

SARC-F questionnaire identifies physical limitations and predicts post discharge outcomes in elderly patients with cardiovascular disease

Shinya Tanaka¹, Kentaro Kamiya², Nobuaki Hamazaki^{1,3}, Ryota Matsuzawa³, Kohei Nozaki³, Yuta Ichinosawa⁴, Manae Harada⁴, Takeshi Nakamura⁴, Emi Maekawa⁵, Chiharu Noda⁵, Minako Yamaoka-Tojo^{1,2}, Atsuhiko Matsunaga^{1,2}, Takashi Masuda^{1,2}, Junya Ako^{1,5}

1 Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kitasato University, Sagamihara, Japan; **2** Department of Rehabilitation, School of Allied Health Sciences, Kitasato University, Sagamihara, Japan; **3** Department of Rehabilitation, Kitasato University Hospital, Sagamihara, Japan; **4** Department of Rehabilitation Sciences, Graduate School of Medical Sciences, Kitasato University, Sagamihara, Japan; **5** Department of Cardiovascular Medicine, Kitasato University School of Medicine, Sagamihara, Japan

Abstract

Background A simple and inexpensive sarcopenia screening tool would be beneficial in clinical practice. This study was performed to determine whether SARC-F questionnaire can be used to identify physical limitations and poor prognosis in elderly cardiovascular disease (CVD) patients.

Methods and results The study population consisted of 257 Japanese patients ≥ 65 years old admitted to our hospital for CVD. Prior to discharge from hospital, SARC-F, handgrip strength, usual gait speed, short physical performance battery score, and 6-minute walking distance were measured in all patients. The patients were divided into two groups according to SARC-F score: SARC-F < 4 and SARC-F ≥ 4 . The study endpoint was the first occurrence of all-cause emergency readmission or all-cause mortality. The prevalence rate of SARC-F ≥ 4 was 26.8%, and increased with age and number of comorbidities. Even after adjusting for covariates, physical function was significantly poorer and the risks of physical function measurements below the critical cut-off values were higher in the SARC-F ≥ 4 group compared to the SARC-F < 4 group. Sixty (23.3%) patients were readmitted and 17 (6.6%) died over a median follow-up period of 11 months (interquartile range: 6–13 months). SARC-F score was a significant predictor of adverse events after discharge. Patients with SARC-F ≥ 4 showed higher event risk than those with SARC-F < 4 (adjusted hazard ratio: 1.78; 95% confidence interval: 1.03–3.07; $P = 0.040$).

Conclusions SARC-F questionnaire is useful to identify patients at high risk of physical limitations and to predict post-discharge outcomes in elderly CVD patients.

Address for correspondence: Kentaro Kamiya, Department of Rehabilitation, School of Allied Health Sciences, Kitasato University, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa, 252-0373 Japan, Tel: +81-42-778-8111; Fax: +81-42-778-9686, E-mail: k-kamiya@kitasato-u.ac.jp

Keywords: Sarcopenia, Physical function, Prognosis, Cardiovascular disease

Received 30 November 2017 Accepted 15 January 2018

Introduction

Sarcopenia is a syndrome characterized by age-related loss of skeletal muscle mass and physical function, which is responsible for frailty, disability, falls, and poor prognosis [1-3]. The incidence of sarcopenia will most likely increase over the next 40 years due to the aging of the world's population [1], as its prevalence rate is known to increase with age [4]. In addition to increased risk of cardiovascular disease (CVD) in the community-dwelling elderly population [5], sarcopenia was also reported to be related to adverse outcomes in elderly patients with CVD [6-8]. Sarcopenia is now recognized as a distinct disease entity with its own

ICD-10-CM code (M62.84) [9], and sarcopenia in the elderly is becoming an increasingly important issue in cardiovascular medicine [10,11].

SARC-F questionnaire is a screening tool used for rapid assessment of sarcopenia status, which does not require special measurements or equipment [12,13]. The performance of this questionnaire in identifying elderly people with impaired physical function and sarcopenia was reported to be comparable to more rigorous tests [14-17], and it showed good predictive capabilities for physical limitations and mortality in the community-dwelling elderly population [18-21]. Previously, we reported that SARC-F was a useful screening tool for impaired physical function in

hospitalized elderly CVD patients [22]. Despite the strong predictive capability of physical functional impairment for readmission and mortality [23-25], there have been no previous studies regarding the prognostic value of SARC-F in elderly CVD patients. The present study was therefore performed to determine whether SARC-F can be used to identify physical limitations and predict poor prognosis in elderly CVD patients.

Methods

This study involved a retrospective review of 257 consecutive Japanese patients ≥ 65 years old admitted to the Cardiovascular Center, Kitasato University Hospital, for CVD that were examined by SARC-F and evaluation of physical function between September 2015 and July 2016. Patients that were unable to walk were excluded from the study. The study protocol was approved by the Ethics Committee of Kitasato University Hospital, and informed consent was obtained from all patients.

The characteristics of the patients, including age, sex, body mass index (BMI), and clinical details of presentation (living status, comorbidities, and medication use), as well as demographic, echocardiographic, and biochemical data just prior to hospital discharge, along with information on adverse events after hospital discharge were recorded from electronic medical records. The estimated glomerular filtration rate (eGFR) was defined according to the Japanese Society of Nephrology formula: $194 \times (\text{serum creatinine})^{-1.094} \times (\text{age})^{0.287}$ for men and $194 \times (\text{serum creatinine})^{-1.094} \times (\text{age})^{0.287} \times 0.739$ for women [26].

Comorbidity score was calculated by assigning a value of 1 point to each of the following conditions: atrial fibrillation, diabetes, hypertension, dyslipidemia, chronic kidney disease (eGFR < 60 mL/min/1.73 m²), stroke, and anemia (hemoglobin < 13.0 g/dL for men and < 12.0 g/dL for women).

At the time of hospital discharge, the patients were asked to complete the SARC-F questionnaire, which has five components: strength, assistance in walking, rise from a chair, climb stairs, and falls (Table 1) [13]. The SARC-F scores ranged from 0 to 10, with 0 – 2 points for each component (0 = best to 10 = worst); patients with a total score of ≥ 4 were classified as having a risk of sarcopenia [15]. The original version of SARC-F was adapted for use in Japanese [22]. SARC-F has been shown to have good test-retest reliability [27], and high specificity but low sensitivity for classification of sarcopenia in older adults [15,18].

Physical function was evaluated and electrocardiographic data were monitored continuously via telemetry at discharge from hospital. Handgrip strength was measured using a digital dynamometer (TKK 5101 Grip-D; Takei, Tokyo, Japan) with the patient in the sitting position. data on two maximal isometric voluntary contractions of the hands for 3-s each with the

elbow joint fixed at 90° flexion were collected for both hands, and the greatest strength, expressed as absolute value (kg), was used in the analyses. The short physical performance battery (SPPB) consisting of three components (usual gait speed, repeated chair stands, standing balance) was measured according to the established methods [28]. SPPB scores ranged from 0 to 12, i.e., 0–4 points for each component (0 = worst to 12 = best). The 6-minute walking distance (6MWD) was determined according to the guidelines established by the American Thoracic Society [29]. Patients received standardized instructions to cover as much distance as possible within the allotted time, and were allowed to use assistive devices for the walking test.

The endpoint in this study was set as the first occurrence of all-cause emergency readmission or all-cause mortality, and the time to the endpoint was calculated as the number of days from the date of hospital discharge to the date of the event.

The results of normally distributed continuous variables are expressed as the means \pm standard deviation, and variables not normally distributed are presented as medians (interquartile range). Categorical variables are expressed as numbers and percentages. The patients were divided into two groups according to SARC-F score: SARC-F < 4 and SARC-F ≥ 4 [15]. The unpaired Student's *t* test, Mann–Whitney U test, and Fisher's exact test were used to compare the baseline patient characteristics and physical function between the two groups as appropriate. A number of physical function outcome measures at hospital discharge—i.e., low handgrip strength (< 26 kg for males and < 18 kg for females), slow gait speed (≤ 0.8 and ≤ 1.0 m/s), low SPPB score (≤ 8 points), and short 6MWD (< 300 and < 400 m)—were examined according to SARC-F score by logistic regression analyses with adjustment for age, sex, and BMI as potential confounders [30]. Adjusted odds ratios (ORs) are reported with corresponding 95% confidence intervals (95% CI). The endpoint of first occurrence of all-cause emergency readmission or death was evaluated using the Kaplan–Meier method and compared by the log-rank test. The relations between SARC-F score and adverse events after discharge were evaluated by Cox regression analyses with adjustment for age, sex, BMI, living status, and comorbidity score. Hazard ratios (HRs) are reported with corresponding 95% CI. Receiver-operating characteristic (ROC) curves for endpoint of first emergency readmission or death were used to compare the accuracy of adding physical function to SARC-F score to determine whether physical function complemented the predictive ability of the SARC-F score. The areas under the curves (AUCs) were compared according to the method of DeLong et al. [31]. Statistical analyses were performed using SPSS version 23.0 (IBM Corporation, Armonk, NY) and R version 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria). Two-tailed $P < 0.05$ was taken to indicate statistical significance.

Table 1 SARC-F score

Component	Question	Scoring
Strength	How much difficulty do you have in lifting and carrying 10 lb?	None = 0
		Some = 1
		A lot or unable = 2
Assistance in walking	How much difficulty do you have walking across a room?	None = 0
		Some = 1
		A lot, use aids, or unable = 2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None = 0
		Some = 1
		A lot or unable without help = 2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None = 0
		Some = 1
		A lot or unable = 2
Falls	How many times have you fallen in the past year?	None = 0
		1 – 3 falls = 1
		≥ 4 falls = 2

Results

Table 2 shows the baseline characteristics, SARC-F, and physical function of all patients and for groups stratified by SARC-F score. The gender distribution of the study population was 65.0% male/35.0% female, with a mean age of 75.8 ± 6.5 years, and 41.2% had heart failure, 36.2% had coronary artery disease, and 22.6% had other clinical entities. At discharge, beta-blockers were prescribed in 82.1% of cases, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in 75.1%, and statins in 69.3%. The median SARC-F score in the total patient population was 2, and 26.8% had SARC-F score ≥ 4 . Relative to patients with SARC-F < 4 , those with SARC-F ≥ 4 were older and had a higher prevalence of comorbidities. Physical function was consistently poorer in the SARC-F score ≥ 4 group, and this groups had significantly higher percentages of patients with low handgrip strength and SPPB score, slow gait speed, and short 6MWD than the SARC-F score < 4 group (Table 2). Table 3 shows the results of logistic regression analyses. SARC-F ≥ 4 showed an independent association with physical limitations. All components of SARC-F also showed significant associations with physical limitations.

In the present study, the prevalence rate of SARC-F ≥ 4 was 26.8% and increased significantly with age from 18.9% in patients 65–74 years old to 32.9% in those ≥ 75 years old ($P = 0.015$) (Figure 1). The prevalence rate of SARC-F ≥ 4 also increased with comorbidities from

17.5% in patients with none to two comorbidities, 27.7% in those with three to four comorbidities, and 37.9% in those with five to seven comorbidities (P trend = 0.007).

A total of 60 (23.3%) patients were readmitted to hospital and 17 (6.6%) died during a median follow-up period of 11 months (interquartile range: 6–13 months). The rates of adverse events were significantly higher in the SARC-F ≥ 4 group compared to the SARC-F < 4 group (log rank, $P = 0.009$) (Figure 2). SARC-F score was a significant and independent predictor of first emergency readmission or death in our study population, even after adjusting for age, sex, BMI, living status, and comorbidity score (Table 4). On multivariate Cox regression analysis, SARC-F ≥ 4 was shown to be associated with a 1.78-fold increase in risk of adverse events (95% CI: 1.03–3.07; $P = 0.040$). Furthermore, the relations between SARC-F score and endpoint of first occurrence of all-cause emergency readmission or death within 90 and 180 days after hospital discharge were examined. Even after adjusting for age, sex, BMI, living status, and comorbidity score, SARC-F score and SARC-F ≥ 4 showed similar associations with adverse events within 90 and 180 days after discharge (Table 4). The logistic regression models of SARC-F score only and SARC-F score + physical function were subjected to ROC curve analysis, as shown in Table 5. The AUCs on ROC curve analysis were greater with addition of usual gait speed, SPPB, or 6MWD to SARC-F, although the differences were not statistically significant.

Table 2 Baseline characteristics, SARC-F, and physical function

Variable	Group			P value
	Overall (n = 257)	SARC-F <4 (n = 188 [73.2%])	SARC-F ≥4 (n = 69 [26.8%])	
Age, yrs	75.8 ± 6.5	74.7 ± 5.9	78.7 ± 7.1	<0.001
≥75	146 (56.8)	98 (52.1)	48 (69.6)	0.015
Male	167 (65.0)	124 (66.0)	43 (62.3)	0.658
BMI, kg/m ²	22.1 ± 4.1	21.9 ± 3.7	22.6 ± 5.1	0.231
<18.5	36 (14.0)	25 (13.3)	11 (15.9)	
18.5 to 24.9	173 (67.3)	130 (69.1)	43 (62.3)	
≥25	48 (18.7)	33 (17.6)	15 (21.7)	
Left ventricular ejection fraction, %	51.5 ± 15.6	51.6 ± 15.3	51.2 ± 16.5	0.854
SBP, mmHg	129 ± 35	131 ± 36	124 ± 31	0.164
DBP, mmHg	75 ± 24	75 ± 24	73 ± 23	0.413
Heart rate, beats/min	82 ± 24	82 ± 24	84 ± 25	0.546
Living alone	38 (15.1)	24 (12.8)	15 (21.7)	0.081
Comorbidities				
Atrial fibrillation	56 (21.8)	33 (17.6)	23 (33.3)	0.010
Diabetes	98 (38.1)	68 (36.2)	30 (43.5)	0.312
Hypertension	169 (65.8)	123 (65.4)	46 (66.7)	0.883
Dyslipidemia	118 (45.9)	85 (45.2)	33 (47.8)	0.778
Chronic kidney disease	192 (74.7)	138 (73.4)	54 (78.3)	0.518
Stroke	40 (15.6)	25 (13.3)	15 (21.7)	0.120
Anemia	171 (66.5)	119 (63.3)	52 (75.4)	0.075
Comorbidity score	3 (2 - 4)	3 (2 - 4)	4 (3 - 5)	0.014
Total of comorbidities				0.026
0 to 2	80 (31.1)	66 (35.1)	14 (20.3)	
3 to 4	119 (46.3)	86 (45.7)	33 (47.8)	
5 to 7	58 (22.6)	36 (19.1)	22 (31.9)	
Current smoker	28 (10.9)	21 (11.2)	7 (10.1)	1.000
Laboratory data				
Albumin, g/dL	3.4 ± 0.5	3.4 ± 0.5	3.3 ± 0.5	0.112
Hemoglobin A1c, %	6.1 (5.7 - 6.6)	6.0 (5.7 - 6.6)	6.1 (5.8 - 6.4)	0.894
Total cholesterol, mg/dL	164 ± 41	166 ± 42	159 ± 39	0.231
HDL cholesterol, mg/dL	53 ± 18	54 ± 19	50 ± 14	0.113
eGFR, mL/min/1.73 m ²	47.4 ± 20.4	47.8 ± 19.7	46.3 ± 22.2	0.614
Hemoglobin, g/dL	11.8 ± 2.0	11.9 ± 2.1	11.6 ± 1.9	0.196
Medications				
ACE inhibitor or ARB	193 (75.1)	138 (73.4)	55 (79.7)	0.333
Beta-blocker	211 (82.1)	155 (82.4)	56 (81.2)	0.855

Statins	178 (69.3)	129 (68.6)	49 (71.0)	0.762
SARC-F	2 (0 - 4)	1 (0 - 2)	5 (4 - 5)	<0.001
Strength				<0.001
None (0)	112 (43.6)	108 (57.4)	4 (5.8)	
Some (1)	94 (36.6)	66 (35.1)	28 (40.6)	
A lot or unable (2)	51 (19.8)	14 (7.4)	37 (53.6)	
Assistance in walking				<0.001
None (0)	203 (79.0)	178 (94.7)	25 (36.2)	
Some (1)	47 (18.3)	10 (5.3)	37 (53.6)	
A lot, use aids, or unable (2)	7 (2.7)	0 (0.0)	7 (10.1)	
Rise from a chair				<0.001
None (0)	197 (76.7)	173 (92.0)	24 (34.8)	
Some (1)	54 (21.0)	15 (8.0)	39 (56.5)	
A lot or unable without help (2)	6 (2.3)	0 (0.0)	6 (8.7)	
Climb stairs				<0.001
None (0)	114 (44.4)	112 (59.6)	2 (2.9)	
Some (1)	113 (44.0)	69 (36.7)	44 (63.8)	
A lot or unable (2)	30 (11.7)	7 (3.7)	23 (33.3)	
Falls				<0.001
None (0)	183 (71.2)	157 (83.5)	26 (37.7)	
1-3 falls (1)	65 (25.3)	28 (14.9)	37 (53.6)	
≥4 falls (2)	9 (3.5)	3 (1.6)	6 (8.7)	
Handgrip strength, kg	23.7 ± 7.6	24.7 ± 7.5	21.0 ± 7.0	<0.001
Male <26 kg, Female <18 kg	126 (49.0)	81 (43.1)	45 (65.2)	0.002
Usual gait speed, m/s	0.96 ± 0.33	1.05 ± 0.30	0.70 ± 0.25	<0.001
≤0.8 m/s	79 (30.7)	33 (17.6)	46 (66.7)	<0.001
≤1.0 m/s	131 (51.0)	72 (38.3)	59 (85.5)	<0.001
SPPB, points	11 (9 - 12)	12 (10 - 12)	8 (5 - 11)	<0.001
≤8 point	51 (19.8)	17 (9.0)	34 (49.3)	<0.001
6MWD, m	331 ± 123	368 ± 106	228 ± 105	<0.001
<300 m	96 (37.4)	48 (25.5)	48 (69.6)	<0.001
<400 m	176 (68.5)	111 (59.0)	65 (94.2)	<0.001

Values are expressed as means ± SD, n (%), or medians (interquartile range).

6MWD, 6-minute walking distance; ACE inhibitor, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; SBP, systolic blood pressure; SPPB, short physical performance battery.

Table 3 Logistic regression analyses for physical limitations

Variable	Handgrip strength Male <26 kg, Female <18 kg		Usual gait speed ≤0.8 m/s		Usual gait speed ≤1.0 m/s	
	Adj. OR (95% CI) *	P value	Adj. OR (95% CI) *	P value	Adj. OR (95% CI) *	P value
SARC-F (continuous)	1.33 (1.15 - 1.55)	<0.001	2.11 (1.70 - 2.63)	<0.001	1.94 (1.58 - 2.37)	<0.001
Individual components of SARC-F						
Strength	1.81 (1.24 - 2.65)	0.002	3.18 (2.04 - 4.96)	<0.001	2.70 (1.77 - 4.10)	<0.001
Assistance in walking	2.17 (1.18 - 4.00)	0.013	4.90 (2.56 - 9.38)	<0.001	4.81 (2.25 - 10.03)	<0.001
Rise from a chair	1.94 (1.09 - 3.47)	0.024	5.25 (2.78 - 9.91)	<0.001	5.71 (2.66 - 10.22)	<0.001
Climb stairs	1.64 (1.07 - 2.51)	0.023	5.68 (3.41 - 9.45)	<0.001	4.74 (2.83 - 7.94)	<0.001
Falls	1.95 (1.15 - 3.32)	0.014	3.01 (1.72 - 5.25)	<0.001	2.63 (1.49 - 4.62)	<0.001
SARC-F ≥4 (vs. SARC-F <4)	2.12 (1.11 - 4.03)	0.022	8.18 (4.07 - 16.40)	<0.001	8.17 (3.68 - 10.81)	<0.001
Variable	SPPB ≤8 point		6MWD <300 m		6MWD <400 m	
	Adj. OR (95% CI) *	P value	Adj. OR (95% CI) *	P value	Adj. OR (95% CI) *	P value
SARC-F (continuous)	1.82 (1.49 - 2.22)	<0.001	1.81 (1.50 - 2.20)	<0.001	1.87 (1.49 - 2.34)	<0.001
Individual components of SARC-F						
Strength	2.36 (1.48 - 3.75)	<0.001	3.14 (2.03 - 4.87)	<0.001	3.09 (1.91 - 4.98)	<0.001
Assistance in walking	5.23 (2.76 - 9.90)	<0.001	3.57 (1.88 - 6.75)	<0.001	10.32 (3.08 - 50.64)	<0.001
Rise from a chair	6.82 (3.54 - 10.31)	<0.001	4.13 (2.19 - 7.79)	<0.001	3.51 (1.52 - 8.09)	0.003
Climb stairs	3.36 (1.95 - 5.77)	<0.001	3.50 (2.14 - 5.74)	<0.001	3.29 (1.93 - 5.61)	<0.001
Falls	1.77 (1.00 - 3.13)	0.049	2.39 (1.38 - 4.15)	0.002	2.42 (1.26 - 4.62)	0.008
SARC-F ≥4 (vs. SARC-F <4)	7.53 (3.66 - 15.50)	<0.001	5.39 (2.71 - 10.70)	<0.001	9.13 (3.08 - 27.10)	<0.001

6MWD, 6-minute walking distance; Adj, adjusted; CI, confidence interval; OR, odds ratio; SPPB, short physical performance battery.

*Adjusted for age, sex, and BMI.

Table 4 Cox regression analyses for the endpoint of first occurrence of all-cause emergency readmission or death after hospital discharge

	No. of Events (%)	Unadjusted			Adjusted *		
		HR (95% CI)	P value	HR (95% CI)	P value		
Adverse events through follow up	63 (24.5)						
SARC-F (continuous)		1.20 (1.07 - 1.34)	0.002	1.17 (1.04 - 1.32)	0.012		
Individual components of SARC-F							
Strength		1.50 (1.09 - 2.06)	0.012	1.45 (1.04 - 2.03)	0.030		
Assistance in walking		1.52 (0.98 - 2.36)	0.062	1.27 (0.80 - 2.04)	0.312		
Rise from a chair		1.73 (1.10 - 2.71)	0.017	1.57 (0.97 - 2.53)	0.065		
Climb stairs		1.27 (0.89 - 1.81)	0.185	1.20 (0.82 - 1.76)	0.339		
Falls		1.85 (1.24 - 2.77)	0.003	1.64 (1.07 - 2.51)	0.023		
SARC-F ≥4 (vs. SARC-F <4)		1.96 (1.18 - 3.25)	0.010	1.78 (1.03 - 3.07)	0.040		
Adverse events within 180 days after discharge	41 (16.0)						
SARC-F (continuous)		1.27 (1.11 - 1.45)	<0.001	1.23 (1.07 - 1.42)	0.004		
Individual components of SARC-F							
Strength		1.91 (1.29 - 2.84)	0.001	1.81 (1.19 - 2.74)	0.005		
Assistance in walking		1.61 (0.96 - 2.69)	0.071	1.32 (0.76 - 2.28)	0.319		
Rise from a chair		1.86 (1.11 - 3.13)	0.019	1.68 (0.96 - 2.94)	0.070		
Climb stairs		1.66 (1.08 - 2.54)	0.020	1.53 (0.97 - 2.41)	0.068		
Falls		1.78 (1.08 - 2.91)	0.023	1.50 (0.90 - 2.51)	0.119		
SARC-F ≥4 (vs. SARC-F <4)		2.69 (1.45 - 4.97)	0.002	2.31 (1.20 - 4.45)	0.013		
Adverse events within 90 days after discharge	27 (10.5)						
SARC-F (continuous)		1.26 (1.08 - 1.48)	0.004	1.23 (1.04 - 1.45)	0.018		
Individual components of SARC-F							
Strength		2.15 (1.31 - 3.53)	0.002	2.11 (1.26 - 3.53)	0.005		
Assistance in walking		1.75 (0.95 - 3.21)	0.071	1.50 (0.80 - 2.83)	0.210		
Rise from a chair		1.95 (1.05 - 3.61)	0.035	1.76 (0.91 - 3.38)	0.093		
Climb stairs		1.63 (0.96 - 2.75)	0.069	1.54 (0.88 - 2.71)	0.131		
Falls		1.22 (0.62 - 2.38)	0.564	1.02 (0.52 - 2.01)	0.950		
SARC-F ≥4 (vs. SARC-F <4)		2.38 (1.12 - 5.09)	0.025	2.17 (1.02 - 4.83)	0.048		

BMI, body mass index; CI, confidence interval; HR, hazard ratio; No., number.

*Adjusted for age, sex, BMI, living status, and comorbidity score.

Adverse events represent first occurrence of all-cause emergency readmission or death.

Table 5 ROC curves for the endpoint of first occurrence of all-cause emergency readmission or death

Model	AUC	95% CI	P value
SARC-F	0.614	0.538 - 0.690	[Reference]
SARC-F + handgrip strength	0.618	0.544 - 0.693	0.533
SARC-F + usual gait speed	0.640	0.563 - 0.718	0.338
SARC-F + SPPB	0.632	0.557 - 0.708	0.358
SARC-F + 6MWD	0.638	0.560 - 0.712	0.342

P values represent pairwise relationships relative to reference group.

6MWD, 6-minute walking distance; AUC, area under the curve; CI, confidence interval; HR, hazard ratio; ROC, receiver-operating characteristic SPPB, short physical performance battery.

Figure 1. Prevalence of SARC-F ≥ 4 by age, sex, BMI, and comorbidities. (AF, atrial fibrillation; BMI, body mass index; CKD, chronic kidney disease.)

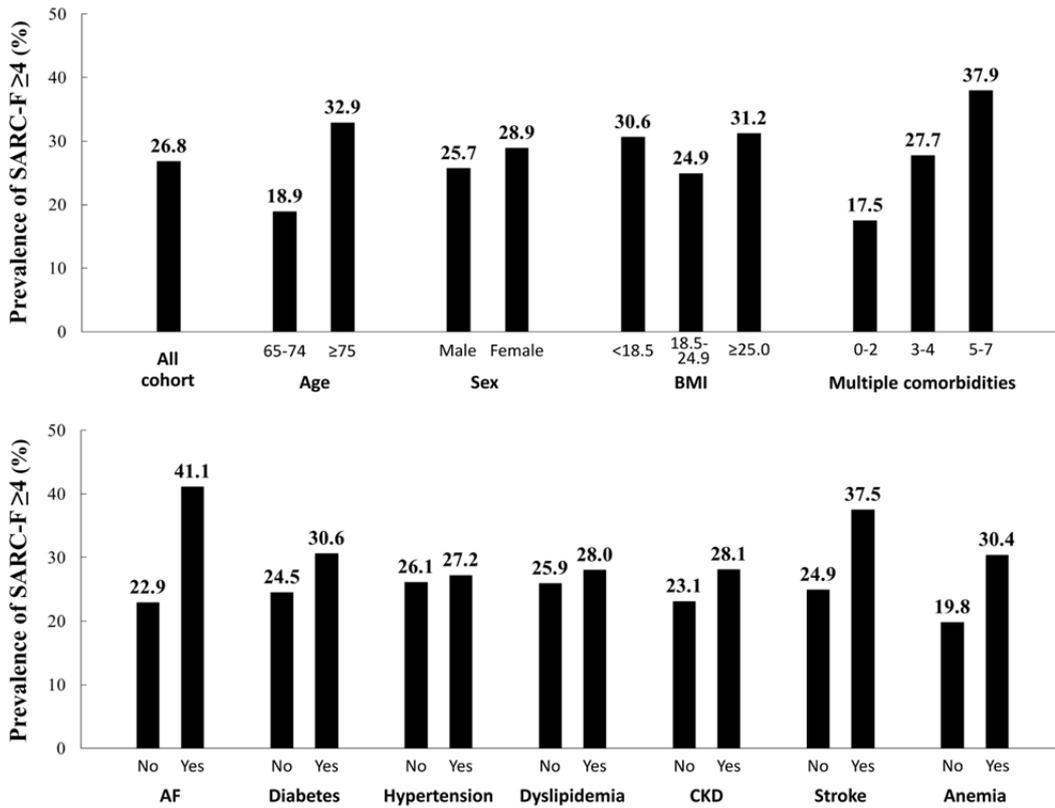
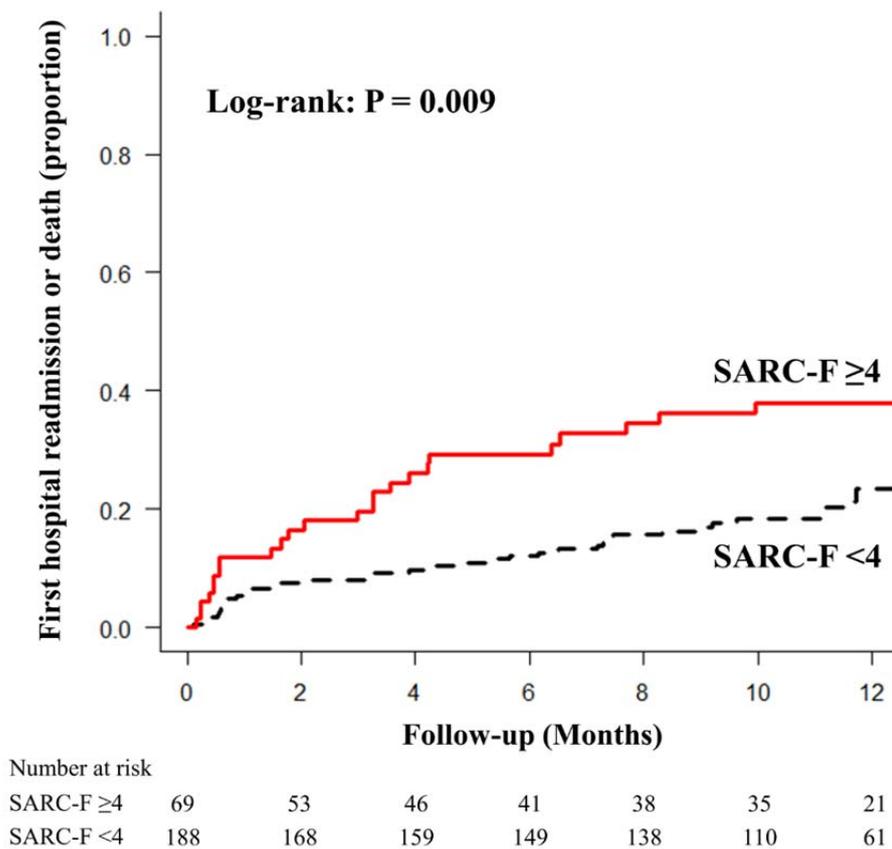


Figure 2. Kaplan–Meier curve for post discharge adverse events stratified by SARC-F.



Discussion

In our study population, 26.8% of patients had SARC-F score ≥ 4 , indicating a risk of sarcopenia, and the prevalence of SARC-F ≥ 4 increased with both age and comorbidities. The degrees of physical limitations were more severe in the SARC-F ≥ 4 group compared to the SARC-F < 4 group. Elderly patients hospitalized for CVD with SARC-F ≥ 4 had a higher risk of readmission or death after hospital discharge than those with SARC-F < 4 . Thus, SARC-F was suggested to be a useful screening tool for risk stratification in hospitalized elderly CVD patients.

Consistent with previous reports, the prevalence of SARC-F ≥ 4 increased with age, and the rate among CVD patients was higher than that in the general community-dwelling elderly population in the present study [17-19,21]. The prevalence of SARC-F ≥ 4 also increased with number of comorbidities in our cohort. There are multiple etiological mechanisms underlying the development of sarcopenia with age [32,33]. Patients with muscle loss associated with the development of various diseases show accelerated loss of muscle mass and strength [34], and hospitalization itself has been shown to adversely affect physical function [35]. Both muscle mass and strength have been shown to be related to circulating inflammatory markers in patients with chronic diseases [36,37]. Therefore, increased awareness and the development of preventive strategies for sarcopenia, comorbidities, and general health status, as well as cardiovascular status, in hospitalized elderly CVD patients.

Consistent with previous observations [22], SARC-F ≥ 4 was related to physical limitations in elderly CVD patients, including reduced handgrip strength, gait speed, SPPB, and 6MWD, all of which were reported to be strong predictors of quality of life, mobility, hospitalization, and mortality [23-25,38,39]. Moreover, SARC-F ≥ 4 was associated with higher probabilities of physical function measurements below critical cut-off values, including gait speed ≤ 1.0 m/s and 6MWD < 400 m, indicating limited mobility [39]. These observations suggest that SARC-F is useful for identifying patients with physical limitations that require treatment.

The results presented here indicated that SARC-F can be used to predict first occurrence of all-cause emergency readmission or all-cause mortality after hospital discharge in elderly CVD patients. In several recent studies, SARC-F was shown to have performance equivalent to more rigorous definitions for predicting adverse outcomes in community-based elderly populations [15,18,21]. Sarcopenia diagnosed according to the standard definitions was shown to be associated with increased rates of hospital readmission and mortality in hospitalized elderly patients [40,41]. To our knowledge, this is the first report regarding the prognostic value of SARC-F in elderly CVD patients. In addition, although not statistically significant, the AUCs for adverse events after discharge were higher when usual gait speed, SPPB, or 6MWD was added to SARC-F in

the present study. These results suggested that a multi-item measure including physical function outperformed SARC-F alone in elderly patients hospitalized with CVD. However, if there is no time to carry out physical function measures in a busy ward, SARC-F is recommended as a screening tool for predicting the prognosis in this population.

Risk stratification after hospitalization for CVD is important with regard to planning of medical care as well as to improve the prognosis of vulnerable populations. One of the most important reasons for assessing sarcopenia status, including impaired physical function, is the fact that this is an at least partially reversible condition. Previous studies have shown that improved physical function is associated with lower risk of adverse events in CVD patients [42,43]. Therefore, methods for the rapid and accurate assessment of sarcopenia status are important to facilitate treatment with various interventions, including cardiac rehabilitation, resistance and aerobic exercise, nutritional recommendations, reduction of polypharmacy (if possible), and self-care [4,44]. These interventions could ameliorate adverse outcomes after discharge in elderly CVD patients determined to be at risk of sarcopenia. Previous studies indicated that SARC-F has a low false positive rate in the diagnosis of sarcopenia [15,18]. Therefore, SARC-F represents a simple and rapid screening tool for clinical use to assess sarcopenia status, and it may be useful in predicting the prognosis of hospitalized elderly CVD patients.

This study had several limitations. First, this was a single-center study with a small patient population and limited follow-up. In addition, this was a retrospective study, and therefore the accuracy of some variables relied on the accuracy of medical records. Second, as patients that were unable to walk were excluded from the analysis, the prevalence of sarcopenia may have been underestimated in our study population. Third, as we did not evaluate muscle mass, it was not possible to compare SARC-F to standard definitions of sarcopenia. Finally, this study was conducted only in Asian patients hospitalized for CVD. Therefore, further studies are needed for validation of SARC-F in other populations and in comparison with standard definitions of sarcopenia.

Conclusions

SARC-F questionnaire is useful for identifying patients at high risk of physical functional limitations and for predicting post-discharge outcomes in elderly CVD patients. The results presented here support the use of SARC-F for screening in hospital settings.

Acknowledgments

This study was supported by the Grant for Clinical and Epidemiologic Research of the Joint Project

of Japan Heart Foundation and the Japanese Society of Cardiovascular Disease Prevention Sponsored by AstraZeneca.

Conflicts of Interest

The authors declare no conflicts of interest.

Statement on Human and Animal Rights

This study was approved by the Ethics Committee of Kitasato University Hospital and meets all standards for ethical conduct in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Statement on Ethical Guidelines

Kentaro Kamiya (corresponding author) certifies that all work is original, has not been submitted elsewhere for publication, certifies authors listed on the manuscript have approved its submission and publication as to Journal of Cachexia, Sarcopenia and Muscle Clinical Reports, and certifies each author has made an independent material contribution to the work submitted for publication. The authors certify that they comply with the ethical guidelines for authorship and publishing of the Journal of Cachexia, Sarcopenia and Muscle - Clinical Reports (von Haehling S, Ebner N, Morley JE, Coats AJS, Anker SD. Ethical guidelines for authorship and publishing in the Journal of Cachexia, Sarcopenia and Muscle - Clinical Reports. *J Cachexia Sarcopenia Muscle Clinical Reports* 2016; 1:e28:1 - 2

References

- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinkova E, Vandewoude M, Zamboni M. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010;39:412-23.
- Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, Abellan van Kan G, Andrieu S, Bauer J, Breuille D, Cederholm T, Chandler J, De Meynard C, Donini L, Harris T, Kannt A, Keime Guibert F, Onder G, Papanicolaou D, Rolland Y, Rooks D, Sieber C, Souhami E, Verlaan S, Zamboni M. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc* 2011;12:249-56.
- Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, Chou MY, Chen LY, Hsu PS, Krairit O, Lee JS, Lee WJ, Lee Y, Liang CK, Limpawattana P, Lin CS, Peng LN, Satake S, Suzuki T, Won CW, Wu CH, Wu SN, Zhang T, Zeng P, Akishita M, Arai H. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc* 2014;15:95-101.
- Morley JE. Frailty and Sarcopenia: The New Geriatric Giants. *Rev Invest Clin* 2016;68:59-67.
- Sanada K, Miyachi M, Tanimoto M, Yamamoto K, Murakami H, Okumura S, Gando Y, Suzuki K, Tabata I, Higuchi M. A cross-sectional study of sarcopenia in Japanese men and women: reference values and association with cardiovascular risk factors. *Eur J Appl Physiol* 2010;110:57-65.
- Srikanthan P, Horwich TB, Tseng CH. Relation of Muscle Mass and Fat Mass to Cardiovascular Disease Mortality. *Am J Cardiol* 2016;117:1355-60.
- Pulignano G, Del Sindaco D, Di Lenarda A, Alunni G, Senni M, Tarantini L, Cioffi G, Tinti MD, Barbati G, Minardi G, Uguccioni M. Incremental Value of Gait Speed in Predicting Prognosis of Older Adults With Heart Failure: Insights From the IMAGE-HF Study. *JACC Heart Fail* 2016;4:289-98.
- Izawa KP, Watanabe S, Osada N, Kasahara Y, Yokoyama H, Hiraki K, Morio Y, Yoshioka S, Oka K, Omiya K. Handgrip strength as a predictor of prognosis in Japanese patients with congestive heart failure. *Eur J Cardiovasc Prev Rehabil* 2009;16:21-7.
- Cao L, Morley JE. Sarcopenia Is Recognized as an Independent Condition by an International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10-CM) Code. *J Am Med Dir Assoc* 2016;17:675-7.
- Springer J, Anker MS, Anker SD. Advances in cachexia and sarcopenia research in the heart failure context: call for action. *J Cardiovasc Med (Hagerstown)* 2016;17:860-2.
- Kinugasa Y, Yamamoto K. The challenge of frailty and sarcopenia in heart failure with preserved ejection fraction. *Heart* 2017;103:184-9.
- Malmstrom TK, Morley JE. Sarcopenia: The Target Population. *J Frailty Aging* 2013;2:55-6.
- Malmstrom TK, Morley JE. SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. *J Am Med Dir Assoc* 2013;14:531-2.
- Cao L, Chen S, Zou C, Ding X, Gao L, Liao Z, Liu G, Malmstrom TK, Morley JE, Flaherty JH, An Y, Dong B. A pilot study of the SARC-F scale on screening sarcopenia and physical disability in the Chinese older people. *J Nutr Health Aging* 2014;18:277-83.
- Woo J, Leung J, Morley JE. Validating the SARC-F: a suitable community screening tool for sarcopenia? *J Am Med Dir Assoc* 2014;15:630-4.
- Parra-Rodriguez L, Szlejf C, Garcia-Gonzalez AI, Malmstrom TK, Cruz-Arenas E, Rosas-Carrasco O. 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* 2016;17:1142-6.
- Rolland Y, Dupuy C, Abellan Van Kan G, Cesari M, Vellas B, Faruch M, Dray C, de Souto Barreto P. Sarcopenia Screened by the SARC-F Questionnaire and Physical Performances of Elderly Women: A Cross-Sectional Study. *J Am Med Dir Assoc* 2017;18:848-52.
- Woo J, Leung J, Morley JE. Defining sarcopenia in terms of incident adverse outcomes. *J Am Med Dir Assoc* 2015;16:247-52.
- Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. *J Cachexia Sarcopenia Muscle* 2016;7:28-36.
- Licini A, Malmstrom TK. Frailty and Sarcopenia as Predictors of Adverse Health Outcomes in Persons With Diabetes Mellitus. *J Am Med Dir Assoc* 2016;17:846-51.
- Wu TY, Liaw CK, Chen FC, Kuo KL,

- Chie WC, Yang RS. Sarcopenia Screened With SARC-F Questionnaire Is Associated With Quality of Life and 4-Year Mortality. *J Am Med Dir Assoc* 2016;17:1129-35.
22. Tanaka S, Kamiya K, Hamazaki N, Matsuzawa R, Nozaki K, Maekawa E, Noda C, Yamaoka-Tojo M, Matsunaga A, Masuda T, Ako J. Utility of SARC-F for Assessing Physical Function in Elderly Patients With Cardiovascular Disease. *J Am Med Dir Assoc* 2017;18:176-81.
 23. Alahdab MT, Mansour IN, Napan S, Stamos TD. Six minute walk test predicts long-term all-cause mortality and heart failure rehospitalization in African-American patients hospitalized with acute decompensated heart failure. *J Card Fail* 2009;15:130-5.
 24. Chiarantini D, Volpato S, Sioulis F, Bartalucci F, Del Bianco L, Mangani I, Pepe G, Tarantini F, Berni A, Marchionni N, Di Bari M. Lower extremity performance measures predict long-term prognosis in older patients hospitalized for heart failure. *J Card Fail* 2010;16:390-5.
 25. Matsuzawa Y, Konishi M, Akiyama E, Suzuki H, Nakayama N, Kiyokuni M, Sumita S, Ebina T, Kosuge M, Hibi K, Tsukahara K, Iwahashi N, Endo M, Maejima N, Saka K, Hashiba K, Okada K, Taguri M, Morita S, Sugiyama S, Ogawa H, Sashika H, Umemura S, Kimura K. Association between gait speed as a measure of frailty and risk of cardiovascular events after myocardial infarction. *J Am Coll Cardiol* 2013;61:1964-72.
 26. Ando Y, Ito S, Uemura O, Kato T, Kimura G, Nakao T, Hattori M, Fukagawa M, Horio M, Mitarai T. CKD Clinical Practice Guidebook. The essence of treatment for CKD patients. *Clin Exp Nephrol* 2009;13:191-248.
 27. Ida S, Murata K, Nakadachi D, Ishihara Y, Imataka K, Uchida A, Monguchi K, Kaneko R, Fujiwara R, Takahashi H. Development of a Japanese version of the SARC-F for diabetic patients: an examination of reliability and validity. *Aging Clin Exp Res* 2017;29:935-42.
 28. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, Scherr PA, Wallace RB. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994;49:M85-94.
 29. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;166:111-7.
 30. Kamiya K, Hamazaki N, Matsuzawa R, Nozaki K, Tanaka S, Ichinosawa Y, Maekawa E, Noda C, Yamaoka-Tojo M, Matsunaga A, Masuda T, Ako J. Sarcopenia: prevalence and prognostic implications in elderly patients with cardiovascular disease. *JCSM Clinical Reports* 2017;2:e00041.
 31. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988;44:837-45.
 32. Chen L, Nelson DR, Zhao Y, Cui Z, Johnston JA. Relationship between muscle mass and muscle strength, and the impact of comorbidities: a population-based, cross-sectional study of older adults in the United States. *BMC Geriatr* 2013;13:74.
 33. McKee A, Morley JE, Matsumoto AM, Vinik A. SARCOPIENIA: AN ENDOCRINE DISORDER? *Endocr Pract* 2017;23:1140-9.
 34. Morley JE, Anker SD, von Haehling S. Prevalence, incidence, and clinical impact of sarcopenia: facts, numbers, and epidemiology-update 2014. *J Cachexia Sarcopenia Muscle* 2014;5:253-9.
 35. Ehlenbach WJ, Larson EB, Curtis JR, Hough CL. Physical Function and Disability After Acute Care and Critical Illness Hospitalizations in a Prospective Cohort of Older Adults. *J Am Geriatr Soc* 2015;63:2061-9.
 36. Brinkley TE, Leng X, Miller ME, Kitzman DW, Pahor M, Berry MJ, Marsh AP, Kritchevsky SB, Nicklas BJ. Chronic inflammation is associated with low physical function in older adults across multiple comorbidities. *J Gerontol A Biol Sci Med Sci* 2009;64:455-61.
 37. Beenakker KG, Ling CH, Meskers CG, de Craen AJ, Stijnen T, Westendorp RG, Maier AB. Patterns of muscle strength loss with age in the general population and patients with a chronic inflammatory state. *Ageing Res Rev* 2010;9:431-6.
 38. Ferreira JP, Duarte K, Graves TL, Zile MR, Abraham WT, Weaver FA, Lindenfeld J, Zannad F. Natriuretic Peptides, 6-Min Walk Test, and Quality-of-Life Questionnaires as Clinically Meaningful Endpoints in HF Trials. *J Am Coll Cardiol* 2016;68:2690-707.
 39. Morley JE, Abbatecola AM, Argiles JM, Baracos V, Bauer J, Bhasin S, Cederholm T, Coats AJ, Cummings SR, Evans WJ, Fearon K, Ferrucci L, Fielding RA, Guralnik JM, Harris TB, Inui A, Kalantar-Zadeh K, Kirwan BA, Mantovani G, Muscaritoli M, Newman AB, Rossi-Fanelli F, Rosano GM, Roubenoff R, Schambelan M, Sokol GH, Storer TW, Vellas B, von Haehling S, Yeh SS, Anker SD. Sarcopenia with limited mobility: an international consensus. *J Am Med Dir Assoc* 2011;12:403-9.
 40. Vetrano DL, Landi F, Volpato S, Corsonello A, Meloni E, Bernabei R, Onder G. Association of sarcopenia with short- and long-term mortality in older adults admitted to acute care wards: results from the CRIME study. *J Gerontol A Biol Sci Med Sci* 2014;69:1154-61.
 41. Yang M, Hu X, Wang H, Zhang L, Hao Q, Dong B. Sarcopenia predicts readmission and mortality in elderly patients in acute care wards: a prospective study. *J Cachexia Sarcopenia Muscle* 2017;8:251-8.
 42. Grazi G, Mazzoni G, Myers J, Codeca L, Pasanisi G, Napoli N, Guerzoni F, Volpato S, Conconi F, Chiaranda G. Improved walking speed is associated with lower hospitalisation rates in patients in an exercise-based secondary prevention programme. *Heart* 2016;102:1902-8.
 43. Passantino A, Lagioia R, Mastropasqua F, Scrutinio D. Short-term change in distance walked in 6 min is an indicator of outcome in patients with chronic heart failure in clinical practice. *J Am Coll Cardiol* 2006;48:99-105.
 44. Morley JE. Pharmacologic Options for the Treatment of Sarcopenia. *Calcif Tissue Int* 2016;98:319-33.