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ORIGINAL RESEARCH

Race-Specific Impact of Conventional Surgical Risk Score on 1-Year Mortality After Transcatheter Aortic Valve Replacement

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ABSTRACT

BACKGROUND Interracial differences in the distribution and prognostic value of conventional Society of Thoracic Surgeons (STS) score on long-term mortality after transcatheter aortic valve replacement (TAVR) are uncertain.

OBJECTIVES This study aims to compare the impact of STS scores on clinical outcomes at 1-year after TAVR between Asian and non-Asian populations.

METHODS We used the Trans-Pacific TAVR (TP-TAVR) registry, a multinational multicenter, observational registry involving patients undergoing TAVR at 2 major centers in the United States and 1 major center in Korea. Patients were classified into 3 groups (low, intermediate, and high-risk) according to the STS score and compared between STS risk groups and race. The primary outcome was all-cause mortality at 1-year.

RESULTS Among 1,412 patients, 581 were Asian and 831 were non-Asian. The distribution of the STS risk score group was different between Asian and non-Asian groups (62.5% low-, 29.8% intermediate-, and 7.7% high-risk in Asian vs 40.6% low-, 39.1% intermediate-, and 20.3% high-risk in non-Asian). In the Asian population, the all-cause mortality at 1-year was substantially higher in the high-risk STS group than in the low- and intermediate-risk groups (3.6% low-risk, 8.7% intermediate-risk, and 24.4% high-risk; log-rank $P < 0.001$), which was primarily driven by noncardiac mortality. In the non-Asian group, there was a proportional increase in all-cause mortality at 1-year according to the STS risk category (5.3% low-risk, 12.6% intermediate-risk, and 17.8% high-risk; log-rank $P < 0.001$).

CONCLUSIONS In this multiracial registry of patients with severe aortic stenosis who underwent TAVR, we identified a differential proportion and prognostic impact of STS score on 1-year mortality between Asian and non-Asian patients (TP-TAVR [Transpacific TAVR Registry]; NCT03826264) (JACC: Asia 2023;3:376–387) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Based on cumulative evidence from multiple large-sized randomized clinical trials, transcatheter aortic valve replacement (TAVR) has become the established treatment for severe, symptomatic aortic stenosis (AS) of all surgical risks.[1-11] In such clinical trials as well as in the daily clinical practice, the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score has been used as the default risk stratification index for consideration of TAVR procedures. The STS-PROM uses an algorithm based on the presence of coexisting illnesses to predict 30-day operative mortality (with scores ranging from 0 to 100% and higher scores indicating a greater risk of death within 30 days after the surgical procedure).[12,13]

This STS risk algorithm was originally developed to predict operative mortality after cardiac surgery, so awareness of the limitations of this conventional surgical risk score for TAVR risk stratification has increased. The predictive value of the STS score on long-term mortality and adverse outcomes after the TAVR procedure is still limited. Furthermore, whether the prognostic impact of STS scores uniformly or differentially affects the relative clinical outcomes among different racial or ethnic groups is uncertain. In this regard, several small to moderate-sized studies have provided conflicting results.[14-19] Using the international, multicenter Trans-Pacific TAVR (TP-TAVR) registry, we compared the distribution of STS risk groups, and the prognostic impact of the STS risk score on 1-year mortality after TAVR across different racial groups (Asian vs non-Asian).

METHODS

STUDY POPULATION AND DATABASE. The TP-TAVR registry contains data from a multinational, multicenter, observational cohort study that included all consecutive patients with symptomatic severe AS who underwent TAVR at 2 major academic medical centers in the United States (Stanford University School of Medicine, Stanford, California, and the Feinberg School of Medicine at Northwestern University, Chicago, Illinois) and 1 in South Korea (Asan Medical Center, Seoul) (NCT03826264).[20,21] Beginning in February 2019, data were retrospectively collected for cases performed before initiation and prospectively thereafter. Each center's institutional review board or ethics committee approved the registry protocol. The TP-TAVR registry was partly funded by the CardioVascular Research Foundation (Seoul, Korea) and a supporting grant (2020IF0016) from the Asan Institute for Life Sciences and Corporate Relations of Asan Medical Center, Seoul, South Korea.

All 3 databases were standardized according to the common database model and merged per the policy of data use agreement among participating centers. Patient demographics, surgical risk score (STS-PROM score), functional status, clinical risk factors or comorbidities, anatomic or hemodynamic parameters by cardiac computed tomography or echocardiography, procedural details, and in-hospital and follow-up outcomes were collected in the common database. The STS-PROM uses an algorithm that is based on the presence of coexisting illnesses to predict 30-day operative mortality and this score itself includes the race-specific differences for calculating the estimated mortality rates.[12] The STS-PROM score equals the predicted mortality expressed as a percentage. In the current analysis, all patients had their baseline STS scores and the study population was categorized into 3 conventional risk groups: low surgical risk (STS score <4), intermediate surgical risk (STS score 4-8), and high surgical risk (STS score >8), to evaluate the clinical impact of baseline STS-PROM score on mortality and adverse clinical events.

TAVR PROCEDURES

A multidisciplinary heart team evaluated the candidacy of each patient for TAVR or surgical aortic valve replacement based on their age, underlying comorbidities, surgical risk, frailty status, anatomic characteristics, and preference at each participating center. All TAVR procedures were conducted following local guidelines using standard techniques and were performed with commercially approved TAVR devices. Procedural planning, including the type (eg, balloon-expandable or self-expandable devices) and size of the TAVR valve, access site, and pre-implantation balloon aortic valvuloplasty, were

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

BMI = body mass index

MI = myocardial infarction

STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality

TAVR = transcatheter aortic valve replacement

TP-TAVR = Trans-Pacific TAVR registry

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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determined based on the review of multimodality imaging by the local multidisciplinary heart team.[20,21] After the TAVR procedure, the patients were prescribed single or dual antiplatelet therapy or oral anticoagulants (eg, warfarin or direct oral anticoagulants) if clinically indicated.

OUTCOMES. The primary outcome was all-cause mortality at 1 year after the procedure. Secondary outcomes included cardiac or noncardiac death, stroke, a composite of death or stroke, rehospitalization, and a composite of death, stroke, or rehospitalization. In addition, in-hospital events such as death, stroke, myocardial infarction (MI), life-threatening or disabling bleeding, major vascular complications, new permanent pacemaker insertion, or new-onset atrial fibrillation were also assessed. All adverse events were defined using the Valve Academic Research Consortium criteria.[22,23] All stroke events were confirmed by a trained neurologist or stroke specialist. Rehospitalization was defined as any hospitalization related to the procedure, the valve, or heart failure. All components of the primary and secondary clinical outcomes were adjudicated by an independent group of clinicians blinded to the participating centers, race, and device type.[20,21]

STATISTICAL ANALYSIS. The principal purpose of this study was to determine if there are race-based (Asian vs non-Asian) differences in the proportion and prognostic impact of the STS scores on mortality or adverse clinical events. The baseline characteristics of all patients were compared and stratified according to STS score category (low-, intermediate-, or high-risk) and racial group (Asian or non-Asian). Continuous variables, presented as means with standard deviations, were compared using the Student's *t*-test or the Wilcoxon rank-sum test, depending on their distribution. Categorical and ordinal variables, presented as frequencies and percentages, were compared using the chi square test or Fisher exact test (expected frequency: <5). Event rates were based on Kaplan-Meier estimates in time-to-first-event analyses and were compared using the log-rank test.

To investigate the relative risk according to the STS score category in the 2 racial groups, Cox proportional hazards models were used to compare the rates of primary and secondary outcomes, and hazard ratios were calculated and presented with 95% confidence intervals. After unadjusted analyses were initially performed, multivariable Cox regression analyses were conducted. In the adjusted models, the following relevant covariates were included; age, body mass index (BMI), NYHA functional class of III or IV, diabetes mellitus, peripheral vascular disease, prior MI, chronic lung disease, end-stage renal disease, aortic valve area, mean aortic valve pressure gradient, bicuspid aortic valve, and left ventricular ejection fraction, which were significantly associated with all-cause death at 1 year in the univariable analysis. After then, the interaction across the STS score categories and racial groups for the primary and secondary outcomes were also tested to determine whether differential risks in clinical outcomes according to STS categories might exist according to different racial groups. The assumptions of the Cox model were assessed statistically based on Schoenfeld residuals and graphically by log-log plots and were approximately satisfied for all variables. Finally, receiver operating characteristic curves were generated to evaluate the capacity of discrimination of the STS score for the primary outcome of all-cause mortality as well as cause-specific mortality (cardiac or noncardiac) in the 2 groups.

All statistical analyses were performed using SAS software version 9.4 (SAS Institute) and R software version 4.0.3 (R Foundation for Statistical Computing). All reported *P* values are 2-sided, and a *P* value of <0.05 was considered to indicate statistical significance. No adjustment for multiple testing was undertaken.

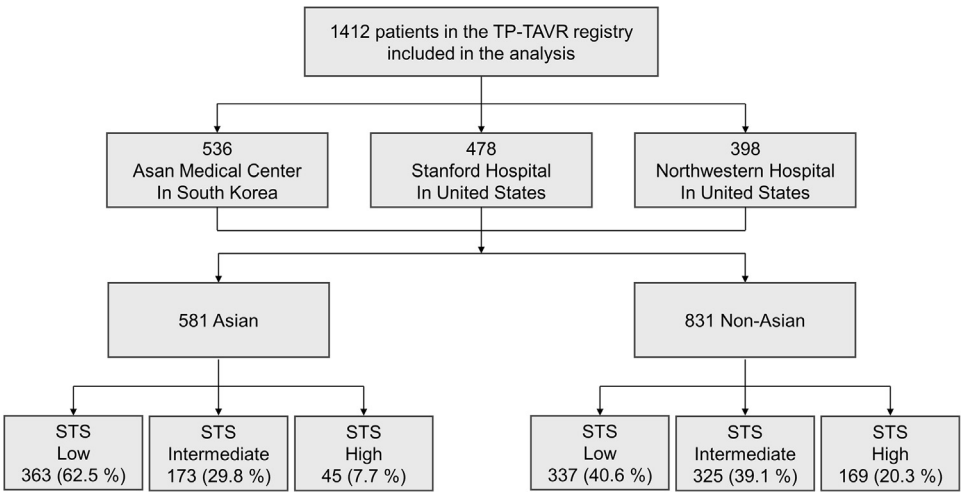
RESULTS

PATIENTS CHARACTERISTICS AND THE DISTRIBUTION OF STS SCORE. Among 1,412 patients of the TP-TAVR registry with valid information on the baseline STS-PROM score, 581 (41.1%) patients were Asian, and 831 (58.9%) patients were non-Asian (87.5% were White, 1.7% Black, 6.1% Hispanic, and 4.7% others). There were differences in the relative proportion of STS risk category between Asian and non-Asian groups (**Figure 1**); the proportion of low-risk patients was greater in the Asian cohort, whereas the proportion of high-risk patients was larger in the non-Asian cohort.

Baseline clinical, anatomical, and procedural characteristics according to the STS score category in each racial group are presented in **Table 1**. There were significant interracial differences in baseline characteristics for age, BMI, prior MI, atrial fibrillation, and aortic valve or annulus area. In general, patients with higher STS scores were older and had more clinical and anatomic risk factors.

CLINICAL OUTCOMES. During a median follow-up of 12.9 months (IQR: 7.1-24.7 months), there were 194

FIGURE 1 Study Flow Diagram of Patients



Study flow diagram and the relative proportion of Society of Thoracic Surgeons (STS) score risk category between Asian and non-Asian groups are shown. TAVR = transcatheter aortic valve replacement; TP-TAVR = Trans-Pacific TAVR registry.

deaths, 50 strokes, and 362 rehospitalizations. The observed event rates of in-hospital adverse events and primary and secondary outcomes at 30 days and at 1 year stratified by the STS risk category in the overall population are summarized in Supplemental Table 1. As expected, there were more frequent adverse events in the highest STS risk score group. In-hospital and 30-day outcomes according to the STS risk score category stratified by the racial group are summarized in Supplemental Tables 2 and 3.

The primary and secondary outcomes at 1 year by the STS score category in the Asian and non-Asian groups are shown in **Table 2**. Rates of the primary outcome of all-cause mortality at 1 year in the Asian group were substantially higher in the high STS group than in the intermediate- and low-STS groups (3.6% vs 8.7% vs 24.4% in low-, intermediate-, and high-STS groups, respectively; $P < 0.001$) (**Figure 2**). This trend was mainly driven by noncardiac mortality rather than cardiac mortality (**Figure 3**). However, there was a proportional increase in all-cause mortality according to STS levels in the non-Asian group (5.3%, 12.6%, and 17.8% in low-, intermediate-, and high-STS groups, respectively; $P < 0.001$) (**Figure 2**). This pattern was similar for cardiac and noncardiac mortality (**Figure 3**).

With respect to secondary outcomes, there was a trend toward the highest rates of stroke or rehospitalization in the high-STS category in both groups. However, a proportional increase of such events was not evident across the STS score category (**Table 2**).

ADJUSTED MARGINAL AND INTERACTION ANALYSES. The adjusted marginal and interaction analyses for the primary and secondary outcomes according to race groups are summarized in **Table 3**. After multivariable adjustment for clinical, hemodynamic, and anatomic important covariates, the HRs for the primary outcome of all-cause mortality at 1 year in the overall population was 2.16 (95% CI: 1.37-3.39; $P < 0.001$) in the intermediate-risk group, and 3.12 (95% CI: 1.78-5.48; $P < 0.001$) in the high-risk group as compared with the low-risk STS group. There was a remarkable increase in the risk of all-cause death in the high-risk STS group in the Asian group compared with the non-Asian group. This difference was mainly driven by noncardiac mortality. Therefore, although there was no significant interaction between racial group and the STS score category for all-cause mortality (P for interaction = 0.31), these race-specific HRs were significantly different regarding noncardiac mortality (P for interaction = 0.02). Also, a significant interaction was present between racial groups and the STS score category for the risk of stroke ($P = 0.008$) and a composite of death, stroke, or rehospitalization ($P = 0.003$).

DISCRIMINATIVE CAPABILITY OF THE STS SCORE IN EACH RACIAL GROUP. The area under the receiver operating characteristic curves for predicting all-

TABLE 1 Baseline Demographics, Clinical, Imaging, and Procedural Characteristics According to the STS Score and Racial Group

	Asian				Non-Asian				
	STS Score				STS Score				
	Low (<4%) (n = 363, 62.5%)	Intermediate (4%-8%) (n = 173, 29.8%)	High (>8%) (n = 45, 7.7%)	*P* Value	Low (<4%) (n = 337, 40.6%)	Intermediate (4%-8%) (n = 325, 39.1%)	High (>8%) (n = 169, 20.3%)	*P* Value	*P* Value [a]
Demographics									
Age, y	78.8 ± 5.0	82.1 ± 5.6	82.5 ± 8.3	<0.001	75.9 ± 9.1	82.9 ± 7.7	84.2 ± 9.0	<0.001	<0.001
Male	200 (55.1)	73 (42.2)	21 (46.7)	0.02	217 (64.4)	165 (50.8)	79 (46.7)	<0.001	0.58
BMI, kg/m^2	24.4 ± 3.4	23.6 ±4.0	22.5 ± 3.0	0.001	29.6 ± 6.7	28.3 ± 6.8	26.2 ± 6.5	<0.001	<0.001
NYHA functional class lll/IV	103 (28.4)	77 (44.5)	26 (57.8)	<0.001	148 (43.9)	158 (48.6)	98 (58.0)	0.01	0.05
Comorbidities									
Diabetes mellitus	175 (48.2)	103 (59.5)	28 (62.2)	0.02	96 (28.5)	112 (34.5)	76 (45.0)	0.001	0.64
Hypertension	309 (85.1)	156 (90.2)	43 (95.6)	0.06	261 (77.4)	287 (88.3)	160 (94.7)	<0.001	0.66
Current smoking	35 (9.6)	10 (5.8)	2 (4.4)	0.20	7 (2.1)	11 (3.4)	4 (2.4)	0.56	0.20
Hyperlipidemia	270 (74.4)	127 (73.4)	40 (88.9)	0.08	235 (69.7)	244 (75.1)	130 (76.9)	0.15	0.18
Prior MI	9 (2.5)	18 (10.4)	5 (11.1)	<0.001	41 (12.2)	47 (14.5)	40 (23.7)	0.003	0.02
Prior PCI	87 (24.0)	57 (32.9)	17 (37.8)	0.028	94 (27.9)	94 (28.9)	56 (33.1)	0.46	0.27
Prior CABG	9 (2.5)	16 (9.2)	6 (13.3)	<0.001	42 (12.5)	62 (19.1)	43 (25.4)	0.001	0.14
Prior stroke	47 (12.9)	21 (12.1)	9 (20.0)	0.37	34 (10.1)	24 (7.4)	25 (14.8)	0.03	0.80
Atrial fibrillation or flutter	43 (11.8)	38 (22.0)	10 (22.2)	0.005	155 (46.0)	161 (49.5)	73 (43.2)	0.38	0.04
Peripheral vascular disease	9 (2.5)	6 (3.5)	7 (15.6)	<0.001	54 (16.0)	80 (24.6)	71 (42.0)	<0.001	0.36
Chronic lung disease	30 (8.3)	28 (16.2)	3 (6.7)	0.01	35 (10.4)	46 (14.2)	35 (20.7)	0.007	0.09
Current dialysis	1 (0.3)	6 (3.5)	16 (35.6)	<0.001	0 (0)	7 (2.2)	23 (13.6)	<0.001	0.53
Echocardiographic or CT findings									
Aortic valve area, cm^2	0.61 ± 0.16	0.62 ± 0.18	0.64 ± 0.18	0.59	0.75 ± 0.21	0.70 ± 0.20	0.67 ± 0.23	0.001	<0.001
Aortic valve mean gradient, mm Hg	58.3 ± 21.7	56.0 ± 19.5	46.6 ± 22.0	0.002	46.2 ± 14.2	44.7 ± 14.2	44.1 ± 18.4	0.26	>0.99
Bicuspid aortic valve	45 (12.5)	12 (6.9)	1 (2.2)	0.03	25 (7.4)	3 (0.9)	4 (2.4)	<0.001	0.08
LV ejection fraction, %	59.6 ± 9.7	56.0 ± 13.1	50.4 ± 15.1	<0.001	59.5 ± 11.8	55.7 ± 13.9	51.9 ± 15.3	<0.001	>0.99
Mitral insufficiency (moderate/severe)	38 (10.5)	20 (11.6)	12 (26.7)	0.007	37 (11.0)	72 (22.3)	44 (26.0)	<0.001	0.09
Tricuspid insufficiency (moderate/severe)	15 (4.1)	20 (11.6)	4 (8.9)	0.005	25 (7.4)	58 (17.9)	43 (25.7)	<0.001	0.48
systolic annular perimeter on CT, mm	76.4 ± 7.3	74.4 ± 8.1	73.2 ± 8.0	0.001	79.7 ± 8.0	77.6 ± 8.5	75.3 ± 9.0	<0.001	<0.001
Systolic annular area on CT, mm^2	450.7 ± 86.8	424.7 ± 92.1	411.9 ± 83.6	0.001	476.4 ± 93.4	453.1 ± 95.6	428.1 ± 101.9	<0.001	0.002
Procedural characteristics									
Valve type				0.33				0.003	0.49
Balloon-expandable	305 (84.5)	134 (79.8)	34 (79.1)		274 (89.8)	227 (83.5)	105 (77.8)		
Self-expandable	56 (15.5)	34 (20.2)	9 (20.9)		31 (10.2)	45 (16.5)	30 (22.2)		
Prosthesis size	26.0 ± 2.2	25.5 ± 2.	25.0 ± 2.2	0.003	26.0 ± 2.6	25.8 ± 2.9	25.1 ± 2.7	0.008	0.32
Moderate to severe paravalvular leakage	10 (2.8)	4 (2.3)	0 (0)	0.76	5 (1.6)	3 (1.1)	2 (1.3)	0.92	0.97
Conversion to open cardiac surgery	4 (1.1)	0 (0)	0 (0)	0.50	2 (0.6)	5 (1.5)	1 (0.6)	0.53	>0.99

Values are mean ± SD or n (%). [a]*P* values for comparison between the Asian and non-Asian groups.

BMI = body mass index; CABG = coronary artery bypass graft; CT = computed tomography; LV = left ventricular; MI = myocardial infarction; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgery risk.

cause, cardiac, and noncardiac mortality in the Asian and non-Asian groups are shown in Figure 4. The discriminative capability of the STS score on mortality prediction as measured by the C statistics was more limited in the Asian population than in the non-Asian population, especially for cardiac mortality.

DISCUSSION

In this registry-based, multinational, multicenter study of patients with severe AS who underwent TAVR, we determined the differential prognostic impact of the STS score on 1-year mortality and adverse clinical events according to racial group (Asian vs non-Asian). Our study has 3 major findings. First, the proportion of the STS risk category was significantly different between the Asian and non-Asian groups; a low-risk TAVR population was more common in Asian patients. Second, the rate of all-cause mortality was substantially higher in the high-risk STS category than in the low- and intermediate-risk groups among the Asian population. By contrast, there was a proportional increase in all-cause mortality according to the higher

TABLE 2 Observed Clinical Outcomes at 12 Months According to the STS Score and Racial Group[a]

	Low	Intermediate	HR (95% CI)	*P* Value	High	HR (95% CI)	*P* Value	*P* Value for Interaction[b]
Asian group								
Primary outcome of all-cause mortality	13 (3.6)	15 (8.7)	2.55 (1.21–5.36)	0.01	11 (24.4)	9.25 (4.14–20.66)	<0.001	0.13
Cardiac death	8 (2.2)	4 (2.3)	1.10 (0.33–3.64)	0.88	2 (4.4)	2.58 (0.55–12.18)	0.23	0.33
Noncardiac death	5 (1.4)	11 (6.4)	4.87 (1.69–14.02)	0.003	9 (20.0)	20.07 (6.72–59.93)	<0.001	0.006
Stroke	17 (4.7)	3 (1.7)	0.37 (0.11–1.26)	0.11	4 (8.9)	2.08 (0.70–6.18)	0.19	0.009
Death or stroke	27 (7.4)	17 (9.8)	1.35 (0.73–2.47)	0.34	12 (26.7)	4.61 (2.33–9.11)	<0.001	0.07
Rehospitalization	75 (20.7)	25 (14.5)	0.70 (0.44–1.10)	0.12	12 (26.7)	1.62 (0.88–2.98)	0.12	0.05
Composite of death, stroke, or rehospitalization	83 (22.9)	36 (20.8)	0.91 (0.62–1.35)	0.64	19 (42.2)	2.36 (1.43–3.89)	<0.001	0.02
Non-Asian group								
Primary outcome of all-cause mortality	18 (5.3)	41 (12.6)	2.57 (1.47–4.47)	<0.001	30 (17.8)	3.98 (2.22–7.14)	<0.001	
Cardiac death	2 (0.6)	6 (1.9)	3.34 (0.67–16.55)	0.12	11 (6.5)	12.78 (2.83–57.67)	<0.001	
Noncardiac death	16 (4.8)	35 (10.8)	2.47 (1.37–4.47)	0.003	19 (11.2)	2.86 (1.47–5.57)	0.002	
Stroke	3 (0.9)	14 (4.3)	5.06 (1.46–17.62)	0.01	5 (3.0)	3.61 (0.86–15.10)	0.08	
Death or stroke	21 (6.2)	52 (16.0)	2.82 (1.70–4.68)	<0.001	34 (20.1)	3.83 (2.22–6.59)	<0.001	
Rehospitalization	65 (19.3)	78 (24.0)	1.38 (0.99–1.92)	0.06	46 (27.2)	1.72 (1.18–2.51)	0.005	
Composite of death, stroke, or rehospitalization	78 (23.2)	114 (35.1)	1.69 (1.27–2.26)	<0.001	67 (39.6)	2.11 (1.52–2.93)	<0.001	

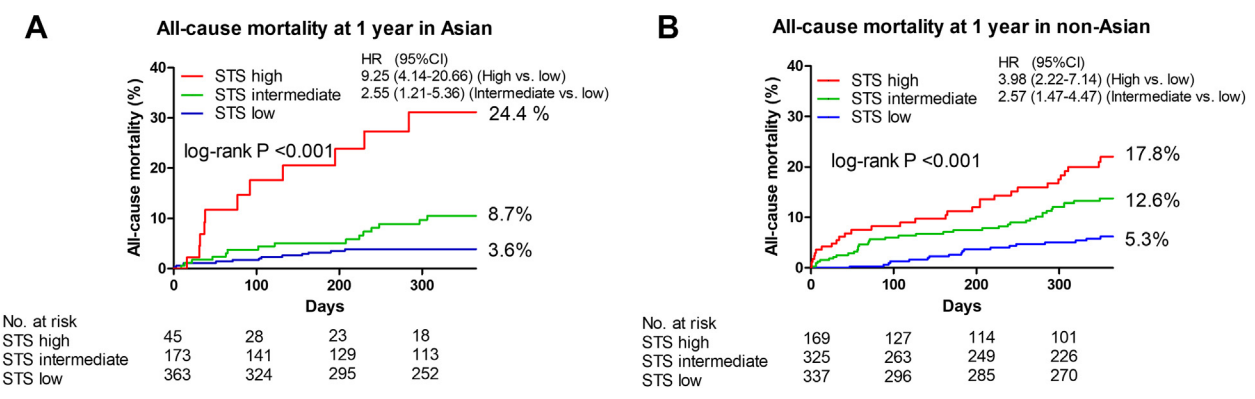
[a]Event numbers (%) were estimated using the Kaplan–Meier method, and the relative risk was described by HR (for intermediate- or high-risk STS categories compared with the low-risk category) and corresponding 95% CIs. [b]*P* value for interaction between the STS risk category and the racial group (Asian vs non-Asian).

Abbreviation as in Table 1.

levels of STS category among the non-Asian group (Central Illustration). Third, the discriminative capacity of the STS score on mortality prediction was relatively limited in the Asian cohort compared to the non-Asian cohort.

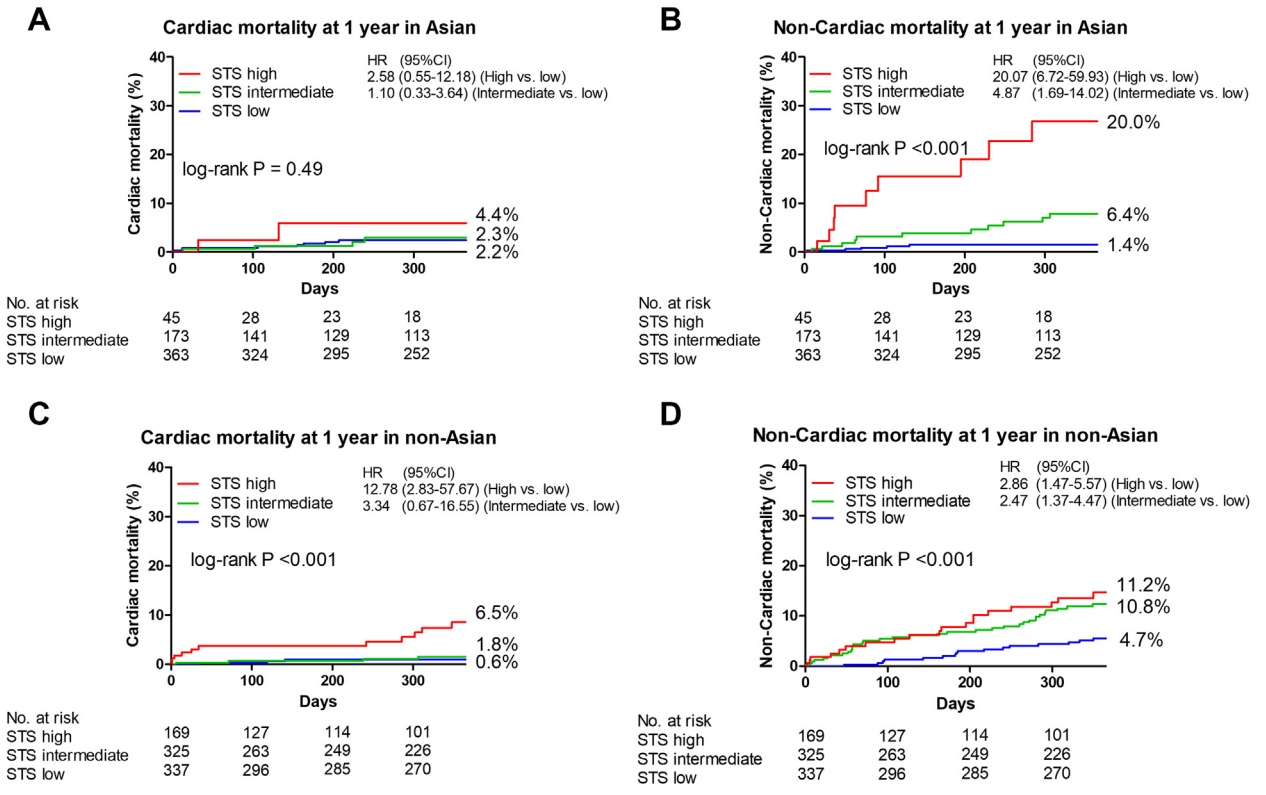
Previous consecutive randomized controlled trials have compared clinical outcomes of TAVR and surgical aortic valve replacement in a diverse spectrum of patients at high, intermediate, and low surgical risk, mainly based on STS risk score.[1-11,24,25] However, because most of the trials were conducted on the Western population, Asian populations are underrepresented (only 5% of enrolled participants). Also, because Asian patients have several different clinical, anatomic, and procedural characteristics as compared with non-Asian patients, it is still unknown regarding direct and unconditional applicability of prior trial findings into the Asian population.[26] Until recently,

FIGURE 2 Cumulative Incidence Curves of All-Cause Mortality at 1-Year



Kaplan–Meier curves for the primary outcome of all-cause mortality at 1 year, determined by STS score, are shown in **(A)** Asian and **(B)** non-Asian patients. *P* values were obtained from the overall log-rank test. Abbreviation as in Figure 1.

FIGURE 3 Cumulative Incidence Curves for Cardiac and Noncardiac Mortality at 1-Year



(A) Cardiac and **(B)** noncardiac mortality in Asian patients. **(C)** Cardiac and **(D)** noncardiac mortality in non-Asian patients. Abbreviation as in Figure 1.

data examining the long-term prognostic value of the STS score in Asian patients who underwent TAVR have been lacking.[19] There were also no available studies directly comparing the prognostic impact of the STS score in different racial groups. In this clinical context, the present study sought to investigate whether there is an inter-racial (Asian vs non-Asian) difference in the relative proportion of the STS score category and its clinical impact on long-term mortality.

Considering that the STS score was originally developed to predict operative mortality, in the current study, the rates of 30-day mortality in overall population were 0.6%, 2.6%, and 4.2% in low-, intermediate-, and high-risk STS groups, respectively ($P < 0.001$), in which those were 1.1%, 1.7%, and 2.2% in the Asian group, respectively, and 0%, 3.1%, and 4.7% in the non-Asian group, respectively. Observed early mortality rates were lower than predicted mortality rates which was defined by the STS risk category. Thus, these findings may suggest that the estimated early mortality risk of cardiac surgery cannot be directly applied to the interventional TAVR procedure. Also, these findings may provide evidence that there is a limitation in TAVR risk stratification by the STS score.

Several observational studies have analyzed clinical outcomes according to the different levels of STS scores.[14,15,18,19] In the Bern TAVI registry, all-cause mortality at 1 year was highest in the STS high-risk group, followed by intermediate- and low-risk groups (34.5% vs 16.1% vs.10.1%, respectively; $P = 0.0003$), mainly driven by increased cardiovascular risk mortality.[14] In a multicenter study from Israel, 1-year all-cause mortality proportionally increased with increasing levels of the STS score category (5.9% in the low-risk, 10.9% in the intermediate-risk, and 22.9% in the high-risk group).[15] A large Australian multicenter cohort also reported that 30-day mortality was low across

TABLE 3 Adjusted Marginal and Interaction Analyses for Clinical Outcomes at 12 Months[a]

	Marginal Analysis		Interaction Analysis				
	Overall		Asian		Non-Asian		
	Adjusted HR[b] (95% CI)	*P* Value	Adjusted HR[b] (95% CI)	*P* Value	Adjusted HR[b] (95% CI)	*P* Value	*P* Value for Interaction[a]
Primary outcome of all-cause mortality							0.31
Low	Referent		Referent		Referent		
Intermediate	2.16 (1.37–3.39)	<0.001	2.15 (1.01–4.57)	0.05	2.14 (1.21–3.76)	0.009	
High	3.12 (1.78–5.48)	<0.001	5.28 (2.17–12.89)	<0.001	2.71 (1.41–5.21)	0.003	
Cardiac death							0.34
Low	Referent		Referent		Referent		
Intermediate	1.05 (0.42–2.61)	0.92	0.95 (0.27–3.28)	0.93	2.12 (0.41–10.86)	0.009	
High	2.76 (0.96–7.90)	0.06	1.36 (0.24–7.72)	0.73	7.14 (1.39–36.74)	0.02	
Noncardiac death							0.02
Low	Referent		Referent		Referent		
Intermediate	2.75 (1.62–4.68)	<0.001	4.09 (1.40–11.92)	0.01	2.25 (1.23–4.12)	0.008	
High	3.32 (1.70–6.49)	<0.001	12.36(3.80–40.17)	<0.001	2.11 (1.01–4.45)	0.05	
Stroke							0.008
Low	Referent		Referent		Referent		
Intermediate	1.18 (0.60–2.30)	0.64	0.35 (0.10–1.20)	0.10	4.62 (1.31–16.28)	0.02	
High	1.57 (0.62–3.99)	0.35	2.20 (0.65–7.48)	0.21	3.05 (0.67–13.96)	0.15	
Death or stroke							0.10
Low	Referent		Referent		Referent		
Intermediate	1.85 (1.26–2.70)	0.002	1.20 (0.65–2.23)	0.57	2.47 (1.48–4.14)	<0.001	
High	2.66 (1.63–4.34)	<0.001	3.29 (1.53–7.08)	0.002	2.92 (1.60–5.33)	<0.001	
Rehospitalization							0.31
Low	Referent		Referent		Referent		
Intermediate	1.10 (0.98–1.24)	0.12	1.00 (0.83–1.20)	0.97	1.17 (1.00–1.36)	0.05	
High	1.41 (1.18–1.69)	<0.001	1.53 (1.09–2.14)	0.01	1.39 (1.14–1.71)	0.001	
Composite of death, stroke, or rehospitalization							0.03
Low	Referent		Referent		Referent		
Intermediate	1.30 (1.03–1.64)	0.03	0.85 (0.57–1.27)	0.42	1.63 (1.22–2.19)	0.001	
High	1.79 (1.31–2.45)	<0.001	1.76 (1.01–3.09)	0.05	1.93 (1.34–2.78)	<0.001	

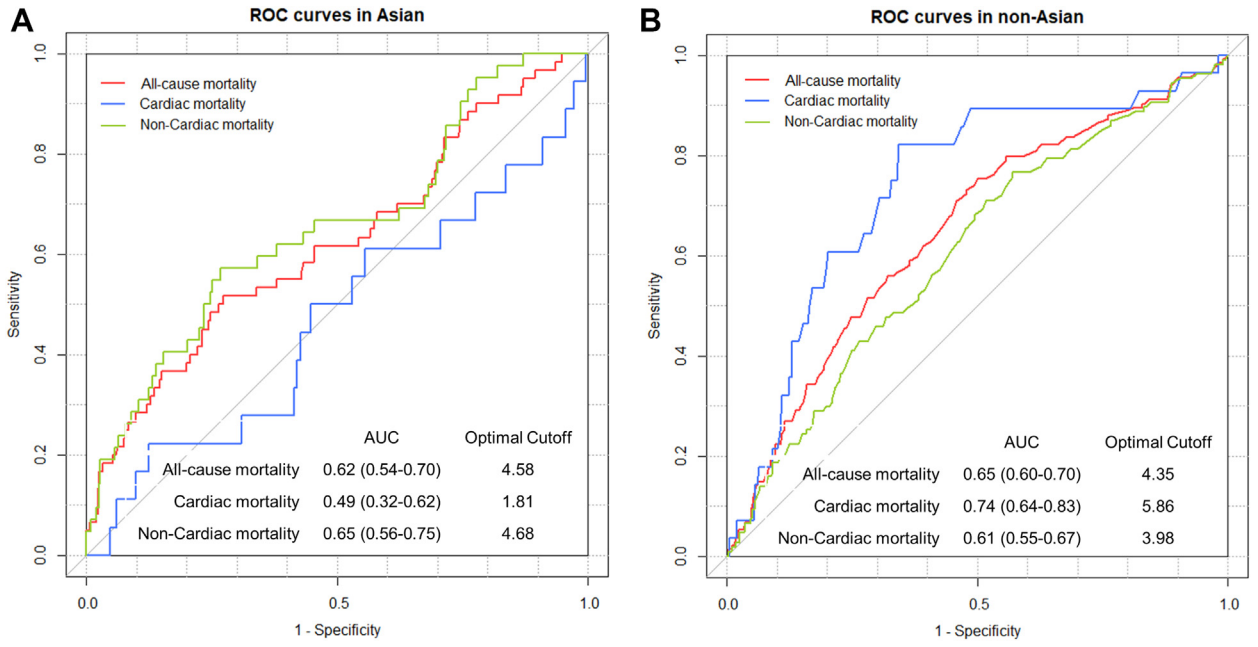
[a]The marginal analyses and interaction analyses included the STS risk category and race in the Cox proportional hazards regression models without and with their interaction term, respectively. HRs are for the intermediate- or high-risk STS categories compared with the low-risk category. [b]The models were adjusted for age, BMI, NYHA functional class of III or IV, diabetes, peripheral vascular disease, prior myocardial infarction, chronic lung disease, end-stage renal disease, aortic valve area, mean aortic valve pressure gradient, bicuspid aortic valve, and LV ejection fraction, which were significantly associated with all-cause mortality at 1 year in the univariable Cox analysis.

Abbreviations as in Table 1.

all 3 groups (1.1%, 1.7%, and 1.4%, respectively; $P = 0.80$).[18] Such findings from the Western population were similar to the non-Asian cohort of our study. By contrast, recent data from the OCEAN-TAVI (Optimized Transcatheter Valvular Intervention) registry of 2,588 Japanese patients showed that the long-term (4-year) incidence of all-cause mortality was extremely higher in high-risk STS group (49.0%) compared with low- (22.6%) and intermediate-risk STS groups (28.7%)[19]; such findings were also similar to the major findings from the Asian cohort in the present study.

In a prior study, procedural complications, including coronary obstruction, cardiac tamponade, conversion to open surgery, vascular complications, and early clinical outcomes were comparable irrespective of baseline STS score.[15] Similar findings were observed in our registry. However, the long-term prognostic impact of the STS score remains poorly understood. As noted in the present study, the exact reasons for the differential prognostic pattern of the STS score category on 1-year mortality between the Asian and the non-Asian populations are unclear. Given that the differential prognostic impact of the STS score on all-cause mortality was primarily driven by noncardiac mortality in the Asian population, the current STS score system might not fully reflect disability, frailty status, and nonconventional comorbidities in this population, which may be significantly associated with long-term all-cause or noncardiac mortality. In addition, there may be important epidemiological

FIGURE 4 ROC Curves of the STS Score for 1-Year Mortality

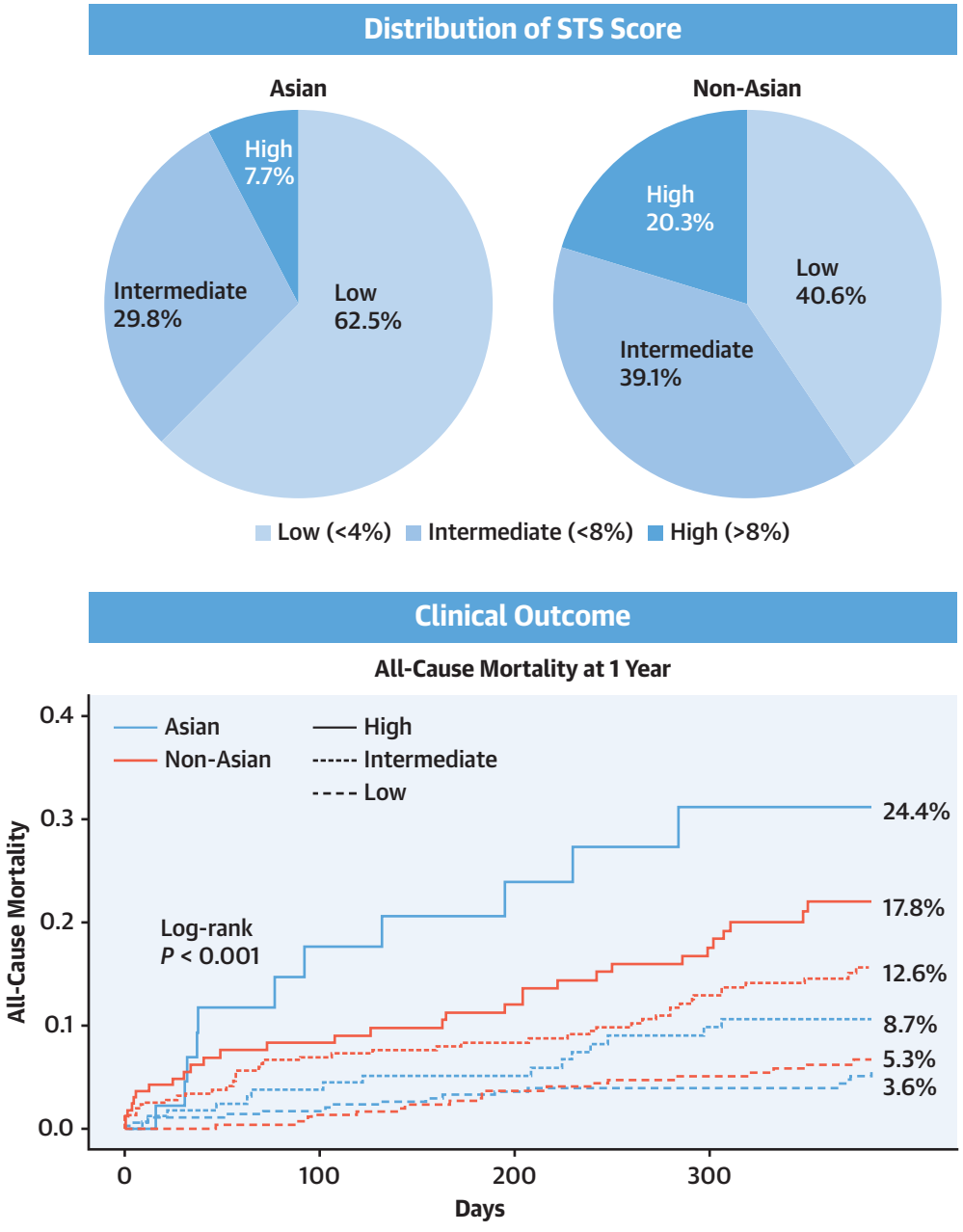


Receiver-operating characteristic (ROC) curves for **(A)** all-cause, cardiac, and noncardiac mortality in Asian patients, and **(B)** all-cause, cardiac, and noncardiac mortality in non-Asian patients. AUC, Area under the curve; other abbreviations as in Figure 1.

differences between elderly Asian (South Korean) and non-Asian (American) individuals that could account for differences in the causes of death observed following TAVR. In South Korea, cancer is by far the leading cause of death in the elderly, followed by heart disease, pneumonia, and cerebrovascular disease.[27] In the United States, heart disease is the leading cause of death in the elderly, followed by cancer as the second leading cause.[28] Therefore, it is possible that, although the application of TAVR in the oldest and highest risk subjects may have a similar beneficial effect on long-term cardiac mortality, it would not be expected to have a differential effect on noncardiac mortality. Such limited prognostic value of conventional STS score in the Asian cohort was also confirmed by the poor discriminative capacity determined by the area under the curve for predicting all-cause mortality at 1 year. Although some different risk prediction models have been tested in patients with TAVR, racial-based TAVR-dedicated risk scores with good discriminative ability for all- and cause-specific mortality should be further developed and validated through further large-sized studies.[29-33]

STUDY LIMITATIONS. First, the observational nature of this study may have affected the observed results because of selection bias and unknown potential confounders. Therefore, the overall findings should be interpreted as exploratory and regarded as hypothesis-generating only. Second, the multicenter design of the registry could yield intersite variability in care (eg, the selection of eligible patients for TAVR, TAVR technique, and post-TAVR surveillance and medical care). Third, because our study evaluated clinical outcomes for up to 1 year, longer-term follow-up data would help detect the long-term differential prognostic impact of the STS score in both racial groups. Fourth, the observed distribution of low, intermediate, and high risk stratified by STS score between Asian and non-Asian groups might be substantially influenced by the limited number of centers and the sample volume. Lastly, despite risk adjustment of a wide range of clinical covariates, other important risk factors associated with poorer outcomes post-TAVR, including frailty, socioeconomic factors, or concomitant medications, were not captured in this database and thus not fully adjusted.

CENTRAL ILLUSTRATION **Distribution and Clinical Impact of STS Score on Mortality**



Kim H, et al. JACC: Asia. 2023;3(3):376–387.

The **upper panel** shows the distribution of the Society of Thoracic Surgeons (STS) scores between Asian and non-Asian patients, whereas the **lower panel** shows the primary outcome of all-cause mortality at 1 year according to the STS score and racial group.

CONCLUSIONS

In this multinational, multicenter registry cohort of patients who underwent TAVR for severe AS, STS score had a differential prognostic effect on 1-year mortality between Asian and non-Asian patients. The discriminative capacity of the STS score for predicting mortality were also different between the 2 cohorts. Further research is warranted to develop practical race-based risk prediction and stratification tools for selecting appropriate candidates for TAVR and predicting long-term outcomes.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Although the STS score has been widely used for decision-making and risk stratification for TAVR in patients with severe AS, the relative proportion and clinical impact on long-term mortality across different racial groups remains unknown.

COMPETENCY IN PATIENT CARE: In this multinational multicenter registry, the relative proportion of the STS risk category was substantially different between the Asian and non-Asian groups. Importantly, there was a differential prognostic effect of STS score on 1-year mortality between Asian and non-Asian patients.

TRANSLATIONAL OUTLOOK: Further large-sized research is required to develop the race-based new risk prediction and stratification tools for selecting appropriate candidates for TAVR and predicting outcomes.

REFERENCES

1. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364(23):2187–2198.

2. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med*. 2012;366(18):1686–1695.

3. Mack MJ, Leon MB, Smith CR, et al. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet*. 2015;385(9986):2477–2484.

4. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370(19):1790–1798.

5. Reardon MJ, Adams DH, Kleiman NS, et al. 2-Year outcomes in patients undergoing surgical or self-expanding transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2015;66(2):113–121.

6. Gleason TG, Reardon MJ, Popma JJ, et al. 5-Year outcomes of self-expanding transcatheter versus surgical aortic valve replacement in high-risk patients. *J Am Coll Cardiol*. 2018;72(22):2687–2696.

7. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2016;374(17):1609–1620.

8. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2017;376(14):1321–1331.

9. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med*. 2019;380(18):1695–1705.

10. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med*. 2019;380(18):1706–1715.

11. Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the All-Comers NOTION randomized clinical trial. *J Am Coll Cardiol*. 2015;65(20):2184–2194.

12. O'Brien SM, Shahian DM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2—isolated valve surgery. *Ann Thorac Surg*. 2009;88(suppl 1):S23–S42.

13. Puskas JD, Kilgo PD, Thourani VH, et al. The Society of Thoracic Surgeons 30-day predicted risk of mortality score also predicts long-term survival. *Ann Thorac Surg*. 2012;93(1):26–35.

14. Wenaweser P, Stortecky S, Schwander S, et al. Clinical outcomes of patients with estimated low or intermediate surgical risk undergoing transcatheter aortic valve implantation. *Eur Heart J*. 2013;34(25):1894–1905.

15. Barbash IM, Finkelstein A, Barsheshet A, et al. Outcomes of patients at estimated low, intermediate, and high risk undergoing transcatheter aortic valve implantation for aortic stenosis. *Am J Cardiol*. 2015;116(12):1916–1922.

16. Compagnone M, Moretti C, Marcelli C, et al. Surgical risk scores applied to transcatheter aortic valve implantation: friends or foes? Short-term

and long-term outcomes from a single-center registry. *J Invasive Cardiol*. 2019;31(10):E282–E288.

17. Saji M, Tobaru T, Higuchi R, et al. Usefulness of the transcatheter aortic valve replacement risk score to determine mid-term outcomes. *Circ J*. 2019;83(8):1755–1761.

18. Quine EJ, Duffy SJ, Stehli J, et al. Comparison of early outcomes in patients at estimated low, intermediate and high risk undergoing transcatheter aortic valve implantation: a multicentre Australian experience. *Heart Lung Circ*. 2020;29(8):1174–1179.

19. Ishizu K, Shirai S, Isotani A, et al. Long-term prognostic value of the society of thoracic surgery risk score in patients undergoing transcatheter aortic valve implantation (From the OCEAN-TAVI Registry). *Am J Cardiol*. 2021;149:86–94.

20. Park H, Ahn JM, Kang DY, et al. Racial differences in the incidence and impact of prosthesis-patient mismatch after transcatheter aortic valve replacement. *J Am Coll Cardiol Intv*. 2021;14(24):2670–2681.

21. Kang DY, Ahn JM, Kim JB, et al. Inter-racial differences in patients undergoing transcatheter aortic valve implantation. *Heart*. 2022;108(19):1562–1570.

22. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Am Coll Cardiol*. 2012;60(15):1438–1454.

23. VARC-3 Writing Committee, Genereux P, Piazza N, et al. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *J Am Coll Cardiol*. 2021;77(21):2717–2746.

24. Thyregod HGH, Ihlemann N, Jørgensen TH, et al. Five-year clinical and echocardiographic outcomes from the Nordic Aortic Valve Intervention (NOTION) randomized clinical trial in lower surgical risk patients. *Circulation*. 2019;139:2714–2723. https://doi.org/10.1161/circulationaha.118.036606

25. Jørgensen TH, Thyregod HGH, Ihlemann N, et al. Eight-year outcomes for patients with aortic valve stenosis at low surgical risk randomized to transcatheter vs. surgical aortic valve replacement. *Eur Heart J*. 2021;42(30):2912–2919.

26. Lee CH, Inohara T, Hayashida K, Park D-W. Transcatheter aortic valve replacement in Asia: present status and future perspectives. *JACC: Asia*. 2021;1(3):279–293.

27. Korea VSDS, Shin H-Y, Kim J, et al. Cause-of-death statistics in 2018 in the Republic of Korea. *J Korean Med Assoc*. 2020;63(5):286–297.

28. Heron M. Deaths: leading causes for 2018. *Natl Vital Stat Rep*. 2021;70(4):1–115.

29. Capodanno D, Barbanti M, Tamburino C, et al. A simple risk tool (the OBSERVANT score) for prediction of 30-day mortality after transcatheter aortic valve replacement. *Am J Cardiol*. 2014;113(11):1851–1858.

30. Ribeiro HB, Rodés-Cabau J. The multiparametric FRANCE-2 risk score: one step further in improving the clinical decision-making process in transcatheter aortic valve implantation. *Heart*. 2014;100(13):993–995.

31. Iung B, Laouénan C, Himbert D, et al. Predictive factors of early mortality after transcatheter aortic valve implantation: individual risk assessment using a simple score. *Heart*. 2014;100(13):1016–1023.

32. Debonnaire P, Fusini L, Wolterbeek R, et al. Value of the "TAVI2-SCORe" versus surgical risk scores for prediction of one year mortality in 511 patients who underwent transcatheter aortic valve implantation. *Am J Cardiol*. 2015;115(2):234–242.

33. Hermiller JB, Yakubov SJ, Reardon MJ, et al. Predicting early and late mortality after transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2016;68(4):343–352.

KEY WORDS aortic valve stenosis, mortality, Society of Thoracic Surgeons score, transcatheter aortic valve replacement

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