Sarcopenia: Prevalence and Prognostic Implications in Elderly Patients with Cardiovascular Disease

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Abstract

Aims Sarcopenia has recently been given an ICD-10 code. However, there have been no systematic investigations regarding the prevalence or prognostic value of sarcopenia in cardiovascular disease (CVD) according to the international consensus definition. The present study was performed to investigate the prevalence and prognostic value of sarcopenia in elderly patients with CVD.

Methods and results The study population consisted of 1603 admitted patients aged ≥65 years (74.4 ± 6.2 years, 1049 men) with CVD. Sarcopenia was defined according to the recommended diagnostic algorithm of the Asia Working Group for Sarcopenia. The endpoint for the study was all-cause mortality. The overall sarcopenia prevalence rate was 29.7% (19.6% in men and 48.7% in women). The prevalence rates of sarcopenia across major diagnostic categories were as follows: acute coronary syndrome, 17.8%; post-cardiac surgery, 31.8%; and heart failure, 35.2%. During the 2.3 ± 2.1-year follow-up period, 175 deaths occurred. Patients with sarcopenia showed higher risk of all-cause mortality compared with non-sarcopenic patients (adjusted hazard ratio: 1.44; 95% confidence interval: 1.01–2.05; P = 0.044).

Conclusions Sarcopenia is highly prevalent among elderly patients with CVD and is associated with increased mortality risk.

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Key words: Sarcopenia; Cardiovascular disease; Elderly; Prevalence; Prognosis

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Introduction

Sarcopenia is becoming a major health issue with the aging of the world’s population [1-7]. Depending on the diagnostic criteria used, sarcopenia has estimated prevalence rates of approximately 1% – 29% in people dwelling in the community [8-10], 10.2% – 60% in hospitalized patients [11-14], and 14.3% – 32.8% in those in long-term care [15, 16]. In addition, the number of patients with sarcopenia has been suggested to increase over the next 30 years [17]. Therefore, it is becoming a major public health issue[18].

Based on the international recommendations [19-21], a diagnosis of sarcopenia is made in patients with low skeletal muscle mass plus low handgrip strength (weakness) and/or a low gait speed (slowness). The Asian Working Group for Sarcopenia (AWGS) has recently proposed a diagnostic algorithm for sarcopenia
based on currently available evidence in Asia [21]. However, there have been no systematic investigations of the prevalence and prognostic values of sarcopenia in elderly patients with cardiovascular disease (CVD) according to the recommended diagnostic strategy. Therefore, the present study was performed to investigate the prevalence and prognostic value of sarcopenia in elderly patients with CVD.

**Methods**

In the Kitasato University Cardiac Rehabilitation Database, we identified a total of 2792 consecutive patients with CVD aged ≥ 65 years old admitted between May 1, 2006, and December 31, 2015. After excluding patients with unstable medical condition or severe disability (n = 705), those that died before evaluation of sarcopenia (n = 210), and those for whom information regarding sarcopenia evaluation was missing (n = 274), 1603 patients were included in this study. We underwent evaluation of both usual gait speed and grip strength at hospital discharge as routine geriatric assessment.

Data on all variables were collected from electronic medical records. Height was measured to the nearest 0.1 cm using a stadiometer, weight was determined using a calibrated scale to the nearest 0.1 kg at hospital discharge, and body mass index (BMI) was calculated as body weight (kg) divided by height (m) squared. The endpoint of this study was all-cause mortality, and the time for the endpoint was calculated as the number of days from the date of handgrip and gait speed measurements to the date of the event.

We measured handgrip strength and usual gait speed before hospital discharge [22]. Handgrip strength was measured using a digital dynamometer (TKK 5101 Grip-D; Takei, Tokyo, Japan). Sitting on a bench with the elbow joint flexed at 90°, the participant squeezed gradually and continuously for 3 s, performing the test with the right and left hands in turn. The greatest strength values on the right and left sides were averaged and expressed as absolute values (kg). For measurement of usual gait speed, the patients were asked to walk at their usual speed, and were timed over the middle 10 m of a 16-m walkway. In accordance with the recommended diagnostic algorithm of the AWGS [21], weakness was defined as handgrip strength < 26 kg for men and < 18 kg for women, and slowness was defined as ≤ 0.8 m/s for both sexes.

Appendicular skeletal muscle mass (ASM) was estimated according to an anthropometric equation previously validated in Asian populations [4, 23, 24].

\[
\text{ASM} = 0.193 \times \text{body weight} + 0.107 \times \text{height} - 4.157 \times \text{sex} - 0.037 \times \text{age} - 2.631
\]

With dual-energy X-ray absorptiometry as the gold standard, the equation model was reported to have an adjusted \(R^2\) of 0.90 [23]. Low muscle mass was defined as skeletal muscle index (SMI, defined as ASM/height\(^2\)) < 7.0 kg/m\(^2\) in men and < 5.4 kg/m\(^2\) in women [21].

A diagnosis of sarcopenia was made in subjects with a low muscle mass plus weakness and/or slowness [21].

Continuous variables are expressed as the means ± standard deviation, and categorical variables are expressed as numbers and percentages. The cohort was divided into two groups according to weakness, slowness, and sarcopenia. Baseline characteristics were compared by unpaired t test or Fisher’s exact test where appropriate.

The cumulative incidence of mortality during follow-up was calculated according to the presence of weakness, slowness, and sarcopenia using the Kaplan–Meier curves. Intergroup differences were estimated by the log-rank test. Cox regression analysis was performed to evaluate the prognostic capabilities of weakness,
Sarcopenia: Prevalence and Prognostic Implications in Elderly Patients with Cardiovascular Disease

The overall prevalence of sarcopenia using the AWGS definition was 29.7%. Figure 2 shows the prevalence rates of weakness, slowness, and sarcopenia across age and gender categories. The prevalence rate increased with age and in women (P < 0.001), especially in patients over 75 years old. Female patients had significantly higher prevalence rates of sarcopenia than male patients (48.9% vs. 19.6%, respectively; P < 0.001). The prevalence rates of weakness and slowness were 56.8% and 27.6%, respectively. The prevalence rates of sarcopenia across major diagnostic categories were as follows: acute coronary syndrome, 17.8%; post-cardiac surgery, 31.8%; and heart failure, 35.2% (Figure 3). Figure 4 shows the prevalence rates across BMI categories. The prevalence of sarcopenia was increased with lower BMI categories. On the other hand, BMI and prevalence of weakness showed an inverse J-shaped relation, and that with slowness showed a U-shaped relation.

During the 2.3 ± 2.1-year follow-up period, 175 deaths occurred. Kaplan–Meier curves followed by log-rank test showed that all-cause mortality increased significantly in patients with weakness, slowness, and sarcopenia (Figure 5 A–C), and these associations were similar in both men and women.

Table 2 shows the results of univariate and multivariate Cox regression analyses for all-cause mortality. Weakness, slowness, and sarcopenia were all independent predictors of mortality after adjusting for age, sex (Model 1), cardiovascular risk factors (Model 2), and the presence of cancer (Model 3).

Figure 6 shows the dose–response associations of handgrip strength and gait speed with mortality. Mortality risk increased with decreasing handgrip strength and gait speed in both sexes, with an inverse J-shaped association, although the slopes of the curves for women were steeper than those for men.
### Table 1: Baseline Characteristics

<table>
<thead>
<tr>
<th>Factor</th>
<th>All Patients</th>
<th>Weakness</th>
<th>Slowness</th>
<th>Sarcopenia</th>
<th>P value</th>
<th>No weakness</th>
<th>Weakness</th>
<th>Slowness</th>
<th>No sarcopenia</th>
<th>Sarcopenia</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>1603</td>
<td>692 (43.2)</td>
<td>911 (56.8)</td>
<td>1160 (72.4)</td>
<td>443 (27.6)</td>
<td>1127 (70.3)</td>
<td>476 (29.7)</td>
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<tr>
<td>Age, yrs</td>
<td>74.4 ± 6.2</td>
<td>72.1 ± 5.2</td>
<td>76.1 ± 6.4</td>
<td>73.1 ± 5.5</td>
<td>77.7 ± 6.7</td>
<td>73.0 ± 5.7</td>
<td>77.5 ± 6.4</td>
<td>&lt;0.001</td>
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<tr>
<td>Male (%)</td>
<td>1049 (65.4)</td>
<td>531 (76.7)</td>
<td>518 (56.9)</td>
<td>826 (71.2)</td>
<td>223 (50.3)</td>
<td>843 (74.8)</td>
<td>206 (43.3)</td>
<td>&lt;0.001</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>22.7 ± 3.5</td>
<td>23.6 ± 3.3</td>
<td>22.1 ± 3.6</td>
<td>22.8 ± 3.4</td>
<td>22.6 ± 3.9</td>
<td>24.1 ± 3.1</td>
<td>19.5 ± 1.9</td>
<td>&lt;0.001</td>
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<tr>
<td>Diagnostic category (%)</td>
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<tr>
<td>Heart failure</td>
<td>702 (43.8)</td>
<td>252 (36.4)</td>
<td>450 (49.4)</td>
<td>455 (39.2)</td>
<td>247 (55.8)</td>
<td>455 (40.4)</td>
<td>247 (51.9)</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>ACS</td>
<td>359 (22.4)</td>
<td>224 (32.4)</td>
<td>135 (14.8)</td>
<td>315 (27.2)</td>
<td>44 (9.9)</td>
<td>295 (26.2)</td>
<td>64 (13.4)</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>Cardiac surgery</td>
<td>337 (21.0)</td>
<td>120 (17.3)</td>
<td>217 (23.8)</td>
<td>247 (21.3)</td>
<td>90 (20.3)</td>
<td>230 (20.4)</td>
<td>107 (22.5)</td>
<td>0.349</td>
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<tr>
<td>Others</td>
<td>205 (12.8)</td>
<td>96 (13.9)</td>
<td>109 (12.0)</td>
<td>143 (12.3)</td>
<td>62 (14.0)</td>
<td>147 (13.0)</td>
<td>58 (12.2)</td>
<td>0.683</td>
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<tr>
<td>Hypertension (%)</td>
<td>1114 (69.5)</td>
<td>481 (69.5)</td>
<td>633 (69.5)</td>
<td>793 (68.4)</td>
<td>321 (72.5)</td>
<td>811 (72.0)</td>
<td>303 (63.4)</td>
<td>0.001</td>
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<tr>
<td>Dyslipidemia (%)</td>
<td>826 (51.5)</td>
<td>386 (55.8)</td>
<td>440 (48.3)</td>
<td>620 (53.4)</td>
<td>206 (46.5)</td>
<td>629 (55.9)</td>
<td>197 (41.2)</td>
<td>&lt;0.001</td>
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<tr>
<td>Diabetes mellitus (%)</td>
<td>625 (39.0)</td>
<td>243 (35.1)</td>
<td>382 (41.9)</td>
<td>435 (37.5)</td>
<td>190 (42.9)</td>
<td>465 (41.3)</td>
<td>160 (33.6)</td>
<td>0.004</td>
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<tr>
<td>Obesity (%)</td>
<td>381 (23.8)</td>
<td>214 (30.8)</td>
<td>167 (18.4)</td>
<td>284 (24.5)</td>
<td>97 (21.9)</td>
<td>381 (33.8)</td>
<td>0 (0.0)</td>
<td>&lt;0.001</td>
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<tr>
<td>Prior MI (%)</td>
<td>326 (20.3)</td>
<td>144 (20.8)</td>
<td>182 (20.0)</td>
<td>234 (20.2)</td>
<td>92 (20.8)</td>
<td>246 (21.8)</td>
<td>80 (16.8)</td>
<td>0.021</td>
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<tr>
<td>Cancer (%)</td>
<td>188 (11.7)</td>
<td>75 (10.8)</td>
<td>113 (12.4)</td>
<td>138 (11.9)</td>
<td>50 (11.3)</td>
<td>133 (11.8)</td>
<td>55 (11.6)</td>
<td>0.932</td>
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<tr>
<td>Grip strength, kg</td>
<td>22.3 ± 8.3</td>
<td>29.4 ± 6.1</td>
<td>17.0 ± 5.1</td>
<td>23.9 ± 8.0</td>
<td>18.1 ± 7.6</td>
<td>25.0 ± 7.8</td>
<td>16.1 ± 5.8</td>
<td>&lt;0.001</td>
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<tr>
<td>Gait speed, m/sec</td>
<td>0.97 ± 0.29</td>
<td>1.08 ± 0.26</td>
<td>0.88 ± 0.27</td>
<td>1.10 ± 0.20</td>
<td>0.61 ± 0.13</td>
<td>1.02 ± 0.28</td>
<td>0.84 ± 0.27</td>
<td>&lt;0.001</td>
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<tr>
<td>SMI, kg/m²</td>
<td>6.69 ± 1.22</td>
<td>7.13 ± 1.03</td>
<td>6.36 ± 1.26</td>
<td>6.84 ± 1.15</td>
<td>6.30 ± 1.31</td>
<td>7.17 ± 0.96</td>
<td>5.56 ± 1.00</td>
<td>&lt;0.001</td>
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<tr>
<td>Sarcopenia (%)</td>
<td>477 (29.8)</td>
<td>18 (2.6)</td>
<td>458 (50.3)</td>
<td>265 (22.8)</td>
<td>211 (47.6)</td>
<td>476 (100.0)</td>
<td>&lt;0.001</td>
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<tr>
<td>All-cause death (%)</td>
<td>175 (10.9)</td>
<td>49 (7.1)</td>
<td>126 (13.8)</td>
<td>102 (8.8)</td>
<td>73 (16.5)</td>
<td>101 (9.0)</td>
<td>74 (15.5)</td>
<td>&lt;0.001</td>
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</tbody>
</table>

Values are means ± SD or %.

ACS = acute coronary syndrome; MI = myocardial infarction; SMI = skeletal muscle index.
Figure 1: Application of the Asian Working Group for Sarcopenia algorithm to identify sarcopenia. (SMI = skeletal muscle index)

Figure 2: Prevalence rates of weakness, slowness, and sarcopenia by age and gender.

Figure 3: Prevalence rates of weakness, slowness, and sarcopenia according to major diagnostic categories in all patients and patients aged ≥ 75 years. (ACS = acute coronary syndrome)
Figure 4: Prevalence rates of weakness, slowness, and sarcopenia across BMI categories.

Figure 5: Associations of weakness, slowness, and sarcopenia with mortality.
Table 2: Univariate and multivariate cox regression models for all-cause mortality

<table>
<thead>
<tr>
<th></th>
<th>Weakness (HR [95% CI])</th>
<th>P value</th>
<th>Slowness (HR [95% CI])</th>
<th>P value</th>
<th>Sarcopenia (HR [95% CI])</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate</td>
<td>1.98 (1.42 - 2.75)</td>
<td>&lt;0.001</td>
<td>2.74 (2.02 - 3.71)</td>
<td>&lt;0.001</td>
<td>2.02 (1.50 - 2.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 1:</td>
<td></td>
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</tr>
<tr>
<td>Adjusted by age and gender</td>
<td>1.72 (1.21 - 2.44)</td>
<td>0.002</td>
<td>2.44 (1.76 - 3.38)</td>
<td>&lt;0.001</td>
<td>1.87 (1.34 - 2.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2:</td>
<td></td>
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<tr>
<td>Model 1 + cardiovascular risk factors</td>
<td>1.48 (1.04 - 2.10)</td>
<td>0.031</td>
<td>2.32 (1.66 - 3.23)</td>
<td>&lt;0.001</td>
<td>1.46 (1.03 - 2.08)</td>
<td>0.036</td>
</tr>
<tr>
<td>Model 3:</td>
<td>Model 2 + presence of cancer</td>
<td>1.47 (1.03 - 2.10)</td>
<td>0.033</td>
<td>2.33 (1.67 - 3.25)</td>
<td>0.001</td>
<td>1.44 (1.01 - 2.05)</td>
</tr>
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</table>

HR = hazard ratio; CI = confidence interval.

Figure 6: Dose–response associations of handgrip strength and gait speed with all-cause mortality.

Discussion

The present study was performed to examine the prevalence and prognostic value of sarcopenia in elderly patients with CVD. The overall prevalence of sarcopenia using the AWGS definition was 29.7% (19.6% in men and 48.7% in women). Sarcopenia was associated with all-cause mortality in both sexes after adjusting for potential confounders. To our knowledge, this is the first study to demonstrate the prognostic value of sarcopenia defined by muscle function and muscle mass in elderly patients.
with CVD. Furthermore, this report represents one of the largest studies of sarcopenia research in a clinical population.

Recent studies estimated the prevalence rates of sarcopenia to be approximately 1% – 29% in people dwelling within the community [8-10], 10.2% – 60% in hospitalized patients [11-14], and 14.3% – 32.8% in those in long-term care [15, 16]. A recent meta-analysis of studies in the general population, including 35 reports with a total of 58404 individuals, showed that the prevalence of sarcopenia defined by low muscle mass was 10% in both sexes [25], and the prevalence was higher for BIA-based methods than DXA-based methods (BIA: 13%, DXA: 8% in both sexes). Using the AWGS criteria, Han et al. [26] reported that the prevalence rates of sarcopenia in 1069 older men and women in China were 6.4% and 11.5%, respectively. In another study, the prevalence of sarcopenia among 2000 community-dwelling older men in Hong Kong was 9.4% [27]. Yuki et al. [10] reported the prevalence rates of sarcopenia in 720 community-dwelling Japanese individuals aged 65 – 79 years old as 4.9% in men and 4.5% in women. In the present study, the prevalence rate of sarcopenia in elderly CVD patients was 29.7%; the rates for men and women were 19.6% and 48.7%, respectively, which were as much as 5× and 10× higher than those in the general population for men and women, respectively. These data suggest that there is a need to increase awareness and develop effective preventive strategies for sarcopenia in elderly patients with CVD.

Sarcopenia was more common in patients with heart failure, and in women. In the present study, the prevalence rate of sarcopenia in heart failure was highest among all CVD categories (35.2% in all heart failure patients, 46.7% in heart failure patients ≥ 75 years old) (Figure 3). Previously reported prevalence rates of sarcopenia were 19.5% – 26.1% in patients with chronic heart failure [28-30]. However, these study populations consisted of ambulatory patients, including non-elderly patients, and sarcopenia was defined only by low muscle mass. The prevalence of sarcopenia in hospitalized heart failure patients was as high as 45% in a recent multicenter cohort study performed in hospitalized geriatric patients in Italy, which was consistent with the results reported here in hospitalized patients with heart failure. Previous studies indicated higher prevalence rates of frailty and physical disability in older female CVD patients. The prevalence of sarcopenia in women in the present study was 48.7%. These results indicate that the prevalence rate of sarcopenia in elderly CVD patients, especially women and those with heart failure is markedly higher than that in the general elderly population.

Handgrip strength and gait speed have been widely used for evaluation of physical function in older adults, and weakness and slowness are core components of frailty and sarcopenia.[31-33] The prevalence rates of weakness and slowness among elderly participants vary depending on the population and the definitions used [34]. In the NILS-LSA study, a population-based survey of aging, the prevalence rates of weakness and slowness defined according to the AWGS criteria were 15.7% and 7.3%, respectively (10.0% and 5.4% in men, and 15.7% and 9.1% in women) [35]. A recent report in China did not present the prevalence of weakness in the entire population, but the rate of slowness was 17.6% (13.1% in men and 21.1% in women) [26]. The prevalence rates of weakness and slowness were extremely high in our cohort, and were 3.6× and 3.8× higher than those in the general population of Japan, respectively.

Sarcopenic or dynapenic obesity has recently attracted the attention of medical professionals with regard to disability in the elderly. In the present study, the prevalence of sarcopenia was increased with lower BMI categories. On the other hand, BMI and the
prevalence of weakness showed an inverse J-shaped relation, and that with slowness showed a U-shaped relation. The low prevalence of sarcopenia in patients with higher BMI was consistent with previous studies regarding sarcopenic obesity [36, 37]. This could be explained by the strong correlation between BMI and SMI [38]. The increased prevalence rates of weakness and slowness in the higher BMI categories would be more clinically important. The combination of obesity and weakness (dynapenic obesity) would cause greater impairment of the activities of daily living than either obesity or weakness alone. The prevalence of sarcopenic or dynapenic obesity differed significantly among studies depending on the methods used for muscle mass quantification and the cutoff values. Similarly, the methods used to define obesity differed substantially among studies, including BMI, bioimpedance, and visceral fat area. Cut-off values for obesity were also different among studies. Therefore, a consensus definition of sarcopenic or dynapenic obesity is needed to promote standardized diagnosis and management.

The results of the present study indicated that sarcopenia predicted all-cause mortality in elderly patients with CVD. Several studies have assessed the association of sarcopenia with mortality. Bianchi et al. [39] reported that sarcopenia among community-dwelling older adults in Italy, defined by the European Working Group on Sarcopenia in Older People (EWGSOP) criteria, was associated with a 1.88-fold higher mortality rate compared to the general population. Similarly, in a multicenter observational study, Vetrano et al. reported significant associations between sarcopenia and both inhospital (adjusted hazard ratio: 3.45; 95% CI: 1.35 – 8.86) and 1-year mortality (adjusted hazard ratio: 1.59; 95% CI: 1.10 – 2.41) among 770 older adults admitted to acute care wards [40]. These results were confirmed in a recent systematic review and meta-analysis [41]; they examined the prognostic influence of sarcopenia defined by the EWGSOP criteria in older people, in a meta-analysis including 12 cohort studies, and found a higher mortality rate among sarcopenic subjects (pooled odds ratio = 3.60; 95% CI = 2.96 – 4.37) [41]. Although the prognostic value of sarcopenia is controversial in general Asian populations [10, 42], it is robust in hospitalized elderly patients [4].

In the present study, we demonstrated the dose–response associations of handgrip strength and gait speed with mortality rate in elderly patients with CVD. Mortality risk increased as handgrip strength and gait speed decreased in both sexes with an inverse J-shaped association, and the slopes of the curves were steeper for women than for men. Importantly, the hazard ratio for mortality increased around the established cutoff value in both sexes. Consistent with our results, a recent study indicated a similar dose–response association of gait speed with operative mortality in older patients undergoing cardiac surgery [43]. These results support the consensus cutoff of sarcopenia for identifying risk in elderly patients with CVD.

This study had several limitations. First, this was a single-center observational study with limited follow-up. Second, our study population included only CVD patients admitted to an acute care hospital, and the external validity of our results to CVD patients in the community is unclear. Third, there were some unmeasured factors associated with sarcopenia and mortality, such as physical activity, socioeconomic status, and dementia. Fourth, we estimated muscle mass using an anthropometric equation, which has previously been validated in Asian populations, rather than bioimpedance analysis (BIA) or dual energy X-ray absorptiometry (DEXA), as recommended by the EWGSOP [19] and AWGS [21]. However, BIA and DEXA are rarely available in developing or developed countries [4, 44, 45]. Furthermore, common conditions in hospitalized CVD patients (e.g., peripheral edema, low albuminuria, kidney
Sarcopenia: Prevalence and Prognostic Implications in Elderly Patients with Cardiovascular Disease

Sarcopenia is highly prevalent among elderly patients with CVD and is associated with increased mortality risk. Our data suggest that there is a need to increase awareness and develop effective preventive strategies for sarcopenia in elderly patients with CVD.

Conflicts of Interest

All authors have 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.)

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consensus on definition and diagnosis:


23. Of note, the authors of the report state that the definition of sarcopenia is based on the percentage of body mass lost, which is different from the original definition based on muscle mass.


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