Sarcopenia based on the Asian Working Group for Sarcopenia criteria and all-cause mortality risk in older Japanese adults

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Aim: The association between sarcopenia diagnosed according to the criteria of the Asian Working Group for Sarcopenia and increased mortality risk is currently unknown. The present study assessed the longitudinal relationship between sarcopenia and mortality risk in an elderly Japanese population.

Methods: Participants were 720 community-dwelling Japanese individuals aged 65–79 years at baseline (November 1997 to April 2000). The participants were followed from baseline to 31 December 2014 (mean duration 11.0 years). Sarcopenia was diagnosed according to the Asian Working Group for Sarcopenia criteria, using extremity muscle mass assessed by dual-energy X-ray absorptiometry, grip strength and gait speed. A population dynamics survey was used to obtain information on deaths. The relationship between sarcopenia and mortality was assessed using Kaplan–Meier survival curves and Cox proportional hazards regression. The Cox proportional hazards model was used to control for potential confounders, including age at baseline, body mass index, total caloric intake, alcohol intake, current smoking habits, leisure-time physical activity and the number of current diseases.

Results: The fully adjusted hazard ratio for all-cause mortality among men in the sarcopenia group was 1.95 (95% confidence interval 1.04–3.67) compared with that in the normal group. No significant association between sarcopenia and all-cause mortality was observed among women.

Conclusion: The complications of sarcopenia, including low muscle mass, low grip strength and low gait speed, appear to be significant risks for mortality in older Japanese men.

Keywords: gait speed, grip strength, hazard ratio, muscle mass.

Introduction

There are currently approximately 32 million older adults in Japan, and this number is predicted to increase.1 Recent studies have reported the prevalence of sarcopenia as 9.6% in men and 7.7% in women based on the presence of low muscle mass, low muscle strength and low physical performance.2 Furthermore, elderly populations are increasing in Asian countries.3 The prevalence of sarcopenia in 1069 older men and women in China was 6.4% and 11.5%, respectively,4 and in Taiwan was 9.3% and 4.1%, respectively.5 Frailty syndrome and reduced physical ability are accelerated by sarcopenia.6,7 Accordingly, an investigation of the clinical outcomes associated with sarcopenia is essential in Japan’s aging society, and other Asian countries.

The European Working Group on Sarcopenia in Older People (EWGSOP) includes death as an adverse outcome of sarcopenia.6 Sarcopenia according to the EWGSOP criteria is associated with a poor survival rate in older Mexican and older Italian individuals.8,9 Recently, a definition and criteria for sarcopenia in older Asians was developed by the Asian Working Group for Sarcopenia (AWGS).10 Studies evaluating the association between the AWGS criteria and adverse outcomes are necessary to validate the clinical utility of these criteria. In addition, the association between sarcopenia diagnosed according to the AWGS criteria and mortality has yet to be elucidated.

The purpose of the present study was to determine the association between sarcopenia diagnosed according to the AWGS criteria and an algorithm, and all-cause mortality in a large population of older Japanese adults living in the community.
Methods

Participants

Participants were identified from the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA). The NILS-LSA is a population-based biennial survey of a cohort of approximately 2300 persons. Participants in the NILS-LSA were randomly selected from registered residents, and stratified according to both sex and decade of age. The NILS-LSA is a facility-based study with access to many types of testing equipment. Examinations, such as medical examinations, body composition, dietary intake, physical fitness tests and daily physical activity, were used for the diagnosis of sarcopenia in the NILS-LSA. The present study protocol was approved by the ethics committee of the National Institute for Geriatrics and Gerontology. All participants provided written informed consent for participation in the present study.

Participants included in the study at baseline were 412 men and 404 women aged 65–79 years who had participated in the first-wave examination of the NILS-LSA between November 1997 and April 2000. Individuals with missing data regarding sarcopenia or other variables were excluded. Accordingly, a total of 365 men and 355 women were included in the final study analysis.

Follow up

Participants were followed from baseline to 31 December 2014. The residential registry was used for the confirmation of residence status. Within the follow-up period, five participants moved out of the study area. A population dynamics survey was used to acquire information on deaths. Registrations of residence and death are required by law in Japan.

Muscle mass measurement

Skeletal muscle mass (in kg) in the extremities and the percentage of body fat were assessed by dual-energy X-ray absorptiometry (QDR-4500; Hologic, Bedford, MA, USA). Extremity fat-free mass minus bone mineral content was used as an index of the amount of muscle mass in the extremities.

Skeletal muscle index (SMI; kg/m²), which was calculated by extremity muscle mass divided by height squared, was used to evaluate sarcopenia. The cut-off point of SMI for low muscle mass was <7.0 kg/m² in men and <5.4 kg/m² in women.

Grip strength measurement

Grip strength (in kg) was measured using a handgrip dynamometer (T.K.K.4301a; Takei, Niigata, Japan) to assess muscle strength. Participants compressed the dynamometer with maximum force, alternating between the left and right hands. The maximum value from four trials for both hands was recorded. The cut-off point for low grip strength was 26 kg in men and 18 kg in women.

Gait speed measurement

A comfortable gait speed was used for the assessment of gait speed. Gait speed was measured using a walking analysis system that comprised light sensors to determine the start and end-points along an 11-m straight line, including acceleration and deceleration (YW-3; Yagami, Aichi, Japan). Gait speed was calculated by the time taken to walk for 10 m. The cut-off point for low gait speed was 0.8 m/s in men and women.

Sarcopenia definition

Sarcopenia was defined according to the AWGS algorithm. Participants who met the criteria for both low grip strength and/or low gait speed and low muscle mass were considered to have sarcopenia.

Other parameters

Height and weight were measured using digital scales with participants wearing only underwear, and were used to calculate body mass index (BMI; kg/m²). Data regarding current smoking habits, alcohol intake and medical history were assessed using self-completed questionnaires and were confirmed by a physician after a medical examination. A history of all medications used during the previous 2 weeks was self-reported by the participants. The participants also brought current medications to the study site. A record of the medications used was verified and coded by examining physicians. The number of comorbidities was defined as the sum of a history of cancer, heart disease, cerebrovascular disease, liver disease, chronic bronchitis, kidney disease, hypertension and diabetes. Trained interviewers used a questionnaire to assess physical activity using questions regarding activity intensity and frequency over the preceding year. The mean leisure-time physical activity per day was calculated (metabolic equivalents [MET]; MET × min/day). Participants were asked to weigh foods on a scale before cooking. Participants also took photographs of all meals before and after eating using a disposable camera. Photographs were used to complete missing data. Registered dieticians telephoned participants to obtain information in order to resolve discrepancies as necessary. The average for the intake of 123 nutrients over 3 days was calculated. The mean total caloric intake per day (kcal/day) was calculated from the 3-day dietary record.

Statistical analysis

Data are presented as mean ± standard error (SE). SAS 9.4 (SAS Institute, Cary, NC, USA) was used for all statistical analyses. P-values <0.05 were considered statistically
significant. Student’s t-test and the χ²-test were used to compare continuous and categorical variables, respectively, between the sarcopenia and normal groups. Differences in the history of kidney disease or diabetes between the sarcopenia and normal groups were assessed using Fisher’s exact test, because the minimum expected cell size was less than five.

The relationship between sarcopenia and survival rate was assessed using Kaplan–Meier survival curves. The equality of survival between the sarcopenia and normal groups was assessed using the log–rank test. Cox proportional hazards regression was used to assess the relationship between sarcopenia and mortality. Analyses using the Cox proportional hazards model were carried out using two adjusted models with different combinations of confounders. Age at baseline (continuous variable) was considered a confounder in model 1 for men and women. Age, BMI (kg/m²; <18.5, ≥18.5), leisure-time physical activity (MET × min/day; <59.2, 59.2–200.5 or ≥200.6), total caloric intake (kcal/day; <2172.8, ≥2172.8), alcohol intake (g; 0, <23, ≥23), current smoking (no, yes) and number of diseases (continuous variable) were adjusted in model 2 for men. Age (continuous variable), BMI (kg/m²; <18.5, ≥18.5), leisure-time physical activity (MET × min/day; <11.5, 11.5–92.0 or ≥92.1), total caloric intake (kcal/day; <1797.0, ≥1797.0) and number of comorbidities (continuous variable) were adjusted in model 2 for women.

Results

Table 1 presents data on participants at baseline according to sarcopenia status. In men, no significant differences in age were observed between the sarcopenia and normal groups. Body height (P < 0.01), bodyweight (P < 0.01) and BMI (P < 0.01) were significantly lower in the sarcopenia group than in the normal group. No significant differences in percentage body fat were noted between the normal and sarcopenia groups. Extremity muscle mass was significantly lower in the sarcopenia group than in the normal group (P < 0.0001). SMI (P < 0.0001), grip strength (P < 0.01) and gait speed (P < 0.01), which were used to make the diagnosis of sarcopenia, were significantly lower in the sarcopenia group than in the normal group. Total caloric intake (P < 0.05) and leisure-time physical activity (P < 0.01) were significantly lower in the sarcopenia group than in the normal group. No differences in alcohol intake or the ratio of current smokers were observed between groups. The proportion of patients with a history of kidney disease (P < 0.05) in the

Table 1 Characteristics of participants at baseline

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 365)</th>
<th>Women (n = 355)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal (n = 347)</td>
<td>Sarcopenia (n = 18)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>71.2 ± 0.2</td>
<td>72.6 ± 0.9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.2 ± 0.3</td>
<td>157.1 ± 1.6**</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>58.9 ± 0.5</td>
<td>51.4 ± 2.2**</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.6 ± 0.2</td>
<td>20.7 ± 0.7***</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>22.0 ± 0.2</td>
<td>21.7 ± 1.2</td>
</tr>
<tr>
<td>Extremity muscle mass (kg)</td>
<td>18.6 ± 0.1</td>
<td>15.6 ± 0.6***</td>
</tr>
<tr>
<td>Skeletal muscle index (kg/m²)</td>
<td>7.1 ± 0.1</td>
<td>6.3 ± 0.2***</td>
</tr>
<tr>
<td>Grip strength (kg)</td>
<td>36.5 ± 0.3</td>
<td>29.0 ± 1.9***</td>
</tr>
<tr>
<td>Gait speed (m/s)</td>
<td>1.3 ± 0.1</td>
<td>1.1 ± 0.1**</td>
</tr>
<tr>
<td>Leisure-time physical activity (MET × min/day)</td>
<td>184.3 ± 10.9</td>
<td>111.3 ± 34.8***</td>
</tr>
<tr>
<td>Total caloric intake (kcal/day)</td>
<td>2232.5 ± 22.3</td>
<td>2011.1 ± 97.9***</td>
</tr>
<tr>
<td>Alcohol intake (g/day)</td>
<td>12.2 ± 0.9</td>
<td>6.0 ± 3.1</td>
</tr>
<tr>
<td>Current smoking (n)</td>
<td>97 (28.0%)</td>
<td>7 (38.9%)</td>
</tr>
<tr>
<td>Medical history (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>21 (6.1%)</td>
<td>1 (5.6%)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>70 (20.2%)</td>
<td>5 (27.8%)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>29 (8.4%)</td>
<td>2 (11.1%)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>36 (10.4%)</td>
<td>1 (5.6%)</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>19 (5.5%)</td>
<td>1 (5.6%)</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>25 (7.2%)</td>
<td>4 (22.2%)**</td>
</tr>
<tr>
<td>Hypertension</td>
<td>115 (33.1%)</td>
<td>10 (55.6%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>43 (12.4%)</td>
<td>4 (22.2%)</td>
</tr>
<tr>
<td>No. comorbidities</td>
<td>1.0 ± 0.1</td>
<td>1.6 ± 0.3**</td>
</tr>
</tbody>
</table>

*P < 0.05, **P < 0.01, ***P < 0.0001. P-values were obtained using the t-test or χ²-test. MET; metabolic equivalents.
sarcopenia group was significantly higher than in the normal group. No differences in the proportions of patients with a history of cancer, heart disease, cerebral vascular disease, liver disease, chronic bronchitis, hypertension or diabetes were observed between groups. The number of comorbidities \( P < 0.05 \) was significantly higher in the sarcopenia group compared with the normal group.

Among women, participants with sarcopenia were older than those without sarcopenia \( P < 0.05 \). No significant differences in body height and percentage body fat were observed between the sarcopenia and normal groups. Bodyweight, BMI, and extremity muscle mass were significantly lower in the sarcopenia group compared with the normal group \( P < 0.0001 \) for all. SMI \( P < 0.0001 \) and grip strength \( P < 0.01 \), which were used to determine the diagnosis of sarcopenia, were significantly lower in the sarcopenia group compared with the normal group. However, no significant difference in gait speed was observed between the sarcopenia and normal groups. Bodyweight, BMI, and extremity muscle mass were significantly lower in the sarcopenia group compared with the normal group \( P < 0.0001 \) for all. SMI \( P < 0.0001 \) and grip strength \( P < 0.01 \), which were used to determine the diagnosis of sarcopenia, were significantly lower in the sarcopenia group compared with the normal group. However, no significant difference in gait speed was observed between the sarcopenia and normal groups. Total caloric intake \( P < 0.05 \) was significantly lower in the sarcopenia group than in the normal group. No significant differences in leisure-time physical activity were observed between the sarcopenia and normal groups. No differences in the proportion of current smokers or alcohol intake were observed between groups. Similarly, no differences in the proportions of patients with comparable medical histories were observed. No significant differences in the number of comorbidities were observed between the sarcopenia and normal groups.

A total of 173 deaths among men and 86 deaths among women occurred during the study follow-up periods. Among men, 12 (66.7%) with sarcopenia died compared with 161 (46.4%) without sarcopenia \( P < 0.01 \). Among women, five (31.3%) with sarcopenia died compared with 81 (23.9%) without sarcopenia (no significant difference). Kaplan–Meier survival curves for survival rate are shown according to sarcopenia in Figure 1. Among men, the survival rate during the follow-up period was lower in the sarcopenia group than in the normal group \( P < 0.01 \), log-rank test). However, no significant differences in survival rate were observed between the sarcopenia and normal groups in women.

Among men, the hazard ratio for all-cause mortality in the sarcopenia group in model 1 and model 2 was 1.86 (95% confidence interval [CI] 1.03–3.37) and 1.90 (95% CI 1.04–3.46), respectively (Table 2). Excluding deaths within the first 2 years, the hazard ratios of all-cause mortality with sarcopenia in model 1 and model 2 were 1.97 (95% CI 1.09–3.58), and 2.06 (95% CI 1.13–3.76), respectively (Table 2). Among women, no significant association was observed between sarcopenia and all-cause mortality. Furthermore, no significant association between sarcopenia and all-cause mortality was observed after the exclusion of early deaths (Table 2).

**Discussion**

The present study showed an association between sarcopenia diagnosed according to the AWGS criteria and algorithm and all-cause mortality in older Japanese men. Sarcopenia diagnosed according to the EWGSOP criteria has been associated with poor survival in older Mexican and older Italian adults. However, the association between sarcopenia diagnosed according to the AWGS criteria and mortality has not been reported in older Asian populations. In the present study, significant associations between sarcopenia diagnosed according to the AWGS criteria and all-cause mortality persisted in men after controlling for age, BMI, caloric intake, smoking habits, alcohol intake, leisure-time physical activity and medical history. These results confirm that the AWGS criteria are associated with an adverse outcome in older Asian men.

In the present study cohort, the risk of all-cause mortality was approximately twofold greater among men in the sarcopenia group than among those in the normal group. In previous studies of older Japanese individuals, the fully adjusted hazard ratio of 2-year mortality in the first tertile \(<23.5 \text{ cm}^2\) of the mid-upper-arm muscle area in frail older individuals, including women, was 2.03 (95% CI

![Figure 1](image-url)  
Kaplan–Meier survival curves according to the presence of sarcopenia in (a) men and (b) women. *P*-values were obtained using the log-rank test. NS, not significant.
Table 2  Relationship between sarcopenia and all-cause mortality

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
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<tbody>
<tr>
<td></td>
<td>Model 1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.86 (1.03–3.37)</td>
</tr>
<tr>
<td>Women</td>
<td>1.03 (0.41–2.60)</td>
</tr>
<tr>
<td>Excluding deaths</td>
<td></td>
</tr>
<tr>
<td>with first 2 years</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.97 (1.09–3.58)</td>
</tr>
<tr>
<td>Women</td>
<td>1.06 (0.42–2.68)</td>
</tr>
</tbody>
</table>

Model 1: adjusted for age. Model 2: adjusted for age, body mass index, leisure-time physical activity, total caloric intake, alcohol intake status, current smoking and number of comorbidities in men; adjusted for age, body mass index, leisure-time physical activity, total caloric intake and number of comorbidities in women.

1.36–3.02) compared with that in the third tertile.15 The fully adjusted relative risk of all-cause mortality, except external causes, in the first quintile (representative figure of the first quintile is approximately 26 kg) of grip strength in healthy men aged 65–74 years was 1.38 (95% CI 1.01–1.89) compared with that in the third quintile.16 Recently, older individuals, including women, with a subjective slow walking speed have been reported to have a higher hazard mortality ratio than elderly individuals with a subjective normal walking speed.17 These results are in line with previous studies. The AWGS diagnostic criteria for sarcopenia appear to reflect a decline in physical ability in older Japanese men.10

No associations between sarcopenia and all-cause mortality were observed in women. Similarly, sarcopenia diagnosed according to the modified criteria of EWGSOP was not associated with mortality in elderly Korean women.18 Muscle mass decrease is an essential requirement for the diagnosis of sarcopenia according to the AWGS criteria.10 However, muscle mass decrease was not found to be associated with aging among Asian women, including Japanese women.2,19,20 In the present study, there might have been older women with low muscle strength and/or low physical function without low muscle mass who were not diagnosed with sarcopenia. Adjusted muscle mass for weight or different cut-off values of low muscle mass according to age grade might relate sarcopenia to mortality in older Asian women.21 In addition, the coexistence of low muscle mass and metabolic syndrome increases the risk of type 2 diabetes mellitus and hypertension in Japanese women.22 High abdominal circumference was shown to be an independent risk factor of metabolic syndrome in older Korean women, but not in men.23 In the present study, BMI was significantly lower in the sarcopenia group than in the normal group, with no significant differences in body fat noted between the normal and sarcopenia groups in participants at baseline. Interestingly, a previous study using the same participants of the first-wave examination of the NILS-LSA reported increased fat mass in elderly men, but no change after 6 years of follow up in older women.24 The absence of sarcopenia in patients with obesity could contribute to survival in older women. However, Japanese women have greater longevity than men.1 Furthermore, the mortality rate in men with sarcopenia was 66.7%, whereas the mortality rate in women with sarcopenia was 31.3% during the follow-up period. A previous study with more than 20 years of follow up from baseline reported that grip strength was a significant predictor of poor survival in middle-aged and older adults in Japan.16 Further studies with longer follow-up periods are required to accurately determine the association between mortality and sarcopenia in older women.

The present study had several limitations. First, the association between the cause of death and sarcopenia was unclear. As there were fewer participants in the present study than in a previous study, the analysis regarding cause of death was statistically underpowered. Second, the mechanism of excess death induced by sarcopenia was not elucidated. Recent studies have shown that skeletal muscles secrete myokines, such as SPARC,25 which suppress colon tumorigenesis; and irisin,26,27 which is associated with adipose metabolism. The loss of skeletal muscles that occurs with sarcopenia might reduce myokine secretion. Furthermore, exercise could stimulate the production of myokines from skeletal muscles.25,26 Inactive lifestyles caused by sarcopenia might decrease muscular contractions.

In conclusion, the present study evaluated the association between sarcopenia based on the AWGS criteria and all-cause mortality in community-dwelling older adults over an 11-year follow-up period. The present results confirm that sarcopenia significantly increases the risk of all-cause mortality in older men. The findings of the present study could contribute to the prevention of sarcopenia.

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A Yuki developed the study concept, designed the study, carried out the statistical analyses and prepared the draft of the manuscript. F Ando and H Shimokata commented on the manuscript. R Otsuka and H Shimokata managed the overall project. All authors collected data and approved manuscript submission.

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Disclosure statement

The authors declare no conflict of interest.

References


