortality, with the lowest odds of death at a platelet count of 200,000/μl and increased odds of death above and below that level. From a procedural standpoint, need for nonfemoral access, higher acuity status, and an earlier date of procedure were each associated with increased odds of death. Lower baseline KCCQ scores were associated with increased odds of death, as was inability to complete the 5-m walk test. Gait speed as a continuous measure, however, was not significantly associated with 30-day death.

The model C statistic was 0.713, and the calibration of the observed with predicted data was excellent (**Figure 1A**). The expected rate of death was 4.55%, with an observed rate of 4.61% (95% CI: 4.28% to 4.96%). The model was also able to separate patients into a wide range of risk categories, ranging from 1.1% in the lowest decile of predicted risk to 13.8% in the highest decile. Calibration was also good in several pre-defined patient cohorts, including subgroups defined according to sex, age, ejection fraction, NYHA functional class, and prior aortic valve procedure (Online Figure 1). In the validation cohort, discrimination and calibration remained good, with a C statistic of 0.703 and an expected mortality rate of 4.63% compared with an observed rate of 5.01% (95% CI: 4.49% to 5.57%) (**Figure 1B**). In comparison, the model that included NYHA functional class IV instead of gait speed and KCCQ had C statistics of 0.708 in the derivation cohort and 0.694 in the validation cohort, and the AIC was 7,718.84 versus 7,695.64 in the KCCQ/gait speed model, indicating that the updated model better fit the data. After adjusting for patient-level risk, there was no evidence of variation in risk-adjusted mortality rate across sites (**Figure 2**). The point estimate of the between-hospital variance, according to the random-effects model, was close to zero, causing all hospitals to have estimated odds ratios close to 1.00.

DEVELOPMENT AND VALIDATION OF IN-HOSPITAL MODEL. Among 26,867 patients in the in-hospital cohort, 876 (3.3%) did not survive to hospital discharge after TAVR. The demographic and clinical factors of patients who survived and those who died are shown in Online Table 1, and the multivariate-adjusted odds ratios with 95% CIs are shown in Online Table 3. There were few meaningful differences in the covariates most strongly associated with

TABLE 1 Characteristics of Patients by Survival Status at 30 Days After TAVR

	All Patients (N = 21,661)	Alive (n = 20,636)	Dead (n = 1,025)
Age (yrs)			
<75	20.7%	20.9%	16.5%
75–84	36.8%	37.0%	33.8%
≥85	42.5%	42.2%	49.8%
Female	48.4%	48.2%	52.6%
Nonwhite race or Hispanic ethnicity	6.3%	6.4%	5.6%
Body surface area (m^2)			
<1.80	41.4%	40.8%	52.8%
1.80–2.19	49.0%	49.4%	41.6%
≥2.20	9.6%	9.8%	5.7%
Prior myocardial infarction	25.1%	24.9%	29.9%
Prior coronary stenting	34.8%	34.8%	34.6%
Prior coronary bypass surgery	27.7%	27.8%	25.0%
Prior aortic procedure	12.8%	12.6%	16.7%
Prior non-aortic procedure	2.3%	2.4%	1.9%
Number of prior cardiac surgeries			
0	70.0%	70.0%	72.3%
1	26.4%	26.5%	24.6%
≥2	3.6%	3.5%	3.1%
Left main coronary artery stenosis ≥50%	10.0%	9.9%	12.1%
Proximal LAD stenosis ≥70%	19.9%	19.9%	19.9%
Prior stroke or transient ischemic attack	19.3%	19.2%	19.5%
Carotid stenosis	23.4%	23.3%	26.8%
Peripheral artery disease	30.6%	30.2%	39.2%
Atrial fibrillation/flutter	41.4%	41.1%	48.1%
Conduction defect	36.5%	36.5%	36.6%
Implantable defibrillator	3.9%	3.9%	4.6%
Diabetes mellitus	37.4%	37.6%	33.5%
Severe chronic lung disease	14.0%	13.8%	18.4%
Home oxygen use	12.3%	11.9%	19.3%
Current smoker	5.8%	5.7%	6.1%
Renal function			
GFR ≥60 ml/min/1.73 m^2, no dialysis	52.7%	53.1%	44.0%
GFR 30–59 ml/min/1.73 m^2, no dialysis	42.1%	41.9%	45.9%
GFR <30 ml/min/1.73 m^2, no dialysis	5.2%	5.0%	10.1%
Current dialysis	3.7%	3.6%	6.1%
Ejection fraction (%)			
<35	11.0%	10.8%	14.3%
35–54	24.7%	24.6%	25.9%
≥55	64.3%	64.5%	59.8%
Hemoglobin <10 g/dl	14.4%	14.0%	21.6%
Platelet <100,000/μl	4.0%	4.0%	5.2%
Hostile chest	7.0%	6.9%	7.5%
Porcelain aorta	5.8%	5.8%	7.3%
Endocarditis	0.8%	0.8%	0.6%
Degenerative aortic valve	95.6%	95.6%	94.9%
Tricuspid aortic valve	94.7%	94.7%	95.1%
Aortic insufficiency moderate or greater	20.3%	20.3%	20.1%
Mitral insufficiency moderate or greater	29.7%	29.4%	34.8%
Tricuspid insufficiency moderate or greater	24.4%	23.9%	35.2%
Nonfemoral access	21.5%	20.7%	37.9%
Acuity category			
Elective	89.1%	89.7%	77.6%
Urgent	7.6%	7.3%	14.5%
Pre-procedure shock	2.9%	2.7%	6.1%
Emergent/salvage	0.4%	0.3%	1.8%
5-m walk test			
Unable to walk	11.8%	11.4%	19.8%
Gait speed by quartiles			
Q1 (speed <0.417 m/s)	25.3%	24.8%	35.6%
Q2 (speed 0.417–0.624 m/s)	28.5%	28.5%	28.7%
Q3 (speed 0.625–0.788 m/s)	20.1%	20.3%	17.5%
Q4 (speed ≥0.789 m/s)	26.0%	26.4%	18.2%
KCCQ by quartiles			
Q1 (KCCQ <23.96)	25.0%	24.6%	34.0%
Q2 (KCCQ 23.96–40.09)	26.1%	26.0%	30.0%
Q3 (KCCQ 40.10–58.32)	22.9%	23.1%	19.6%
Q4 (KCCQ ≥58.33)	25.9%	26.3%	16.5%
Length of stay (days), median (IQR)	5 (3–8)	5 (3–8)	5 (3–16)

GFR = glomerular filtration rate; LAD = left anterior descending coronary artery; IQR = interquartile range; KCCQ = Kansas City Cardiomyopathy Questionnaire; Q = quartile.

Continued in the next column

in-hospital versus 30-day death. Similar to the 30-day mortality model, lower KCCQ scores and inability to complete the 5-m walk test were also associated with increased odds of in-hospital death. The C statistic of the model was 0.723 in the derivation cohort and 0.707 in the internal validation cohort. The calibration of the observed with predicted data was excellent in both the derivation and validation cohorts (Online Figures 2A and 2B), with the expected rate of death being 3.29% versus the observed rate of 3.30% (95% CI: 3.05% to 3.56%). In comparison, the model that included NYHA functional class IV instead of gait speed and KCCQ had C statistics of 0.717 in the derivation cohort and 0.704 in the validation cohort, and the AIC was 7,155.77 versus 7,099.82 in the KCCQ/gait speed model, indicating that the updated model better fit the data. Similar to the 30-day model, there was no evidence of variation in risk-adjusted mortality rate for in-hospital death across sites after accounting for patient risk (Online Figure 3).

DISCUSSION

In a national registry of patients undergoing TAVR, we developed and validated models for 30-day and

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TABLE 2 TVT Registry 30-Day Mortality Risk Adjustment Model

	Odds Ratio (95% CI)	p Value
Age (per 5 yrs when ≤75)	0.91 (0.82–1.01)	0.089
Age (per 5 yrs when >75)	1.19 (1.11–1.28)	<0.001
Sex (female at BSA 1.7 m^2 vs. male at BSA 1.9 m^2)	1.00 (0.87–1.16)	0.959
Race (nonwhite race or Hispanic ethnicity)	1.15 (0.87–1.52)	0.341
Body surface area (per 1 m^2 for male)	0.33 (0.21–0.54)	<0.001
Body surface area (per 1 m^2 for female)	0.45 (0.28–0.71)	<0.001
Prior myocardial infarction	1.21 (1.04–1.42)	0.015
Prior coronary stenting	0.89 (0.77–1.03)	0.117
Prior coronary bypass surgery	0.76 (0.57–1.03)	0.080
Prior cardiac operations (1 vs. 0)	0.99 (0.75–1.31)	0.953
Prior cardiac operations (≥2 vs. 0)	0.80 (0.51–1.27)	0.349
Prior aortic valve procedure	1.11 (0.92–1.33)	0.272
Prior non-aortic valve procedure	0.69 (0.42–1.15)	0.156
Left main coronary artery stenosis ≥50%	1.34 (1.07–1.67)	0.011
Proximal LAD stenosis ≥70%	1.08 (0.90–1.31)	0.409
Prior stroke or transient ischemic attack	0.91 (0.77–1.07)	0.250
Carotid stenosis	1.09 (0.94–1.27)	0.272
Peripheral artery disease	1.23 (1.06–1.41)	0.006
Atrial fibrillation or flutter	1.13 (0.99–1.29)	0.081
Conduction defect	0.97 (0.85–1.12)	0.703
Pacemaker	0.92 (0.77–1.10)	0.345
Implantable defibrillator	1.18 (0.85–1.65)	0.316
Diabetes mellitus	0.89 (0.77–1.02)	0.100
Severe chronic lung disease	1.15 (0.96–1.38)	0.143
Home oxygen	1.54 (1.28–1.84)	<0.001
Current smoker	0.92 (0.70–1.23)	0.586
GFR (per 5 ml/min/1.73 m^2)	0.96 (0.94–0.97)	<0.001
Current dialysis vs no dialysis and GFR 90 ml/min/1.73 m^2	2.04 (1.49–2.79)	<0.001
Ejection fraction (per 5%)	0.99 (0.96–1.01)	0.306
Hemoglobin (per 1 g/dl)	0.98 (0.94–1.02)	0.353
Platelet count (per 10,000/μl when ≤200,000/μl)	0.97 (0.95–0.99)	0.007
Platelet count (per 10,000/μl when >200,000/μl)	1.02 (1.00–1.03)	0.014
Hostile chest	1.25 (0.97–1.61)	0.088
Porcelain aorta	1.14 (0.88–1.47)	0.317
Endocarditis	0.63 (0.27–1.51)	0.303
Aortic etiology (degenerative vs. other)	0.89 (0.66–1.21)	0.467
Valve morphology (tricuspid vs. other)	1.12 (0.82–1.51)	0.486
Aortic insufficiency (moderate/severe)	0.86 (0.73–1.02)	0.080
Mitral insufficiency (moderate/severe)	0.92 (0.79–1.06)	0.242
Tricuspid insufficiency (moderate/severe)	1.49 (1.29–1.73)	<0.001
Nonfemoral access	1.89 (1.61–2.21)	<0.001
Acuity: urgent	1.67 (1.37–2.04)	<0.001
Acuity: shock	1.89 (1.42–2.52)	<0.001
Acuity: emergent	5.12 (2.94–8.93)	<0.001
Unable to walk vs. able to walk and speed first percentile	1.27 (1.02–1.58)	0.036
Gait speed (per 0.2 m/s)	0.95 (0.89–1.02)	0.146
Baseline KCCQ score (per 25 points)	0.82 (0.76–0.89)	<0.001
Date of procedure (per 30 day)	0.99 (0.98–0.99)	<0.001

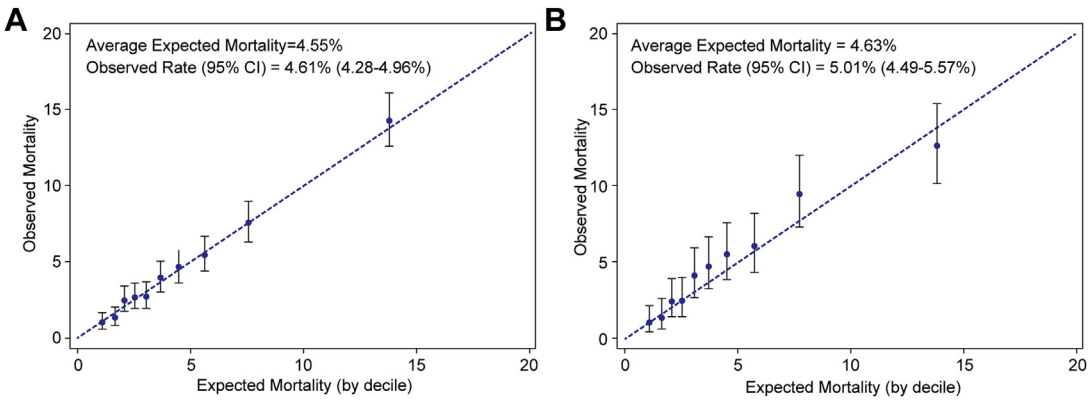
CI = confidence interval; GFR = glomerular filtration rate; LAD = left anterior descending coronary artery; KCCQ = Kansas City Cardiomyopathy Questionnaire; TVT = Transcatheter Valve Therapy.

in-hospital mortality that can be used to adjust for the risk of the patient. These models will permit an objective comparison of short-term mortality rates among hospitals that treat patients with different risk profiles. The hope is that providing this type of quality assessment, benchmarking, and feedback to providers and sites performing TAVR will translate into quality improvement efforts, both nationally and locally, that result in improved patient outcomes (20-24).

KCCQ AND GAIT SPEED. Importantly, both the 30-day and in-hospital mortality models included baseline patient health status and gait speed, 2 factors that are known to be prognostically important (10,11,19,25) but have rarely been included in similar models because of the difficulty in routinely assessing these factors in large data sets (particularly outside of clinical trials). Although NYHA functional class can be used as a means for capturing patients' symptoms and functional status, it has substantial limitations. Physicians' estimations of patients' symptoms have been known to correlate poorly with symptoms reported directly from patients on validated instruments (10,26), particularly before a procedure in which physicians tend to overestimate patients' symptom burden (27). This issue becomes greater when dealing with risk adjustment, as "upcoding" of symptoms will result in the patient appearing to be at higher risk than he or she truly is (thereby gaming the system). Furthermore, NYHA functional class is a coarse assessment of health status with only 4 levels. By using gait speed and KCCQ score, 2 objective and reproducible measurements, we were able to more accurately phenotype the patients and to avoid the possibility of gaming. Because of the importance of these factors for risk adjustment, we also re-estimated the in-hospital mortality model with these factors included, even though it had been previously developed and validated with NYHA functional class (12).

As expected, lower baseline KCCQ scores were strongly associated with increased risk for mortality at 30 days, with similar strength of association as had been previously observed (10). Gait speed as a continuous measure was not significantly associated with 30-day death, but inability to complete the 5-m walk test was associated with an increased risk for in-hospital and 30-day death. Although prior studies have shown slower gait speed to be modestly associated with increased risk for short-term mortality (11,19), those studies did not adjust for baseline health status, which captures much of the disease-specific functional limitations that are more strongly associated with short-term mortality. Gait speed, along with other frailty markers, appears to be more strongly associated with increased risk for poor intermediate and long-term outcomes (28). Frail patients often can survive the procedure but then will

FIGURE 1 **Calibration of the 30-Day Risk Adjustment Model in the Derivation (A) and Validation (B) Cohorts**

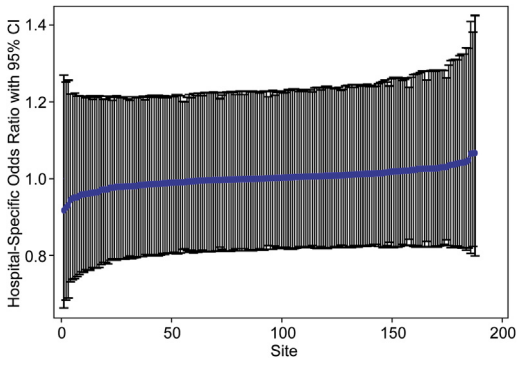


Deciles of predicted odds are plotted against the observed odds of death at 30 days after transcatheter aortic valve replacement, with 95% confidence intervals (CIs). The **dashed line** represents perfect calibration.

fail to recover because of the lack of reserve. As such, it would be expected that the association of slow gait speed with mortality would strengthen as the time frame for analysis lengthens.

SITE-LEVEL VARIABILITY. Another important finding of our analysis is the apparent lack of site-level variability in outcomes. This finding contrasts with that from a previous study (also from the TVT Registry) that suggested that there was variability in risk-adjusted in-hospital mortality rates among hospitals in the early commercial experience (the study analyzed outcomes after TAVR from November 2011 to October 2014). There are a number of potential explanations for these divergent findings. First, as our goal was to create a model that reflects current experience, we excluded TAVR procedures performed before June 2013, and these early cases may have been a source of variation because of the learning curve (29). Second, we excluded 225 sites because of high rates of missing KCCQ or gait speed data—sites that had been included in the prior analysis. A smaller number of sites can lead to narrowing of the range of risk-adjusted outcomes because of shrinkage correction for hospital sample sizes. Furthermore, differences in modeling strategies (i.e., hierarchical logistic regression in the present study vs. full Bayesian risk adjustment in the prior study) may have masked some variation in the present analysis. Third, the addition of KCCQ and gait speed could have improved risk adjustment that explained some of the previously seen variation. Although the second 2 explanations have more to do with modeling, the first would suggest a true lack of variation in outcomes. As TAVR has been expanded to new sites in a relatively controlled manner with some oversight and monitoring, it is possible that outcomes, at least in the short term, are reasonably similar across sites. Obviously, this will need to be tracked over time as TAVR expands to lower risk patients and to less experienced sites.

FIGURE 2 **Distribution of Estimated Hospital-Specific Odds Ratios and 95% Confidence Intervals for 30-Day Mortality**



CI = confidence interval.

STUDY LIMITATIONS. Our findings should be interpreted in the context of the following potential limitations. As described earlier, we excluded a number of sites because of incomplete ascertainment of baseline health status and gait speed. It is unlikely that this influenced our modeling, as there were few meaningful differences between included and excluded sites and the patients treated at these sites

(and the factors that did differ were not significantly associated with mortality). Online Table 2 presents these findings in detail, confirming that the characteristics of sites used in model development are essentially the same as those of excluded sites. However, the smaller number of analyzed sites limited our ability to examine site-level variability.

Second, although statistical techniques such as Bayesian modeling and multiple imputation for missing data might have produced slightly more accurate risk adjustment models, the need to provide frequent reports to sites and to regularly update the model made these techniques impractical.

Third, the inclusion of KCCQ and gait speed as opposed to NYHA functional classification, which is easier to assess, only modestly improved discrimination of the models. However, as described earlier, we believe that the empirical inclusion of directly measured functional status and patient-reported symptoms and quality of life, compared with physician-estimated NYHA functional class, is important regardless of the degree of statistical improvement in the models, as these objective assessments are both more accurate and less subject to gaming.

Finally, these models were designed to allow center-to-center comparisons of outcomes and not for individual patient counseling regarding the risk for TAVR or for comparisons with the predicted risk for surgical valve replacement. As such, all clinically relevant variables were included in the models with no model reduction for parsimony. Other studies are ongoing for this latter purpose.

CONCLUSIONS

We developed and validated risk adjustment models to predict 30-day and in-hospital mortality after TAVR to permit objective comparisons of outcomes across sites by accounting for differences in case mix. Importantly, these models included patient-reported health status and gait speed at baseline, 2 factors known to be prognostically important beyond traditional demographic and clinical factors but that are rarely included in such models because of the burden of collecting these data. Finally, after exclusion of the early TAVR experience, we found no evidence of site-level variability in short-term mortality. Whether this finding represents a statistical anomaly due to limited number of sites or modeling technique or this represents a true lack of variability in risk-adjusted mortality outcomes is not known and will need to be followed over time, particularly as the use of TAVR expands further to lower risk patients and less experienced sites and operators.

ADDRESS FOR CORRESPONDENCE: Dr. Suzanne V. Arnold, Saint Luke's Mid America Heart Institute, 4401 Wornall Road, Kansas City, Missouri 64111. E-mail: suz.v.arnold@gmail.com.

PERSPECTIVES

WHAT IS KNOWN? Assessment of risk for TAVR is important both for patient selection and provider comparisons but previously had been limited to in-hospital mortality.

WHAT IS NEW? We developed and validated a risk adjustment model for 30-day mortality, a time frame recommended by the American Heart Association and STS for reporting. We also included patient health status and gait speed in the model, 2 factors known to be associated with outcomes but are rarely included in such models because of difficulties in routinely collecting them.

WHAT IS NEXT? This model will allow quality assessment, benchmarking, and feedback to providers and sites of risk adjusted site-level outcomes, which can be used to spur quality improvement efforts, both nationally and locally.

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KEY WORDS mortality, transcatheter aortic valve replacement, variation

APPENDIX For supplemental tables and figures, please see the online version of this paper.