Prognostic Value of Baseline Sarcopenia on 1-year Mortality in Patients Undergoing Transcatheter Aortic Valve Implantation

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There is limited data regarding the association between sarcopenia and clinical outcomes in patients who underwent transcatheter aortic valve implantation (TAVI). From the prospective ASAN-TAVI registry, we evaluated a total of 522 patients with severe aortic stenosis who underwent TAVI between March 2010 and November 2018. Routine pre-TAVI computed tomography scan was used to calculate the skeletal muscle index (SMI), which was defined as skeletal muscle area at the L3 level divided by height squared; subject patients were classified into the gender-specific tertile groups of SMI. The patients' mean age was 79 years and 49% were men. Mean SMI values were 41.3 ± 6.7 cm^2/m^2 in men and 34.1 ± 6.5 cm^2/m^2 in women. The Kaplan−Meier estimates of all-cause mortality at 12 months were higher in the low-tertile group than in the mid- and high-tertile groups (15.5%, 7.1%, and 6.2%, respectively; p = 0.036). In multivariate analysis, low-tertile of SMI was an independent predictor of mortality (vs high-tertile of SMI, hazard ratio 2.69; 95% confidence interval, 1.18 to 6.12; p = 0.019). The all-cause mortality was substantially higher in the groups with high-surgical risk plus low SMI tertile. The risk assessment with addition of SMI on conventional STS-PROM score was significantly improved by statistical measures of model reclassification and discrimination. In patients who underwent TAVI, sarcopenia measured by SMI was significantly associated with an increased risk of 1-year mortality. The prognostic impact of SMI-measured sarcopenia was more prominent in patients with high surgical risks. **(Am J Cardiol 2021;139:79−86)**

Aortic stenosis (AS) is a degenerative disease that mainly occurs in the old population. Over the last decade, transcatheter aortic valve implantation (TAVI) has become an established treatment for symptomatic severe AS, and the application has been extended to patients with low surgical risk.[1,2] Therefore, it is important to understand the risk factors related to the future risk of mortality and adverse cardiovascular events in older adults who underwent TAVI beyond the conventional risk assessment tools. Sarcopenia is a progressive skeletal muscle disorder characterized by loss of muscle mass and function as an age-related process in older people.[3] Importantly, sarcopenia significantly affects the quality of life by leading to frequent falls and fractures, loss of independence, postoperative complications, and even mortality.[4] Skeletal muscle mass might play an important role in predicting clinical outcomes in patients who underwent TAVI. We therefore evaluated the association of the degree of sarcopenia with mortality and adverse clinical events in patients who underwent TAVI.

Methods

The ASAN-TAVI registry is a prospective, "real-world" registry that includes all consecutive patients with symptomatic severe AS who undergo TAVI at Asan Medical Center (Seoul, Korea).[5-9] The current study included consecutive patients who underwent TAVI between March 2010 and November 2018 in this registry. The decisions on TAVI and the details of procedures (e.g., valve type, valve size, access route, and type of anesthesia) were made by discussions in a multidisciplinary heart team according to

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pre-TAVI 3-dimensional multidetector CT and transesophageal echocardiography. Surgical risks were assessed with the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM score) and the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE II). TAVI was performed using standard methods.[10,11] After TAVI procedures, all patients were prescribed dual anti-platelet therapy (aspirin [100 mg once daily] and clopidogrel [75 mg once daily]) for at least 6 months.[12] Prolonged use of the dual anti-platelet therapy or concomitant use of oral anticoagulants were carried out at the discretion of the attending physician considering the patient's co-morbidities. This study was approved by the institutional review board of Asan Medical Center, and all patients provided written informed consent.

Body compositions including skeletal muscle area, visceral fat area, and subcutaneous fat area were measured at the inferior margin of L3 vertebra in the abdominal scan of pre-TAVI CT. Experienced operators (Y. K and K.W. Kim) analyzed the CT images using the automated Asan J-Morphometry software (http://datasharing.aimaicro.com/morphometry), which is an ImageJ-based software (NIH, Bethesda, Maryland) for measuring the abdominal muscle and fat areas (Figure 1). Interscan and inter-reader agreement of this method were reported previously.[13] Skeletal muscle areas were demarcated using predetermined thresholds (−29 to +190 Hounsfield units).[14] Visceral fat areas and subcutaneous fat areas were also demarcated using fat tissue thresholds (−190 to -30 Hounsfield units). Skeletal muscle index (SMI) was calculated as skeletal muscle area divided by height squared (cm^2/m^2).[15] Study subjects were classified into 3 groups according to gender-specific tertiles of SMI. Visceral fat index and subcutaneous fat index were also calculated by dividing the visceral fat area and subcutaneous fat area by height squared (cm^2/m^2), respectively.

The primary outcome of the study was all-cause mortality at 1 year. We also assessed various secondary outcomes including the rates of stroke, myocardial infarction, rehospitalization, new pacemaker insertion, acute kidney injury, vascular events, and bleeding. All study endpoints were defined according to the VARC-2 criteria.[16] Myocardial infarction was defined as periprocedural (occurred as a complication after TAVI) or spontaneous (diagnosed at readmission during follow-up). Stroke was defined as new neurological deficits with available neuroimaging documents a new hemorrhage or infarct confirmed by a neurologist. Transient ischemic attacks, which were neurological deficit lasting < 24 hours without documentation of hemorrhage or infarcts on neuroimaging, were also included in clinical outcomes. Rehospitalization was regarded as any hospitalization during follow-up owing to either cardiovascular or noncardiovascular causes. Acute kidney injury included all levels of severity from stage 1 to stage 3. Vascular injury consists of major and minor injury. Bleeding events comprised life-threatening, major, and minor bleeding. All events were reviewed and adjudicated by an independent group of clinicians blinded to the study purpose.

Clinical, procedural, and outcome data were collected using a dedicated electronic case report form that included baseline clinical, laboratory, echocardiographic, and CT data as well as procedural and clinical follow-up data. Clinical follow-up after TAVI was performed via clinical visit and/or telephone interview at 1, 6, and 12 months and every 6 months thereafter. At each follow-up contact, data pertaining to the patients' clinical status and occurrence of any adverse clinical events were collected. Referring cardiologists, general practitioners, and patients were contacted to obtain further information as necessary.

The baseline clinical, anatomic, and procedural characteristics of the patients were compared according to their SMI tertiles. Continuous variables were compared using 1-way analysis of variance or Kruskal-Wallis test and presented as mean ± standard deviation; categorical variables were compared using the chi-squared or Fisher's exact test as appropriate and presented as counts or percentages.

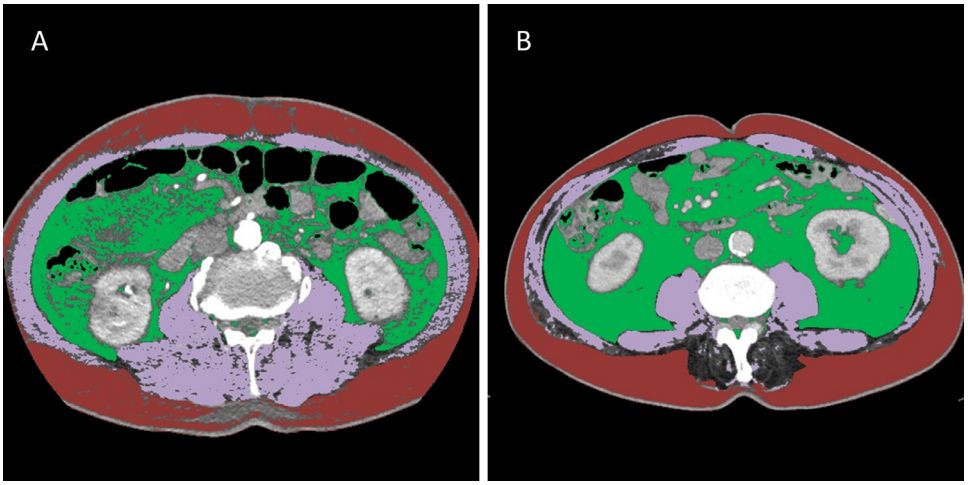

Figure 1. The images of CT scan show skeletal muscle, visceral fat, and subcutaneous fat area at L3 vertebra level which are measured by automated Asan J-Morphometry software. Panel A shows CT image of 80-year old man in mid-tertile group. (SMI = 42.1 cm^2/m^2, body mass index = 24.83 kg/m^2, STS-PROM score = 3.487, logistic EuroSCORE II = 15.62) Panel B shows CT image of 73-year old man in low-tertile group (SMI = 28.0 cm^2/m^2, body mass index = 25.83 kg/m^2, STS-PROM score = 1.289, logistic EuroSCORE II = 8.27). There showed fat degeneration in paraspinal muscle. White, green, and brown colors indicate skeletal muscle, visceral fat, and subcutaneous fat, respectively.

Event rates and curves of the primary and secondary outcomes at 12 months were calculated using the Kaplan−Meier estimates and compared using the log-rank test. The entire follow-up period was used to analyze time-to-event outcomes and patients were censored at the time of death, outcome of interest, or last follow-up, whichever came first. Multivariable Cox proportional hazards models with backward elimination under stratification of sex were used to assess the independent associations between SMI levels and clinical outcomes. The initial input variables were age, body-mass index, STS-PROM score, hypertension, diabetes mellitus, low ejection fraction (<40%), previous stroke, peripheral vascular disease, chronic kidney disease, balloon-expandable valve, transfemoral approach, and type of anesthesia. The muscle index was input both as a categorical variable and a continuous variable in separate models.

The relation between SMI levels and the primary outcome of all-cause mortality was also investigated in groups with different baseline surgical risks. The all-cause mortality according to SMI grades (low or mid-high) were assessed in low-intermediate and high-risk groups as defined by the STS-PROM score and the logistic EuroSCORE II. Net reclassification index, integrated discrimination index, and C-index were calculated in the Cox proportional hazard models with or without SMI tertile to assess additive value of SMI in the risk prediction. We also performed receiver operating characteristics curve analysis separately in men and women with measurement of area under the curve (AUC), in which a higher AUC indicated better performance in distinguishing between patients with and without events. The optimal cutoff value was defined as the value with the maximal sum of sensitivity and specificity. All reported p values are 2-sided and were not adjusted for multiple testing. All statistical analyses were performed with R version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria).

Result

Between March 2010 and November 2018, a total of 533 patients with severe symptomatic AS who underwent TAVI were enrolled in the ASAN-TAVI registry. In them, 6 patients were excluded from the data analysis due to the lack of available 3-dimensional, multi-detector CT images before TAVI, and 5 patients were excluded due to poor CT image quality that hindered valid measurement of SMI. Finally, a total of 522 patients were included in the present analysis. The mean (±SD) age of the patients was 78.9 ± 5.2 years and 49.4% were men. The mean STS-PROM score and logistic EuroSCORE II were 4.1 ± 3.0 and 14.7 ± 11.7, respectively. Most patients (96.4%) underwent TAVI through the transfemoral access. The mean SMIs of men and women in pre-TAVI CT scan analysis were 41.3 ± 6.7 cm^2/m^2 and 34.1 ± 6.5 cm^2/m^2 (p<0.001), respectively.

The study population was then categorized according to the gender-specific SMI tertile levels (low ≤38.9 cm^2/m^2, mid >38.9 cm^2/m^2 and ≤43.9 cm^2/m^2, high >43.9 cm^2/m^2 in men; low ≤31.3 cm^2/m^2, mid >31.3 cm^2/m^2 and ≤36.8 cm^2/m^2, high >36.8 cm^2/m^2 in women). Baseline clinical, anatomic, and procedural characteristics of the study population according to the gender-specific SMI tertiles are shown in Table 1. Patients in the low SMI groups tended to have older age, lower body-mass index, higher STS-PROM score, and higher logistic EuroSCORE II; conversely, the prevalence of other risk factors and known cardiovascular diseases were not significantly different according to the SMI tertiles. In addition, the hemodynamic and anatomic characteristics measured by echocardiography and CT analysis did not show significant differences according to the SMI tertiles. Procedural characteristics such as use of the balloon-expandable valve, transfemoral access, and type of anesthesia also did not show significant differences in the groups.

The median follow-up duration was 12.3 months, and the rate of complete follow-up was 97.6% in the patients as a whole. The Kaplan−Meier estimates of all-cause mortality at 12 months were 6.2% in the high-tertile group, 7.1% in the mid-tertile group, and 15.5% in the low-tertile group (p = 0.036) (Table 2 and Figure 2). After multivariable adjustment for the potential explanatory factors for mortality, the low-tertile group showed a significantly higher risk of mortality (referent: high-tertile group; hazard ratio [HR] 2.69; 95% confidence interval [CI], 1.18 to 6.12; p = 0.019). There were no significant associations between the SMI tertiles and secondary clinical outcomes in multivariate analysis. Univariate and multivariate analyses for the predictors of all-cause mortality are summarized in Table 3 and Online Table 1 in the Supplementary Appendix. The SMI was an independent risk factor for mortality both as a categorical (tertile) and a continuous variable, whereas other body compositions including the visceral and subcutaneous fat index were not significant determinants for increased mortality.

Stratified analyses for primary outcomes according to SMI tertile in combination with baseline the STS-PROM score or the logistic EuroSCORE II are illustrated in Figure 3. The 1-year rate of primary outcome was 39.8% in STS-PROM score >8 and low SMI tertile, 18.3% in STS-PROM score >8 and mid-high SMI tertile, 12.5% in STS-PROM score ≤8 and low SMI tertile, 5.8% in STS-PROM score ≤8 and mid-high SMI tertile. The 1-year rate of primary outcome was 29.8% in logistic EuroSCORE II score >20 and low SMI tertile, 9.1% in logistic EuroSCORE II score >20 and mid-high SMI tertile, 8.4% in logistic EuroSCORE II score ≤20 and low SMI tertile, 5.6% in logistic EuroSCORE II score ≤20 and mid-high SMI tertile. Rate of all-cause mortality was substantially higher in the groups with high-surgical risk and low SMI tertile. In the Cox proportional hazard models involving STS-PROM score, sex, diabetes, and ejection fraction, predictive performance was significantly improved as integrated discrimination index 0.026 (95% CI, 0.001 to 0.079; p = 0.027), continuous net reclassification index 0.227 (95% CI, 0.025 to 0.395; p = 0.04), C-index from 0.735 to 0.746 by adding SMI tertile to this prediction model.

The predictive power of SMI and its best cut-off points for mortality separately in men or women are illustrated in Figure 4. Overall, the power of SMI for predicting mortality was higher in men than in women (AUC: 0.707 and 0.578, respectively). The best cut-off levels of SMI were 40.7

Table 1
Baseline patient characteristics

Variable	Skeletal muscle index tertile			p Value
	High (n=174)	Mid (n=174)	Low (n=174)	
Age (years)	77.7±5.2	78.5±5.0	80.6±5.0	<0.001
Men	86 (49.4%)	86 (49.4%)	86 (49.4%)	>0.99
Body weight (kg)	60.5 ± 8.8	59.2 ± 9.8	57.3 ± 9.4	0.006
Height (cm)	156.0 ± 9.0	156.8 ± 8.5	158.6 ± 9.2	0.023
Body mass index (kg/m^2)	24.8 ± 3.0	24.1 ± 3.6	22.8 ± 2.9	<0.001
STS score	3.7 ± 3.4	3.9 ± 2.6	4.6 ± 3.1	0.011
EuroSCORE II	14.2 ± 11.2	13.1 ± 9.9	17.0 ± 13.1	0.005
Hypertension	143 (82.2%)	134 (77%)	137 (78.7%)	0.479
Diabetes mellitus	64 (36.8%)	50 (28.7%)	57 (32.8%)	0.278
Dyslipidemia	94 (58%)	86 (52.8%)	94 (57.3%)	0.583
Congestive heart failure	25 (15.4%)	26 (16%)	40 (24.4%)	0.065
Previous myocardial infarction	9 (5.2%)	10 (5.7%)	11 (6.3%)	0.899
Previous stroke	22 (12.6%)	26 (14.9%)	17 (9.8%)	0.342
Peripheral vascular disease	8 (4.6%)	7 (4%)	11 (6.3%)	0.591
Chronic kidney disease	47 (27%)	53 (30.5%)	55 (31.6%)	0.621
Echocardiography data				
Ejection fraction (%)	58.9 ±10.5	58.5 ±10.8	58.3 ±11.1	0.867
Ejection fraction (<40%)	12 (6.9%)	15 (8.6%)	17 (9.8%)	0.624
Mean aortic-valve gradient (mmHg)	57.7 ± 20.1	60.9 ± 21.7	59.4 ± 24.0	0.409
Aortic-valve area (cm^2)	0.6 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	0.427
Computed tomography data				
Aortic annulus maximal diameter (mm)	25.5 ± 3.5	25.4 ± 3.4	25.7 ± 3.4	0.715
Aortic annulus minimal diameter (mm)	22.2 ± 3.3	22.4 ± 3.7	21.7 ± 3.4	0.147
Aortic annulus area (mm^2)	439.1 ± 81.0	442.0 ± 88.4	432.5 ± 93.8	0.611
Aortic annulus perimeter (mm)	75.6 ± 7.0	75.8 ± 7.4	75.2 ± 7.8	0.778
Skeletal muscle index	44.7 ± 5.0	37.8 ± 4.1	30.4 ± 5.1	<0.001
Subcutaneous fat index	52.4 ± 26.9	52.7 ± 27.1	50.4 ± 25.2	0.678
Visceral fat index	51.0 ± 24.9	50.7 ± 28.7	47.6 ± 25.5	0.412
Procedural characteristics				
Type of deployment				0.364
Balloon-expandable	118 (67.8%)	130 (74.7%)	124 (71.3%)	
Self-expandable	56 (32.2%)	44 (25.3%)	50 (28.7%)	
Type of valve				0.561
SAPIEN	6 (3.4%)	2 (1.1%)	2 (1.1%)	
SAPIEN XT	39 (22.4%)	42 (24.1%)	38 (21.8%)	
SAPIEN 3	73 (42%)	86 (49.4%)	84 (48.3%)	
CoreValve	29 (16.7%)	20 (11.5%)	29 (16.7%)	
Evolut R	24 (13.8%)	23 (13.2%)	20 (11.5%)	
Lotus	3 (1.7%)	1 (0.6%)	1 (0.6%)	
Valve size (mm)	26.1 ± 2.2	26.0 ± 2.3	25.9 ± 2.3	0.799
Access route				0.622
Transfemoral	168 (96.6%)	167 (96%)	168 (96.6%)	
Transapical	4 (2.3%)	6 (3.4%)	5 (2.9%)	
Transaortic	2 (1.1%)	-	1 (0.6%)	
Transsubclavian	-	1 (0.6%)	-	
Monitored anesthesia care	106 (60.9%)	113 (64.9%)	96 (55.2%)	0.173

EuroSCORE indicates the European System for Cardiac Operative Risk Evaluation; STS, Society of Thoracic Surgeons. Data are shown as mean (SD) for continuous variables and absolute numbers (percentage) for dichotomous variables.

cm^2/m^2 in men (sensitivity: 75.1%, specificity: 62.8%) and 34.0 cm^2/m^2 in women (sensitivity: 73.2%, specificity: 51.2%).

Discussion

In this study, we used a prospective, real-world cohort of consecutive patients with severe AS undergoing TAVI to evaluate the prognostic role of baseline sarcopenia measured by CT-determined SMI. The major findings are that (1) a higher degree of sarcopenia (i.e., a lower level of SMI) was significantly associated with a higher risk of all-cause mortality at 1 year, (2) the prognostic impact of lower SMI on mortality was substantially higher in patients who were at baseline higher surgical risks of the STS-PROM score and the logistic EuroSCORE II, (3) the addition of SMI substantially improves the risk stratification for mortality beyond that of a model based only on conventional risk factors, and (4) the discriminative capacity of SMI for predicting mortality was higher in men than in women.

Table 2
Primary and secondary clinical outcomes at 12 months according to skeletal muscle index tertile

	Event rate at 12 Mo*, n (%)				Adjusted Hazard Ratio (95% CI)†			
	High	Mid	Low	p Value	Mid	p Value	Low	p Value
Primary outcome: death from any cause	8 (6.2%)	11 (7.1%)	20 (15.5%)	0.036	1.66 (0.66−4.18)	0.282	2.69 (1.18−6.12)	0.019
Secondary outcomes								
Stroke or TIA	7 (4.7%)	9 (6.1%)	7 (4.9%)	0.826	1.59 (0.58−4.37)	0.373	1.12 (0.38−3.29)	0.840
Stroke	6 (3.9%)	9 (6.1%)	4 (2.5%)	0.355	1.74 (0.61−5.02)	0.303	0.69 (0.19−2.51)	0.573
Myocardial infarction	11 (6.3%)	11 (6.6%)	12 (7.2%)	0.957	1.05 (0.45−2.42)	0.914	1.21 (0.52−2.82)	0.663
Any rehospitalization	35 (26%)	33 (26.4%)	33 (26.3%)	0.996	1.08 (0.67−1.75)	0.744	1.19 (0.73−1.94)	0.491
New permanent pacemaker insertion	8 (7%)	11 (10.4%)	8 (6.8%)	0.659	2.22 (0.85−5.78)	0.102	1.46 (0.55−3.87)	0.446
Acute kidney injury	14 (8%)	17 (9.8%)	19 (11%)	0.659	1.51 (0.74−3.12)	0.259	1.28 (0.64−2.58)	0.487
Vascular access site complication	10 (5.7%)	10 (6%)	20 (12.2%)	0.063	1.15 (0.48−2.76)	0.761	2.06 (0.96−4.45)	0.065
Bleeding	61 (36.2%)	74 (44.9%)	78 (45.4%)	0.101	1.28 (0.91−1.80)	0.154	1.26 (0.89−1.79)	0.195

CI indicates confidence interval; TIA, transient ischemic attack.

* The percentages are Kaplan−Meier estimates of the rates of the endpoints at 12 months.

† Hazard ratios are for comparison with the high-tertile group (reference). Models were adjusted for age, body mass index, STS score, hypertension, diabetes mellitus, baseline ejection fraction, coronary artery disease, prior stroke, peripheral vascular disease, renal insufficiency, valve type, and type of anesthesia with sex-stratification.

The evaluation of frailty is a critical task for risk prediction and patient selection in TAVI.[17] Sarcopenia is one of the determining factors for the functional status of the old patients and important biological substrates of frailty.[3,17,18] Sarcopenia was defined according to the European Working Group on Sarcopenia in Older People[18] as the copresence of low muscle mass and strength, operationally defined as low psoas muscle area by CT imaging. In this regard, our results suggest that the degree of sarcopenia as measured by CT-derived SMI substantially improve the risk stratification for mortality in patients who underwent TAVI.

By analyzing the CT images in the context of TAVI, physicians can obtain information on body composition in the trunk. Several studies used the psoas muscle area as a convenient marker for estimating the skeletal muscle mass.[19-21] However, there is still a lack of evidence that psoas muscle area can appropriately represent the total body muscle; therefore, utilizing an entire cross-sectional scan to calculate the skeletal muscle mass in the abdomen provides a better estimation of the entire muscle mass.[22] By using an automated software system, the amount of muscle mass in patients can be simply obtained with routine pre-TAVI CT scan. This information on body composition would improve the risk stratification of TAVI candidates as well as patient care including nutritional support and rehabilitation, especially in old patients with lower skeletal muscle mass.

In the present study, low SMI was an independent predictor for 1-year mortality. Our findings are consistent with previous studies showing that sarcopenic patients had longer hospitalization periods and increased mortality after TAVI.[23-25] The addition of SMI to conventional risk model resulted in significant increases in the ability to classify 1-year mortality risk. This finding was similar to recent report

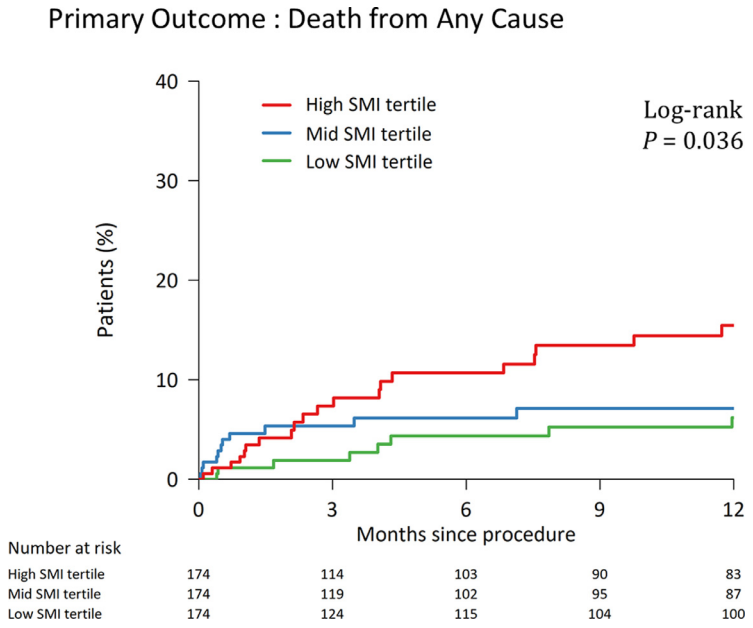

Figure 2. Kaplan-meier curve of all-cause mortality at 12 months according to skeletal muscle index tertiles. SMI indicates skeletal muscle index.

Table 3
Predictors for all-cause mortality at 12 months in univariate and multivariate cox proportional hazards analyses with sex-stratification

	Univariate		Multivariate	
	Hazard ratio (95% CI)	p Value	Hazard ratio (95% CI)	p Value
Skeletal muscle index (categorical)				
High tertile	1 (referent)		1 (referent)	
Mid tertile	1.46 (0.59−3.63)	0.416	1.66 (0.66−4.18)	0.282
Low tertile	2.74 (1.20−6.22)	0.016	2.69 (1.18−6.12)	0.019
Age (per 1-year increase)	1.02 (0.96−1.09)	0.476		
Body mass index	0.96 (0.87−1.06)	0.445		
STS-PROM score	1.11 (1.06−1.16)	<0.001	1.08 (1.01−1.15)	0.020
Hypertension	1.91 (0.67−5.38)	0.224		
Diabetes mellitus	2.65 (1.41−4.99)	0.003	2.27 (1.17−4.40)	0.015
Ejection fraction <40%	3.85 (1.82−8.13)	<0.001	2.73 (1.24−6.04)	0.013
Previous stroke	1.23 (0.51−2.94)	0.649		
Peripheral vascular disease	2.53 (0.99−6.48)	0.053		
Chronic kidney disease	2.51 (1.34−4.71)	0.004		
Balloon-expandable valve	1.10 (0.59−2.03)	0.766		
Transfemoral approach	0.41 (0.15−1.17)	0.096		
Monitored anesthesia care	0.74 (0.39−1.40)	0.354		

CI indicates confidence interval.

from FRAILTY-AVR (Frailty in Aortic Valve Replacement) registry.[26] Interestingly, the mortality risk according to the degree of SMI was substantially different in combination with the conventional surgical risk categories. The additive prognostic impact of low SMI was the highest in patients who were at high surgical risks. In this context, further categorization using CT-measured skeletal muscle mass may be a more useful anatomic profile for the prediction of mortality in higher-risk patients who underwent TAVI.

The amount of skeletal muscle is affected by various factors such as race, age, and sex.[3,4] In the current study, the mean SMI was significantly higher in men, and the discriminative capacity of SMI for predicting mortality was also substantially higher in men. Until recently, there were no accepted cut-off values of CT-measured skeletal muscle for diagnosing sarcopenia in different clinical groups. In older patients and especially the TAVI candidates, the prevalence of sarcopenia may be much higher than in other patient groups. When using the diagnostic criteria for sarcopenia in the Korean population with malignant disease,[27] nearly 80% and 30% of men and women in our registry would be classified into sarcopenia. However, the direct adoption of criteria used in other ethnic populations could lead to misclassification and misinterpretation of the results.

This study has several limitations. First, our study is an analysis from a nonrandomized, observational data, and thus the confounding variables not taken into account may have influenced the observed findings. Therefore, the overall findings should be considered as hypothetical and hypothesis-generating only. Second, we included TAVI patients from a tertiary center in Korea. Therefore, the

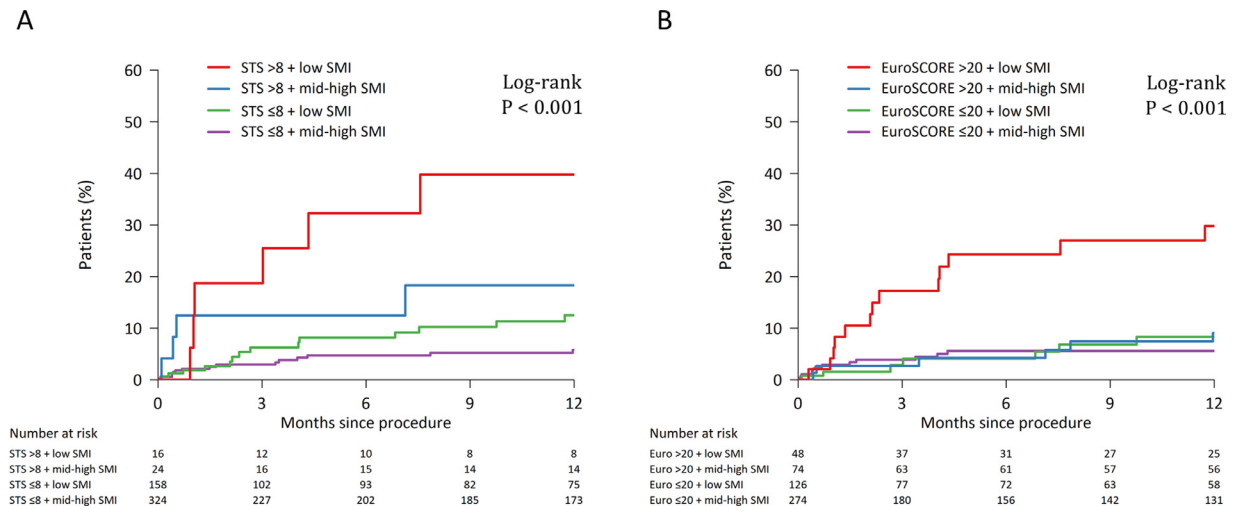

Figure 3. Kaplan-meier curves of all-cause mortality at 12 months according to stratified groups by skeletal muscle index tertiles combined with traditional surgical risk categories. Panel A shows all-cause mortality at 12 months in groups according to skeletal muscle index grades (low or mid-high) stratified by the STS-PROM score (≤8 or >8). Panel B shows all-cause mortality at 12 months in groups according to skeletal muscle index grades (low or mid-high) stratified by the logistic EuroSCORE II (≤20 or >20). EuroSCORE indicates the European System for Cardiac Operative Risk Evaluation; STS, Society of Thoracic Surgeons.

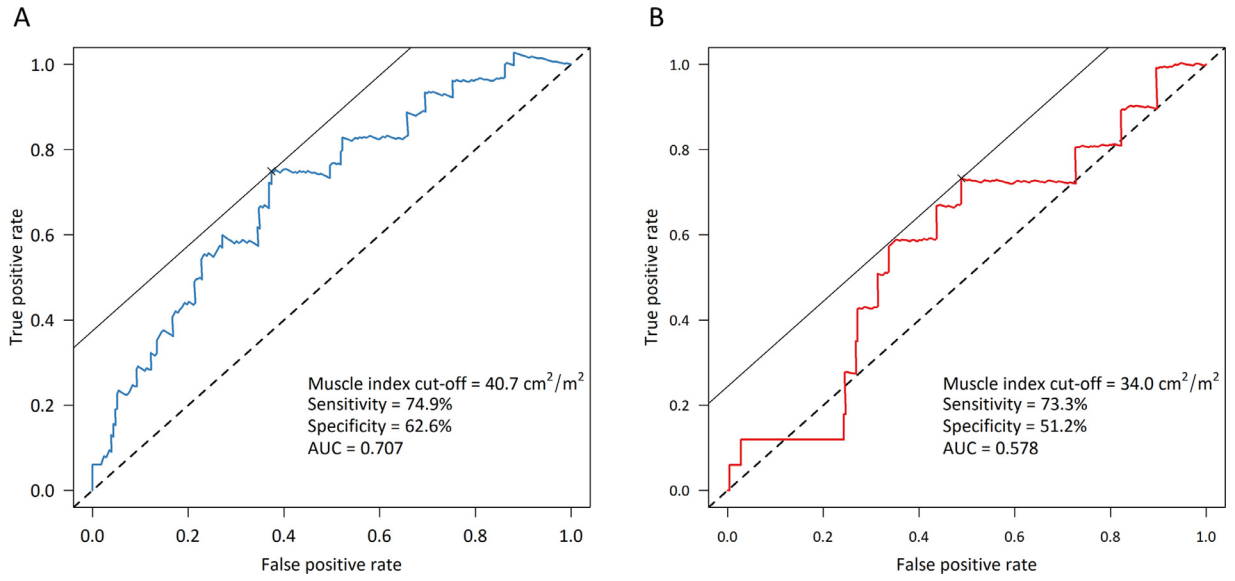

Figure 4. Best cut-off levels of skeletal muscle index for risk prediction of mortality in men and women. AUC indicates area under the curve.

direct application of our findings to other ethnic populations or different clinical settings might be limited. Third, given that the sample size of patients and clinical events was relatively small, our study was underpowered to detect clinically relevant differences in terms of the outcomes. Also, even though all-cause mortality was related with severity of SMI, most of other surrogate endpoints were not associated significantly. The reason of higher mortality in low SMI was not fully elucidated. Lastly, we did not include detailed information on the functional status, physiologic muscle strength, and quality of life, which might be important manifestations of sarcopenia in the old population.[26]

This study has prospectively demonstrated the incremental prognostic value of sarcopenia in patients who underwent TAVI. This association was more prominent in patients who were at high surgical risk. Physiological risk stratification with SMI as an adjunct to clinical and anatomical risk factors may be useful. In the clinical viewpoint, one of the most important rationale to adopt a sarcopenia-based assessment of frailty is its actionable therapeutic responsiveness to exercise and nutrition-based interventions. Further researches are required to elucidate whether sarcopenic patients benefit from effective preventive and therapeutic strategies to counteract their frailty and improve their outcomes following TAVI.

Authors contribution

Yong-Hoon Yoon: Methodology, Software, Validation, Investigation, Resources, Data Curation, Writing − Original Draft, Visualization. **Yousun Ko:** Methodology, Software, Resources, Investigation, Writing − Original Draft. **Kyung Won Kim:** Methodology, Software, Resources, Investigation, Writing − Original Draft. **Do-Yoon Kang:** Investigation, Resources. **Jung-Min Ahn:** Investigation, Resources. **Euihong Ko:** Investigation, Resources. **Hanbit Park:** Investigation, Resources, Data Curation. **Sang-Cheol Cho:** Investigation, Resources, Data Curation. **Ho Jin Kim:** Resources. **Joon Bum Kim:** Validation, Resources, Writing - Review & Editing. **Suk Jung Choo:** Resources. **Seung-Ah Lee:** Validation, Resources, Writing - Review & Editing. **Dae-Hee Kim:** Validation, Resources, Writing - Review & Editing. **Duk-Woo Park:** Conceptualization, Methodology, Validation, Investigation, Resources, Writing - Review & Editing, Supervision, Project administration, Funding acquisition. **Seung-Jung Park:** Validation, Investigation, Resources, Writing - Review & Editing, Supervision, Project administration, Funding acquisition.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.10.039.

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