Experimental Gerontology 171 (2023) 112021

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

SARC-F predicts poor motor function, quality of life, and prognosis in older patients with cardiovascular disease and cognitive impairment

Takumi Noda [a,b], Kentaro Kamiya [a,c,*], Nobuaki Hamazaki [d], Kohei Nozaki [d], Takafumi Ichikawa [d], Masashi Yamashita [a,e], Shota Uchida [a], Kensuke Ueno [a], Emi Maekawa [f], Tasuku Terada [b], Jennifer L. Reed [b,g,h], Minako Yamaoka-Tojo [a,c], Atsuhiko Matsunaga [a,c], Junya Ako [f]

[a] Department of Rehabilitation Sciences, Kitasato University Graduate School of Medical Sciences, Sagamihara, Japan
[b] Exercise Physiology and Cardiovascular Health Lab, Division of Cardiac Prevention and Rehabilitation, University of Ottawa Heart Institute, Ottawa, Canada
[c] Department of Rehabilitation, Kitasato University School of Allied Health Sciences, Sagamihara, Japan
[d] Department of Rehabilitation, Kitasato University Hospital, Sagamihara, Japan
[e] Division of Research, ARCE Inc., Sagamihara, Japan
[f] Department of Cardiovascular Medicine, Kitasato University School of Medicine, Sagamihara, Japan
[g] School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Canada
[h] School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Canada

ARTICLE INFO

Section Editor: Christiaan Leeuwenburgh

Keywords:
Sarcopenia
SARC-F
Physical function
Quality of life
Mortality
Cognitive impairment

ABSTRACT

Objectives: We investigated whether SARC-F scores were associated with motor function, quality of life (QOL) related to physical function, and prognosis in older patients with cardiovascular disease (CVD) and cognitive impairment.

Methods: This was a retrospective cross-sectional cohort study. The study population consisted of 408 patients with CVD (≥60 years old) who completed the SARC-F questionnaire and Mini-Cog, a cognitive function test, at discharge. Sarcopenia was defined as a total SARC-F score ≥ 4 points. Patients who were cognitively-preserved (Mini-Cog score ≥ 3 points) were excluded. Patients completed the handgrip strength, leg strength, usual gait speed, 6-minute walking distance, short physical performance battery score, and 36-item Short-Form Health Survey Physical Functioning (SF-36PF) tests before discharge. Associations of SARC-F with physical function, QOL, and prognoses (i.e., composite of all-cause death and emergency CVD rehospitalization and the number of CVD rehospitalizations) were investigated.

Results: Sarcopenia (SARC-F score ≥ 4 points) was associated with poorer motor function test outcomes and SF-36PF scores (all $P < 0.001$). The correlations remained significant after adjusting for comorbidities (e.g., anemia, prior heart failure, and renal dysfunction). Sarcopenia was also associated with a poorer prognosis (hazard ratio: 1.574; 95 % confidence interval [CI], 1.011–2.445) and an increased risk of CVD rehospitalization (incidence rate ratio: 1.911; 95 % CI, 1.312–2.782) after adjusting for comorbidities.

Conclusions and implications: In older patients with CVD and cognitive impairment, the SARC-F questionnaire may be a simple and inexpensive tool for identifying patients with decreased motor function and a poor prognosis.

1. Introduction

Sarcopenia is prevalent in older patients with cardiovascular disease (CVD) (31.4 %) due to aging, chronic inflammatory conditions, decreased physical activity, and poor nutrition (Bauer et al., 2019; Kamiya et al., 2017; Sasaki and Fukumoto, 2022). Older patients with

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; IQR, interquartile range; IRR, incidence rate ratio; LVEF, left ventricular ejection fraction; QOL, quality of life; SF-36PF, 36-item Short-Form Health Survey Physical Functioning; SPPB, short physical performance battery.

* Corresponding author at: Department of Rehabilitation, Kitasato University School of Allied Health Sciences, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa 252-0375, Japan.
E-mail address: k-kamiya@kitasato-u.ac.jp (K. Kamiya).

https://doi.org/10.1016/j.exger.2022.112021
Received 31 August 2022; Received in revised form 1 November 2022; Accepted 3 November 2022
Available online 8 November 2022

CVD and sarcopenia reportedly have lower physical function, higher rehospitalization rates, and mortality than those without sarcopenia (Kamiya et al., 2017; Tanaka et al., 2018; Yasuda et al., 2017). In addition, quality of life (QOL) is lower among older people with sarcopenia compared to those without sarcopenia (Rizzoli et al., 2013). Therefore, the early detection of sarcopenia in older patients with CVD is essential in daily clinical practice to provide individualized interventions.

The SARC-F questionnaire, which consists of five questions, is a simple and inexpensive tool for assessing sarcopenia (Malmstrom and Morley, 2013). With this tool, sarcopenia can be evaluated in a short period of time. SARC-F has also been translated and used in various languages and is widely used to identify older adults at risk for sarcopenia (Bauer et al., 2019). Studies have shown that SARC-F is associated with motor function and prognosis in patients with CVD (Tanaka et al., 2018; Tanaka et al., 2017). SARC-F may be helpful for the early detection of sarcopenia and for assessing motor function and prognosis in patients with CVD.

However, many older adults have dementia (12.0 %) or a mild cognitive decline (15.5 %) (Jia et al., 2020). Additionally, individuals with CVD or sarcopenia have exacerbated cognitive dysfunction (Aprahamian et al., 2020; Iadecola et al., 2019), which may decrease self-perception of behavior and dysfunction (Onor et al., 2006). It is unclear whether sarcopenia assessed by a questionnaire can predict poor motor function and prognosis in older patients with CVD and cognitive impairment. If SARC-F scores are associated with physical function, QOL, and prognosis in older patients with CVD and cognitive impairment, then the SARC-F questionnaire can be used to efficiently and easily assess sarcopenia and identify patients at risk of poor prognosis. Thus, this study aimed to determine the relationship between SARC-F scores and motor function tests, QOL, and prognosis in older patients with CVD and cognitive impairment.

2. Methods

2.1. Study population

This was a retrospective cross-sectional cohort study. The participants were admitted to the Kitasato University Hospital Cardiovascular Center for CVD treatment between August 2015 and December 2020. Patients were assessed at discharge using the SARC-F questionnaire and Mini-Cog, a cognitive function test. Patients not evaluated by the SARC-F or Mini-Cog and those assessed as having preserved cognitive function based on Mini-Cog results were excluded from the study. The study protocol was prepared according to the tenets of the Declaration of Helsinki and approved by the Ethics Committee of Kitasato University Medical Ethics Organization (No. KMEO B18-075). Since this was an observational study without invasive procedures or interventions, written informed consent was not required following the principles of the Japanese Ministry of Health, Labour and Welfare's "Ethical Guidelines for Medical and Health Research Involving Human Subjects." Therefore, the requirement for informed consent was waived under the "Institutional Guidelines for Backward-looking Observational Research" set forth by the Kitasato University Medical Ethics Organization.

2.2. Data collection and measurement of Mini-Cog and SARC-F

In this study, we used data from the Kitasato University Cardiac Rehabilitation Database. Age, sex, body mass index (BMI), vital signs (systolic blood pressure, diastolic blood pressure, and heart rate), diagnosis (heart failure [HF], acute coronary syndrome [ACS], aortic disease, others), biochemical data, and echocardiograms were collected from electronic medical records as recorded at the time of discharge (or closest to that point in time). Patients were classified according to the BMI categories recommended by the World Health Organization as follows: BMI $<$ 18.5 kg/m^2 (underweight), BMI 18.5–24.9 kg/m^2 (normal), BMI $\geq$ 25.0 kg/m^2 (obese) (Organization, 2000). Comorbidities (e.g., hypertension, diabetes, and dyslipidemia) diagnosed by specialists were extracted from medical records, and medications prescribed at the time of discharge were reviewed. The estimated glomerular filtration rate (eGFR) was defined using the formula of the Japanese Society of Nephrology (male: $=194 \times (\textit{serum creatinine})^{1.094} \times (\textit{age})^{0.287}$; female: $194 \times (\textit{serum creatinine})^{1.094} \times (\textit{age})^{0.287} \times 0.739$) (Ando et al., 2009). We defined an eGFR $<$ 60 mL/min/1.73 m^2 as renal dysfunction.

The Mini-Cog test and SARC-F questionnaires were administered before hospital discharge. The Mini-Cog test comprised two items: the word recall test and clock drawing (Borson et al., 2000). Trained rehabilitation staff or nurses administered the test by asking patients to repeat three unrelated words, followed by a clock-drawing test, and finally recalling the three words. All instructions suggested on the Mini-Cog© website (https://mini-cog.com/) were followed. The total test score used a 5-point scale (1 point per correctly recalled word for each of three words and 2 points for correctly drawing the clock). Scores $\leq$ 2 points were considered abnormal and evaluated as cognitive impairment (Borson et al., 2000).

For the SARC-F, patients were asked to complete the SARC-F questionnaire consisting of five items: strength (S), assistance in walking (A), rising from a chair (R), climbing stairs (C), and falling (F) (Woo et al., 2014). Each SARC-F element had 0–2 points, and patients were rated on a total score of 0–10 points (0 = best physical performance to 10 = worst physical performance). Patients with total scores $\geq$ 4 were classified as having sarcopenia. The original version of the SARC-F was modified for use in Japanese, as in previous studies (Tanaka et al., 2017).

2.3. Measurement of physical function tests and QOL

Patients were placed in a sitting position, and their muscle strength was measured by trained rehabilitation staff. The handgrip strength was assessed using a digital dynamometer (TKK 5101 Grip-D; Takei, Tokyo, Japan) with the elbows held in 90° flexion, and the maximum isometric voluntary contraction of both hands was measured twice for 3 s each. The maximum handgrip strength, expressed as an absolute value (kg), was used for the analysis since the maximum is less likely to be affected by the number of trials than the mean is (Roberts et al., 2011). The leg strength was assessed using isometric quadriceps strength measured using a handheld dynamometer (μ-Tas; ANIMA, Tokyo, Japan). The patient sat with a strain gauge secured to the ankle using a non-stretch strap. The maximum 5-s isometric voluntary contraction of the quadriceps muscle was recorded twice for each leg while the hip joint was flexed at approximately 90°. The top muscle strength values for both measured leg strengths were averaged and expressed as relative to the body mass (%BM).

The gait speed was measured based on the patient's comfortable speed. The rehabilitation staff instructed the patient to walk comfortably along a 16-m sidewalk. Moreover, the assessor timed and measured the speed in the center of the sidewalk (at 10 m). Each patient's usual gait speed was calculated by dividing the distance (m) by time (s). Six-minute walking distances (6 MWD) were measured according to the American Thoracic Society guidelines (Laboratories, 2002) under the supervision of the rehabilitation staff. Patients were instructed to walk at their own pace along a straight, flat corridor marked at 1-m intervals, and the distance (m) was recorded after 6 min. The Short Physical Performance Battery (SPPB), comprising three components (comfortable walking speed, five-repetition standing and sitting test, and standing balance), was measured according to established methods (Guralnik et al., 1994). Comfortable walking speed was measured as the time taken to walk 4 m, and it was scored based on a previous study (de Fátima Ribeiro Silva et al., 2021). In the five-repetition standing and sitting test, patients were evaluated by their ability to stand and sit on a chair five times in a row, followed by the time taken to complete these tasks. Balance tests consisted of three postures: side-by-side stand, semi-

tandem stand, and tandem stand. In each balance test, patients were assessed by their ability to stand upright for a maximum of 10 s. The SPPB scores were evaluated using the total score (0 = worst to 12 = best), with each element scored from 0 to 4.

For the 36-item Short-Form Health Survey Physical Functioning (SF-36PF), which consists of 10 items on mobility and physical movement (Ware, 1993), the total score for each question was recorded. Scores ranged from 0 (severely limited physical activity) to 100 (free physical activity).

2.4. Prognostic outcomes

A composite outcome of all-cause death and first emergency CVD (e.g., HF, ACS, and aortic dissection) rehospitalization was defined as the study endpoint. The prognosis of registered patients within 3 years of discharge was retrospectively collected. The time to the endpoint was calculated as the number of days from the discharge date to the event's occurrence (all-cause death or CVD rehospitalization). Follow-up was performed in the order of discharge. The last day on which we could confirm that the patients were alive without events during the study period was recorded as the censoring date of the composite outcome. Additionally, for patients with multiple hospitalizations, the number of times a patient had an emergency hospitalization for CVD was assessed as the second prognostic outcome. In this case, for the outcome of the number of rehospitalizations in patients hospitalized more than once, the date of the last visit was used as the censoring date.

2.5. Statistical analysis

Continuous data are presented as median and interquartile range (IQR), while categorical data are presented as frequency and percentages. Participants were classified into two groups based on their SARC-F scores, i.e., those with $\geq$4 and <4 points, as previously reported (Tanaka et al., 2017). SARC-F scores $\geq$ 4 were defined as sarcopenia. To investigate differences in baseline characteristics between groups with and without sarcopenia, the Mann–Whitney *U* test was used for continuous variables and the chi-square test for categorical variables. Multiple imputations using R with the "mice" package version 3.14.0 (Zhang, 2016) generated 20 datasets with complementary missing values.

Multivariate linear regression models were used to examine the association between the total SARC-F scores and motor functions (handgrip strength, leg strength, gait speed, 6 MWD, and SPPB) and QOL (SF-36PF). Additionally, physical functioning and QOL were compared between sarcopenia and non-sarcopenia using multivariate linear regression models. The models in each analysis were adjusted for age, sex, BMI, left ventricular ejection fraction (LVEF), hemoglobin, albumin, prior HF, and renal dysfunction.

We calculated 100 person-years for each participant from the day participants were evaluated with SARC-F up to the event occurrence date. Kaplan–Meier curves for cumulative survival were generated, and the prognostic significance of dividing patients into the non-sarcopenia (SARC-F < 4) or sarcopenia (SARC-F $\geq$ 4) groups was evaluated using a log-rank test. The Cox proportional hazards model was used to construct unadjusted and adjusted models using the resulting equations to calculate hazard ratios (HRs) and 95 % confidence intervals (CIs) for consecutive total SARC-F scores, and the prognostic ability when divided into two groups with the absence/presence of sarcopenia. The adjusted model was constructed based on age, sex, BMI, LVEF, hemoglobin level, albumin level, prior HF, and renal dysfunction. The endpoint was the composite outcome of all-cause death and CVD rehospitalization. To examine the association between the total number of post-discharge emergency CVD readmissions and SARC-F scores and the absence/presence of sarcopenia, we performed Poisson regression models with robust variance estimators, adjusted for age, sex, BMI, LVEF, hemoglobin, albumin, prior HF, and renal dysfunction, to estimate the incidence rate ratio (IRR) of CVD readmissions and 95 % CI.

All statistical analyses were performed using the R Studio statistical software, version 4.2.0 (Vienna, Austria, https://www.R-project.org). The statistical significance level was set at $P < 0.05$.

3. Results

3.1. Study population

We included 2171 patients aged $\geq$60 years who completed the SARC-F questionnaire and Mini-Cog test during the study period. We excluded 1763 patients with Mini-Cog scores $\geq$3; a total of 408 patients were analyzed (Supplementary Fig. S1). Table 1 presents the baseline patient characteristics. Of the 408 patients, 267 (65.4 %) were men and 141 (34.6 %) were women, with a median age of 78 years (IQR: 73–84 years), median BMI of 21.4 kg/m^2 (IQR: 19.1–23.7 kg/m^2), and median LVEF of 56.1 % (IQR: 42.0–66.0 %). The median length of stay in the hospital of all patients was 18 days (IQR: 11–26 days). A total of 242 patients (59.3 %) were in the intensive care unit (ICU), where the median length of stay was 2 days (IQR: 1–4 days). Of 408 participants, 52.7 % were hospitalized with HF, 15.9 % with ACS, and 14.2 % with aortic disease. The median SARC-F score was 2 points (IQR: 1–4 points), and 32.6 % had SARC-F $\geq$ 4 points. The percentages of participants with SARC-F $\geq$ 4 points according to the Mini-Cog score were 37.5 %, 32.8 %, and 31.7 % for 0, 1, and 2 points, respectively (Supplementary Fig. S2). Individuals in the group with SARC-F $\geq$ 4 points were older (77 vs. 81 years, $P < 0.001$), had a higher HF diagnosis rate (43.6 % vs. 54.9 %, $P = 0.035$), and lower LVEF (56.7 % vs. 51.0 %, $P = 0.029$) than those in the group with SARC-F < 4 points. They also had lower serum albumin levels ($P = 0.003$) and eGFR ($P = 0.010$).

3.2. Association of SARC-F, physical function, and QOL in patients with CVD and cognitive impairment

Table 2 shows the association between SARC-F scores, motor function test results, and SF-36PF scores. Higher SARC-F scores were inversely associated with handgrip strength, leg strength, usual gait speed, 6 MWD, SPPB, and SF-36PF, even after adjustment for age, sex, BMI, LVEF, hemoglobin, albumin, prior HF, and renal dysfunction (all $P < 0.001$). Furthermore, the individuals in the sarcopenia group (SARC-F $\geq$ 4) had lower estimated mean values for all motor functions and lower SF-36PF scores than those in the non-sarcopenia group (SARC-F < 4) after adjusting for the same variables (Fig. 1).

3.3. Association of SARC-F with prognosis

The median follow-up period was 323 days (IQR: 98–669 days), and during the follow-up period, all-cause death or CVD rehospitalization occurred in 40 and 78 cases, respectively. Additionally, 100 events occurred with the composite outcome, i.e., all-cause death or CVD rehospitalization, and the incidence rate of the composite events was 21.2/100 person-years. Fig. 2 shows Kaplan–Meier survival curves for composite outcome events in the sarcopenia and non-sarcopenia groups. Individuals in the sarcopenia group had a worse prognosis than those in the non-sarcopenia group ($\chi^2 = 5.62$; log-rank test, $P = 0.018$).

Table 3 shows the univariate and multivariate Cox regression analyses of the composite outcome and results of the Poisson regression analysis when the outcome was the number of CVD readmissions. The results of the univariate analysis indicated that the HR for the SARC-F score was 1.156 (95 % CI: 1.055–1.265, $P = 0.002$), suggesting that a higher SARC-F score was a predictor of poorer prognosis in patients with CVD. Additionally, the HR of the sarcopenia group was 1.620 (95 % CI: 1.078–2.434, $P = 0.021$), indicating poorer prognosis than that of the non-sarcopenia group. After adjusting for age, sex, BMI, LVEF, hemoglobin, albumin, prior HF, and renal dysfunction in the multivariate analysis, the HR for the SARC-F score was 1.125 (95 % CI: 1.019–1.242, $P = 0.020$), and the HR of the sarcopenia group was 1.574 (95 % CI:

Table 1
Patient characteristics.

	Overall	Non-sarcopenia (SARC-F < 4)	Sarcopenia (SARC-F ≥ 4)	*P*-value
	n = 408	n = 275; 67.4 %	n = 133; 32.6 %	
Age [years]	78 [73–84]	77 [72–82]	81 [77–86]	<0.001
Male, n (%)	267 (65.4)	188 (68.4)	79 (59.4)	0.094
BMI [kg/m^2]	21.4 [19.1–23.7]	21.3 [19.3–23.5]	21.6 [18.8–24.1]	0.934
Underweight (BMI < 18.5 kg/m^2), n (%)	79 (19.4)	51 (18.5)	28 (21.1)	0.548
Normal (BMI 18.5–24.9 kg/m^2), n (%)	265 (65.0)	183 (66.5)	82 (61.7)	0.332
Obese (BMI ≥ 25.0 kg/m^2), n (%)	64 (15.7)	41 (14.9)	23 (17.3)	0.535
Heart rate [beats/min]	75 [64–86]	75 [66–86]	76 [64–88]	0.511
Systolic blood pressure [mm Hg]	116 [105–129]	117 [107–128]	114 [100−130]	0.170
Diastolic blood pressure [mm Hg]	65 [57–74]	66 [57–74]	65 [56–74]	0.511
Diagnosis, n (%)				
Heart failure	193 (52.7)	120 (43.6)	73 (54.9)	0.035
Acute coronary syndrome	65 (15.9)	47 (17.1)	18 (13.5)	0.390
Aortic disease	58 (14.2)	44 (16.0)	14 (10.5)	0.173
Others	92 (22.5)	64 (23.3)	28 (21.1)	0.705
LVEF [%]	56.1 [42.0–66.0]	56.7 [44.0–66.6]	51.0 [36.0–65.0]	0.029
Comorbidities				
Hypertension, n (%)	287 (70.3)	197 (71.6)	90 (67.7)	0.480
Dyslipidemia, n (%)	134 (32.8)	89 (32.4)	45 (33.8)	0.854
Diabetes mellitus, n (%)	151 (37.0)	99 (36.0)	52 (39.1)	0.618
Renal dysfunction, n (%)	331 (81.1)	220 (80.0)	111 (83.5)	0.483
Prior heart failure, n (%)	103 (25.2)	62 (22.5)	41 (30.8)	0.092
Prior myocardial infarction, n (%)	55 (13.5)	41 (14.9)	14 (30.8)	0.289
Current smoker, n (%)	178 (38.0)	82 (34.2)	96 (41.9)	0.102
Medications				
Beta blocker, n (%)	293 (71.8)	200 (72.7)	93 (69.9)	0.637
ACE inhibitor or ARB, n (%)	278 (68.1)	186 (67.6)	92 (69.2)	0.821
Statin, n (%)	198 (48.5)	133 (48.4)	65 (48.9)	0.999
Laboratory examination				
Albumin [g/dL]	3.4 [3.0–3.9]	3.5 [3.1–3.9]	3.4 [2.9–3.7]	0.003
Hemoglobin [g/dL]	11.0 [9.8–12.7]	11.2 [9.8–12.8]	10.8 [9.7–12.5]	0.327
eGFR [mL/min/1.73 m^2]	43.0 [31.0–58.2]	46.0 [33.0–60.0]	37.0 [25.0–56.0]	0.010
Physical function				
Handgrip strength [kg]	20.9 [15.6–25.3]	22.0 [17.1–26.4]	18.5 [13.4–22.4]	<0.001
Leg strength [% BM]	34.1 [26.0–42.7]	36.4 [29.6–45.6]	27.8 [22.5–35.1]	<0.001
Usual gait speed [m/s]	0.9 [0.7–1.1]	1.0 [0.8–1.2]	0.7 [0.5–0.8]	<0.001
6-minute walking distance [m]	280 [192–360]	329 [245–392]	193 [114–245]	<0.001
SPPB [point]	10 [8–12]	11 [10−12]	8 [6–10]	<0.001
SF-36PF [point]	65 [40–85]	80 [55–90]	40 [20–55]	<0.001
SARC-F	2 [1–4]	2 [1–2]	5 [4–6]	<0.001
Strength				<0.001
None (0)	144 (35.3)	132 (48.0)	12 (9.0)	
Some (1)	166 (40.7)	116 (42.2)	50 (37.6)	
A lot or unable (2)	98 (24.0)	27 (9.8)	71.0 (53.4)	
Assistance in walking				<0.001
None (0)	301 (73.8)	256 (93.1)	45 (33.8)	
Some (1)	79 (19.4)	17 (6.2)	62 (46.6)	
A lot, use aids or unable (2)	28 (6.9)	2 (0.7)	26 (19.5)	
Rise from a chair				<0.001
None (0)	283 (69.4)	239 (86.9)	44 (33.1)	
Some (1)	107 (26.2)	36 (13.1)	71 (53.4)	
A lot or unable without help (2)	18 (4.4)	0 (0.0)	18.0 (13.5)	
Climb stairs				<0.001
None (0)	166 (40.7)	158 (57.5)	8 (6.0)	
Some (1)	165 (40.4)	99 (36.0)	66 (49.6)	
A lot or unable (2)	77 (18.9)	18 (6.5)	59 (44.4)	
Falls				<0.001
None (0)	285 (69.9)	222 (80.7)	63 (47.5)	
1–3 falls (1)	108 (26.5)	50 (18.2)	58 (43.6)	
≥4 falls (2)	15 (3.7)	3 (1.1)	12 (9.0)	
Mini-Cog [points]	2 [1–2]	2 [1–2]	2 [1–2]	0.565
Zero point, n (%)	82 (20.1)	53 (19.3)	29 (21.8)	0.769
One point, n (%)	119 (29.7)	81 (29.5)	40 (30.1)	
Two points, n (%)	205 (50.2)	141 (51.3)	64 (48.1)	
All-cause death, n (%)	40 (9.8)	23 (8.4)	17 (12.8)	0.159
CVD rehospitalization, n (%)	78 (19.1)	46 (16.7)	32 (24.1)	0.077

BMI, body mass index; LVEF, left ventricular ejection fraction; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; BM, body mass; SPPB, short physical performance battery; SF-36PF, the 36-item Short-Form Health Survey Physical Functioning; CVD, cardiovascular disease.
Median [interquartile range]; n, number (%).

1.011–2.445, $P = 0.044$) compared with the non-sarcopenia group. The IRR for the number of CVD readmissions of the SARC-F scores was 1.191 (95 % CI: 1.100–1.289, $P < 0.001$), and in the sarcopenia group, it was 1.950 (95 % CI: 1.378–2.760, $P < 0.001$). After adjusting for the same variables, the IRR of the SARC-F scores was 1.171 (95 % CI: 1.073–1.279, $P < 0.001$). The IRR of the sarcopenia group was also 1.911 (95 % CI: 1.312–2.782, $P < 0.001$) compared with the non-sarcopenia group. A high SARC-F score was associated with rehospitalization and poor prognosis in patients with CVD and cognitive impairment.

4. Discussion

This is the first study to investigate the association between sarcopenia assessed using SARC-F and motor function, QOL, and prognosis in patients with CVD and cognitive impairment. We found that among patients with CVD and cognitive impairment, approximately 33 % had sarcopenia (SARC-F ≥ 4). We also found that sarcopenia was associated with: (1) poor motor function and QOL; (2) higher rates of composite events, such as all-cause death and CVD readmissions; and (3) an increased number of readmissions after discharge. These findings underscore the importance of the SARC-F questionnaire in the evaluation of motor function and prognosis in patients with CVD and cognitive dysfunction.

Many studies have reported the usefulness of SARC-F in older and chronic patients (Kim et al., 2018; Malmstrom et al., 2016; Parra-Rodríguez et al., 2016; Tanaka et al., 2018; Tanaka et al., 2017; Woo et al., 2014). While the population is aging and more people are living with an increased incidence of mild cognitive impairment or dementia

Table 2
Associations of SARC-F score with motor function tests and quality of life.

Effect	Handgrip strength				Leg strength				Gait speed			
	B coefficient	β	t value	*P*-value	B coefficient	β	t value	*P*-value	B coefficient	β	t value	*P*-value
SARC-F score	−0.582	−0.171	−4.853	<0.001	−1.957	−0.311	−6.884	<0.001	−0.067	−0.467	−11.704	<0.001
Age	−0.164	−0.172	−4.740	<0.001	−0.199	−0.113	−2.379	0.018	−0.010	−0.235	−5.753	<0.001
Sex (male)	8.834	0.606	17.335	<0.001	3.927	0.146	3.222	0.001	0.065	0.103	2.662	0.008
Body mass index	0.167	0.085	2.433	0.015	−0.288	−0.080	−1.733	0.084	0.001	0.001	0.329	0.743
LVEF	0.008	0.019	0.488	0.626	−0.052	−0.067	−1.269	0.206	−0.000	−0.035	−0.769	0.443
Hemoglobin	0.449	0.129	3.479	<0.001	0.258	0.041	0.833	0.405	0.004	0.027	0.591	0.555
Albumin	1.440	0.130	3.566	<0.001	5.492	0.247	5.666	<0.001	0.064	0.131	3.275	0.001
Prior heart failure	0.362	0.023	0.652	0.515	2.318	0.077	1.740	0.083	−0.004	−0.015	−0.155	0.877
Renal dysfunction	0.863	0.055	1.479	0.140	−1.710	−0.053	−1.202	0.230	−0.055	−0.078	−1.987	0.048

Effect	6-minute walking distance				Short physical performance battery				SF-36-PF			
	B coefficient	β	t value	*P*-value	B coefficient	β	t value	*P*-value	B coefficient	β	t value	*P*-value
SARC-F score	−28.180	−0.489	−13.053	<0.001	−0.678	−0.515	−12.689	<0.001	−7.401	−0.537	−13.032	<0.001
Age	−3.944	−0.241	−6.318	<0.001	−0.073	−0.198	−4.696	<0.001	−0.482	−0.126	−2.879	0.004
Sex (male)	29.756	0.119	3.238	0.001	0.227	0.040	0.993	0.321	5.929	0.100	2.436	0.015
Body mass index	−1.974	−0.056	−1.576	0.116	0.051	0.067	1.647	0.100	−0.972	−0.125	−2.904	0.004
LVEF	0.126	0.012	0.437	0.063	−0.001	−0.007	−0.096	0.924	0.126	0.074	1.663	0.097
Hemoglobin	5.011	0.087	2.149	0.032	0.069	0.052	1.212	0.226	0.335	0.024	0.544	0.587
Albumin	29.933	0.162	4.074	<0.001	0.673	0.157	3.712	<0.001	0.642	0.013	0.332	0.740
Prior heart failure	−8.976	−0.031	−0.887	0.375	0.213	0.035	0.853	0.394	−3.637	−0.057	−1.360	0.175
Renal dysfunction	−23.544	−0.086	−2.238	0.026	0.043	0.006	0.164	0.870	0.929	0.012	0.331	0.741

β, standardized regression coefficient; LVEF, left ventricular ejection fraction; SF-36PF, the 36-item Short-Form Health Survey Physical Functioning.

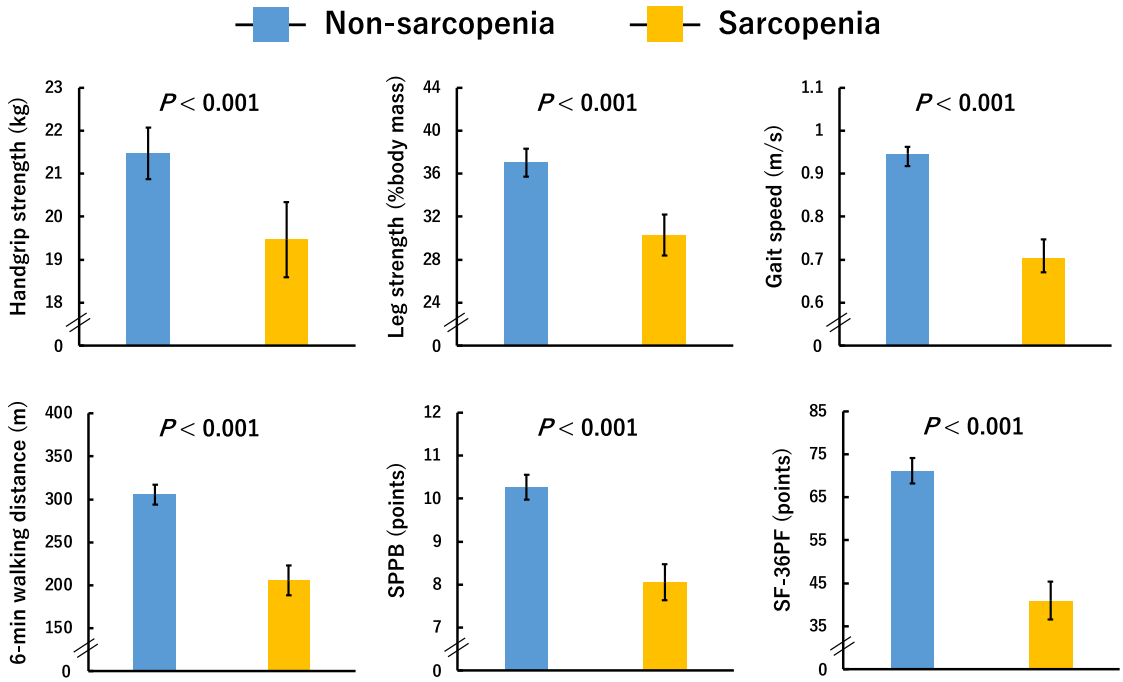

Fig. 1. Multiple linear regression models of sarcopenia (SARC-F ≥ 4) with motor function tests (handgrip strength, leg strength, gait speed, and 6-min walking distance, SPPB) and quality of life (SF-36PF). Estimated mean values with 95 % confident interval of motor function tests and quality of life in multiple regression models were adjusted for age, sex, body mass index, left ventricular ejection fraction, hemoglobin, albumin, prior heart failure, and renal dysfunction. SPPB, short physical performance battery; SF-36PF, the 36-item Short-Form Health Survey Physical Functioning.

(Jia et al., 2020), no studies have assessed whether SARC-F predicts physical function or prognosis in CVD patients with cognitive impairment. Some studies have found that patients with sarcopenia are more likely to have cognitive impairment (Ida et al., 2017; Peng et al., 2020). Furthermore, older patients with HF who had both cognitive and physical dysfunction had a poorer prognosis than those with just one of them (Matsue et al., 2020; Yamamoto et al., 2022). Therefore, early assessment and intervention for sarcopenia are essential especially in patients with cognitive impairment. In our study, 32.6 % of all participants had sarcopenia, and those with lower Mini-Cog scores (i.e., more severe cognitive impairment) had a higher prevalence of sarcopenia. Thus, it is important to assess sarcopenia even in patients with cognitive dysfunction; the SARC-F questionnaire might be useful to assess sarcopenia in patients with CVD and cognitive impairment.

Several studies have investigated the association between the SARC-F scores and motor functions in community-dwelling older adults and

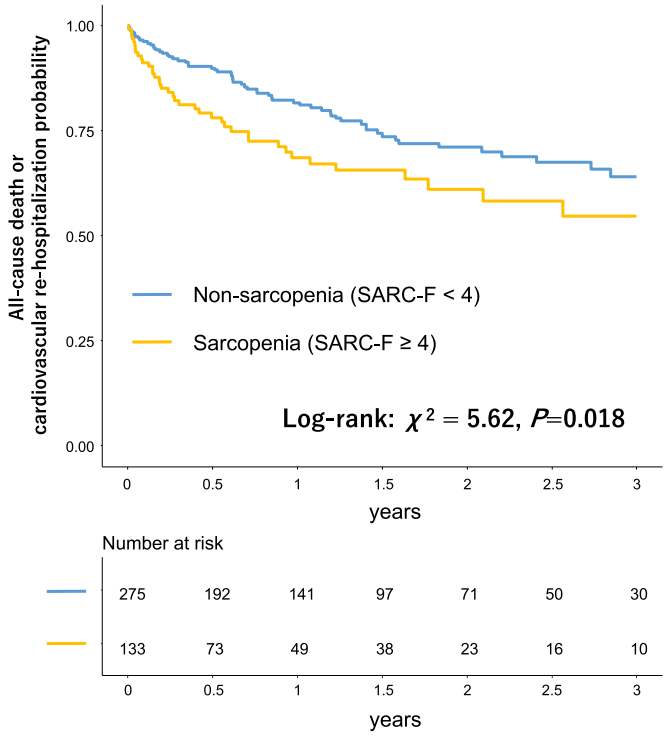

Fig. 2. Kaplan–Meier curves for all-cause death and cardiovascular rehospitalization events stratified by SARC-F.

patients with chronic diseases and found that SARC-F scores is strongly associated with physical functions such as muscle strength, walking speed, balance function, and 6 MWD (Ha et al., 2020; Ida et al., 2019; Malmstrom et al., 2016; Parra-Rodríguez et al., 2016; Tanaka et al., 2018; Tanaka et al., 2017). The present study showed that SARC-F can predict motor function decline in older patients with CVD and cognitive impairment. Additionally, in this study, higher SARC-F scores were associated with lower QOL in older patients with CVD. These results indicate that SARC-F is not only a simple assessment of physical dysfunction or sarcopenia but is also a predictor of patients' daily QOL.

Sarcopenia assessed by SARC-F was associated with all-cause mortality and emergency CVD rehospitalization events. Previous studies have found that SARC-F is associated with higher in-hospital mortality in older patients and higher short-term mortality in patients with CVD (Tanaka et al., 2018; Ueshima et al., 2021). This study shows that SARC-F can be used to predict the long-term prognosis of cognitively-impaired patients with CVD. Additionally, this study examined the association between SARC-F and the number of emergency CVD readmissions after discharge in patients with CVD. Individuals in the sarcopenia group had a significantly increased risk of readmission. Patients with CVD having cognitive impairment face more difficulties with self-management, which limits at-home care (Lee et al., 2013). Therefore, they have a higher risk of rehospitalization than patients without cognitive impairment (Adachi et al., 2022). These results show that SARC-F should be used as a screening tool to predict rehospitalization risk and life expectancy in older patients with CVD and cognitive impairment at the time of hospitalization.

Differences in the type of cognitive function may explain why the SARC-F questionnaire's relationship with motor function tests and prognosis were correctly reflected, even in patients with more severe cognitive impairments. Memory impairment in patients with dementia has recently been reported to result in short-term and episodic memory loss, which is evident in the performance of a task at present, i.e. when going somewhere or doing something (Duff et al., 2020; Ogoh et al., 2019). Despite this, they tend to maintain procedural memory, such as the things one has done in their life for a long time or their lifestyle (Duff et al., 2020; Ogoh et al., 2019). Additionally, several studies have shown that the QOL of individuals with cognitive impairment is lower than that of individuals without cognitive impairment (Banerjee et al., 2006; Missotten et al., 2008; Pressler et al., 2010). These findings indicate that even those with cognitive impairment or dementia might experience anxiety and difficulty in performing their daily activities, such as walking, climbing stairs, and standing up. We believe that SARC-F is related to motor function and sarcopenia because these feelings are reflected in the responses to the SARC-F questionnaire.

This study had several limitations. First, because this was a retrospective single-center study and included only Asian patients with CVD, further studies in other populations that account for racial and regional differences are needed. In addition, some patients who were rehospitalized in other hospitals or died might have been censored. We could not find this information. Second, data on medications prescribed at the time of discharge and the start and duration of these medications were unknown. Third, this study used Mini-Cog scores to assess cognitive function, which does not cover a wide variety of cognitive functions. Therefore, differences in the type of dementia (e.g., Alzheimer's or Lewy bodies) may have affected the results. Fourth, this study may not have included patients with severe dementia or cognitive dysfunction because we excluded patients who were not able to complete SARC-F. Finally, sarcopenia was not diagnosed, and muscle mass was not assessed.

5. Conclusions and implications

In older patients with CVD and cognitive impairment, the SARC-F questionnaire was associated with decreased motor function and QOL related to physical functioning. Additionally, sarcopenia assessed using

Table 3
Hazard ratio for all-cause death and cardiovascular rehospitalization, and incidence rate ratio for the number of cardiovascular rehospitalization events.

	Unadjusted			Adjusted		
	HR	95 % CI	*P*-value	HR	95 % CI	*P*-value
All-cause death and cardiovascular rehospitalization events						
SARC-F (continuous)	1.156	1.055–1.265	0.002	1.125	1.019–1.242	0.020
SARC-F ≥ 4 (vs. SARC-F < 4)	1.620	1.078–2.434	0.021	1.574	1.011–2.445	0.044

	Unadjusted			Adjusted		
	IRR	95 % CI	*P*-value	IRR	95 % CI	*P*-value
Number of cardiovascular rehospitalization events						
SARC-F (continuous)	1.191	1.100–1.289	<0.001	1.171	1.073–1.279	<0.001
SARC-F ≥ 4 (vs. SARC-F < 4)	1.950	1.378–2.760	<0.001	1.911	1.312–2.782	<0.001

Adjusted for age, sex, body mass index, left ventricular ejection fraction, hemoglobin, serum albumin, prior heart failure, and renal dysfunction.
HR, hazard ratio; CI, confidence interval; IRR, incidence rate ratio.

SARC-F $\geq$ 4 was related to a higher risk of death and readmission after discharge. These results indicate that SARC-F is a simple and inexpensive predictor of physical dysfunction, lower QOL, and worse prognosis in patients with CVD and cognitive dysfunction.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2022.112021.

CRediT authorship contribution statement

All gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

Takumi Noda: Conceptualization, Methodology, Software, Formal analysis, Writing - Original draft, and Visualization.
Kentaro Kamiya: Conceptualization, Methodology, Validation, Writing - Original draft, Visualization, Project administration, and Funding acquisition.
Nobuaki Hamazaki: Validation, Investigation, Resources, Data curation, and Writing - Review & editing.
Kohei Nozaki: Investigation and Resources.
Takafumi Ichikawa: Investigation, and Resources.
Masashi Yamashita: Software, Formal analysis, and Data curation.
Shota Uchida: Software, Formal analysis, and Data curation.
Kensuke Ueno: Software, Formal analysis, and Data curation.
Emi Maekawa: Investigation and Resources.
Tasuku Terada: Methodology and Writing - Original draft.
Jennifer L. Reed: Methodology, Validation, and Writing - Review & editing.
Minako Yamaoka-Tojo: Methodology, Validation, and Writing - Review & editing.
Atsuhiko Matsunaga: Conceptualization, Validation, and Writing - Review & editing.
Junya Ako: Conceptualization, Writing - Review & editing, Supervision, and Project administration.

Conflict of interest

The authors have no conflicts of interest directly relevant to the content of this article. Although Mr. Yamashita has no conflict of interest related to the conduct of this study, he holds company stock (less than 5% of the total) and receives a salary as one of the directors of an employer.

Acknowledgments

The authors certify that they comply with the ethical guidelines for authorship and publishing. The authors thank all the collaborators from our teams at Kitasato University Hospital for their clinical work.

Funding

This study was partially supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI (grant number: 21H03309).

References

Adachi, T., Tsunekawa, Y., Tanimura, D., 2022. Association among mild cognitive impairment, social frailty, and clinical events in elderly patients with cardiovascular disease. Heart Lung 55, 82–88.
Ando, Y., Ito, S., Uemura, O., Kato, T., Kimura, G., Nakao, T., Hattori, M., Fukagawa, M., Horio, M., Mitarai, T., 2009. CKD clinical practice guidebook. The essence of treatment for CKD patients. Clin. Exp. Nephrol. 13, 191–248.
Aprahamian, I., Cipolli, G.C., Yassuda, M.S., 2020. Sarcopenia and cognitive impairment: possible physiopathological causation or just a spurious association? Clin. Nutr. 39, 1622.
Banerjee, S., Smith, S., Lamping, D., Harwood, R., Foley, B., Smith, P., Murray, J., Prince, M., Levin, E., Mann, A., 2006. Quality of life in dementia: more than just cognition. An analysis of associations with quality of life in dementia. J. Neurol. Neurosurg. Psychiatry 77, 146–148.
Bauer, J., Morley, J.E., Schols, A., Ferrucci, L., Cruz-Jentoft, A.J., Dent, E., Baracos, V.E., Crawford, J.A., Doehner, W., Heymsfield, S.B., Jatoi, A., Kalantar-Zadeh, K., Lainscak, M., Landi, F., Laviano, A., Mancuso, M., Muscaritoli, M., Prado, C.M., Strasser, F., von Haehling, S., Coats, A.J.S., Anker, S.D., 2019. Sarcopenia: a time for action. An SCWD position paper. J. Cachexia. Sarcopenia Muscle 10, 956–961.
Borson, S., Scanlan, J., Brush, M., Vitaliano, P., Dokmak, A., 2000. The mini-cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. Int. J. Geriatr. Psychiatry 15, 1021–1027.
de Fátima Ribeiro Silva, C., Ohara, D.G., Matos, A.P., Pinto, A., Pegorari, M.S., 2021. Short physical performance battery as a measure of physical performance and mortality predictor in older adults: a comprehensive literature review. Int. J. Environ. Res. Public Health 18.
Duff, M.C., Covington, N.V., Hilverman, C., Cohen, N.J., 2020. Semantic memory and the hippocampus: revisiting, reaffirming, and extending the reach of their critical relationship. Front. Hum. Neurosci. 13, 471.
Guralnik, J.M., Simonsick, E.M., Ferrucci, L., Glynn, R.J., Berkman, L.F., Blazer, D.G., Scherr, P.A., Wallace, R.B., 1994. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J. Gerontol. 49, M85–M94.
Ha, Y.-C., Won, C.W., Kim, M., Chun, K.-J., Yoo, J.-I., 2020. SARC-F as a useful tool for screening sarcopenia in elderly patients with hip fractures. J. Nutr. Health Aging 24, 78–82.
Iadecola, C., Duering, M., Hachinski, V., Joutel, A., Pendlebury, S.T., Schneider, J.A., Dichgans, M., 2019. Vascular cognitive impairment and dementia: JACC scientific expert panel. J. Am. Coll. Cardiol. 73, 3326–3344.
Ida, S., Kojima, Y., Hamaoka, S., Urawa, N., Araki, J., Kaneko, R., Murata, K., 2019. Validity of japanese version of SARC-F questionnaire in patients with chronic liver disease. J. Gastroenterol. Hepatol. 34, 947–953.
Ida, S., Nakai, M., Ito, S., Ishihara, Y., Imataka, K., Uchida, A., Monguchi, K., Kaneko, R., Fujiwara, R., Takahashi, H., 2017. Association between sarcopenia and mild cognitive impairment using the Japanese version of the SARC-F in elderly patients with diabetes. J. Am. Med. Dir. Assoc. 18, 809 e809-809. e813.
Jia, L., Du, Y., Chu, L., Zhang, Z., Li, F., Lyu, D., Li, Y., Li, Y., Zhu, M., Jiao, H., Song, Y., Shi, Y., Zhang, H., Gong, M., Wei, C., Tang, Y., Fang, B., Guo, D., Wang, F., Zhou, A., Chu, C., Zuo, X., Yu, Y., Yuan, Q., Wang, W., Li, F., Shi, S., Yang, H., Zhou, C., Liao, Z., Lv, Y., Li, Y., Kan, M., Zhao, H., Wang, S., Yang, S., Li, H., Liu, Z., Wang, Q., Qin, W., Jia, J., 2020. Prevalence, risk factors, and management of dementia and mild cognitive impairment in adults aged 60 years or older in China: a cross-sectional study. Lancet Public Health 5, e661–e671.
Kamiya, K., Hamazaki, N., Matsuzawa, R., Nozaki, K., Tanaka, S., Ichinosawa, Y., Maekawa, E., Noda, C., Yamaoka-Tojo, M., Matsunaga, A., 2017. Sarcopenia: prevalence and prognostic implications in elderly patients with cardiovascular disease. JCSM Clin. Rep. 2, 1–13.
Kim, S., Kim, M., Won, C.W., 2018. Validation of the Korean version of the SARC-F questionnaire to assess sarcopenia: Korean frailty and aging cohort study. J. Am. Med. Dir. Assoc. 19, 40–45 e41.
<collab>Laboratories, A.C.o.P.S.f.C.P.F</collab>, 2002. ATS statement: guidelines for the six-minute walk test. Am. J. Respir. Crit. Care Med. 166, 111–117.
Lee, C.S., Gelow, J.M., Bidwell, J.T., Mudd, J.O., Green, J.K., Jurgens, C.Y., Woodruff-Pak, D.S., 2013. Blunted responses to heart failure symptoms in adults with mild cognitive dysfunction. J. Cardiovasc. Nurs. 28, 534–540.
Malmstrom, T.K., Miller, D.K., Simonsick, E.M., Ferrucci, L., Morley, J.E., 2016. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J. Cachexia. Sarcopenia Muscle 7, 28–36.
Malmstrom, T.K., Morley, J.E., 2013. SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. J. Am. Med. Dir. Assoc. 14, 531–532.
Matsue, Y., Kamiya, K., Saito, H., Saito, K., Ogasahara, Y., Maekawa, E., Konishi, M., Kitai, T., Iwata, K., Jujo, K., Wada, H., Kasai, T., Nagamatsu, H., Ozawa, T., Izawa, K., Yamamoto, S., Aizawa, N., Yonezawa, R., Oka, K., Momomura, S.I., Kagiyama, N., 2020. Prevalence and prognostic impact of the coexistence of multiple frailty domains in elderly patients with heart failure: the FRAGILE-HF cohort study. Eur. J. Heart Fail. 22, 2112–2119.
Missotten, P., Squelard, G., Ylieff, M., Di Notte, D., Paquay, L., De Lepeleire, J., Buntinx, F., Fontaine, O., 2008. Relationship between quality of life and cognitive decline in dementia. Dement. Geriatr. Cogn. Disord. 25, 564–572.
Ogoh, S., Hashimoto, T., Ando, S., 2019. Does Exercise Improve False Episodic Memory in Dementia? Multidisciplinary Digital Publishing Institute.
Onor, M.L., Trevisiol, M., Negro, C., Aguglia, E., 2006. Different perception of cognitive impairment, behavioral disturbances, and functional disabilities between persons with mild cognitive impairment and mild Alzheimer's disease and their caregivers. Am. J. Alzheimers Dis. Other Dement. 21, 333–338.
<collab>Organization, W.H</collab>, 2000. The Asia-Pacific Perspective: Redefining Obesity and its Treatment.
Parra-Rodríguez, L., Szlejf, C., García-González, A.I., Malmstrom, T.K., Cruz-Arenas, E., Rosas-Carrasco, O., 2016. Cross-cultural adaptation and validation of the Spanish-language version of the SARC-F to assess sarcopenia in Mexican community-dwelling older adults. J. Am. Med. Dir. Assoc. 17, 1142–1146.
Peng, T.C., Chen, W.L., Wu, L.W., Chang, Y.W., Kao, T.W., 2020. Sarcopenia and cognitive impairment: a systematic review and meta-analysis. Clin. Nutr. 39, 2695–2701.
Pressler, S.J., Subramanian, U., Kareken, D., Perkins, S.M., Gradus-Pizlo, I., Sauvé, M.J., Ding, Y., Kim, J., Sloan, R., Jaynes, H., 2010. Cognitive deficits and health-related quality of life in chronic heart failure. J. Cardiovasc. Nurs. 25, 189.
Rizzoli, R., Reginster, J.Y., Arnal, J.F., Bautmans, I., Beaudart, C., Bischoff-Ferrari, H., Biver, E., Boonen, S., Brandi, M.L., Chines, A., Cooper, C., Epstein, S., Fielding, R.A., Goodpaster, B., Kanis, J.A., Kaufman, J.M., Laslop, A., Malafarina, V., Mañas, L.R.,

Mitlak, B.H., Oreffo, R.O., Petermans, J., Reid, K., Rolland, Y., Sayer, A.A., Tsouderos, Y., Visser, M., Bruyère, O., 2013. Quality of life in sarcopenia and frailty. Calcif. Tissue Int. 93, 101–120.
Roberts, H.C., Denison, H.J., Martin, H.J., Patel, H.P., Syddall, H., Cooper, C., Sayer, A. A., 2011. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing 40, 423–429.
Sasaki, K.I., Fukumoto, Y., 2022. Sarcopenia as a comorbidity of cardiovascular disease. J. Cardiol. 79, 596–604.
Tanaka, S., Kamiya, K., Hamazaki, N., Matsuzawa, R., Nozaki, K., Ichinosawa, Y., Harada, M., Nakamura, T., Maekawa, E., Noda, C., 2018. SARC-F questionnaire identifies physical limitations and predicts post discharge outcomes in elderly patients with cardiovascular disease. JCSM Clin. Rep. 3, 1–11.
Tanaka, S., Kamiya, K., Hamazaki, N., Matsuzawa, R., Nozaki, K., Maekawa, E., Noda, C., Yamaoka-Tojo, M., Matsunaga, A., Masuda, T., Ako, J., 2017. Utility of SARC-F for assessing physical function in elderly patients with cardiovascular disease. J. Am. Med. Dir. Assoc. 18, 176–181.
Ueshima, J., Maeda, K., Ishida, Y., Shimizu, A., Inoue, T., Nonogaki, T., Matsuyama, R., Yamanaka, Y., Mori, N., 2021. SARC-F predicts mortality risk of older adults during hospitalization. J. Nutr. Health Aging 25, 914–920.
Ware, J.E., 1993. SF-36 Health Survey : Manual and Interpretation Guide. Health Institute.
Woo, J., Leung, J., Morley, J.E., 2014. Validating the SARC-F: a suitable community screening tool for sarcopenia? J. Am. Med. Dir. Assoc. 15, 630–634.
Yamamoto, S., Yamasaki, S., Higuchi, S., Kamiya, K., Saito, H., Saito, K., Ogasahara, Y., Maekawa, E., Konishi, M., Kitai, T., 2022. Prevalence and prognostic impact of cognitive frailty in elderly patients with heart failure: sub-analysis of FRAGILE-HF. ESC Heart Failure 9, 1574–1583.
Yasuda, T., Nakajima, T., Sawaguchi, T., Nozawa, N., Arakawa, T., Takahashi, R., Mizushima, Y., Katayanagi, S., Matsumoto, K., Toyoda, S., Inoue, T., 2017. Short physical performance battery for cardiovascular disease inpatients: implications for critical factors and sarcopenia. Sci. Rep. 7, 17425.
Zhang, Z., 2016. Multiple imputation with multivariate imputation by chained equation (MICE) package. Ann. Transl. Med. 4, 30.