Kihon checklist is useful for predicting outcomes in patients undergoing transcatheter aortic valve implantation

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Highlights	◇これまで介護などで使われていた日本発「基本チェックリスト」は、25 問の「はい／いいえ」で回答するアンケート形式のため非常に簡便。 ◇この基本チェックリストにより算出したフレイルの指標は、従来のフレイルの指標と比較し同等であり、 経カテーテル大動脈弁留置術（TAVI）後 3 年の死亡の独立した因子と判明。 ◇リハビリや治療への介入、予後の予測や改善につながる可能性。
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概要	研究グループは、TAVI 施術者に対する基本チェックリストによるフレイルの評価が経カテーテル大動脈弁留置術（TAVI）後 3 年の総死亡の予測因子として有用であることを明らかにしました。 本研究成果により、基本チェックリストがフレイルを簡便かつ客観的に評価し、適切な治療方針の決定に役立つと期待できます。 フレイルの指標と TAVI との関連性はこれまでに報告されていますが、それらの指標は検査を多く要するものや、簡便であっても客観性に欠けるものがあります。 今回、本研究グループは、2016 年 1 月から 2020 年 12 月に大阪市立大学医学部附属病院で TAVI を施行した 280 例を対象とし、従来のフレイルの指標に加えて基本チェックリストによるフレイルの評価を行いました。その結果、基本チェックリストにより算出したフレイルの指標は、従来のフレイルの指標と比較し同等であり、生存時間分析で TAVI 後 3 年の死亡の独立した因子であることが分かりました。また、基本チェックリストの総スコア（25 点満点）で 3 群に分類して解析したところ、フレイル群（13～25 点）で TAVI 後 3 年の死亡が有意に高いことが分かりました。 ‘日本発の簡便なアンケート形式によるフレイル評価　“基本チェックリスト”によるフレイルの評価が「経カテーテル大動脈弁留置術」後の治療方針決定の一助に’ 大阪市立大学. https://www.osaka-cu.ac.jp/ja/news/2021/211221-2 (参照　2021-12-21)

Kihon checklist is useful for predicting outcomes in patients undergoing transcatheter aortic valve implantation

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Abstract

Background: Frailty is a major risk factor for death and disability following transcatheter aortic valve implantation (TAVI). The Kihon checklist (KCL) is a simple self-reporting yes/no survey consisting of 25 questions and is used as a screening tool to identify frailty in the primary care setting. No clinical studies have focused on frailty calculated by the KCL in the TAVI cohort. We investigated the 3-year prognostic impact of frailty evaluated by the KCL in patients who underwent TAVI.

Methods: This single-center prospective observational study included 280 consecutive patients with symptomatic severe aortic stenosis who underwent TAVI and evaluated pre-procedural physical performance focused on frailty at our institution. We assessed all patients' frailty by the KCL before TAVI, as described previously. We set the primary endpoint as the 3-year all-cause mortality after TAVI.

Results: The median patient age was 84 years (interquartile range, 81–87 years), and 31.1% were men. In the receiver operating characteristics curve, there were no significant differences between the KCL and Cardiovascular Health Study frailty index [area under the curve (AUC) 0.625 versus 0.628; p=0.93), KCL and Rockwood Clinical Frailty Scale (AUC 0.625 versus 0.542; p=0.15), and KCL and Short Physical Performance Battery (AUC 0.625 versus 0.612; p=0.91). The first and second tertiles of

the total KCL score were 8 and 12, respectively. The multivariate Cox regression model indicated that the total KCL score [hazard ratio (HR), 1.104; 95% confidence interval (CI), 1.034–1.179; *p*=0.003], presence of diabetes mellitus (HR, 1.993; CI, 1.055–3.766; *p*=0.03), and presence of liver disease (HR, 3.007; CI, 1.067-8.477; *p*=0.04) were independently associated with 3-year all-cause mortality.

Conclusions: The KCL is a simple and useful tool for evaluating frailty status and predicting 3-year all-cause mortality in patients undergoing TAVI.

Introduction

Severe aortic stenosis (AS) is a common cause of left ventricular outflow impairment and its prevalence has been increasing with the aging society [1,2]. For symptomatic patients with severe AS, transcatheter aortic valve implantation (TAVI) has recently been recognized as a viable therapeutic option, regardless of the surgical risk [3]. Satisfactory mid-term clinical outcomes expand the indication of TAVI to intermediate and low surgical risk patients as candidates [4-8].

Although almost all clinical courses after TAVI are satisfactory, some patients occasionally have unfavorable peri- and post-procedural outcomes. Therefore, to identify the optimal candidates for TAVI, adequate pre-screening and risk stratification are required.

Previous studies have shown that anemia, nutrition, and diabetes mellitus are factors that influence prognosis after TAVI, other than organ dysfunction [9-11]. Moreover, frailty is a major risk factor for death and disability following TAVI [12]. Several clinical scores can be used to evaluate the frailty status of candidate patients for TAVI. For example, the Fried scale reflects strength, mobility, weight loss, fatigue, and habitual activity, and is predictive of survival and quality of life after aortic valve procedures [13,14]. The Short Physical Performance Battery (SPPB) narrowly reflects

the patient's lower-extremity muscle function and is associated with an increased risk of death after TAVI [13,15]. However, it is often difficult for clinicians to calculate these scores in daily practice because not all candidates can perform sufficient examinations, such as walking gait speed, which is required for calculation. However, the Rockwood Clinical Frailty Scale (CFS) is a simple frailty index that broadly reflects the patient's functional abilities and has a predictive value for survival after TAVI [16]. Although the reliability of CFS has already been confirmed in many clinical settings, the CFS is semiquantitative and subjective, as described in several study limitations; therefore, it is predisposed to interobserver variability [16,17]. The Kihon checklist (KCL), developed by the Ministry of Health Labor and Welfare in Japan, is a simple self-reporting yes/no survey consisting of 25 questions [18]. It is extensively used to assess seniors' physical, mental, and social functions in daily life and to identify older adults who are at risk of requiring support or care in the near future [19]. It is also a good screening tool to identify frailty in the primary care setting or in outpatient clinics to facilitate public health [20]. The KCL score is correlated with the number of frailty phenotypes according to the Cardiovascular Health Study (CHS) frailty index criteria in elderly outpatients [19]. However, no clinical studies have focused on frailty calculated by the

KCL in the TAVI cohort. In this study, we investigated the 3-year prognostic impact of frailty evaluated by the KCL in patients who underwent TAVI.

Methods

Study population

This single-center prospective observational study included 280 consecutive patients with symptomatic severe AS who underwent TAVI and whose pre-procedural physical performance was evaluated focused on frailty at Osaka City University Hospital between January 2016 and December 2020 (**Fig. 1**). Patients at intermediate or high risk for surgery were indicated for TAVI at our institution during the study period. The inclusion criteria were as follows: (1) presence of symptoms, (2) presence of degenerative AS, (3) an estimated mean aortic valve pressure gradient of >40 mmHg or a jet velocity of >4.0 m/s, and/or (4) an aortic valve area of <1.0 cm^2 (or an effective orifice area index of <0.6 cm^2/m^2) by transthoracic echocardiography, according to the guidelines for valvular heart disease of the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery [21]. The indication and surgical risk for TAVI were determined based on the clinical consensus of a heart team comprising cardiac surgeons, interventional cardiologists, anesthesiologists, and

imaging specialists. Among the 305 possible candidates, we excluded five cases of in-hospital deaths related to periprocedural complications. Additionally, we excluded 20 patients with active cancer because cancer may be an independent risk factor for death. The study protocol complied with the Declaration of Helsinki and was approved by our institutional ethics committee (approval number: 2021-064). Written informed consent was obtained from all patients. The authors had full access to the data and were responsible for their integrity. All authors have read and agreed to the manuscript as written.

TAVI procedure

We chose the transfemoral approach as the first option when patients did not have an excessively narrow access route for insertion of the sheath or aortic arch atheroma. We performed TAVI under general anesthesia in a hybrid operating room, except for six patients who underwent conscious sedation because of pulmonary dysfunction. Transcatheter heart valves were classified as balloon-expandable (Edwards Sapien XT or Sapien 3 Transcatheter Heart Valve; Edwards Lifesciences, Irvine, CA, USA) or self-expandable (Medtronic classic CoreValve or CoreValve Evolut R/ Pro/Pro+; Medtronic, Inc., Minneapolis, MN, USA). Balloon-expandable valves were

the first choice, and self-expandable valves were reserved for patients with a narrow aortic annulus and/or in the case of the trans-subclavian approach.

Data collection

All data shown in the tables and figures were collected prospectively from patient records. Clinical data, including frailty factors, patient characteristics, echocardiographic data, and procedural and outcome information, were prospectively recorded. Procedural and other complications during TAVI were evaluated according to the Valve Academic Research Consortium-2 criteria [22].

Frailty assessment

We assessed patient frailty by CHS, CFS, and SPPB before TAVI, as described previously [17,23,24]. In addition to these scores, we evaluated the KCL of all participants. The KCL consists of 25 questions regarding instrumental (three questions) and social (four questions) activities of daily living, physical functions (five questions), nutritional status (two questions), oral function (three questions), cognitive function (three questions), and depressive mood (five questions) (Table 1) [18].

Study endpoints

We set the primary endpoint as the 3-year all-cause mortality after TAVI.

Statistical analysis

Continuous variables are summarized using medians and interquartile ranges (quartiles 1 to 3), and categorical variables are summarized using means of counts and percentages. Differences in continuous and categorical variables among the three groups were compared using Kruskal-Wallis test and chi-square test, respectively. We evaluated the impact of the KCL score on the endpoint using univariable and multivariable Cox regression analyses with 95% confidence intervals (CIs). A 3-year all-cause mortality was estimated using the Kaplan-Meier method, and the difference between the groups was evaluated using the log-rank test. The validity of the KCL for estimating frailty status was evaluated using receiver operating characteristic (ROC) curves and area under the curve (AUC) of the total KCL score, CHS, CFS, and SPPB were assessed using ROC analysis tool based on DeLong's method [25]. The total KCL score was compared with the number of each frailty phenotype, using Spearman's correlation coefficient. Statistical analyses were performed using the R software package (version 3.3; R Development Core Team, Vienna, Austria). The significance

level of a statistical hypothesis testing was set at 0.05, and the alternative hypothesis was two or three sided.

Results

Validation of the KCL in estimating frailty status

Baseline patient characteristics are listed in **Table 2**. In the total study population, the median patient age was 84 years (interquartile range, 81–87 years), and 31.1% were men. The median body mass index, mean grip strength, and 15 foot-walk gait speed, plasma albumin level were 22.4 kg/m^2 (19.9–25.1 kg/m^2), 16 kg (13–22 kg), 5.6 m/sec (4.6–7.2 m/sec), 3.8 g/dL (3.5–4.1 g/dL), respectively. The median scores of CHS, CFS, and SPPB were 3 (2–4), 4 (3–4), and 8 (5–10), respectively.

Figure 2 shows a comparison of the frailty status between the KCL and CHS, CFS, and SPPB. In the ROC curve, there were no significant differences between KCL and CHS (AUC 0.625 versus 0.628; p=0.93), KCL and CFS (AUC 0.625 versus 0.542; p=0.15), and KCL and SPPB (AUC 0.625 versus 0.612; p=0.91). The total KCL score significantly correlated with the number of frailty phenotypes defined in the CHS criteria [Spearman's rank correlation coefficient (rs), 0.642; p<0.001], CFS (rs, 0.381; p<0.001), and SPPB (rs, -0.613; p<0.001) according to Spearman's correlation analysis

(**Fig. 3**). These data indicate that KCL can be used to evaluate frailty status, similar to the previously established clinical scoring system in the TAVI cohort.

Comparison of patients' characteristics according to the frailty status by the KCL

The first and second tertiles of the total KCL scores were 8 and 12, respectively. The total study population was divided into three groups by tertiles of total KCL score: 89 patients were categorized as non-frail (KCL from 0 to 8), 95 patients as pre-frail (KCL from 9 to 12), and 96 patients as frail (KCL from 13 to 25). There were significant differences in the body mass index, body surface area, Society of Thoracic Surgeons score, mean grip strength, 15 foot-walk gait speed, presence of atrial fibrillation, plasma albumin level, plasma natrium level, and plasma hemoglobin level between the three groups. The indicators of frailty, CHS, CFS, and SPPB were also significantly different among the three groups.

Table 3 shows peri- and post-procedural outcome information. In the total study population, 86.1% of the patients underwent transfemoral TAVI, and 72.5% underwent balloon-expandable TAVI. There were no significant differences in the TAVI approach and transcatheter heart valve size among the three groups. Significant differences were observed among groups with respect to SAPIEN XT valve [non-frail

group 7 (7.9%) versus pre-frail group 8 (8.4%) versus frail group 22 (22.9%), p=0.004] procedural time [55 (40–82) versus 60 (45–88) versus 70 (45–101) min, p=0.04], all bleeding [2 (2.2%) versus 10 (10.5%) versus 19 (19.8%), p<0.001], and life-threatening/major bleeding [2 (2.2%) versus 6 (6.3%) versus 15 (15.6%), p=0.004]. Post-procedural echocardiographic data were not significantly different between the three groups.

Predictive value of KCL in late mortality

The total number of all-cause deaths was 50 (non-frail group 14, pre-frail group 11, frail group 25). Regarding the cause of death, cardiovascular deaths were four (non-frail group one, pre-frail group one, frail group two) and non-cardiovascular deaths were 46 (non-frail group 13, pre-frail group 10, frail group 23).

The results of the Cox regression analysis for the association between late mortality and clinical findings are presented in **Table 4**. The multivariate Cox regression model indicated that the total KCL score [hazard ratio (HR), 1.104; 95% CI, 1.034–1.179; p=0.003], presence of diabetes mellitus (HR, 1.993; 95% CI, 1.055–3.766; p=0.03), and presence of liver disease (HR, 3.007; 95% CI, 1.067-8.477; p=0.04) were independently associated with 3-year all-cause mortality. In addition, the estimated 3-

year mortality rate was 14.0% (95% CI, 7.7–24.9) for the non-frail group versus 12.0% (95% CI, 6.0-23.3) for the pre-frail group versus 35.1% (95% CI, 23.9-49.5) for the frail group (log-rank *p*=0.0048) **(Fig. 4)**.

Discussion

In this study, we demonstrated that the KCL could be used to evaluate frailty status, similar to the previously established clinical scoring system in the TAVI cohort. In addition, the total KCL score, presence of diabetes mellitus, and presence of liver disease were independently associated with 3-year all-cause mortality. Finally, the estimated 3-year mortality rate was significantly higher in the high KCL group. To the best of our knowledge, this is the first study to demonstrate that frailty evaluated by the KCL is associated with long-term mortality in the TAVI cohort.

Frailty is recognized as a general indicator of a patient's vulnerability, which is highly associated with adverse health outcomes in the geriatric field [24,26]. The KCL was originally developed to identify elderly individuals who were at risk of requiring care/support and to take preventive steps for pre-disabled older adults within the Japanese long-term care insurance system, independent of the concept of frailty. In this study, we utilized the KCL to evaluate frailty in patients who underwent TAVI. Our

data showed good correlation between the total KCL score and established frailty indices, such as CHS, CFS, and SPPB, indicating that KCL could be used as an alternative assessment method to evaluate frailty. CHS and SPPB can more precisely assess frailty status than KCL because these scores are calculated from physical findings and motility function [24,27]. However, it is often difficult for clinicians to calculate these scores in daily practice because not all candidates can perform sufficient examinations that are required for calculation. Although CFS can be an easily measured index for frailty and is associated with 1-year all-cause mortality following TAVI [16], it is easily affected by the environment and physical condition, and it may not be possible to objectively evaluate frailty. However, the KCL can make a general judgment by scoring daily life function, motility function, nutrition, cognitive function, and depression. Although the KCL is a self-reporting survey, it may be possible to make a more objective evaluation by evaluating various indicators related to frailty. The KCL is an index that can be easily calculated without special measurement and is a useful tool that can predict the prognosis after TAVI.

In a previous study, the total KCL score was correlated with CHS, and a cut-off KCL value of 7/8 was adequate for evaluating frailty in elderly outpatients [19]. However, in this study, the frail group (total KCL score13–25) had higher 3-year

mortality than the non-frail group (total KCL score 0–8) and pre-frail group (total KCL score 9–12). There was no significant difference in mortality between the non-frail and pre-frail groups. The cut-off value of frailty in the TAVI cohort might be higher than that in elderly people with chronic conditions. Further studies with more patients are required to clarify this point.

Study limitations

This study has several limitations. First, this study was designed as a single-center design, and the small study population (n=280) underpowered the statistical analysis. Second, since TAVI is a treatment for elderly patients, this study included patients who were unable to answer questions accurately due to severe cognitive impairment. In these cases, frailty evaluated by the KCL could not precisely reflect the patient's frailty status.

Conclusion

The KCL is a simple and useful tool for evaluating frailty status and predicting 3-year all-cause mortality in patients undergoing TAVI. The availability of KCL along with a surgical risk score might be useful in identifying patients who are too frail to

benefit from TAVI. KCL could be an indicator for identifying optimal candidates for TAVI.

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Figure legends

Figure 1 Flowchart of patient selection.

AS, aortic stenosis; KCL, Kihon checklist; TAVI, transcatheter aortic valve implantation.

Figure 2 Comparison between the Kihon checklist (KCL) and Cardiovascular Health Study Frailty Index (CHS), Clinical Frailty Scale (CFS), and Short Physical Performance Battery (SPPB). (a) Receiver operating characteristic (ROC) curves for

total KCL score and CHS. (b) ROC curve for total KCL score and CFS. (c) ROC curves for total KCL score and SPPB.

AUC, area under the curve; CFS, Clinical Frailty Scale; CHS, Cardiovascular Health Study Frailty Index; KCL, Kihon checklist; SPPB, Short Physical Performance Battery.

Figure 3 Correlation between Kihon checklist and Cardiovascular Health Study Frailty Index, Clinical Frailty Scale, and Short Physical Performance Battery. Total KCL score linearly and dependently correlates with the number of frailty phenotypes defined by the CHS, CFS, and SPPB criteria according to Spearman's correlation analysis. (a) Total KCL score and CHS. (b) Total KCL score and CFS. (c) Total KCL score and SPPB.

CFS, Clinical Frailty Scale; CHS, Cardiovascular Health Study Frailty Index; KCL, Kihon checklist; rs, Spearman's rank correlation coefficient; SPPB, Short Physical Performance Battery.

Figure 4 Kaplan-Meier analysis of all-cause mortality.

Table 1. Kihon Checklist

No.	Questions	Answer	
1	Do you go out by bus or train by yourself?	□1. YES	□0. NO
2	Do you go shopping to buy daily necessities by yourself?	□1. YES	□0. NO
3	Do you manage your own deposits and savings at the bank?	□1. YES	□0. NO
4	Do you sometimes visit your friends?	□1. YES	□0. NO
5	Do you turn to your family or friends for advice?	□1. YES	□0. NO
6	Do you normally climb stairs without using handrail or wall for support?	□1. YES	□0. NO
7	Do you normally stand up from a chair without any aids?	□1. YES	□0. NO
8	Do you normally walk continuously for 15 minutes?	□1. YES	□0. NO
9	Have you experienced a fall in the past year?	□1. YES	□0. NO
10	Do you have a fear of falling while walking?	□1. YES	□0. NO
11	Have you lost 2kg or more in the past 6 months?	□1. YES	□0. NO
12	Height: cm, Weight: kg, BMI: kg/m2 If BMI is less than 18.5, this item is scored.	□1. YES	□0. NO
13	Do you have any difficulties eating tough foods compared to 6 months ago?	□1. YES	□0. NO
14	Have you choked on your tea or soup recently?	□1. YES	□0. NO
15	Do you often experience having a dry mouth?	□1. YES	□0. NO
16	Do you go out at least once a week?	□1. YES	□0. NO
17	Do you go out less frequently compared to last year?	□1. YES	□0. NO
18	Do your family or your friends point out your memory loss? e.g."You ask the same question over and over again."	□1. YES	□0. NO
19	Do you make a call by looking up phone numbers?	□1. YES	□0. NO
20	Do you find yourself not knowing today's date?	□1. YES	□0. NO
21	In the last 2 weeks have you felt a lack of fulfillment in your daily life?	□1. YES	□0. NO
22	In the last 2 weeks have you felt a lack of joy when doing the things you used to enjoy?	□1. YES	□0. NO
23	In the last 2 weeks have you felt difficulty in doing what you could do easily before?	□1. YES	□0. NO
24	In the last 2 weeks have you felt helpless?	□1. YES	□0. NO
25	In the last 2 weeks have you felt tired without a reason?	□1. YES	□0. NO

BMI, body mass index

Table 2. Baseline Clinical Characteristic of Study Patients

Baseline Clinical Characteristic	Total n=280	Non-frail KCL 0-8 n=89	Pre-frail KCL 9-12 n=95	Frail KCL 13-25 n=96	p- value
Age, years	84 (81-87)	83 (80-86)	84 (81-86)	85 (81-89)	0.07
Male sex, n (%)	87 (31.1)	37 (41.6)	25 (26.3)	25 (26.0)	0.04
BMI, kg/m^2	22.4 (19.9-25.1)	22.8 (20.8-25.1)	22.2 (20.6-25.4)	20.8 (18.8-24.7)	0.10
BSA, m^2	1.41 (1.3-1.55)	1.46 (1.38-1.60)	1.40 (1.31-1.53)	1.38 (1.25-1.50)	<0.001
NYHA Class III or IV, n (%)	64 (17.9)	14 (15.7)	22 (23.2)	28 (29.2)	0.09
STS score	6.77 (4.80-9.12)	5.7 (4.30-7.20)	7.0 (4.88-9.38)	7.70 (5.65-9.73)	<0.001
CHS, n (%)	3 (2-4)	2 (2-3)	3 (2.5-4)	4 (3-5)	<0.001
CFS, n (%)	4 (3-4)	3 (3-4)	4 (3-4)	4 (4-5)	<0.001
SPPB, n (%)	8 (5-10)	10 (9-12)	8 (6-10)	5 (3-7)	<0.001
Mean grip strength , kg	16.4 (13.3-22.1)	19.7 (16.2-25.4)	15.7 (12.8-19.1)	14.7 (11.7-17.9)	<0.001
15-ft walk gait speed , m/s	5.60 (4.64-7.19)	4.65 (4.07-5.22)	5.57 (4.80-6.57)	7.19 (5.85-8.79)	<0.001
Comorbidity, n (%)					
Diabetes mellitus	77 (27.5)	23 (25.8)	26 (27.4)	28 (29.2)	0.88
Hypertension	260 (92.8)	84 (94.4)	88 (92.6)	88 (91.7)	0.81
Dyslipidemia	164 (58.6)	58 (65.2)	54 (56.8)	52 (54.2)	0.29
Coronary artery disease	80 (28.6)	27 (30.3)	23 (24.2)	30 (31.2)	0.51
Peripheral artery disease	53 (18.9)	13 (14.6)	17 (17.9)	23 (24.0)	0.27
Atrial fibrillation	56 (20.0)	11 (12.4)	26 (27.4)	19 (19.8)	0.04
Previous stroke	25 (8.9)	7 (7.9)	11 (11.6)	7 (7.3)	0.59
Liver disease	11 (3.9)	4 (4.5)	3 (3.2)	4 (4.2)	0.93
Pulmonary disease	37 (13.2)	13 (14.6)	10 (10.5)	14 (14.6)	0.63
Preprocedural laboratory data					
Albumin, g/dL	3.8 (3.5-4.1)	3.9 (3.6-4.1)	3.8 (3.5-4.0)	3.7 (3.4-3.9)	0.002
Creatinine, mg/dL	0.91 (0.74-1.14)	0.92 (0.76-1.14)	0.90 (0.71-1.19)	0.90 (0.74-1.12)	0.92
e-GFR, mL/min/1.73m2	48.8 (38.6-63.4)	49.7 (42.7-63.4)	47.5 (38.5-63.2)	47.9 (37.6-64.7)	0.68

Natrium, mEq/L	140 (138-142)	140 (138-141)	141 (139-142)	140 (138-142)	0.02
Hemoglobin, g/dL	11.6 (10.3-12.4)	11.8 (10.9-13.0)	11.0 (10.3-12.4)	10.9 (10.0-12.2)	<0.001
BNP, pg/mL	185.0 (76.9-381.7)	156.6 (61.6-370.6)	210.7(114.4-399.4)	163.1 (67.1-395.6)	0.34
Preprocedural Echocardiographic data					
LVEF, %	60.0 (55.0-65.0)	61.0 (53.0-65.0)	60.0 (57.0-65.0)	61 (55.0-65.0)	0.51
Peak AV velocity, m/s	4.5 (4.1-5.1)	4.5 (4.3-5.1)	4.5 (4.1-5.3)	4.3 (4.0-4.9)	0.07
Mean AVPG, mmHg	45 (35-59)	46 (39-61)	48 (37-61.5)	43 (33-57)	0.14
AVA, cm^2	0.66 (0.57-.74)	0.68 (0.58-0.73)	0.65 (0.57-0.74)	0.66 (0.58-0.74)	0.87
Moderate or severe AR, n (%)	29 (10.4)	7 (7.9)	8 (8.4)	14 (14.6)	0.29
Moderate or severe MR, n (%)	28 (10.0)	7 (7.9)	8 (8.4)	13 (13.5)	0.39
Preprocedural CT data					
Annulus area, mm^2	392 (346-442)	388 (347-465)	395 (347-439)	392 (348-439)	0.16
Perimeter, mm	70.3 (66.1-75.0)	70.4 (66.1-76.6)	70.9 (66.0-74.5)	70.0 (65.8-74.3)	0.11

Categorical variables are shown as numbers (percentages) and continuous variables are shown as medians (25-75th percentiles). KCL, Kihon Checklist; BSA, body surface area; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons Predictive Risk of Mortality; CHS, Cardiovascular Health Study frailty index; CFS, Clinical Frailty Scale; SPPB, Short Physical Performance Battery; e-GFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; LVEF, left ventricle ejection fraction by modified Simpson methods; AV, aortic valve; AVPG, aortic valve pressure gradient; AVA, aortic valve area; AR, aortic regurgitation; MR, mitral regurgitation; CT, computed tomography

Table 3. Peri- and postprocedural Outcome Information

Procedural and Outcome Information	**Total n=280**	**Non-frail KCL 0-8 n=89**	**Pre-frail KCL 9-12 n=95**	**Frail KCL 13-25 n=96**	**p-value**
Procedural Data, n (%)					
Access route					
Transfemoral	241 (86.1)	80 (89.9)	82 (86.3)	79 (82.3)	0.33
Transapical	30 (10.7)	7 (7.9)	8 (8.4)	15 (15.6)	0.16

Direct-Aorta	1 (0.4)	0 (0.0)	1 (1.0)	0 (0.0)	0.38
Transsubclavian	8 (2.9)	2 (2.2)	4 (4.2)	2 (2.1)	0.62
Valve type					
SAPIEN XT, n (%)	38 (13.6)	7 (7.9)	9 (9.5)	22 (22.9)	0.004
SAPIEN 3, n (%)	165 (58.9)	58 (65.2)	60 (63.2)	47 (49.0)	0.048
Core Valve, n (%)	3 (1.0)	0 (0.0)	3 (3.2)	0 (0.0)	0.052
Evolut R, n (%)	35 (12.5)	13 (14.6)	13 (13.7)	9 (9.4)	0.51
Evolut Pro/Pro+, n (%)	39 (13.9)	11 (12.4)	10 (10.5)	18 (18.8)	0.23
Valve size, mm	26 (23-26)	26 (23-26)	26 (23-26)	26 (23-26)	0.14
Periprocedural Variable					
Procedual time, min	60 (45-91)	55 (40-82)	60 (45-88)	70 (45-101)	0.02
Local anesthesia, n (%)	6 (2.1)	3 (3.4)	0 (0.0)	3 (3.1)	0.21
Contrast, ml	65 (54-81)	65 (54-80)	65 (54-80)	65 (54-82)	0.96
Periprocedural Complications, n (%)					
Coronary occlusion	5 (1.8)	1 (1.1)	2 (2.1)	2 (2.1)	0.85
Permanent pacemaker implantation	10 (3.6)	4 (4.5)	3 (3.2)	3 (3.1)	0.85
Disabling Stroke	5 (1.8)	2 (2.2)	2 (2.2)	1 (1.0)	0.75
Acute kidney injury	15 (5.3)	5 (5.6)	6 (6.3)	4 (4.2)	0.80
All bleeding	31 (11.1)	2 (2.2)	10 (10.5)	19 (19.8)	<0.001
Life-threatening/Major bleeding	23 (8.2)	2 (2.2)	6 (6.3)	15 (15.6)	0.004
All vascular complications	14 (5.0)	1 (1.1)	7 (7.4)	6 (6.2)	0.10
Cardiac tamponade	2 (0.7)	0 (0.0)	2 (2.1)	0 (0.0)	0.22
Postprocedural Echocardiographic Data					
Peak AV velocity, m/s	2.1 (1.9-2.4)	2.2 (1.9-2.4)	2.2 (1.9-2.4)	2.1 (1.8-2.4)	0.66
Mean AVPG, mmHg	9 (7-12)	10 (7-12)	9 (7-13)	9 (7-12)	0.72
EOA, cm^2	1.59 (1.38-1.81)	1.62 (1.43-1.81)	1.57 (1.37-1.79)	1.60 (1.33-1.82)	0.56
Moderate or severe AR, n (%)	16 (5.7)	4 (4.5)	5 (5.3)	7 (7.3)	0.77

Caption is the same as in Table 2. EOA, effective orifice area

Table 4. Cox Regression Analysis for the Association between Cumulative Mortality and Clinical Findings

Parameter	Univariate	Multivariate

	Unadjusted HR	95% CI	p-value	Adjusted HR	95% CI	p-value
Total KCL score	1.107	1.036-1.183	0.003	1.104	1.034-1.179	0.003
Age	0.944	0.891-1.000	0.0501			
BMI	0.947	0.870-1.031	0.21			
NYHA Class III or IV	0.707	0.334-1.496	0.36			
STS score	1.045	0.992-1.101	0.10			
15-ft walk gait speed	1.093	0.992-1.205	0.07			
Mean grip strength	0.978	0.930-1.029	0.39			
Diabetes mellitus	2.024	1.072- 3.818	0.03	1.993	1.055-3.766	0.03
Hypertension	0.555	0.197-1.563	0.27			
Coronary artery disease	1.156	0.587-2.275	0.68			
Peripheral artery disease	1.988	0.992-3.983	0.053			
Liver disease	3.358	1.189-9.482	0.02	3.007	1.067-8.477	0.04
Pulmonary disease	1.857	0.906-3.808	0.09			
Albumin	0.516	0.255-1.046	0.07			
Creatinine	0.917	0.438-1.918	0.82			
Natrium	0.913	0.828-1.006	0.07			
BNP	1.000	1.000-1.001	0.31			
LVEF	1.003	0.972-1.035	0.87			
AVA	1.086	0.106-11.15	0.95			
Mean AVPG	1.003	0.987-1.020	0.71			
Transfemoral	0.482	0.230-1.013	0.054			

Caption is the same as in Table 2. HR, hazard ratio; CI, confidence interval

Grafical abstract

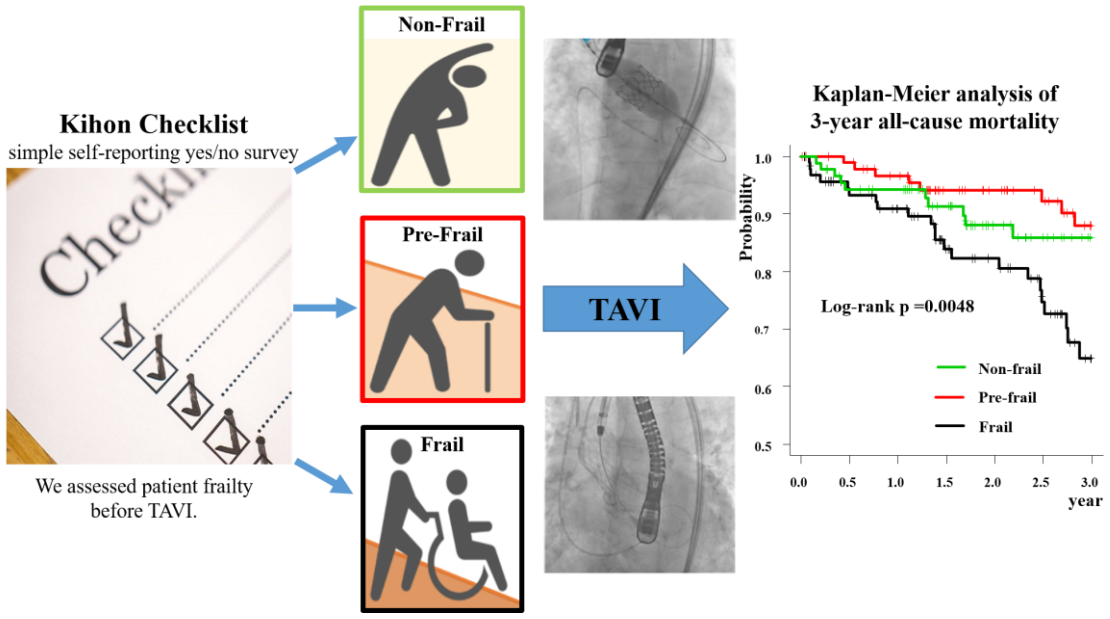


Figure 1. Flowchart of patient selection.

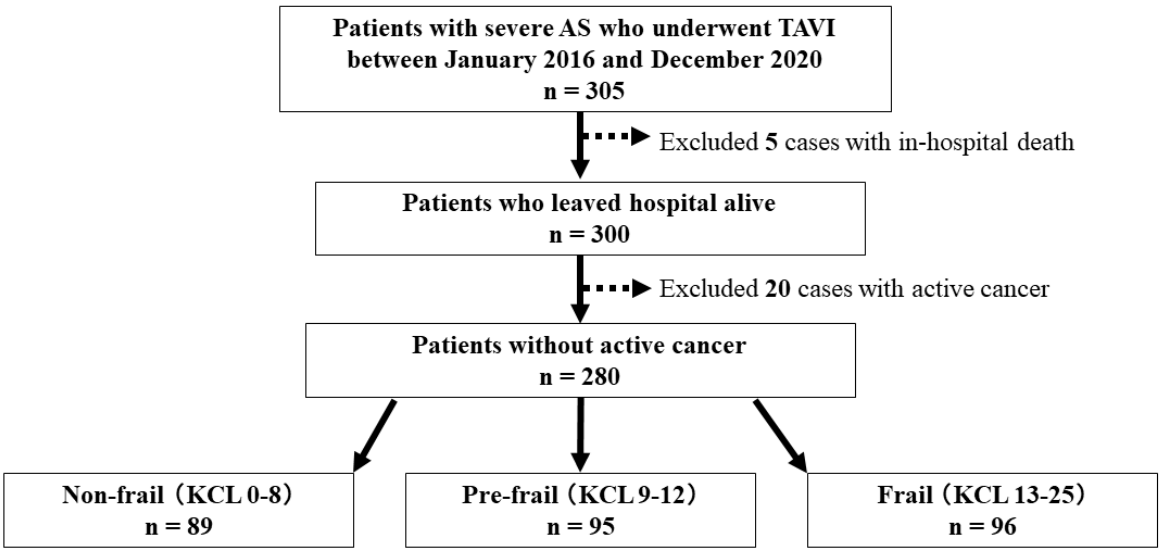
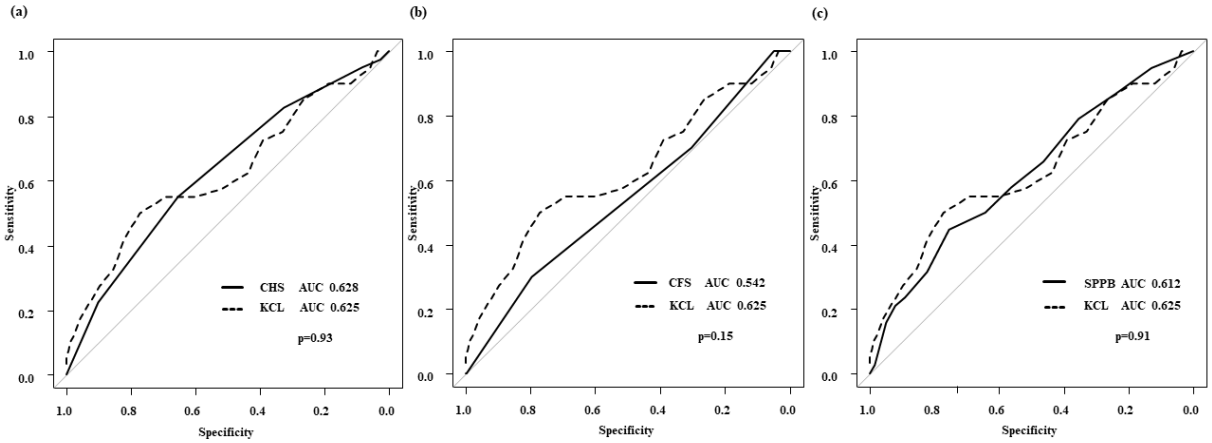


Figure 2. Comparison between KCL and CHS, CFS, SPPB



(a) Receiver operating characteristic (ROC) curves for total KCL score and CHS.
(b) ROC curve for total KCL score and CFS.
(c) ROC curves for total KCL score and SPPB.

Figure 3. Correlation between KCL and CHS, CFS, SPPB

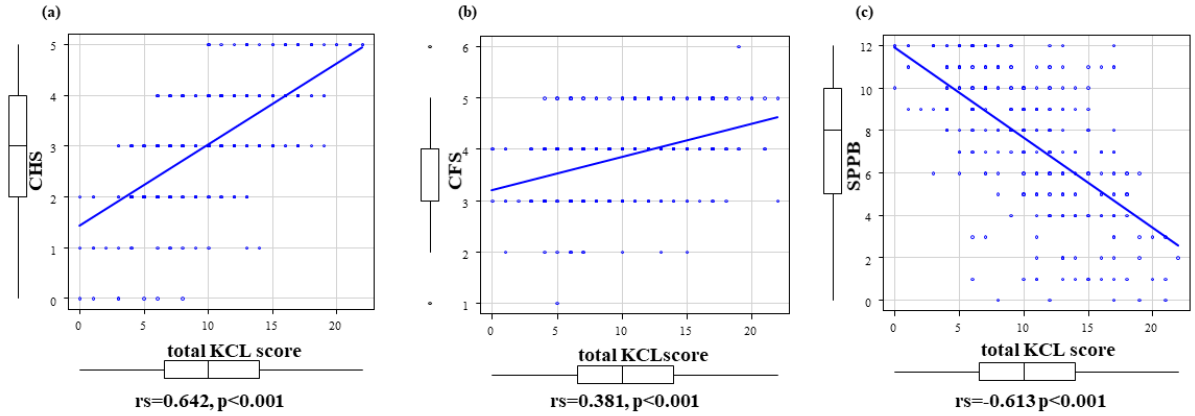
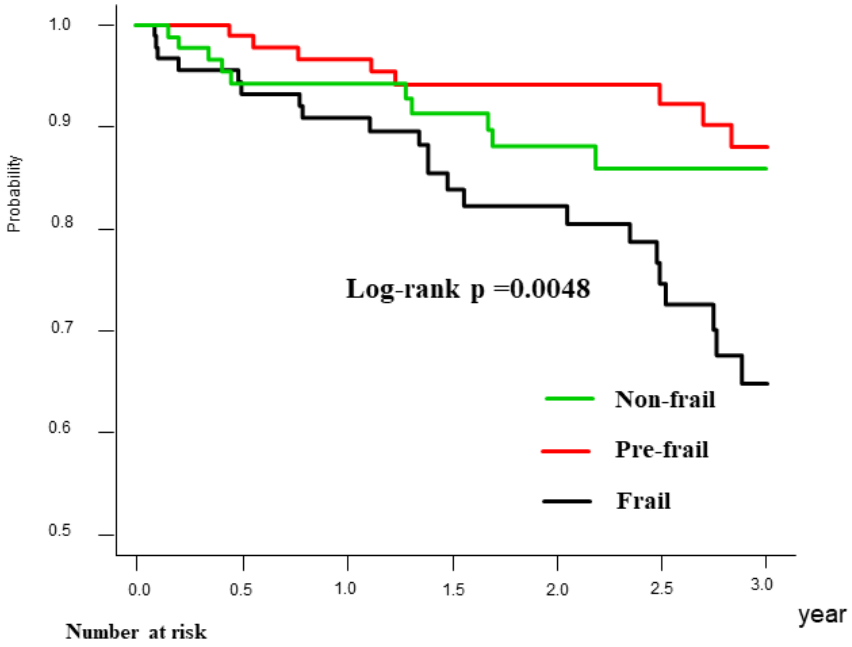


Figure 4. Kaplan-Meier analysis of all-cause mortality of patients in non frail, prefrail and frail group



Number at risk							
Non-frail	85	80	74	60	44	36	27
Pre-frail	95	90	83	62	56	48	37
Frail	96	79	72	54	48	36	22