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Preoperative frailty affects postoperative complications, exercise capacity, and home discharge rates after surgical and transcatheter aortic valve replacement

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Abstract

Assessment of frailty is important for risk stratification among the elderly with severe aortic stenosis (AS) when considering interventions such as surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR). However, evidence of the impact of preoperative frailty on short-term postoperative outcomes or functional recovery is limited. This retrospective study included 234 consecutive patients with severe AS who underwent SAVR or TAVR at Kobe University Hospital between Dec 2013 and Dec 2019. Primary outcomes were postoperative complications, postoperative 6-min walking distance (6MWD), and home discharge rates. The mean age was 82 ± 6.6 years. There were 169 (SAVR: 80, TAVR: 89) and 65 (SAVR: 20, TAVR: 45) patients in the non-frail and frail groups, respectively ($p = 0.02$). The postoperative complication rates in the frail group were significantly higher than those in the non-frail group [30.8% (SAVR: 35.0%, TAVR: 28.9%) vs. 10.7% (SAVR: 15.0%, TAVR: 6.7%), $p < 0.001$]. The home discharge rate in the non-frail group was significantly higher than that in the frail group [85.2% (SAVR: 81.2%, TAVR: 88.8%) vs. 49.2% (SAVR: 55.0%, TAVR: 46.7%), $p < 0.001$]. The postoperative 6MWD in the non-frail group was significantly longer than that in the frail group [299.3 ± 87.8 m (SAVR: 321.9 ± 90.8 m, TAVR: 281.1 ± 81.3 m) vs. 141.9 ± 92.4 m (SAVR: 167.8 ± 92.5 m, TAVR: 131.6 ± 91.3 m), $p < 0.001$]. The TAVR group did not show a decrease in the 6MWD after intervention, regardless of frailty. We report for the first time that preoperative frailty was strongly associated with postoperative complications, 6MWD, and home discharge rates following both SAVR and TAVR. Preoperative frailty assessment may provide useful indications for planning better individualized therapeutic interventions and supporting comprehensive intensive care before and after interventions.

Keywords Frailty · Aortic stenosis · Surgical aortic valve replacement · Transcatheter aortic valve replacement · Exercise capacity

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Introduction

Aortic stenosis (AS) is a progressive age-related disease that develops over decades, increases the risk of heart failure, and is associated with poor survival [1, 2]. As a result of the extension of life expectancy and increase in the prevalence of cardiovascular diseases associated with aging, the demand for AS management in the elderly population is growing. As there is a marked reduction in survival after the onset of symptoms, the options available include invasive interventions, surgical aortic valve replacement (SAVR), and transcatheter aortic valve replacement (TAVR) to improve symptoms and prolong survival [3, 4]. As treatment methods such as surgical techniques and perioperative care have improved dramatically, perioperative mortality has decreased remarkably in recent years; nevertheless, postoperative functional decline has been a growing issue in patients undergoing surgery. Given these circumstances, frailty, which is a leading contributor to functional decline in older adults, is attracting considerable attention in the field of AS surgery. Frailty is of crucial importance, because it can affect postoperative daily physical capacity and home discharge rates, resulting in a decline in quality of life [5–9]. It is important to encourage early ambulation after intervention to maintain postoperative physical and cognitive function in daily activities and to support patients' discharge with multidisciplinary care [10]. However, little evidence exists on whether preoperative risk factors can predict postoperative physical activity.

A previous study reported a strong predictive ability of frailty status for 12 month mortality after TAVR [11]. Another large cohort study has shown that frailty is a major risk factor for death at 30 days and disability at 1 year following either SAVR or TAVR [12]. Considering this background, the current guidelines generally recommend assessment of frailty in patients with severe AS undergoing AVR [13]. However, evidence of the impact of preoperative frailty on short-term postoperative outcomes is limited. This single-center retrospective study sought to investigate whether preoperative frailty status was associated with postoperative short-term adverse events, postoperative physical activity such as 6 min walking distance (6MWD), the home discharge rate, length of intensive care unit stay, independent ambulation days, and length of hospital stay in Japanese patients with severe AS who underwent SAVR or TAVR. To understand the current status in detail and compare the differences in intervention, we analyzed the data of the SAVR and TAVR groups separately.

Materials and methods

Patient population

In this single-center retrospective study, we consecutively enrolled 236 patients aged ≥ 65 years who had undergone SAVR or TAVR in accordance with the American College of Cardiology/American Heart Association (AHA/ACC) guidelines [14] from Dec 2013 to Dec 2019 at Kobe University Hospital. In Kobe University Hospital, TAVR was first performed in Oct 2015. Patients younger than 65 years were excluded as their etiologies of AS were not age-related degeneration; patients whose postoperative data could not be obtained because of hospital death were also excluded. This study was approved by the Ethics Committee of Kobe University (No. B190328), registered with the UMIN Clinical Trials Registry (trial registration No. UMIN000033173) and was performed according to the guidelines of the Declaration of Helsinki. All subjects provided informed consent to participate in this study via the opt-out method.

Decision of intervention

The definition of severe AS and treatment strategy were based on the AHA/ACC guidelines [15, 16]. Briefly, at the completion of the clinical evaluation of the patients, candidates for TAVR were further examined to assess the aortic valve and its surrounding structures as well as the vascular access route, using multi-detector computed tomography. The heart team, which comprised cardiac surgeons, cardiologists, and co-medical members, made a final decision regarding SAVR or TAVR in consideration of the risks and benefits for each intervention.

Clinical characteristics of the patients

Preoperative baseline characteristics, including age, sex, body mass index (BMI), single living, left ventricular ejection fraction, aortic valve area, aortic valve peak velocity, aortic valve mean pressure gradient, comorbidities, and medications, and interventional risk scores such as the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II [17], Society of Thoracic Surgery (STS) risk score [18, 19], logistic EuroSCORE, and preoperative physical functions were extracted. The New York Heart Association functional classification was used to classify the extent of heart failure [20]. Diabetes mellitus was defined based on clinical history, hemoglobin A1c levels ≥ 6.5%, and either a fasting plasma glucose (PG) level of ≥ 126 mg/dL or PG level of ≥ 200 mg/dL 2 h after a 75 g oral glucose tolerance test [21]. Hypertension was defined as blood

pressure > 140/90 mmHg or the use of antihypertensive drugs. Dyslipidemia was defined as low-density lipoprotein cholesterol levels > 140 mg/dL, triglyceride levels > 150 mg/dL, or use of antidyslipidemic drugs, according to the guidelines issued by the Japan Atherosclerosis Society [22].

Measurement of preoperative frailty and exercise capacity

We assessed preoperative frailty within 1 week prior to the intervention. We used frailty status as assessed using the Cardiovascular Health Study (CHS) frailty index [23]. Frailty was defined as a clinical syndrome in which three or more of the following criteria were present: unintentional weight loss (10 lbs in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity [23]. Handgrip strength was measured using a grip strength dynamometer (T.K.K.5401; Takei Scientific Instruments Co., Ltd., Niigata, Japan) [24]. Measurements were taken thrice for each hand while watching for a possible Valsalva effect. We used the highest value of right or left handgrip strength according to the standard protocol [24]. Walking speed was measured twice at the usual speed, as described elsewhere [24]. A 5 m section of the walkway was marked off by two lines, and space and time were allowed for acceleration and deceleration. The participants were allowed to use canes, but no assistance by a caregiver was permitted.

We used the 6MWD to assess exercise capacity. The 6MWD was measured within 1 week before SAVR or TAVR and approximately 14 ± 7 days after intervention.

Postoperative parameters

Postoperative clinical variables such as 6MWD, length of intensive care unit stay, independent ambulation days in the ward, length of hospital stay, postoperative complications, and home discharge rates were recorded. The 6MWD was measured again at approximately 14 ± 7 days after the intervention. Postoperative complications were defined as surgical site infections [25], acute kidney injury [26], stroke, prolonged ventilator management (> 48 h), pacemaker implantation, and reoperation and were evaluated until 2 weeks after SAVR or TAVR. In TAVR, open surgery was also included as a postoperative complication. The judgment of patient's discharge was determined by the attending physician and heart team members according to the team's comprehensive judgment.

Blood sampling

Blood samples were collected after overnight fasting and were used to determine the levels of albumin, brain natriuretic peptide, hemoglobin, estimated glomerular filtration rate, hemoglobin A1c, aspartate aminotransferase, alanine aminotransferase, glutamyl transpeptidase, alkaline phosphatase, total bilirubin, C-reactive protein, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol.

Statistical analysis

All data are presented as mean ± standard deviation or proportions. Differences in continuous parameters among the four groups were calculated using one-way analysis of variance for parametric data. Tukey's test was performed as a post-hoc analysis for continuous variables. Non-parametric variables were compared using the Games-Howell test. Categorical variables are expressed as frequencies and percentages, and intergroup comparisons were analyzed using Fisher's exact test. Differences in continuous parameters between the two groups were calculated using a two-tailed paired t test. For statistical correlation between two parameters, simple linear correlations were calculated using the method of least squares and by determining Pearson's correlation coefficient. To evaluate the differences and perioperative changes in the 6MWD, two-way repeated measures analysis of variance was used to compare the effects of frailty and intervention method (frail group vs. non-frail group, SAVR group vs. TAVR group) on functional recovery pre- and postoperatively.

The within-subject factor was time (time effect), and the between-subject factor was group (group effect). We analyzed the effect of time (before and after intervention), group (SAVR and TAVR), and time-group interaction.

Logistic regression analysis was used to examine the association between home discharge and each clinical characteristic. In this analysis, home discharge was used as the dependent variable, whereas the independent variables included frailty and other clinical characteristics. Univariate analysis was first performed, and all variables with $p < 0.10$ were entered en bloc in the multivariate model, along with age, sex, and type of intervention as background variables. Analyses were performed using commercially available software (JMP version 11.0, SAS Institute). Values of $p < 0.05$ were considered statistically significant.

Results

Baseline patient characteristics

Two hundred and thirty-six patients were considered eligible for inclusion. We did not extract any outcome of interest for two patients due to death. Finally, 234 patients with a mean age of 82.0 ± 6.6 years were the participants of the present

study. The baseline characteristics, echocardiographic parameters, medications, and laboratory data are shown in Table 1. The patients were divided into the SAVR group ($n = 100$) and TAVR group ($n = 134$) according to the type of intervention. In all patients in the SAVR group, surgery was performed through median sternotomy using cardiopulmonary bypass with hypothermic circulatory arrest. All patients were selected for the biological valve, and none were selected for the mechanical valve. In the TAVR group, the procedure was performed under general anesthesia in 132 patients (98.5%); nevertheless, local anesthesia was used in two patients (1.5%) who had a history of severe interstitial pneumonia. We further divided the patients according to the presence of preoperative frailty in each group. The number of patients in each group was 80, 20, 89, and 45 in the SAVR non-frail, SAVR frail, TAVR non-frail, and TAVR frail groups, respectively.

Patient age was significantly higher in the TAVR group than in the SAVR group (85.5 ± 4.2 vs. 77.3 ± 6.5, $p < 0.001$). There was no significant difference in BMI between the SAVR and TAVR groups (23.0 ± 0.4 vs. 22.3 ± 0.3 kg/m^2, $p = 0.196$). The ratio of women was higher in the TAVR group than in the SAVR group (73 vs. 51%, $p < 0.001$). Interestingly, the rate of single living was significantly lower in the SAVR group than in the TAVR group (17.0 vs. 36.7%, $p = 0.003$). The TAVR group had lower albumin, hemoglobin, alanine aminotransferase, and high-density lipoprotein cholesterol levels than the SAVR group ($p < 0.05$ for each).

There were no significant differences in AS severity with echocardiographic parameters such as aortic valve area determined by the continuity equation, AS peak jet velocity, mean transvalvular pressure gradient, and left ventricular ejection fraction among the four groups. While the mean age in the intra groups of SAVR was significantly different (76.5 ± 6.0 in non-frail vs. 80.6 ± 7.4 in frail, $p = 0.01$), the mean age in the intra groups of TAVR was almost similar (85.5 ± 3.7 in non-frail vs. 85.6 ± 5.0 in frail, $p = 1.00$).

We then analyzed the impact of frailty on patient characteristics in the SAVR and TAVR groups. The proportion of women was not statistically different in the intra-group analysis (SAVR, 47.5% in non-frail vs. 65.0% in frail; TAVR, 71.9% in non-frail vs. 75.6% in frail). The SAVR frail group tended to have a higher rate of single living than the SAVR non-frail group (30.0% vs. 13.7, $p = 0.084$). There was no significant difference in laboratory data between the SAVR non-frail and frail groups. On the other hand, the TAVR frail group had significantly lower albumin, hemoglobin, and high-density lipoprotein cholesterol levels than the TAVR non-frail group. In terms of medications, the frail SAVR and TAVR groups tended to take diuretics more frequently than the non-frail SAVR and TAVR groups. No significant differences in comorbidities were observed among the four groups.

The EuroSCORE II was not significantly different between the non-frail and frail groups. Therefore, we did not evaluate the logistic EuroSCORE and STS risk scores in the SAVR group. The EuroSCORE II in the TAVR frail group was significantly higher than that in the TAVR non-frail group (15.4 ± 9.6 vs. 11.6 ± 6.7, $p = 0.006$). Similarly, the logistic EuroSCORE and STS risk scores in the TAVR frail group were significantly higher than those in the TAVR non-frail group ($p = 0.001$ and $p = 0.021$, respectively).

Preoperative physical function

The SAVR group had significantly higher physical function than the TAVR group, as assessed by grip strength, gait speed, and 6MWD ($p < 0.001$) (Table 1). The frail group had significantly lower physical function than the non-frail group in the SAVR and TAVR groups (p < 0.001 for each).

Primary outcomes

In the patients who underwent SAVR, postoperative complication rates in the frail group were significantly higher than those in the non-frail group (35.0 vs. 15.0%, $p < 0.041$). The distribution of the complications was as follows: two surgical site infections, three strokes, two prolonged ventilator management, seven pacemaker implantations, and four reoperations (Fig. 1a, b). In the TAVR group, the postoperative complication rate was significantly higher in the frail group than in the non-frail group (28.9 vs. 6.7%, $p < 0.001$). The distribution of the complications was: 1 acute kidney injuries, two strokes, 12 pacemaker implantations, and four reoperations (Fig. 1c, d).

Table 2 and Fig. 2 show a comparison of the 6MWD pre- and post-intervention. The 6MWD in the non-frail group was always better than that in the frail group, regardless of the type of intervention ($p < 0.001$ for each) (Fig. 2b, c). It is worth noting that patients in the TAVR group could maintain the 6MWD after the intervention (Fig. 2a, c). On the other hand, the postoperative 6MWD significantly decreased in patients who underwent SAVR (Fig. 2a, b). The decline in the 6MWD throughout the perioperative period did not show statistically significant differences between the non-frail and frail groups in the same intervention (interaction: SAVR: 0.541, and TAVR: 0.812) (Fig. 2b, c, Table 2).

Table 1 Baseline characteristics and laboratory data of the study population

Variables	All, n = 234	SAVR all, n = 100	TAVR all, n = 134	P value SAVR all vs. TAVR all	SAVR Non-frail n = 80	Frail n = 20	P value SAVR non-frail vs. SAVR frail	TAVR Non-frail n = 89	Frail n = 45	P value TAVR non-frail vs. TAVR frail
Age, years	82.0 ± 6.6	77.3 ± 6.5	85.5 ± 4.2	< 0.001	76.5 ± 6.0	80.6 ± 7.4	0.01	85.5 ± 3.7	85.6 ± 5.0	0.9998
BMI, kg/m^2	22.7 ± 3.7	23.1 ± 3.7	22.4 ± 3.7	0.196	23.2 ± 3.8	22.5 ± 3.3	0.880	23.0 ± 3.5	21.3 ± 3.9	0.052
Female, n (%)	149 (63.7)	51 (52.0)	98 (73.1)	< 0.001	38 (47.5)	13 (65.0)	0.161	64 (71.9)	34 (75.6)	0.653
Single living, n (%)	66 (31.6)	17 (17.0)	49 (36.6)	< 0.001	11 (13.7)	6 (30.0)	0.084	32 (36.0)	17 (37.8)	0.836
Echocardiographic parameters										
LV dimension diastolic, mm	42.1 ± 6.9	42.8 ± 7.1	41.6 ± 6.7	0.209	43.3 ± 6.6	40.7 ± 8.4	0.417	41.8 ± 6.7	41.3 ± 6.7	0.982
LV Dimension systolic, mm	27.4 ± 6.8	27.2 ± 6.5	27.5 ± 7.1	0.762	27.4 ± 6.6	26.4 ± 6.1	0.940	27.1 ± 7.2	28.2 ± 68	0.839
LVEF, %	62.7 ± 12.3	63.6 ± 11.0	62.1 ± 13.2	0.352	64.3 ± 10.7	60.8 ± 11.7	0.669	63.1 ± 13.2	60.1 ± 13.2	0.531
E	4.6 ± 4.3	5.0 ± 5.5	4.4 ± 3.2	0.274	5.2 ± 6.1	4.2 ± 1.7	0.748	4.6 ± 3.7	3.8 ± 1.5	0.818
E/E	21.2 ± 10.6	20.6 ± 11.0	21.6 ± 10.3	0.520	19.5 ± 9.7	24.6 ± 14.4	0.262	21.1 ± 10.9	22.6 ± 9.0	0.912
LAD, mm	41.8 ± 7.3	41.3 ± 8.0	42.2 ± 6.8	0.334	41.4 ± 8.3	40.8 ± 6.9	0.988	41.6 ± 7.3	43.5 ± 5.7	0.500
AVA, cm^2	0.6 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	0.992	0.7 ± 0.2	0.6 ± 0.2	0.527	0.7 ± 0.2	0.6 ± 0.2	0.505
Peak velocity, m/s	4.5 ± 0.6	4.4 ± 0.7	4.5 ± 0.6	0.372	4.5 ± 0.7	4.3 ± 0.8	0.537	4.5 ± 0.5	4.5 ± 0.6	0.963
Mean PG, mmHg	50.4 ± 16.3	51.3 ± 18.6	49.8 ± 14.7	0.509	52.5 ± 18.5	46.8 ± 18.5	0.523	50.5 ± 14.2	48.3 ± 15.6	0.880
Comorbidities, n (%)										
Hypertension	104 (44.4)	42 (42.0)	62 (46.2)	0.516	35 (43.8)	7 (35.0)	0.478	41 (46.1)	21 (46.7)	0.948
Diabetes mellitus	74 (20.1)	32 (32.0)	42 (31.3)	0.915	26 (32.5)	6 (30.0)	0.830	24 (27.0)	18 (40.0)	0.124
Dyslipidemia	59 (25.2)	29 (29.0)	30 (22.3)	0.249	24 (30.0)	5 (25.0)	0.659	23 (25.8)	7 (15.6)	0.177
NYHA, n (%)										
I	16 (6.8)	8 (8.0)	8 (6.0)	< 0.001	8 (10.0)	0 (0)	0.003	7 (7.9)	1 (2.2)	< 0.001
II	131 (56.0)	70 (70.0)	61 (45.5)		60 (75.0)	10 (50.0)		50 (56.2)	11 (24.4)	
III	80 (34.2)	21 (21.0)	59 (44.0)		12 (15.0)	9 (45.0)		31 (34.8)	28 (62.2)	
IV	7 (3.0)	1 (1.0)	6 (4.5)		0 (0)	1 (5.0)		1 (1.1)	5 (11.1)	
Laboratory data										
Albumin, g/dL	3.6 ± 0.5	3.8 ± 0.4	3.5 ± 0.5	< 0.001	3.9 ± 0.4	3.6 ± 0.5	0.064	3.6 ± 0.5	3.3 ± 0.4	0.003
Hemoglobin, g/dL	11.6 ± 1.6	12.2 ± 1.6	11.2 ± 1.5	< 0.001	12.3 ± 1.6	11.5 ± 1.6	0.182	11.4 ± 1.5	10.7 ± 1.4	0.041
eGFR, ml/min/1.73m^2	49.4 ± 19.4	51.0 ± 20.0	48.3 ± 19.0	0.317	53.3 ± 18.9	41.9 ± 22.1	0.099	49.6 ± 17.8	45.8 ± 21.0	0.686
HbA1c, %	6.0 ± 0.7	6.1 ± 0.9	5.9 ± 0.6	0.112	6.1 ± 0.9	6.0 ± 0.7	0.939	6.0 ± 0.6	5.8 ± 0.7	0.923
AST, U/L	24.0 ± 12.6	24.7 ± 10.3	23.4 ± 14.0	0.433	25.1 ± 11.0	28.7 ± 25.2	0.760	23.5 ± 14.2	23.2 ± 13.8	0.999
ALT, U/L	16.7 ± 10.7	18.5 ± 12.2	13.3 ± 9.2	0.023	18.5 ± 12.0	18.8 ± 13.2	0.999	15.6 ± 9.5	14.8 ± 8.9	0.976

Table 1 (continued)

Variables	All, n = 234	SAVR all, n = 100	TAVR all, n = 134	P value SAVR all vs. TAVR all	SAVR Non-frail n = 80	SAVR Frail n = 20	P value SAVR non-frail vs. SAVR frail	TAVR Non-frail n = 89	TAVR Frail n = 45	P value TAVR non-frail vs. TAVR frail
ALP, U/L	233.5 ± 91.7	232.7 ± 101.5	233.8 ± 84.1	0.122	224.5 ± 96.7	264.9 ± 115.6	0.288	222.0 ± 71.5	257.2 ± 101.6	0.339
γ-GTP, U/L	28.5 ± 24.3	31.4 ± 25.2	26.4 ± 23.5	0.924	32.1 ± 27.0	28.6 ± 16.2	0.941	24.1 ± 20.7	30.9 ± 28.0	0.151
Total bilirubin, mg/dL	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.720	0.7 ± 0.2	0.6 ± 0.2	0.285	0.7 ± 0.2	0.6 ± 0.2	0.676
CRP, mg/dL	0.4 ± 1.0	0.5 ± 1.2	0.4 ± 0.9	0.339	0.4 ± 1.2	0.8 ± 1.4	0.523	0.3 ± 0.6	0.6 ± 1.3	0.980
T-Cho, mg/dL	172.5 ± 38.1	178.1 ± 40.8	168.5 ± 35.7	0.063	181.1 ± 35.6	165.4 ± 57.3	0.394	169.4 ± 36.7	166.7 ± 33.9	0.501
Triglycerides, mg/dL	116.9 ± 60.4	123.8 ± 64.8	111.9 ± 56.7	0.145	126.3 ± 66.3	113.0 ± 58.7	0.833	106.7 ± 57.5	122.3 ± 54.3	0.427
HDL, mg/dL	54.5 ± 16.3	57.2 ± 18.0	52.7 ± 14.8	0.044	57.8 ± 18.1	54.8 ± 17.8	0.894	54.7 ± 15.6	48.6 ± 12.3	0.018
LDL, mg/dL	104.0 ± 30.2	108.4 ± 32.2	101.0 ± 28.5	0.076	110.1 ± 32.6	101.4 ± 30.2	0.706	102.5 ± 29.3	98.1 ± 26.9	0.863
BNP, pg/mL	400.0 ± 625.1	381.0 ± 610.7	413.1 ± 636.8	0.706	348.5 ± 585.1	505.8 ± 703.5	0.760	333.0 ± 447.3	575.2 ± 891.8	0.152
Medications, n (%)										
β-blocker	73 (31.2)	35 (35.0)	38 (28.4)	0.278	28(35.0)	7(35.0)	>0.999	26 (29.2)	12(26.7)	0.757
ACE-I	25 (10.7)	11 (11.0)	14 (10.5)	0.892	11(13.8)	0(0)	0.079	8(9.0)	6(13.3)	0.437
ARB	84 (35.9)	39 (39.0)	45 (33.6)	0.393	30(37.5)	9(45.0)	0.539	34(38.2)	11(24.4)	0.111
Statin	84 (35.9)	40 (40.0)	44 (32.8)	0.258	33(41.3)	7(35.0)	0.609	30(33.7)	14(31.1)	0.762
Calcium-channel blocker	103 (44.0)	42 (42.0)	61 (45.5)	0.591	33(41.3)	9(45.0)	0.761	40(44.9)	21(46.7)	0.850
Diuretics	92 (39.3)	33 (33.0)	59 (44.0)	0.088	23(28.8)	10(50.0)	0.071	34(38.2)	25(55.6)	0.056
Risk scoring										
Logistic EuroSCORE	–	–	15.6 ± 10.3	–	–	–	–	13.5 ± 7.8	20.8 ± 13.5	0.001
STS risk score	–	–	8.1 ± 8.5	–	–	–	–	6.9 ± 3.9	11.7 ± 14.3	0.021
EuroSCORE II	10.2 ± 7.2	6.6 ± 4.0	12.8 ± 7.9	< 0.001	6.2 ± 3.3	8.6 ± 6.0	0.450	11.6 ± 6.7	15.4 ± 9.6	0.006
Pre-operative physical functions										
Grip strength, kg	19.6 ± 7.6	23.2 ± 8.1	16.9 ± 6.0	< 0.001	24.5 ± 7.9	17.8 ± 6.8	< 0.001	19.0 ± 5.5	12.9 ± 4.8	< 0.001
Gait speed, m/s	0.9 ± 0.4	1.0 ± 0.2	0.8 ± 0.4	< 0.001	1.1 ± 0.2	0.8 ± 0.3	0.004	0.9 ± 0.4	0.5 ± 0.2	< 0.001
6MWD, m	281.1 ± 126.6	339.9 ± 108.1	237.2 ± 121.7	< 0.001	372.8 ± 82.3	208.5 ± 100.3	< 0.001	288.1 ± 94.2	136.3 ± 106.7	< 0.001

Data are shown as mean ± standard deviation, or %. The averages of continuous variables were compared using either the two-tailed student's t test. Fisher's exact test was used to compare the proportions of categorical variables between groups. 6MWD, 6 min walking test distance

ACEI angiotensin-converting enzyme inhibitor, *ALP* alkaline phosphatase, *ALT* alanine aminotransferase, *ARB* angiotensin receptor blocker, *AST* aspartate aminotransferase, *AVA* aortic valve area, *BMI* body mass index, *BNP* brain natriuretic peptide, *BUN* blood urea nitrogen, *CRP* C-reactive protein, *EF* ejection fraction, *eGFR* estimated glomerular filtration rate, *γ-GTP* glutamyl transpeptidase, *HbA1c* glycated hemoglobin, *HDL-C* high-density lipoprotein cholesterol, *LAD* left atrial diameter, *LDL-C* low-density lipoprotein cholesterol, *LV* left ventricle, *NYHA* New York Heart Association, *PG* pressure gradient, *SAVR* surgical aortic valve replacement, *STS* Society of thoracic surgeons, *TAVR* transcatheter aortic valve replacement, *T-Cho* total cholesterol

Fig. 1 Incidence of postoperative complications among four groups. Data are shown as percentages (%). *AKI* acute kidney injury, *PMI* pacemaker implantation, *PVM* prolonged ventilator management, *SAVR* surgical aortic valve replacement, *TAVR* transcatheter aortic valve replacement
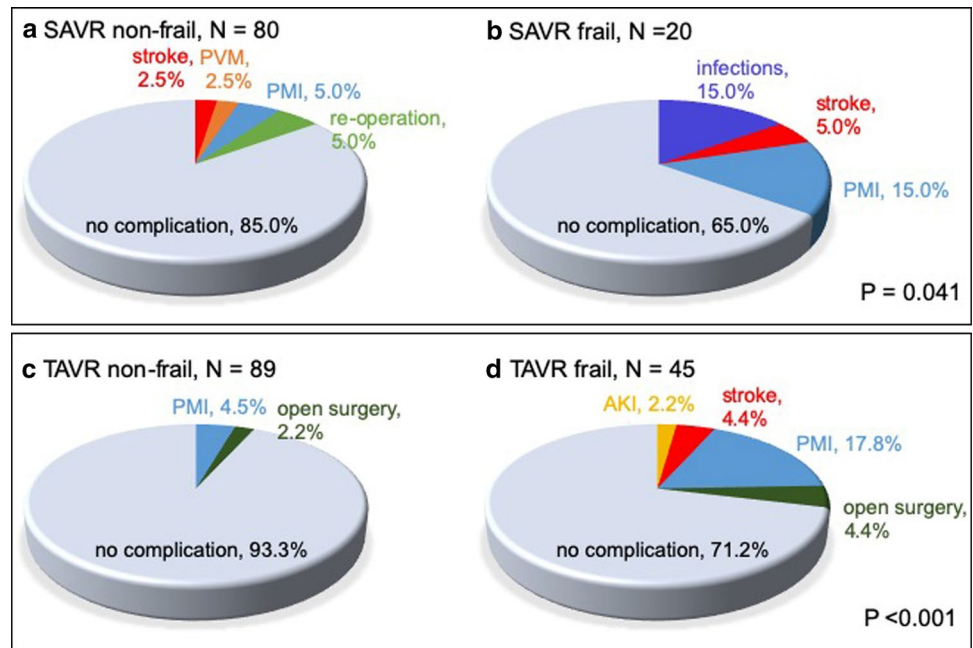

Table 2 Result of 6MWD of pre and post operation

Variables	Pre	Post	p value[b]	Interaction	
				F value	p value[c]
All patients					
SAVR	339.9 ± 108.1[a]	291.1 ± 109.8[a]	< 0.001	27.84	< 0.001
TAVR	237.2 ± 121.7	230.9 ± 110.3	0.16	–	–
SAVR					
Non-frail	372.8 ± 82.3[a]	321.9 ± 90.8[a]	< 0.001	0.376	0.541
Frail	208.5 ± 100.3	167.8 ± 92.5	< 0.001	–	–
TAVR					
Non-frail	288.1 ± 94.2[a]	281.1 ± 81.3[a]	0.202	0.057	0.812
Frail	136.3 ± 106.7	131.6 ± 91.3	0.537	–	–

6MWD, 6 min walking test distance

SAVR surgical aortic valve replacement, *TAVR* transcatheter aortic valve replacement

[a]Significance level for the hypothesis of no group effect

[b]Significance level for the hypothesis of time effect (pre vs. post in the same group)

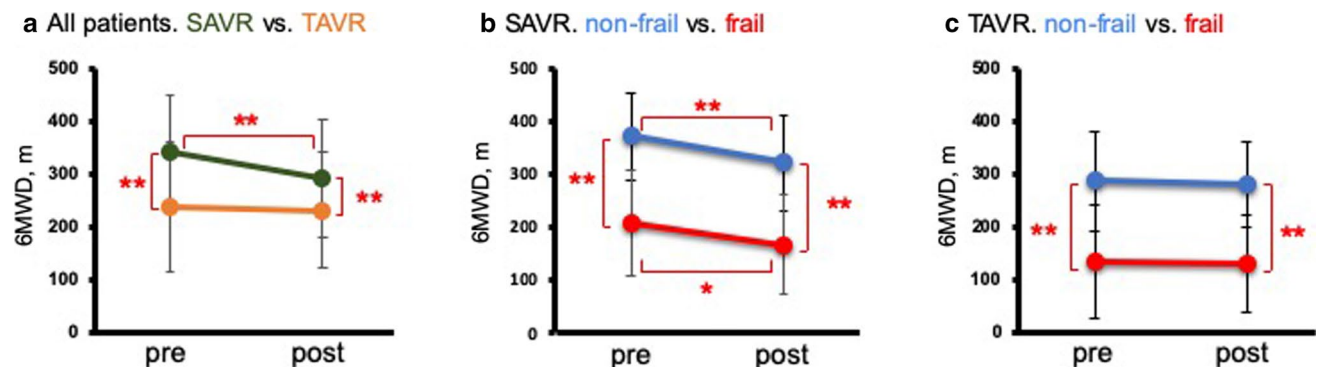[c]Significance level for the hypothesis of no time × group effect

Fig. 2 Change in the pre- and postoperative 6MWD. 6MWD, 6 min walking distance; *SAVR* surgical aortic valve replacement, *TAVR* transcatheter aortic valve replacement *$p < 0.01$, **$p < 0.001$

Home discharge rates of patients in the SAVR non-frail, SAVR frail, TAVR non-frail, and TAVR frail groups were 81.3, 55.0, 88.8, and 46.7%, respectively (Fig. 3).

Home discharge rates in the non-frail group were significantly higher than those in the frail group, regardless of the type of intervention (SAVR, $p = 0.014$; TAVR, $p < 0.001$).

Association between home discharge and variables

The results of the logistic regression analysis of home discharge are shown in Table 3. After adjusting for all confounding factors, age ($p < 0.001$), single living ($p = 0.016$), and frailty (odds ratio: 0.131; 95% confidence interval 0.058–0.285; $p < 0.001$) remained statistically significant predictors of home discharge.

Additional outcomes

The length of stay in the intensive care unit did not differ between the SAVR non-frail and frail groups (Fig. 4a). On the other hand, the TAVR frail group had a longer intensive care unit stay than the TAVR non-frail group (Fig. 4a). The frail group showed longer independent ambulation days in both the SAVR and TAVR groups (Fig. 4b). Postoperative hospital stay did not differ between the SAVR non-frail and frail groups, whereas the TAVR frail group showed a longer postoperative hospital stay than the TAVR non-frail group (Fig. 4c).

Fig. 3 Home discharge rate among four groups. Data are shown as percentages (%). *SAVR* surgical aortic valve replacement, *TAVR* transcatheter aortic valve replacement
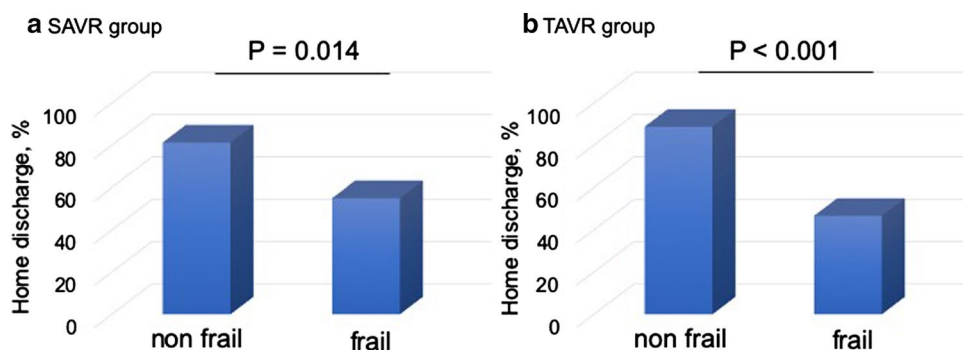
Table 3 Logistic regression model of home discharge

Variable	Univariable		Multivariable	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	0.916 (0.866–0.963)	< 0.001	0.895 (0.829–0.963)	0.003
Sex, (ref. female)	0.591 (0.301–1.115)	0.106	1.087 (0.463–2.521)	0.846
Intervention, (ref. SAVR)	1.077 (0.592–1.980)	0.809	0.382 (0.136–1.046)	0.061
Albumin	2.471 (1.255–5.084)	0.008	1.276 (0.326–2.040)	0.603
CRP	0.762 (0.594–0.946)	0.013	0.764 (0.555–1.016)	0.066
Frail	0.168 (0.087–0.319)	< 0.001	0.131 (0.058–0.285)	< 0.001
Single living	0.401 (0.214–0.752)	0.004	0.378 (0.169–0.831)	0.016

CRP C-reactive protein, *CI* confidence interval, *OR* odds ratio, *SAVR* surgical aortic valve replacement
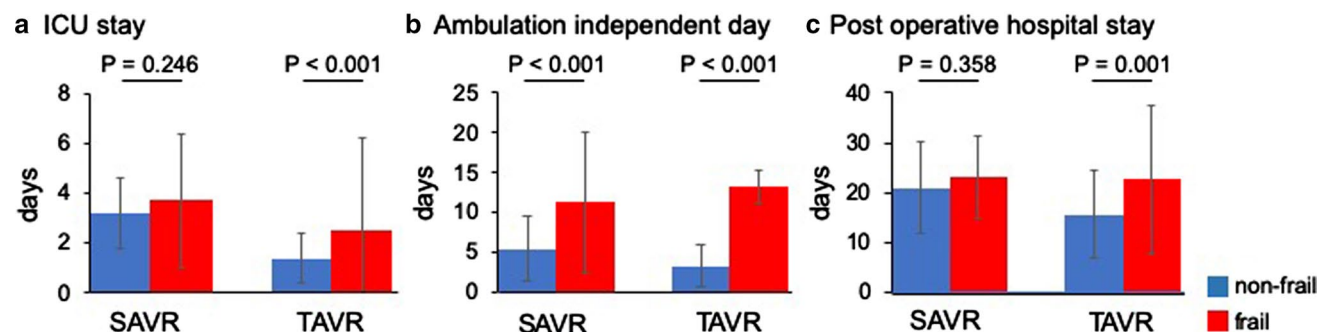

Fig. 4 Data of additional outcomes. *ICU* intensive care unit, *SAVR* surgical aortic valve replacement, *TAVR* transcatheter aortic valve replacement

Discussion

To the best of our knowledge, this is the first report to clearly indicate a significant association between preoperative frailty status as assessed using the CHS Frailty Index and postoperative physical activity in Japanese patients with severe AS who underwent SAVR or TAVR. The main findings of this study are as follows: frailty was an independent risk factor for postoperative complications and the difficulty of home discharge in both the SAVR and TAVR groups and the 6MWD decreased significantly after intervention in patients in the SAVR group; however, there was no significant reduction in 6MWD in patients who underwent TAVR. Our findings suggest that preoperative assessment of frailty may be crucial for predicting short-term postoperative outcomes of both SAVR and TAVR.

In previous studies, frailty was common in patients undergoing cardiac surgery and increased postoperative complications [27, 28]. Our results were similar to those of previous reports, but the incidence of complications was found to vary slightly from study to study. In part, various methods of assessing frailty status can contribute to the observed discrepancy. The SAVR group had a higher incidence of surgical site infection than the TAVR group possibly due to surgical invasion such as sternotomy. The TAVR non-frail group showed a low complication rate; it is one of the benefits of TAVR, in that it requires minimally invasive procedures. Nevertheless, the frail group showed a non-negligible incidence of complications in both intervention groups, such as stroke and the need for pacemaker implantation. Therefore, we should carefully weigh the benefits against the risks when we recommend SAVR or TAVR for frail patients.

Logistic regression analysis showed no significant difference in postoperative complications for each frailty parameter for both the SAVR and TAVR groups. On the other hand, weakness had the greatest contribution to the home discharge rate in the SAVR group (odds ratio, 0.29; 95% CI, 0.088–0.886; $p = 0.029$). Similarly, weakness had the greatest contribution to the home discharge rate in the TAVR group (odds ratio, 0.37; 95% CI, 0.143–0.965; $p = 0.041$). Collectively, our data suggest that frailty, especially weakness, plays an important role in postoperative outcomes. However, we believe that frailty should be assessed comprehensively by a combination of parameters, rather than just a single parameter.

A prior study from the United States showed that the rates of discharge to rehabilitation facilities increased with increasing frailty [29]. Although body weight, BMI, and the hospital and healthcare environment in the previous study were completely different from those in the current study due to county differences, the results of our study

(the home discharge rate was higher in the non-frail group than in the frail group) were consistent with those of the previous study. One of the reasons for the lower home discharge rates in the frail group may be attributed to not only lower physical function but also less physiological reserve in the frail group. In other words, the patients assessed as frail using the CHS frailty index, who have a low nutritional status, low physical activity, and muscle weakness, would have a high frequency of complications and, therefore, have a long hospital stay and require rehabilitation transfer to improve nutrition and activities of daily living. In contemporary TAVR, discharge disposition significantly affects the 1 year risk of cardiovascular death and stroke, and even after adjustment for recorded baseline differences [8], preoperative assessment of frailty is of crucial importance for both SAVR and TAVR. The aim of home discharge is to improve patient prognosis.

In previous studies, the 6MWD was found useful in identifying frailty and those in transition to frailty [30, 31]. Earlier studies in elderly patients with heart failure reported that the 6MWD correlated with frailty and was associated with mortality [32]. Similarly, in this study, the 6MWD was significantly lower in the frail group. Preoperative and postoperative exercise-based cardiac rehabilitation have been reported to improve the 6MWD [33–37]. In addition, comprehensive cardiac rehabilitation may help prevent, reverse, and reduce the severity of frailty and improve the prognosis of frail patients with valvular disease following surgery or intervention [38]. Therefore, for frail patients with a low preoperative 6MWD, exercise-based cardiac rehabilitation is strongly recommended after relief from severe aortic stenosis.

The SAVR group showed a significant decrease in the 6MWD after surgery, whereas the TAVR group did not. To our knowledge, there have been no reports on the change in the 6MWD before and after SAVR or TAVR. We previously reported that the 6MWD decreased about 20% during the perioperative period in patients undergoing valvular surgery, which were regarded to be due to postoperative inflammation and catabolic responses [39]. TAVR, which is a less invasive intervention for AS, could maintain the exercise capacity of patients during the perioperative period. Therefore, the assessment of preoperative exercise capacity and frailty is considered to be of great importance in the decision on the intervention.

In our study, the postoperative hospital stay was long. First, the length of hospital stay after SAVR and TAVR is relatively long in Japan compared to that in other Western countries. Furthermore, the patients who underwent SAVR in the present study were older than those in recent clinical trials. In addition, the patients included in our study had severe symptoms of heart failure before surgery, as indicated by the high preoperative brain natriuretic peptide levels.

These factors could lead to prolonged postoperative management of heart failure and the time required for postoperative rehabilitation, resulting in a prolonged hospital stay.

To treat in the frailty of patients with AS and improve their prognosis, early postoperative exercise therapy and comprehensive multi-disciplinary cardiac rehabilitation, which is available even before surgery, are desirable. Among the comprehensive multi-disciplinary interventions, we consider that preoperative nutritional intervention is effective in preventing postoperative complications.

Approximately 21.3% of the global population will be 60 years or older by 2050 [40] and the number of elderly patients with AS would keep increasing. From a future clinical perspective, our results strongly support the idea that multifactorial intervention is essential to prevent the progression of frailty in patients with AS.

Study limitations

This study has several limitations. First, this was a retrospective, single-center study with a relatively small sample size. Larger prospective multi-center trials could reveal the current frailty status of Japanese patients with severe AS undergoing SAVR or TAVR. Further studies are needed to increase the sample size and perform a sub-analysis to investigate which parameters of frailty affect postoperative outcomes. Second, the results might be biased by the differences in baseline characteristics between the patients undergoing TAVR and SAVR. Third, as this was a clinical study, we were unable to clarify the reason for decreased postoperative physical activity in frail patients. We hope to explore the pathophysiological mechanisms underlying frailty in the future based on the results of this study.

Conclusions

Our results indicate that preoperative frailty status was associated with postoperative complications in patients with severe AS who underwent SAVR or TAVR. Preoperative frailty assessment may provide useful indications for planning better individualized therapeutic interventions and supporting comprehensive intensive care for vulnerable patients with AS following interventions.

Compliance with ethical standards

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