Physical Function and Cardio-Ankle Vascular Index in Elderly Heart Failure Patients

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Summary
The number of heart failure patients is increasing rapidly in Japan because of its large elderly population. As age increases, arterial stiffness and physical dysfunction progress. This study aimed to evaluate the association between the physical function and arterial stiffness in elderly heart failure patients.

This retrospective, observational study includes data from 100 heart failure patients aged ≥ 65 years who were admitted to our hospital and underwent cardiac rehabilitation. The Cardio-Ankle Vascular Index (CAVI) was measured as an indicator of arterial stiffness. Body composition was assessed by bioelectrical impedance analysis. To determine the degree of physical function, we assessed handgrip strength, five-meter walk speed (5MWS), five-repetition sit-to-stand time (5RSST) and six-minute walk distance (6MWD). Sarcopenia was defined using Asian guidelines based on physical function and body composition.

Among 100 patients, 47.0% of patients had sarcopenia. After adjustments for age, sex, atrial fibrillation, and ischemic cardiomyopathy, CAVI was significantly higher in with sarcopenia patients than those without sarcopenia. Age, handgrip strength, 5MWS, 5RSST, and 6MWD were associated with CAVI, and 6MWD was as an independent determinant factor of CAVI.

6MWD was recognized as an accurate physical function indicator. These findings suggested that physical function and arterial stiffness complement each other. To restore cardiac dysfunction, improving both arterial stiffness and physical function might be useful.

Key words: Arterial stiffness, Sarcopenia, Skeletal muscle mass, 6-minute walk distance, Cardiac rehabilitation

The increased number of elderly patients with heart failure in Japan, which coincides with the aging population, has become a significant societal challenge because of increased medical expenditures and the burden on caregivers and patients. In elderly patients with heart failure, the frequently observed skeletal muscle loss, including sarcopenia and associated pathological conditions, are drawing attention. Sarcopenia is an age-associated loss of skeletal muscle and physical function; it is a life-long process with a complex and multifactorial etiology.1 In the United States, the Health, Aging, and Body Composition (“Health ABC”) study focused on the interaction between sex, race, and sarcopenic cardiovascular risk.2 Sarcopenia has become an increasing focus of clinical and basic research, and links to cardiovascular risk factors have been reported.2

Recently, the Cardio-Ankle Vascular Index (CAVI) has become widely used as a blood pressure-independent parameter of arterial stiffness at measuring time. It is a predictor of cardiovascular events and it is also used as an index for managing cardiovascular risks.3,4 Exercise capacity influences heart disease prognosis significantly,5 and skeletal muscle function is a determining factor of exercise capacity.6 In previous study of Japanese community-dwelling older adults, CAVI was shown to be associated with the level of skeletal muscle mass.7

The relationship between arterial stiffness and sarcopenia in patients with heart failure is not understood fully, and factors causing arterial stiffness remain unclear. Therefore, we investigated the relationship between CAVI and skeletal muscle mass in elderly heart failure patients.

Methods

Subjects: The present study is a retrospective observational study using the cardiac rehabilitation database in our hospital. We studied 235 consecutive hospitalized heart failure patients who underwent cardiac rehabilitation from 2017 to 2019 at the Toho University Sakura Medical Center.

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Received for publication January 31, 2020. Revised and accepted April 6, 2020.
Released in advance online on J-STAGE July 18, 2020.
doi: 10.1536/ihj.20-058
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The inclusion criteria were 1) aged ≥ 65 years, and 2) patients who have undergone CAVI and body composition during hospitalization. The exclusion criteria were as follows: 1) age: under 65 years, 2) hemodialysis patients, 3) lacking CAVI and body composition measurements, 4) ABI under 0.9. This study enrolled 100 patients (Figure 1). All parameters were evaluated just before discharge.

**CAVI measurement:** As an indicator of arterial stiffness, CAVI was measured using the vascular screening system, VaSera1500 (Fukuda Denshi Co., Ltd., Tokyo, Japan) according to previously described methods.5,6 Briefly, with the subject supine and the head held in the midline position, the cuffs were applied to bilateral upper arms and ankles, and examinations were performed after a 10-minute rest. A low cuff pressure of 30-50 mmHg was applied to ensure a minimal cuff pressure effect on hemodynamics. Blood pressure (BP) was measured and CAVI was determined by applying the following equation:

\[ CAVI = a \frac{(2p/ΔP) \times \ln(P_s/P_d)}{PWV^2} + b, \]

Where Ps and Pd represent systolic and diastolic BP, respectively, PWV, pulse wave velocity from the aorta origin to the junction of the tibial and femoral arteries, ΔP, is Ps-Pd, p is blood density, and a and b are constants. This equation was modified from Bramwell-Hill’s equation and the stiffness parameter \( \beta \); CAVI was adjusted for BP according to the stiffness parameter \( \beta \). In order to evaluate the CAVI of atrial fibrillation accurately, the forms of pulse wave were checked by three well-trained examiners.

**Body composition measurement:** Body composition was measured via direct segmental multi-frequency bioelectrical impedance analysis (BIA; MC-980A; Tanita Corp., Tokyo, Japan).10-12 Dual energy X-ray absorptiometry has detected a strong correlation between muscle volume and fat mass.13 By inputting the patient’s age, sex and height, the BIA device yielded segmental muscle mass (arms, legs and trunk), absolute fat mass, and body fat percentages. The sum of arm and leg skeletal muscle mass was considered to represent the appendicular skeletal muscle mass (ASM). Here, the skeletal muscle mass index (SMI) was defined as ASM divided by body height (in meters) squared, as follows:

\[ SMI = \frac{ASM}{Height^2} \]

**Assessment of physical function**

**Handgrip strength** An electronic hand dynamometer (Takei Scientific Instruments Co., Ltd., Tokyo, Japan) was used to measure the handgrip strength. Two consecutive measures of handgrip strength were made for both hands and recorded to the nearest kilogram while the patients placed in a standing position with and the arm of the hand measured parallel to the body.

**5-meter walk test** Walking speed is an important predictor of mortality and hospitalization in elderly people.14,15 We measured five-meter walk speed (5MWS) to evaluate sarcopenia. A straight corridor, with one-meter and five-meter lengths marked on the floor, was used for this test. The patients walked the whole length of the corridor, but only the time to finish the inner five-meter range was recorded to control for acceleration and deceleration. Therefore, at the time of the measurement, walking began from one meter before; using a stopwatch, the measurement was started when either the left or right foot touched or crossed the marking on the start point. The measurement was stopped when the left or right foot either touched or exceeded the endpoint marking.

**5 repetition sit-to-stand test** Five-repetition sit-to-stand time (5RSST) was measured to assess physical performance. To test the ability to stand up from a chair, a straight-backed chair was positioned; the patient was asked to fold their arm across their chest and to stand up from the chair one time. If successful, the patient was
asked to stand up and sit down as quickly as possible for five times; the time was measured from the initial sitting position to the final standing position at the end of the fifth stand.\(^\text{16}\)

**6-minute walk test** The 6-minute walk distance (6MWD) was performed indoors, along a long, flat, straight, enclosed corridor (30 m long) with a hard floor surface. The turnaround points were marked with cones. The measurement method and instructions given to the patient were according to the previously published guidelines.\(^\text{17}\)

**Heart failure diagnosis:** The Framingham heart failure criteria were applied in this study. It consists of major criteria (paroxysmal nocturnal dyspnea, orthopnea, jugular venous distension, third heart sound, cardiothoracic ratio > 0.5 on X-ray, pulmonary edema on X-ray, and pulmonary crackling rales) and minor criteria (peripheral edema, nocturnal cough, dyspnea at exercise, hepatomegaly, pleural effusion, and tachycardia).\(^\text{18}\)

**Sarcopenia diagnosis:** Sarcopenia was defined using Asian working group for sarcopenia (AWGS) guidelines.\(^\text{19}\) According to AWGS criteria, sarcopenia was defined as low muscle mass, low muscle strength, and/or slow gait speed. Low muscle mass was classified as ASM/height\(^2\) of less than 7.0 kg/m\(^2\) in males and 5.7 kg/m\(^2\) in females; low muscle strength was defined as handgrip strength < 26 kg and < 18 kg, respectively; slow gait speed was defined as 5 m walk times > 6.25 seconds (< 0.8 m/second). AWGS criteria are shown in Figure 2.

**Ethics:** The Ethics Committee of Toho University Sakura Medical Center (S18042) and Saitama Prefectural University (30501) approved the study protocol. The research followed the Declaration of Helsinki and ethical standards of the responsible committee on human experimentation. Informed consent was obtained in the form of opt-out.

**Statistical analysis:** The Mann-Whitney U test and the Chi-square test were used to compare patient characteristics and clinical parameters with and without sarcopenia. In addition, CAVI was compared by adjusting for age, sex, atrial fibrillation, and ischemic cardiomyopathy using analysis of covariance with or without sarcopenia. We analyzed the relationship between CAVI and other clinical parameters using the Spearman’s rank correlation coefficient. Finally, we used the stepwise multiple regression analysis to evaluate CAVI determinants. Results were expressed as the mean ± standard deviation and median (interquartile range). \(P < 0.05\) was considered significant. Statistical analysis was performed using SPSS package (ver.21.0, Chicago, IL, USA).

**Results**

Table I shows the patient characteristics in this study. In this observational study, 47.0% of elderly patients with heart failure had sarcopenia. Eleven patients had a prior stroke; however, they had no movement disorders such as hemiplegia. Patients with sarcopenia were older (80.0 years to 75.0 years, \(P < 0.01\)), had low body mass index (BMI) (19.3 kg/m\(^2\) to 22.5 kg/m\(^2\), \(P < 0.01\)) and high CAVI (10.1 to 9.5, \(P < 0.01\)). There was no significant difference in the length of hospital stays with or without sarcopenia. 

\[\text{Handgrip strength} + \text{5-meter walk test}\]

| Handgrip strength: male < 26.0 kg, female < 18.0 kg and/or 5-meter walk time > 6.25 second |

| Measurement of body composition analysis for calculating SMI |

| SMI: male ≥ 7.0 kg/m\(^2\), female ≥ 5.7 kg/m\(^2\) |

| Sarcopenia(−) \(n = 53\) |

| Sarcopenia(+) \(n = 47\) |

Figure 2. Patient profile and AWGS criteria for sarcopenia diagnosis. We used the Asia Working Group for Sarcopenia (AWGS) criteria to diagnose sarcopenia. SMI indicates skeletal muscle mass index.
sarcopenia (20.0 days to 19 days, $P = 0.505$). Patients with sarcopenia tended to have longer cardiac rehabilitation periods (6.0 days to 8.0 days, $P = 0.051$). Table II shows body composition and physical function. Patients with sarcopenia had significantly lower SMI, weakened handgrip strength, slower 5MWS, slower 5RSST, and shortened 6MWD.

Figure 3 shows the CAVI values with or without sarcopenia. CAVI was higher in patients with sarcopenia than in those without sarcopenia, even after adjustments of age, sex, arterial fibrillation, and ischemic cardiomyopathy ($P < 0.01$).

Table III shows the relationship between CAVI and clinical parameters. Significant correlations were observed in age ($p = 0.252$, $P < 0.05$), handgrip strength ($p = -0.204$, $P < 0.05$), 5MWS ($p = 0.216$, $P < 0.05$), 5RSST ($p = 0.328$, $P < 0.05$) and 6MWD ($p = -0.347$, $P < 0.01$), respectively. Figure 4 shows scatter plot of 6MWD and CAVI.

There were significant relationships between physical function and cardiac rehabilitation period in handgrip strength ($p = -0.272$, $P = 0.006$), 5MWS ($p = 0.317$, $P = 0.002$), 5RSST ($p = 0.199$, $P = 0.077$) and 6MWD ($p = -0.368$, $P < 0.0001$).

| Variable | All patients $n = 100$ | Sarcopenia (−) $n = 53$ | Sarcopenia (+) $n = 47$ | $P$-value |
|----------|----------------------|---------------------------|--------------------------|---------|
| Male, $n$ (%) | 62 (62.0) | 37 (69.8) | 25 (53.2) | n.s. |
| Age, years | 77.0 (71.0, 81.0) | 75.0 (68.0, 79.5) | 80.0 (75.0, 84.0) | < 0.01 |
| BMI, kg/m² | 20.9 (18.9, 24.3) | 22.5 (20.2, 25.7) | 19.3 (18.1, 21.4) | < 0.01 |
| sBP, mmHg | 121.0 (110.0, 135.8) | 121.0 (107.5, 135.0) | 121.0 (111.0, 136.0) | n.s. |
| dBP, mmHg | 74.0 (68.0, 77.8) | 74.0 (68.5, 80.0) | 73.0 (67.0, 83.0) | n.s. |
| HR, bpm | 68.0 (59.3, 77.8) | 66.0 (59.5, 77.5) | 69.0 (59.0, 78.0) | n.s. |
| Alb. g/dL | 3.80 (3.58, 4.00) | 3.80 (3.60, 4.00) | 3.80 (3.48, 4.00) | n.s. |
| Cre. mg/dL | 1.00 (0.76, 1.29) | 0.94 (0.75, 1.23) | 1.00 (0.77, 1.37) | n.s. |
| BNP, pg/mL | 165.7 (101.9, 373.7) | 158.7 (89.2, 463.4) | 184.6 (115.8, 329.0) | n.s. |
| EF, % | 41.5 (30.0, 63.0) | 40.5 (30.0, 60.8) | 48.0 (30.0, 66.0) | n.s. |
| E/e’ | 15.8 (10.6, 20.4) | 15.6 (9.8, 20.4) | 16.9 (12.9, 24.1) | n.s. |

BMI indicates body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure; HR, heart rate; Alb, albumin; Cre, creatinine; BNP, brain natriuretic peptide; EF, ejection fraction; E/e’, ratio of early transmitial filling velocity to early diastolic velocity; CAVI, cardio-ankle vascular index; ICM, ischemic cardiomyopathy; AF, atrial fibrillation; HT, hypertension; DM, diabetes mellitus; DL, dyslipidemia; Ca-angiotensin; calcium antagonists; and RAS-inhibitors, renin angiotensin aldosterone inhibitors. The dates are presented as median (interquartile range).

Table II. Comparison of Body Composition and Physical Function

| Variable | All patients $n = 100$ | Sarcopenia (−) $n = 53$ | Sarcopenia (+) $n = 47$ | $P$-value |
|----------|----------------------|---------------------------|--------------------------|---------|
| SMI, kg/m² | 6.37 (5.68, 7.38) | 7.14 (6.28, 8.01) | 5.77 (5.30, 6.28) | < 0.01 |
| Handgrip strength, kg | 21.7 (16.2, 28.2) | 25.5 (20.2, 31.8) | 17.1 (13.9, 22.7) | < 0.01 |
| 5MWS, second | 6.00 (4.22, 6.31) | 4.63 (4.10, 5.45) | 5.76 (4.71, 7.33) | < 0.01 |
| 5RSST, second | 13.0 (10.5, 17.6) | 11.2 (9.4, 14.1) | 15.9 (12.3, 24.3) | < 0.01 |
| 6MWD, meter | 357.0 (285.0, 411.0) | 385.0 (323.0, 428.0) | 295.0 (232.0, 375.0) | < 0.01 |

SMI indicates skeletal muscle mass index; 5MWS, 5-meter walk speed; 5RSST, 5 repetition sit-to-stand time; and 6MWD, 6-minute walk distance. The dates are presented as median (interquartile range).
Figure 3. CAVI in elderly heart failure patients with or without sarcopenia (adjusted for age, sex, atrial fibrillation and ischemic cardiomyopathy by analysis of covariance). CAVI indicates Cardio-Ankle Vascular Index.

Table IV shows the contributing factor for CAVI in heart failure patients. Multiple regression analysis shows that 6MWD was identified as an independent factor about CAVI ($\beta = -0.334, P < 0.01$).

**Discussion**

Kirkham reported an independent association between CAVI and sarcopenia in older U.K. adults, which reflected the usefulness of CAVI, but not PWV.20 We investigated the correlation between CAVI and physical function of elderly Japanese heart failure patients. The present study showed that CAVI was higher in patients with sarcopenia than in those without sarcopenia, even after adjustments of age, sex, arterial fibrillation, and ischemic cardiomyopathy. These results suggested that there was some relationship between physical function and CAVI in heart failure patients.

The prevalence of sarcopenia in community-dwelling Japanese elderly individuals aged 65-89 years is reportedly about 22.0%.21 On the other hand, we observed a high prevalence of sarcopenia (47%) in elderly heart failure patients. Although various factors are involved in the onset of sarcopenia, vascular dysfunction, caused by insulin resistance and chronic inflammation, or decreased sex hormones, such as testosterone, may be triggers.22,23 Arterial stiffness increases with age, and it is closely related to arteriosclerosis. Impaired physical function by aging can cause a decrease in activities of daily living, resulting in a vicious cycle of vascular dysfunction.

As for pathological mechanisms of skeletal muscle dysfunction in patients with heart failure, enhanced muscle deterioration due to chronic inflammation and sympathetic nerve activity, increased skeletal muscle catabolism induced by over-production of neurohumoral factors, and molecular mechanisms involving decreased protein assimilation have been reported.24-27 In elderly patients with heart failure, arterial stiffness and skeletal muscle catabolism may mutually affect each other. Insulin resistance may be a potential mechanism for skeletal muscle loss causing elevated arterial stiffness. Skeletal muscle has been recently considered to be a secretory organ that synthesizes and releases various cytokines and other peptides called myokines. Reduced secretion of myokines from skeletal muscle cell may be involved in insulin resistance.28

Although aging influences the progression of both vascular dysfunction and sarcopenia, in the present study, heart failure patients with sarcopenia had higher CAVI. Therefore, the association between vascular dysfunction and skeletal muscle dysfunction may be relevant regardless of age-related changes.

Im, et al.29 reported an association between muscle mass deficits and arterial stiffness in middle-aged men using CAVI. We found no association between SMI and CAVI in elderly heart failure patients. However, CAVI was associated with physical function parameters, such as handgrip strength, 5MWS, 5RSST and 6MWD. We thought this association may be due to heart failure, and they also had skeletal muscle dysfunction. Patients with heart failure often had accompanying skeletal muscle abnormalities (e.g. reduced oxidative capacity of mitochondria and muscle fiber type substitution) in addition to skeletal muscle atrophy.24,30

Therefore, the decrease in skeletal muscle function may have affected muscular strength and motor ability, resulting in a relationship between arteriosclerosis and physical function. Newman, et al.31 also reported that physical function, rather than muscle mass, is associated with mortality risk. In the present study, the multiple regression analysis identified 6MWD as an independent determining factor for arterial stiffness. The 6MWD has been used as part of several assessment parameters—including physical function, exercise capacity, quality of

| Variable | Spearman’s rank correlation coefficient ($\rho$) | P-value |
|----------|---------------------------------------------|--------|
| Age      | 0.252                                       | < 0.05 |
| BMI      | −0.017                                      | n.s.   |
| Alb      | 0.067                                       | n.s.   |
| Cre      | 0.184                                       | n.s.   |
| BNP      | −0.007                                      | n.s.   |
| EF       | −0.047                                      | n.s.   |
| E/e'     | 0.148                                       | n.s.   |
| sBP      | 0.112                                       | n.s.   |
| dBP      | 0.017                                       | n.s.   |
| HR       | 0.005                                       | n.s.   |
| SMI      | −0.144                                      | n.s.   |
| Handgrip strength | −0.204                                 | < 0.05 |
| 5MWS     | 0.216                                       | < 0.05 |
| 5RSST    | 0.328                                       | < 0.05 |
| 6MWD     | −0.347                                      | < 0.01 |

CAVI indicates cardio-ankle vascular index; BMI, body mass index; Alb, albumin; Cre, creatinine; BNP, brain natriuretic peptide; EF, ejection fraction; E/e', ratio of early transient filling velocity to early diastolic velocity; sBP, systolic blood pressure; dBP, diastolic blood pressure; HR, heart rate; SMI, skeletal muscle mass index; 5MWS, 5-meter walk speed; 5RSST, 5 repetition sit-to-stand time; and 6MWD, 6-minute walk distance.
Determinant of CAVI by Multiple Regression Analysis

| Variable | r    | $r^2$ | $\beta$ | P-value |
|----------|------|-------|---------|---------|
| 6MWD     | 0.334 | 0.119 | -0.334  | < 0.01  |

The adjustment factors are: age, sex, atrial fibrillation, ischemia, handgrip strength, 5 repetition sit-to-stand time, and 6-minute walk distance. CAVI indicates cardio-ankle vascular index; 6MWD, 6-minute walk distance; $r$, multiple correlation coefficient; $r^2$, coefficient of determination; and $\beta$, standardized partial regression coefficient.

The adjutment factors are: age, sex, atrial fibrillation, ischemia, handgrip strength, 5 repetition sit-to-stand time, and 6-minute walk distance. CAVI indicates cardio-ankle vascular index; 6MWD, 6-minute walk distance; $r$, multiple correlation coefficient; $r^2$, coefficient of determination; and $\beta$, standardized partial regression coefficient.

Table IV. Determinant of CAVI by Multiple Regression Analysis

Figure 4. Scatter plot of 6MWD and CAVI. 6MWD indicates 6-minute walk distance; and CAVI, Cardio-Ankle Vascular Index.

Conclusions

Physical function and arterial stiffness as a vascular function complemented each other in elderly heart failure patients. Further studies on improving arterial stiffness as well as physical function might be useful for better management of elderly heart failure patients.

Study limitations: The present study has some limitations. First, skeletal muscle mass was assessed by BIA. Since skeletal muscle tissue generally contains much more water than fat tissue in the body, BIA measures body composition using this property. In patients with heart failure, skeletal muscle tissue may have been overestimated because of edema. However, as the patients included in the present study had undergone cardiac rehabilitation during hospitalization, and body composition was measured at discharge when their heart failure would have been stable, the excess body water due to heart failure would have been reduced.

Second, because data in this observational study was obtained under medication for heart failure, the influence of medication cannot be excluded.

Third, about 50% of subjects had atrial fibrillation. When measuring a stable pulse wave, atrial fibrillation is disadvantageous. However, this study confirmed a stable pulse wave. The incidence of atrial fibrillation tends to be higher in elderly patients with heart failure. Therefore, it is important to elucidate the pathology, including atrial fibrillation, to conduct research on elderly patients with heart failure.

Finally, this was an observational study at a single institution, so the number of samples was limited. However, data were obtained from series of tests carried out by some of the most experienced physiological testing specialists and physical therapists at this facility, we believe that the quality of the assessments was high.

Acknowledgments

We thank the cardiac rehabilitation staff of the Toho University Sakura Medical Center, Hajime Kiyokawa,
Disclosure

Conflicts of interest: None.

References

1. Evans WJ. Skeletal muscle loss: cachexia, sarcopenia, and inactivity. Am J Clin Nutr 2010; 91: 1123S-7S.
2. Abbatecola AM, Chiidini P, Gallo C, et al. Health ABC study: Pulse wave velocity is associated with muscle mass decline: Health ABC study. Age (Dordr) 2012; 34: 469-78.
3. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002; 50: 889-96.
4. Karakelides H, Nair KS. Sarcopenia of aging and its metabolic impact. Curr Top Dev Biol 2005; 68: 123-48.
5. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002; 346: 793-801.
6. Karpman VL. The theoretical analysis of Fick's equation. On the centennial of the use of Fick's principle in physiology. Z Kardiol 1975; 64: 801-8.
7. Sampaio RA, Sampaio PY, Yamada M, et al. Arterial stiffness is associated with low skeletal muscle mass in Japanese community-dwelling older adults. Geriatr Gerontol Int 2014; 14 (Supplement 1): 109-14.
8. Brown BH, Karatzas T, Nacielyn R, Clarke RG. Determination of upper arm muscle and fat areas using electrical impedance measurements. Clin Phys Physiol Meas 1988; 9: 45-55.
9. Tuohimaa P, Gallacher D, Grannum J, et al. Bioimpedance analysis: potential for measuring lower limb skeletal muscle mass. J Parenter Enter Nutr 1999; 23: 96-103.
10. Pietrobelli A, Morini P, Battistini N, Chiumello G, Nuitive C, Heymsfield SB. Appendicular skeletal muscle mass: prediction from multiple frequency segmental bioimpedance analysis. Eur J Clin Nutr 1998; 52: 507-11.
11. Malavolti M, Massi C, Poli M, et al. Cross-calibration of eight-polar bioelectrical impedance analysis versus dual-energy X-ray absorptiometry for the assessment of total and appendicular body composition in healthy subjects aged 21-82 years. Ann Hum Biol 2003; 30: 380-91.
12. Cesari M, Kritchevsky SB, Penninx BW, et al. Prognostic value of usual gait speed in well-functioning older people—results from the Health, Aging and Body Composition Study. J Am Geriatr Soc 2005; 53: 1675-80.
13. Lo AX, Donnelly JP, McGwin G, Bittner V, Ahmed A, Brown CJ. Impact of gait speed and instrumental activities of daily living on all-cause mortality in adults 265 years with heart failure. Am J Cardiol 2015; 115: 797-801.
14. Guralnik JM, Simonsick EM, Ferrucci L, et al. 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.
15. ATS. Erratum: ATS Statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2016; 193: 1185.
16. McKee PA, Castelli WP, McNamara PM, Kannell WB. The natural history of congestive heart failure: the Framingham study. N Engl J Med 1971; 285: 1441-6.
17. ATS. Erratum: ATS Statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2016; 193: 1185.
18. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc 2014; 15: 95-101.
19. Kirkham FA, Bunting E, Fantin F, Zamboni M, Rajkumar C. Independent association between cardio-ankle vascular index and sarcopenia in older U.K. Adults. J Am Geriatr Soc 2019; 67: 317-22.
20. Yamada M, Nishiguchi S, Fukutani N, et al. Prevalence of sarcopenia in community-dwelling Japanese older adults. J Am Med Dir Assoc 2013; 14: 911-5.
21. Pasini E, Aquilani R, Dioguardi FS, D’Antona G, Gheorghiade M, Taegmeyer H. Hypercatabolic syndrome: molecular basis and effects of nutritional supplements with amino acids. Am J Cardiol 2008; 101: 11E-5E.
22. Angulo J, El Assar M, Rodriguez-Mañas L. Frailty and sarcopenia as the basis for the phenotypic manifestation of chronic diseases in older adults. Mol Aspects Med 2016; 50: 1-32.
23. Middlekauff HR. Making the case for skeletal myopathy as the major limitation of exercise capacity in heart failure. Circ Heart Fail 2010; 3: 537-46.
24. Yoshida T, Tabony AM, Galvez S, et al. Molecular mechanisms and signaling pathways of angiotensin II-induced muscle wasting: potential therapeutic targets for cardiac cachexia. Int J Biochem Cell Biol 2013; 45: 2322-32.
25. Kinugawa S, Takada S, Matsushima S, Okita K, Tsutsui H. Skeletal muscle abnormalities in heart failure. Int Heart J 2015; 56: 475-84.
26. Kadoguchi T, Kinugawa S, Takada S, et al. Angiotensin II can directly induce mitochondrial dysfunction, decrease oxidative fibre number and induce atrophy in mouse hindlimb skeletal muscle. Exp Physiol 2015; 100: 312-22.
27. Pedersen BK. Muscle as a secretory organ. Compr Physiol 2013; 3: 1337-62.
28. Im HJ, Choi HJ, Jeong SM, Kim HJ, Son JS, Oh HJ. The association between muscle mass deficits and arterial stiffness in middle-aged men. Nutr Metabol Cardiovasc Dis 2017; 27: 1130-5.
29. Drexler H, Riede U, Münzel T, König H, Funke E, Just H. Alterations of skeletal muscle in chronic heart failure. Circulation 1992; 85: 1751-9.
30. Newman AB, Kupelian V, Visser M, et al. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. J Gerontol A Biol Sci Med Sci 2006; 61: 72-7.
31. Brandel MC, Mediano MFF, Ferreira RR, et al. Correlation of 6-min walk test with left ventricular function and quality of life in heart failure due to Chagas disease. Trop Med Int Health 2017; 22: 1314-21.
32. Shoemaker MJ, Curtis AB, Vangsnes E, Dickinson MG. Clinically meaningful change estimates for the six-minute walk test and daily activity in individuals with chronic heart failure. Cardiopulm Phys Ther J 2013; 24: 21-9.
33. Cahan LP, Mathier MA, Semigran MJ, Dec GW, DiSalvo TG. The six-minute walk test predicts peak oxygen uptake and survival in patients with advanced heart failure. Chest 1996; 110: 325-32.
34. Faggiano P, D’Alòia A, Gualeni A, Lavatelli A, Giordano A. Assessment of oxygen uptake during the 6-minute walking test in patients with heart failure: preliminary experience with a portable device. Am Heart J 1997; 134: 203-6.
35. Alkao M, Chun YH, Wada H, et al. Current status of clinical background of patients with atrial fibrillation in a community-based survey: the Fushimi AF Registry. J Cardiol 2013; 61: 260-6.