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A simple sarcopenia screening test predicts future adverse events in patients with heart failure

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ABSTRACT

Background: Progressive loss of skeletal muscle termed "sarcopenia" is an independent risk factor for mortality in patients with cardiovascular diseases. A simple screening test that can identify sarcopenia using three variables (age, grip strength and calf circumference) was recently developed. We evaluated the clinical utility of this screening test in patients with heart failure (HF).

Methods and results: HF patients were divided into the sarcopenia (n = 82) and non-sarcopenia (n = 37) groups based on the sarcopenia score. Circulating BNP and high-sensitive cardiac troponin T levels were significantly higher, and left ventricular ejection fraction was lower in the sarcopenia group than non-sarcopenia group. Kaplan–Meier curve showed that HF event-free survival rate was significantly lower in the sarcopenia group. Multivariate Cox proportional hazards analysis identified BNP (ln[BNP]) (hazard ratio [HR]: 1.58; 95% CI: 1.09–2.29, p = 0.02), hs-CRP (ln[CRP]) (HR: 1.82; 95% CI: 1.23–2.68; p < 0.01) and sarcopenia score (HR: 1.03; 95% CI: 1.01–1.05, p < 0.01) as independent predictors of HF events. In receiver operating characteristic analysis, adding the sarcopenia score to BNP levels increased an area under the curve for future HF events (sarcopenia score alone, 0.77; BNP alone, 0.82; combination, 0.89).

Conclusions: The sarcopenia screening test can be used to predict future adverse events in patients with HF.

1. Introduction

Reduced skeletal muscle mass and function is one of the main features of end-stage heart diseases. The prognostic importance of muscle wasting has been established in patients with chronic heart failure (HF) [1]. Especially, loss of the leg muscle mass has been shown to be an independent risk of heart disease and premature death [2]. Muscle strength is also reported to be an independent predictor of survival in patients with HF [3], and reduced handgrip strength is associated with increased mortality in these patients [4,5]. In HF patients, exercise designed to increase muscle mass and strength could have favorable effects [6–9], and this type of training is recommended as a complementary exercise modality for patient with cardiovascular disease [10].

The term "sarcopenia" was recently coined to progressive loss of skeletal muscle mass and strength associated with aging [11]. Sarcopenia could worsen in the presence of comorbidities such as HF, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD) and cancer [12]. Previous study showed that sarcopenia is associated with risk of adverse events, such as physical disability, poor quality of life and death [13]. In patients with HF, sarcopenia assessed by the fat-free mass index is associated with an unfavorable prognosis [14]. Accordingly, assessment of sarcopenia may be useful to risk stratification in patients with HF.

The European Working Group on Sarcopenia in Older People (EWGSOP) published a practical guideline for the diagnosis of sarcopenia [15]. The guideline recommends the use of computed tomography (CT scan), magnetic resonance imaging (MRI), and dual energy X-ray absorptiometry (DXA) to evaluate muscle mass. Although these modalities allow precise evaluation of muscle mass, they are not available for routine use in daily clinical practice setting. Recently, Ishii et al. [16] developed a simple screening test that can identify sarcopenia with high accuracy using three easily obtainable variables; age, grip strength and calf circumference. In the present study, we used this simple screening test of sarcopenia and assessed its clinical utility in patients with HF.

2. Methods

2.1. Study population

The study subjects were 119 consecutive patients, aged 65 years or older, hospitalized between March 2012 and April 2013 at Kumamoto

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University Hospital for treatment or diagnosis of HF. HF was defined as the typical symptoms (breathlessness, orthopnea, paroxysmal nocturnal dyspnea, fatigue, tiredness, etc) and signs (elevated jugular venous pressure, hepatojugular reflux, third heart sound, laterally displaced apical impulse, etc) evaluated by physical examination, echocardiography, electrocardiogram and chest X-ray [17]. The exclusion criteria included patients with acute coronary syndrome, malignant tumors, acute infection, chronic hemodialysis and inflammatory diseases.

2.2. Protocol

All participants underwent measurement of hand grip strength and calf circumference just before they discharged from the hospital. Hand grip strength was measured using a digital hand grip strength dynamometer (Takei Scientific Instruments, Niigata, Japan). After two measurements of grip strength of the dominant hand, the higher value of the two measurements was used for estimation of the sarcopenia score. Calf circumference was measured using a measuring tape at the maximum circumference of the non-dominant leg in sitting position with the leg bent 90° at the knee. The sarcopenia score was calculated using a score chart or calculation formula for estimated probability of sarcopenia advocated by Ishii et al. [16]. The calculation formula to the score are as following; in men, $0.62 \times (\text{age} - 64) - 3.09 \times (\text{grip strength} - 50) - 4.64 \times (\text{calf circumference} - 42)$; in women, $0.80 \times (\text{age} - 64) - 5.09 \times (\text{grip strength} - 34) - 3.28 \times (\text{calf circumference} - 42)$. In this study, we defined the presence of sarcopenia as a sarcopenia score ≥ 105 in men and ≥ 120 in women, based on the previous study [16].

Serum and plasma samples were withdrawn from resting participants at supine position and kept frozen at −80 °C until analysis. Plasma B-type natriuretic peptide (BNP) levels were measured using the MI02 Shionogi BNP kit (Shionogi, Osaka, Japan). Serum high-sensitive cardiac troponin T (hs-TnT) levels were measured using the Elecsys 2010 Troponin T hs kit (Roche Diagnostics, Indianapolis, IN). Estimated glomerular filtration rate (eGFR) was calculated using following equation according to recommendations of the Japanese Society of Nephrology; eGFR in male $= 194 \times (\text{Serum Creatinine})^{-1.094} \times (\text{Age})^{-0.287}$, eGFR in female $= 194 \times (\text{Serum Creatinine})^{-1.094} \times (\text{Age})^{-0.287} \times 0.739$.

Echocardiography was conducted in all participants using Aplio XG (Toshiba, Tokyo, Japan) or Vivid 7 (GEVingmed Ultrasound, Horton, Norway) ultrasound systems and the results were evaluated by two independent investigators who were blinded to all clinical data. LVEF was calculated by the modified Simpson method. Early (E) diastolic transmitral flow velocity was measured from mitral inflow velocities. Early diastolic mitral annular (e′) velocity was determined after pulsed wave tissue doppler imaging and E/e′ was calculated.

2.3. Follow up for mortality and cardiovascular events

After calculation of sarcopenia score, patients were followed in the outpatient clinic for a median of 495 days (interquartile range [IQR] 211 to 715 days). The endpoint of this study was HF events, included HF-related hospitalization and death due to HF. HF-events were identified by searching the medical records.

2.4. Statistical analysis

Continuous variables were expressed as mean ± SD, but BNP, hs-TnT and high sensitive C reactive protein (hs-CRP) showed skewed distribution and were therefore expressed as median (IQR) and log transformed before other analyses. Categorical variables were expressed as number (percentage). Continuous and categorical variables were compared using Mann–Whitney U-test and Fisher's exact test, respectively. We assessed the prognostic association using the Kaplan–Meier method, log-rank test, and simple and multiple Cox proportional hazards

Table 1
Clinical characteristics of the study participants.

	All patients (n = 119)	Sarcopenia group (n = 82)	Non-sarcopenia group (n = 37)	P-value
Age (years)	76.1 ± 6.2	77.6 ± 5.4	72.0 ± 5.9	<0.01
Male sex	73 (61%)	53(65%)	20 (54%)	0.28
Body mass index (kg/m^2)	23.2 ± 3.6	22.2 ± 3.2	25.5 ± 3.3	<0.01
Abdominal circumference (cm)	85.8 ± 9.8	83.3 ± 9.1	91.3 ± 9.0	<0.01
Hand grip strength (kg)	23.0 ± 8.3	19.9 ± 6.9	29.8 ± 7.0	<0.01
Calf circumference (cm)	30.8 ± 3.3	29.4 ± 2.6	34.0 ± 2.6	<0.01
Sarcopenia score	130.5 ± 36.9	133.5 ± 23.7	86.2 ± 16.1	<0.01
Hypertension	77 (65%)	55 (67%)	22 (59%)	0.27
Diabetes mellitus	46 (39%)	32 (39%)	14 (38%)	0.58
Dyslipidemia	49 (41%)	35 (43%)	14 (38%)	0.58
Current smoker	7 (6%)	3 (4%)	4 (11%)	<0.01
Albumin (g/dl)	3.8 ± 0.5	3.8 ± 0.5	3.9 ± 0.4	0.21
Hemoglobin (g/dl)	12.5 ± 2.0	12.2 ± 2.0	13.1 ± 1.8	0.03
eGFR (ml/min/1.73 m^2)	50.0 ± 20.2	49.0 ± 20.8	52.3 ± 19.0	0.41
BNP (pg/ml)	123.6 (57.7–362.6)	182.6 (77.1–419.2)	72.7 (42.3–139.6)	<0.01
hs-TnT (ng/ml)	0.020 (0.011–0.048)	0.026 (0.014–0.058)	0.011 (0.008–0.022)	0.01
hs-CRP (mg/dl)	0.10 (0.04–0.21)	0.11 (0.04–0.22)	0.06 (0.04–0.21)	0.83
LVEF (%)	55.4 ± 12.3	53.8 ± 12.3	58.8 ± 11.8	0.04
LVDd (mm)	48.3 ± 8.5	48.3 ± 8.5	48.1 ± 8.5	0.87
E/e′	16.5 ± 9.0	16.7 ± 8.2	16.2 ± 10.6	0.78
Medication				
Ca channel blocker	59 (50%)	39 (48%)	20 (54%)	
ACEI or ARB	85 (71%)	63 (77%)	22 (54%)	
β-blocker	64 (54%)	46 (56%)	18 (49%)	
Diuretics	47 (39%)	36 (44%)	11 (30%)	
Etiology				
Ischemia heart disease	39 (33%)	30 (37%)	9 (24%)	
Hypertensive heart disease	16 (13%)	12 (15%)	4 (11%)	
Dilated cardiomyopathy	8 (7%)	6 (7%)	2 (5%)	
Valvular heart disease	20 (17%)	13 (16%)	7 (19%)	
Other causes	36 (30%)	21 (25%)	15 (40%)	

Data are mean ± SD, number (percentage) or (interquartile range).
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; hs-CRP, high-sensitivity C-reactive protein; hs-TnT, high-sensitivity cardiac troponin T; LVEF, left ventricular ejection fraction; LVDd, left ventricular end-diastolic diameter.