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## Effects of computed tomography-defined sarcopenia on patients undergoing transcatheter aortic valve implantation

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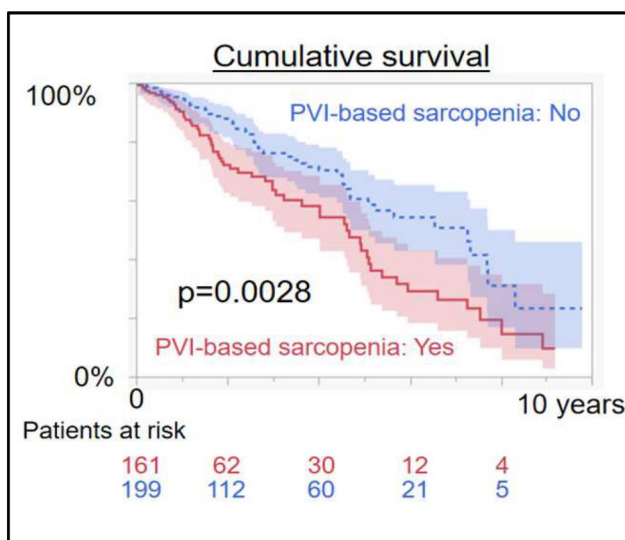
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#### Summary

In this retrospective study, 360 patients undergoing TAVI were enrolled. Preoperative CT scan images were used to diagnose sarcopenia. Computed tomography-defined sarcopenia diagnosed using PVI-based criteria is a good predictor of adverse procedural outcomes and unfavourable long-term outcomes. These findings might facilitate patient stratification for aortic stenosis treatment.



Legend: PVI = psoas muscle volume index; TAVI = transcatheter aortic valve implantation

#### Abstract

**OBJECTIVES:** Stratifying patients with aortic stenosis is crucial for improving their lifetime management. Several studies analysed computed tomography (CT)-defined sarcopenia in patients undergoing transcatheter aortic valve implantation (TAVI). However, the criteria for CT-defined sarcopenia are heterogeneous among these studies. Mostly, they primarily evaluated short-term outcomes; research focusing on long-term outcomes, related to lifetime management in patients with aortic stenosis, is rare. We assessed the effects of CT-defined sarcopenia on the short- and long-term outcomes in patients undergoing TAVI using three different sarcopenia criteria, including two traditional criteria and a novel criterion.

**METHODS:** In this retrospective study, we enrolled 360 patients. Three different sarcopenia criteria (skeletal muscle index [SMI], psoas muscle area [PMA] and psoas muscle volume index [PVI]) were applied to assess safety and early and long-term clinical outcomes.

**RESULTS:** SMI-, PMA- and PVI-sarcopenia were diagnosed in 244 (67.7%), 246 (68.3%) and 161 (44.7%) patients, respectively. However, PMA-sarcopenia was associated with poor long-term survival after TAVI. Furthermore, PVI-sarcopenia was associated with lower safety at 30 days and poor long-term survival. Using Cox regression hazard models, PVI-sarcopenia tended to be a risk factor for overall survival (hazards ratio: 1.49,  $P = 0.052$ ).

**CONCLUSIONS:** In patients undergoing TAVI, CT-defined sarcopenia using PVI-based criteria was a reliable predictor of poor outcomes. This finding might facilitate stratification of patients undergoing TAVI.

**Keywords:** aortic valve stenosis • sarcopenia • transcatheter aortic valve implantation

ABBREVIATIONS	
AS	Aortic stenosis
PMA	Psoas muscle area
PMV	Psoas muscle volume
PVI	Psoas muscle volume index
SMI	Skeletal muscle index
TAVI	Transcatheter aortic valve implantation
VARC-3	Valve Academic Research Consortium 3

INTRODUCTION

In the last decade, the number of transcatheter aortic valve implantation (TAVI) performed has considerably increased. In Europe and the USA, the number of TAVI cases far exceeds that of surgical aortic valve replacement [1, 2]. The number of TAVI cases also exceeds that of surgical aortic valve replacements in Asian countries [3], and it is becoming the mainstream treatment of aortic stenosis (AS).

Stratifying patients with AS is crucial for improving their life-time management. Various studies have reported predictors of clinical outcomes after TAVI [4–6], including sarcopenia [7]. Preprocedural whole-body computed tomography (CT) is required to safely complete TAVI, which is advantageous for measuring muscle mass. Therefore, several studies analysed CT-defined sarcopenia in patients undergoing TAVI. However, the criteria for CT-defined sarcopenia are heterogeneous among these studies [7, 8]. Research focusing on long-term outcomes, which are related to lifetime management in patients with AS, is rare [7, 8].

Therefore, we assessed the effects of CT-defined sarcopenia on the short- and long-term outcomes in patients undergoing TAVI using two traditional criteria and a novel criterion.

PATIENTS AND METHODS

Study population

This retrospective study included 362 consecutive patients who underwent TAVI for symptomatic severe AS at Yamaguchi University Hospital (Ube, Japan) between 2014 and 2023. The Institutional Review Board of Yamaguchi University Hospital (Study ID: H2024-014) approved this study on 9 May 2024. This research protocol complies with the latest version of the Declaration of Helsinki (including the World Medical Association [WMA] Declaration of Taipei) and the “Ethical Guidelines for Life Science and Medical Research Involving Human Subjects”

(partially revised on 10 March 2022). The requirement for written informed consent was waived based on the Ethical Guidelines for Medical and Biological Research Involving Human Subjects. Information on study implementation is publicly available on the website of Yamaguchi University School of Medicine Hospital; patients or their legal representatives who might have participated in the study had been provided with the opportunity to refuse participation.

CT-based definition of sarcopenia

The established abdominal muscle parameters for diagnosing sarcopenia, including the skeletal muscle area at the L3 level, psoas muscle area (PMA) at the L4 level and total psoas muscle volume (PMV), were measured semi-automatically using SYNAPSE VINCENT (Fujifilm, Tokyo, Japan) (Fig. 1).

To identify sarcopenia, we used the skeletal muscle index (SMI), PMA and PMV index (PVI). SMI was defined as the skeletal muscle area indexed to the square of the patient’s height ( $\text{cm}^2/\text{m}^2$ ). PVI was defined as the PMV indexed to the cubic of the patient’s height ( $\text{cm}^3/\text{m}^3$ ). According to CT findings, sarcopenia was defined as:

1. ‘SMI-sarcopenia’ as an SMI of  $<55.4 \text{ cm}^2/\text{m}^2$  in men and  $<38.9 \text{ cm}^2/\text{m}^2$  in women.
2. ‘PMA-sarcopenia’ as a PMA of  $<20.3 \text{ cm}^2$  in men and  $<11.8 \text{ cm}^2$  in women.
3. ‘PVI-sarcopenia’ as a PVI of  $<60.5 \text{ cm}^3/\text{m}^3$  in men and  $<43.6 \text{ cm}^3/\text{m}^3$  in women.

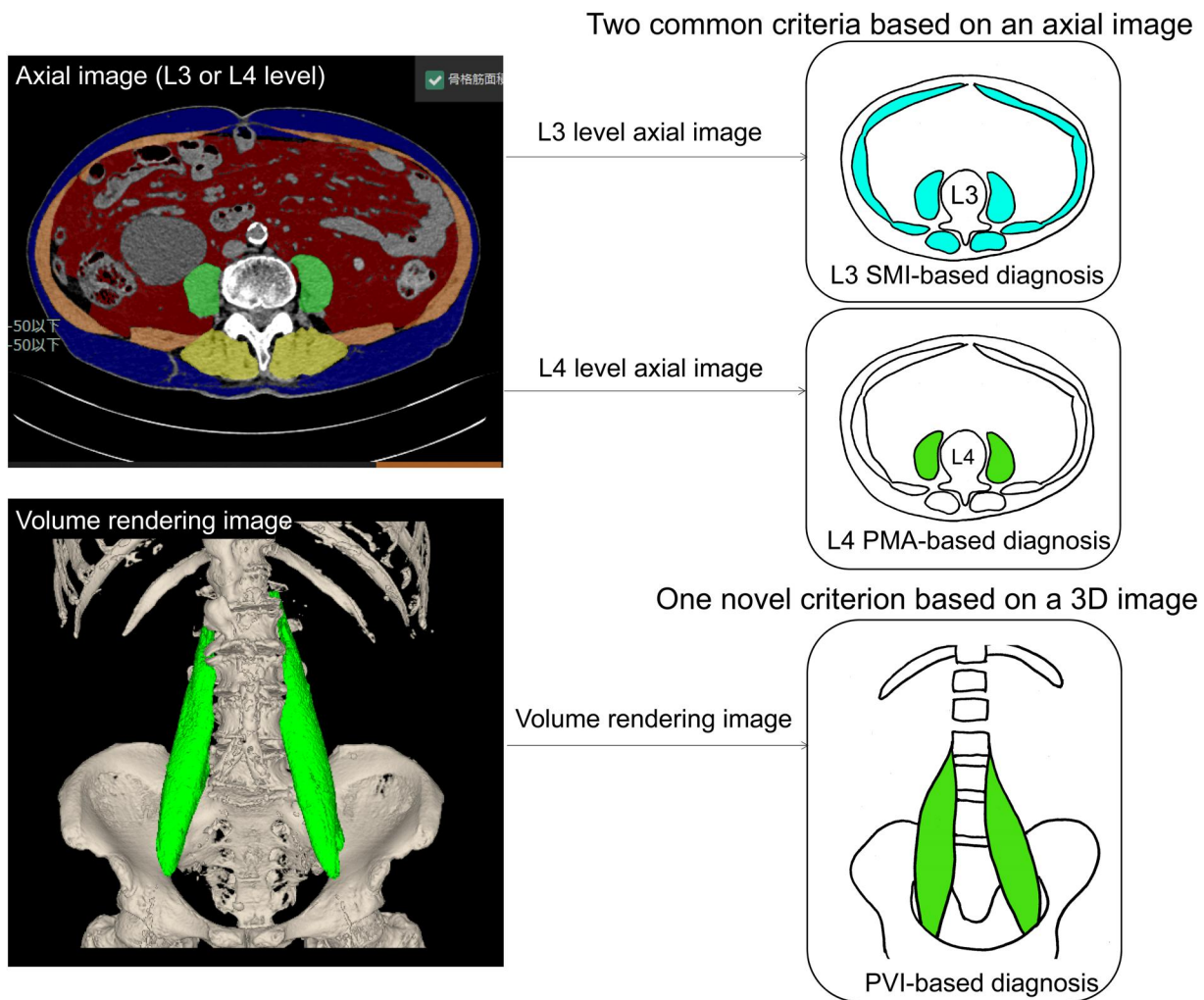
SMI- and PMA-sarcopenia have been defined by the European Working Group on Sarcopenia in Older People [9] and as previously reported [7]. We determined the PVI cut-off value for sarcopenia as the lowest quartile by sex as previously described [10, 11].

Assessments of clinical outcomes

Early clinical outcomes, including technical success, device success and early safety, were assessed according to the Valve Academic Research Consortium 3 (VARC-3) criteria [12].

Statistical analyses

Continuous data are expressed as mean  $\pm$  standard deviation and were evaluated using Student’s  $t$ -test. Categorical data were evaluated using the  $\chi^2$  or Fisher’s exact test, as appropriate. When the sample size was large with expected frequencies of 5



**Figure 1:** Evaluation of CT-defined sarcopenia using SYNAPSE VINCENT. Upper row: The psoas muscle area, erector spinae muscle area and abdominal muscle area are shown in green, yellow and red, respectively. The sum of these areas is defined as the skeletal muscle area (light blue). Lower row: The psoas muscle volume (green) was measured on images obtained using consecutive 1-mm CT slices

or more, the  $\chi^2$  test was used; differently, Fisher's exact test was used.

Time-to-event analyses including overall survival and freedom from cardiac death were performed using the Kaplan-Meier method with the log-rank test. Freedom from cardiac death was also analysed using the Fine-Gray method. The follow-up duration for patients who died was defined as the period from the date of surgery to that of death, whereas the follow-up duration for survivors was defined as the period from the date of surgery to the last confirmed date of survival.

The predictors of early safety of TAVI were analysed using a logistic regression model. Independent risk factors of overall survival after TAVI were analysed using the Cox regression hazard model. Multivariable analyses were performed using stepwise regression with forward selection. Variables with  $P < 0.10$  from univariable analysis were fitted in multivariable models. The confounders related to early safety were primarily selected based on risk factors identified in the EuroSCORE II, Society of Thoracic Surgeons Predictive Risk of Mortality (STS-PROM) and other similar scoring systems. Confounders related to overall survival were primarily selected based on indicators of general cardiovascular diseases, lifestyle-related diseases, and factors

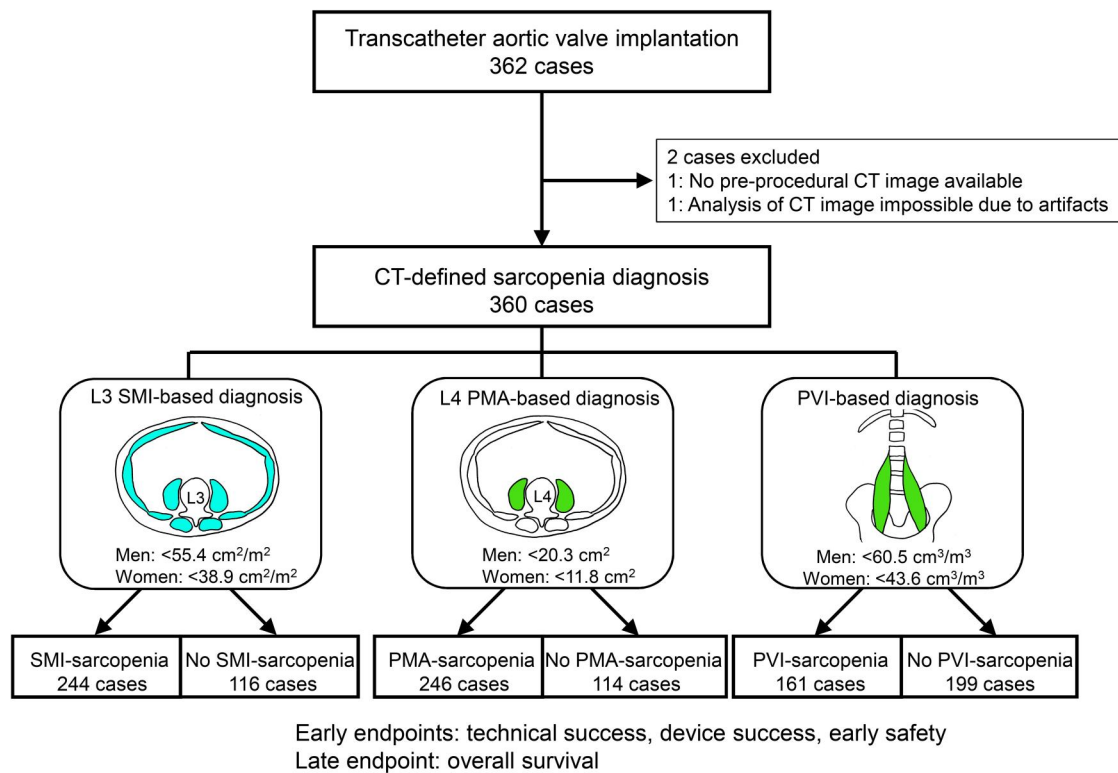
that might impact long-term prognosis, such as cardiac function, renal function, nutrition and frailty.

Statistical analyses were performed using JMP ver. 16 (SAS Institute, Cary, NC, USA) and EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan). Statistical significance was set at  $P < 0.05$ .

## RESULTS

### Study enrolment and baseline characteristics

Of 362 enrolled consecutive patients undergoing TAVI, 360 patients completed CT-defined sarcopenia diagnosis (Fig. 2). Two patients were excluded: preprocedural CT image was unavailable in one patient, and CT images could not be analysed in another due to artefacts caused by metal bolts implanted in the lumbar vertebrae. The baseline patient characteristics are presented in [Supplementary Table S1](#). The mean age of all patients was  $85.3 \pm 4.9$  years; 66.6% were female individuals. SMI-, PMA- and PVI-sarcopenia were diagnosed in 244 (67.7%), 246 (68.3%) and 161 (44.7%) patients, respectively. In all three



**Figure 2:** Study enrolment. Three different definitions of CT-based diagnosis of sarcopenia were applied to categorize the study participants

groups, patients with sarcopenia included fewer female patients. Patients with sarcopenia had lower body weight despite being taller.

### Procedural characteristics of TAVI

The procedural characteristics of TAVI are presented in [Supplementary Table S2](#). Balloon-expandable and self-expandable valves were implanted in 199 (55.3%) and 161 (44.7%) patients, respectively. The transfemoral approach was applied in 287 patients (79.7%). These tendencies were similar across all three sarcopenia definitions in patients with and without sarcopenia. The details of the transcatheter heart valves used are listed in [Supplementary Table S3](#). The incidence of blood transfusion use was significantly lower in the group without sarcopenia than in that with sarcopenia ( $P=0.015$ ), based on the PVI definition ([Supplementary Table S2](#)).

### Early clinical outcomes

Early clinical outcomes are summarized in [Table 1](#). All-cause mortality ( $n=2$ ) included one patient who died in the hospital on postoperative day 10 due to postoperative low output syndrome and another patient who was discharged on postoperative day 11 but died at home on postoperative day 26 from unexplained renal failure.

The incidence rates of in-hospital mortality, 30-day all-cause mortality and cardiovascular mortality were very low in our study population. The incidence of new pacemaker implantation and more-than-moderate patient-prosthesis mismatch was lower in patients with SMI-sarcopenia.

Patients in the PVI-sarcopenia group had a significantly lower incidence of early safety (sarcopenia: 56.5% vs. without sarcopenia: 69.3%,  $P=0.015$ ). We further analysed the predictors of early safety ([Table 2](#)). Multivariable analysis identified that PVI-sarcopenia was a negative predictor for early safety (odds ratio: 0.560, 95% confidence interval (CI): 0.340–0.560,  $P=0.023$ ). The forest plot for early safety is shown in [Supplementary Fig. S1](#). VARC-3 type 2 bleeding was the main reason for the reduced safety in the PVI-sarcopenia group ([Supplementary Table S4](#)).

### Long-term clinical outcomes

The mean follow-up period was  $2.4 \pm 2.2$  (median [interquartile range], 1.9 [0.7–4.0]) years. The overall 5- and 9-year survival rates in all patients were 53.4% and 16.2%, respectively ([Fig. 3A](#)). The 5- and 9-year survival rates stratified by SMI-sarcopenia were 54.0% and 12.4% in patients with sarcopenia and 51.9% and 19.5% in those without sarcopenia, respectively ([Fig. 3B](#)), without significant difference ( $P=0.50$ : log-rank [Sarcopenia group: median time of 5.1 years, 95% CI: 45.2–73.2% vs. No sarcopenia group: median time 5.2 years, 95% CI: 45.6–72.6%]). However, the 5- and 9-year survival rates stratified by PMA-sarcopenia were 47.8% and 9.7% in patients with sarcopenia and 62.9% and 21.2% in those without, respectively ([Fig. 3C](#)), with a significant difference ( $P=0.026$ : log-rank [Sarcopenia group: median time of 4.9 years, 95% CI: 40.2–56.5% vs. No sarcopenia group: median time of 6.5 years, 95% CI: 46.9–76.9%]). The 5- and 9-year survival rates stratified by PVI-sarcopenia were 43.0% and 9.7% in patients with sarcopenia and 60.7% and 23.3% in patients without sarcopenia, respectively ([Fig. 3D](#)), which was significantly different ( $P=0.0028$ : log-rank [Sarcopenia group: median time of 4.6 years, 95% CI: 32.3–51.4% vs. No sarcopenia



**Table 1:** Early clinical outcomes

Variables	Overall (n = 360)	SMI-sarcopenia			PMA-sarcopenia			PVI-sarcopenia		
		Yes (n = 244)	No (n = 116)	P-value	Yes (n = 246)	No (n = 114)	P-value	Yes (n = 161)	No (n = 199)	P-value
30-day outcomes, n (%)										
In-hospital mortality	1 (0.3)	1 (0.4)	0	0.99	1 (0.4)	0	0.99	1 (0.6)	0	0.44
All-cause mortality	2 (0.6)	2 (0.8)	0	0.99	2 (0.8)	0	0.99	1 (0.6)	1 (0.5)	0.99
Cardiovascular mortality	1 (0.3)	1 (0.4)	0	0.99	1 (0.4)	0	0.99	1 (0.6)	0	0.44
Conversion to open surgery	2 (5.5)	1 (0.4)	1 (0.8)	0.54	2 (0.8)	0	0.99	0	2 (1.0)	0.50
Unexpected coronary obstruction	1 (0.3)	0	1 (0.8)	0.33	0	1 (0.8)	0.32	0	1 (0.5)	0.99
Aortic dissection	4 (1.1)	2 (0.8)	2 (1.7)	0.60	3 (1.2)	1 (0.8)	0.99	2 (1.2)	2 (1.0)	0.99
Annulus rupture	1 (0.3)	0	1 (0.8)	0.33	0	1 (0.8)	0.32	0	1 (0.5)	0.99
TAVI in TAVI deployment	3 (0.8)	3 (1.2)	0	0.55	3 (1.2)	0	0.55	0	3 (1.5)	0.26
Unplanned use of PCPS	3 (0.8)	3 (1.2)	0	0.55	2 (0.8)	1 (0.8)	0.99	3 (1.9)	0	0.09
Stroke	8 (2.2)	4 (1.6)	4 (3.4)	0.28	5 (2.0)	3 (2.6)	0.71	5 (3.1)	3 (1.5)	0.47
Cardiac tamponade	2 (5.5)	2 (0.8)	0	0.99	2 (0.8)	0	0.99	1 (0.6)	1 (0.5)	0.99
New pacemaker implantation	32 (8.9)	16 (6.5)	16 (13.7)	<0.05	18 (7.3)	14 (12.2)	0.12	11 (6.8)	21 (10.5)	0.21
PVL ≥ moderate	35 (9.7)	24 (9.8)	11 (9.4)	0.91	25 (10.1)	10 (8.7)	0.67	15 (9.3)	20 (10.0)	0.81
PPM ≥ moderate	17 (4.7)	4 (1.6)	13 (11.2)	<0.001	10 (4.0)	7 (6.1)	0.38	4 (2.4)	13 (6.9)	0.08
ICU stay, days	1.7 ± 2.1	1.7 ± 2.3	1.9 ± 1.7	0.41	1.8 ± 2.4	1.7 ± 2.4	0.65	1.7 ± 1.4	1.8 ± 2.5	0.85
Hospital stay after TAVI, days	10.50 ± 12.2	9.9 ± 8.1	12.2 ± 17.9	0.06	10.3 ± 9.9	10.8 ± 16.8	0.69	10.6 ± 10.0	10.3 ± 13.7	0.79
Composite end-points defined by VARC-3 criteria, n (%)										
Technical success (at exit from procedure room)	352 (97.8)	238 (97.5)	114 (98.2)	0.99	241 (97.9)	111 (97.3)	0.71	159 (98.7)	193 (96.9)	0.30
Device success (at 30 days)	298 (82.7)	208 (85.2)	90 (77.5)	0.07	203 (82.5)	95 (83.3)	0.84	139 (86.3)	159 (79.8)	0.10
Early safety (at 30 days)	230 (63.8)	161 (65.9)	69 (59.4)	0.23	150 (60.9)	80 (70.1)	0.09	91 (56.5)	138 (69.3)	0.011

ICU, intensive care unit; PCPS: percutaneous cardiopulmonary support; PMA: psoas muscle area; PPM: patient-prosthesis mismatch; PVI: psoas muscle index; PVL: paravalvular leakage; SMI: skeletal muscle index; TAVI: transcatheter aortic valve implantation; VARC-3: Valve Academic Research Consortium 3. Bold indicates statistical significance.

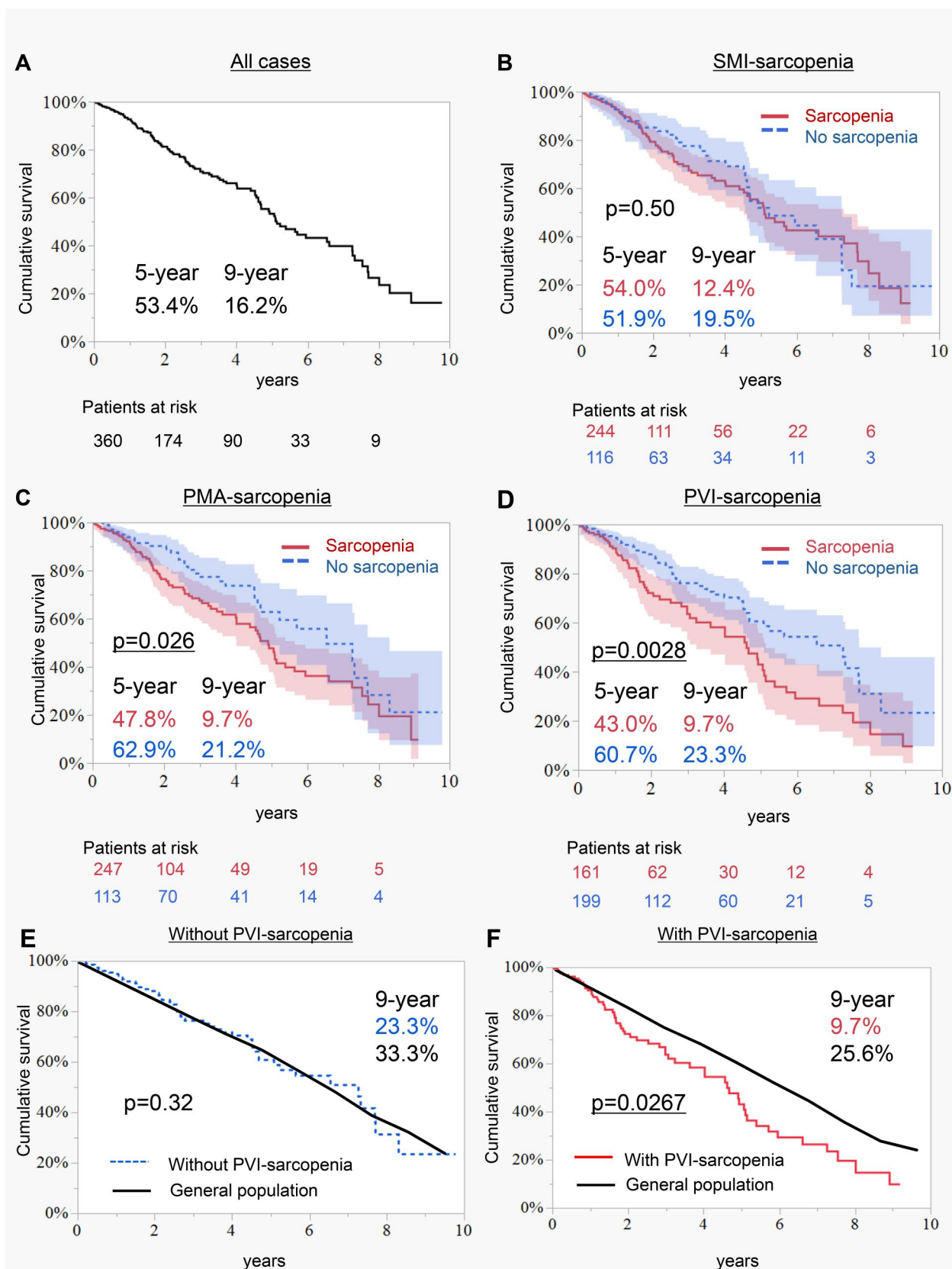
**Table 2:** Predictors for early safety

Variables	Univariable			Multivariable		
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Age, years	0.981	(0.939–1.024)	0.38			
Female sex	0.745	(0.469–1.186)	0.21			
Hypertension	0.641	(0.325–1.263)	0.19			
Dyslipidaemia	0.822	(0.531–1.272)	0.37			
Diabetes mellitus	1.449	(0.855–2.455)	0.16			
Coronary artery disease	0.994	(0.627–1.575)	0.97			
Peripheral arterial disease	0.505	(0.284–0.898)	<b>0.019</b>	0.438	(0.028–6.902)	0.73
Previous cardiac surgery	1.314	(0.526–3.282)	0.55			
Chronic atrial fibrillation	1.402	(0.705–2.486)	0.33			
COPD	1.566	(0.705–3.480)	0.27			
EF, % <sup>a</sup>	1.010	(0.993–1.027)	0.26			
Serum albumin, g/dl <sup>a</sup>	2.587	(1.54–4.345)	<b>&lt;0.001</b>	1.900	(1.051–3.435)	<b>&lt;0.05</b>
eGFR <sup>a</sup>	1.021	(1.007–1.035)	<b>&lt;0.01</b>	1.017	(1.001–1.033)	<b>&lt;0.05</b>
Haemodialysis	0.561	(0.078–4.034)	0.56			
NYHA class <sup>a</sup>	0.601	(0.421–0.858)	<b>&lt;0.01</b>	0.912	(0.586–1.418)	0.68
Clinical frailty scale score <sup>a</sup>	0.619	(0.493–0.777)	<b>&lt;0.0001</b>	0.711	(0.540–0.934)	<b>&lt;0.05</b>
EuroSCORE II, % <sup>a</sup>	0.931	(0.888–0.976)	<b>&lt;0.01</b>	0.981	(0.928–1.037)	0.49
STS-PROM, % <sup>a</sup>	0.953	(0.916–0.991)	<b>0.016</b>	0.992	(0.947–1.039)	0.73
PVI-sarcopenia	0.561	(0.363–0.867)	<b>&lt;0.01</b>	0.560	(0.340–0.924)	<b>&lt;0.05</b>
TA access	0.154	(0.064–0.372)	<b>&lt;0.0001</b>	0.172	(0.063–0.464)	<b>&lt;0.001</b>

<sup>a</sup>Analysed as continuous data, otherwise as categorical data.

CI: confidence interval; COPD: chronic obstructive pulmonary disease; EF: ejection fraction; eGFR: estimated glomerular filtration rate; NYHA: New York Heart Association; PVI: psoas muscle volume index; STS-PROM: Society of Thoracic Surgeons predictive risk of mortality; TA: transapical.

Bold indicates statistical significance.



**Figure 3:** Time-to-event data for survival. **(A)** Curves for cumulative survival in all patients. **(B–D)** Curves for cumulative survival stratified by **(B)** SMI-sarcopenia, **(C)** PMA-sarcopenia, and **(D)** PVI-sarcopenia. The curves of patients with and without sarcopenia are shown as solid red and dashed blue lines, respectively. **(E and F)** Predicted survival for patients without **(E)** and with **(F)** PVI-sarcopenia as shown in **(D)**. Black lines indicate the corresponding curves of a sex- and age-matched Japanese general population

group: median time of 7.2 years, 95% CI: 46.9–77.1%]. [Supplementary Figure S3](#) shows the Kaplan–Meier curves with individual patient information on censoring and [Supplementary Fig. S4](#) shows the inverse Kaplan–Meier curves.

We also compared the 9-year survival of patients who underwent TAVI in this study with that of the sex- and age-matched Japanese population calculated from Japanese abridged life tables. Compared with the general Japanese population, the survival of patients without PVI-sarcopenia was equivalent (23.3% vs. 33.3%,  $P = 0.32$ ; Fig. 3E), whereas the survival rate of patients with PVI-sarcopenia was lower (9.7% vs. 25.6%,  $P = 0.027$ ; Fig. 3F).

Freedom from cardiac death at 5 and 9 years was found in 86.7% and 67.7% of all patients, respectively ([Supplementary Fig. S5A](#)). [Supplementary Figure S5B–D](#) shows freedom from cardiac death for each of the three sarcopenia criteria.

We further analysed the risk factors of overall survival after TAVI by comparing PVI-sarcopenia with other possible clinical factors (Table 3). Univariable analysis identified 10 variables as potential risk factors for overall survival. Multivariable analysis identified five risk factors of overall survival after TAVI and two possible predictors, including PVI-sarcopenia (hazard ratio: 1.495, 95% CI: 0.995–2.247,  $P = 0.052$ ). The forest plot for overall survival is shown in [Supplementary Fig. S2](#).

## DISCUSSION

An SMI-based sarcopenia diagnosis was not a predictor for any poor outcome after TAVI. In contrast, PMA-based sarcopenia diagnosis was associated with poor long-term survival after TAVI; PVI-based sarcopenia diagnosis was associated with lower 30-day safety and poor long-term survival. Using the analysis of predictors of early safety (Table 2), we compared the predictive

value of PVI-sarcopenia with established risk models, including EuroSCORE II and STS-PROM. Using univariate analysis, EuroSCORE II, STS-PROM and PVI-sarcopenia were all identified as predictors. However, using multivariate analysis, only PVI-sarcopenia remained a predictor. This suggests that PVI-sarcopenia is a valuable predictor. Similarly, regarding analysis of risk factors for overall survival (Table 3), EuroSCORE II, STS-PROM and PVI-sarcopenia were included for evaluation. Using this analysis, PVI-sarcopenia was the only factor identified as a risk factor using both univariate and multivariate analyses.

CT-defined sarcopenia has traditionally been diagnosed using a single axial image. However, many recent reports in cardiovascular and non-cardiovascular patients have suggested that volumetric assessment is more accurate than assessments using only a single axial image. We used two traditional criteria for sarcopenia diagnosis based on a single axial image and one novel diagnostic criterion based on volumetric assessments. The prevalence of PVI-sarcopenia diagnosed based on volumetric data was the lowest compared with those of the other two criteria of sarcopenia diagnosis, and PVI-sarcopenia was associated with poor early and long-term outcomes. This indicates that compared with the other two sarcopenia criteria, the PVI criteria can better identify patients with worse prognoses. Although TAVI indications are gradually expanded to younger patients, most patients undergoing TAVI are older adults. Spinal deformities are more common in older patients, which makes measuring the muscle area accurately using a single axial image difficult. Furthermore, the patient's grip strength is more strongly correlated with the PMV than with the cross-sectional PMA. Thus, PMV may more sensitively reflect the patient's frailty [13].

The current study showed that PVI-sarcopenia was associated with lower early safety and poor long-term survival. The main reason for reduced early safety was the occurrence of VARC-3 type 2 bleeding events ([Supplementary Table S4](#)). VARC-3 type 2

**Table 3:** Risk factors for overall survival

Variables	Univariable			Multivariable		
	Hazard ratio	95% CI	P-value	Hazard ratio	95% CI	P-value
Age, years	1.013	(0.976–1.051)	0.50			
Female sex	0.642	(0.435–0.948)	<b>0.0256</b>	0.559	(0.358–0.873)	<b>0.0105</b>
Hypertension	0.567	(0.325–0.982)	<b>0.0427</b>	0.654	(0.362–1.182)	0.156
Dyslipidaemia	0.586	(0.401–0.857)	<b>0.0059</b>	0.689	(0.460–1.030)	0.069
Diabetes mellitus	0.855	(0.542–1.346)	0.49			
Coronary artery disease	0.903	(0.607–1.344)	0.61			
Peripheral arterial disease	1.583	(0.996–2.516)	0.06	1.398	(0.828–2.360)	0.210
Previous cardiac surgery	0.458	(0.169–1.246)	0.12			
Chronic atrial fibrillation	0.952	(0.531–1.704)	0.86			
COPD	1.006	(0.486–2.082)	0.98			
EF, % <sup>a</sup>	1.015	(0.999–1.031)	0.07	1.031	(1.014–1.048)	<b>0.0002</b>
BNP, pg/ml <sup>a</sup>	1.000	(1.000–1.001)	0.78			
Serum albumin, g/dl <sup>a</sup>	0.448	(0.282–0.712)	<b>0.0007</b>	0.400	(0.242–0.663)	<b>0.0004</b>
eGFR <sup>a</sup>	0.982	(0.968–0.995)	<b>0.0077</b>	0.981	(0.966–0.996)	<b>0.010</b>
Haemodialysis	57.127	(6.142–531.364)	<b>0.0004</b>	3.899	(0.350–43.378)	0.268
NYHA class <sup>a</sup>	1.135	(0.849–1.518)	0.39			
Clinical frailty scale score <sup>a</sup>	1.128	(0.956–1.331)	0.15			
EuroSCORE II, % <sup>a</sup>	0.954	(0.903–1.009)	0.11			
STS-PROM, % <sup>a</sup>	1.011	(0.974–1.051)	0.56			
PVI-sarcopenia	1.770	(1.211–2.586)	<b>0.0032</b>	1.495	(0.995–2.247)	0.052
TA access	1.786	(1.118–2.851)	<b>0.015</b>	1.786	(1.063–3.002)	<b>0.028</b>

<sup>a</sup>Analysed as continuous data, otherwise as categorical data.

BNP: brain natriuretic peptide; CI: confidence interval; COPD: chronic obstructive pulmonary disease; EF: ejection fraction; eGFR: estimated glomerular filtration rate; NYHA: New York Heart Association; PVI: psoas muscle volume index; STS-PROM: Society of Thoracic Surgeons predictive risk of mortality; TA: transapical.

Bold indicates statistical significance.

bleeding includes bleeding that requires a transfusion of 2–4 units of red blood cells. Regarding PVI-sarcopenia, patients with and without sarcopenia had haemoglobin levels of  $10.7 \pm 1.6$  g/dl and  $11.1 \pm 1.4$  g/dl, respectively. Patients with PVI-sarcopenia had significantly lower haemoglobin levels ( $P = 0.03$ ). To clarify the reasons for the higher frequency of blood transfusions in patients with PVI-sarcopenia, further analysis was conducted. A correlation between PVI, preoperative haemoglobin levels and intraoperative blood loss was assessed. The results showed that preoperative haemoglobin levels positively correlated with PVI ( $P < 0.0001$ ). Data are shown in [Supplementary Fig. S6](#). Accordingly, low preoperative haemoglobin levels might have been the reason for the higher frequency of blood transfusions in patients with PVI-sarcopenia.

Furthermore, PVI-sarcopenia was also associated with shorter long-term survival, suggesting two crucial implications. First, patient stratification should include the expected long-term outcomes because they are crucial for lifetime management of patients with AS. The European guideline recommends TAVI in patients aged 75 years and older [14]. The Japanese guidelines recommend that the threshold age for TAVI or surgical aortic valve replacement is 75–80 years [15], meaning that TAVI can be considered in 75-year-old patients with AS. The Japanese Ministry of Health, Labour and Welfare reported that the average life expectancies of 75-year-old Japanese are 12 years for men and 16 years for women [16]. Since a single TAVI may not complete the treatment for AS, considering the long-term prognosis in patients when deciding on the initial treatment for AS is important. Second, our study showed that loss of muscle volume was associated with poor long-term outcomes after TAVI. It implies that correcting sarcopenia may improve long-term outcomes after TAVI. Exercise and nutrition interventions in patients with sarcopenia improve physical strength [17]. Thus, pre- or postoperative interventions involving exercise and nutrition may improve poor outcomes in patients with sarcopenia undergoing TAVI. Figure 4 shows a chart representing the lifetime management algorithm in patients undergoing TAVI.

In this study, prognosis in patients undergoing TAVI with concomitant PVI-sarcopenia was poor. Regarding the analysis of long-term outcomes, there was no significant difference between the sarcopenia and non-sarcopenia groups in the proportion of cardiac deaths ([Supplementary Fig. S5](#)). In the PVI-sarcopenia group, 57 deaths were observed during this study period. The causes of death, in order of frequency, were infection in 15 cases (26.3%), senility in 14 (24.5%), heart disease in 10 (17.5%), cerebrovascular disease in 7 (12.2%), malignancy in 6 (10.5%), and other causes in 5. In the non-PVI-sarcopenia group, 51 deaths were observed. The causes of death, in order of frequency, were infection in 15 cases (29.4%), heart disease in 12 (23.5%), senility in 6 (11.7%), malignancy in 6 (11.7%), cerebrovascular disease in 2 (9.8%), and other causes in 10. The sarcopenia group had a higher proportion of senility-related deaths; muscle weakness and frailty progression contributed to poor long-term outcomes.

To improve prognosis in patients undergoing TAVI, active rehabilitation and nutritional therapy interventions could be considered. Hospitalized patients with AS generally exhibit severe symptoms with limited physical activity. Currently, to how much extent preoperative rehabilitation can be tolerated in these patients and how beneficial it would be remain unclear; further research is needed in this area. Conversely, regarding rehabilitation after TAVI, postoperative intensive recovery regimens have been shown to improve functional capacity, quality of life [18] and exercise tolerance, particularly with respect to the 6-min walk test [19] and maximum workload distance [20]. Postoperative rehabilitation may also be beneficial for reducing the risk of non-cardiovascular-related mortality, such as from unintended injuries. Furthermore, nutritional therapy in patients with sarcopenia, such as high-protein diets and nutritional supplements including branched-chain amino acids, vitamin D, whey protein and hydroxymethylbutyrate-enriched milk, has been shown to be effective [17]. Actively implementing these interventions in patients with poor prognosis is important.

The use of CT findings alone for the diagnosis of sarcopenia is a major limitation of this study. Both European and Asian working

### Lifetime management algorithm for patients undergoing TAVI

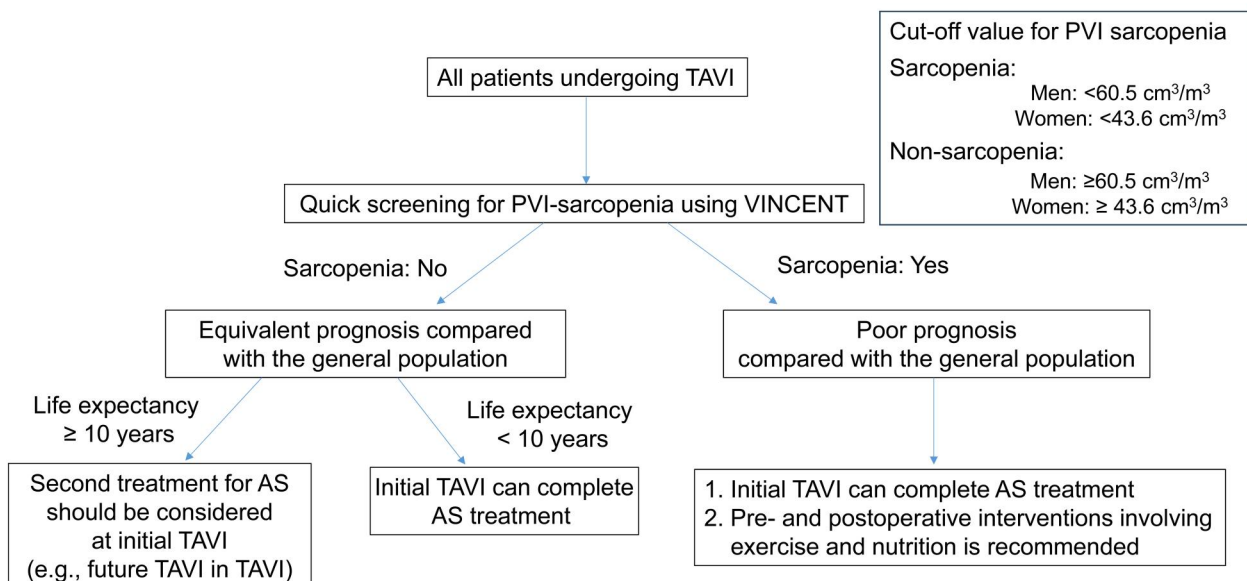


Figure 4: Lifetime management algorithm for patients undergoing TAVI



groups on sarcopenia recommend using the presence of both low muscle mass and low muscle strength for defining this disease [9, 21]. The present study did not assess muscle strength. In real-world clinical settings, some patients have better muscle strength, despite low muscle mass. The use of muscle mass alone for defining sarcopenia might overestimate sarcopenia prevalence. This study has further limitations including its small cohort size, retrospective study design and relatively old population. As our facility is not a high-volume centre, the number of cases is limited. Differences in mortality due to the learning curves of surgeons are an important consideration. However, our results have been favourable, and in-hospital mortality occurred in only 1 out of 360 patients. This death occurred in patient 352, it was not during the learning phase of the procedure, suggesting that the learning curve of surgeons did not significantly affect the study findings. Moreover, the article used to define the cut-off value for PVI is not a clinical study focused on cardiovascular patients. As no prior reports investigated the PVI cut-off value specifically in patients with cardiovascular disorders, we have adopted the cut-off value determined in patients with cancer. We referred to a study including patients with early-stage lung cancer for setting the cut-off value for PVI-sarcopenia. Patients with lung cancer, even if they are in the early stage of cancer, might be frailer. Setting the cut-off value to the lower 25th percentile for patients with early-stage lung cancer might have allowed for a greater probability of identifying severe cases. In the future, establishing an accurate threshold for defining sarcopenia settled may affect the results of this study.

## CONCLUSION

CT-defined sarcopenia differentially predicts safety and patient outcomes based on the criteria employed. However, this study was conducted including only older patients undergoing TAVI, making it an investigation in a limited context. PMA-based sarcopenia was only a predictor for long-term outcomes and PVI-based sarcopenia was a predictor for reduced safety and poor long-term outcomes. These findings may facilitate patient stratification for AS treatment. A more detailed investigation with a larger patient population is warranted.

## SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

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## CONFLICT OF INTEREST

None declared.

## DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Author contributions

**Hiroshi Kurazumi:** Writing—original draft. **Ryo Suzuki:** Writing—review & editing. **Ryosuke Nawata:** Data curation. **Kazumasa Matsunaga:** Data curation. **Yousuke Miyazaki:** Data curation. **Atsuo Yamashita:** Supervision. **Takayuki Okamura:** Supervision. **Akihito Mikamo:** Conceptualization. **Motoaki Sano:** Conceptualization. **Kimikazu Hamano:** Conceptualization

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