厚生労働科学研究費補助金

長寿科学総合研究事業

# サルコペニアの予防を目的とした総合的研究
（H25-長寿-若手-009）

平成25年度　総括研究報告書

研究代表者　山田　実

平成26（2014）年　5月

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# サルコペニアの予防を目的とした総合的研究

研究代表者　山田　実　京都大学大学院医学研究科


## 研究要旨

目的

本研究の目的は、【研究 1】地域在住日本人高齢者（65 歳以上）におけるサルコペニア有症率を明らかにする、【研究 2】骨格筋量の加齢変化を明らかにする、そして【研究 3】骨格筋量に関連するバイオマーカーを検証することである。

方法

【研究 1】

地域在住高齢者 1,882 名（74.9±5.5 歳）を対象に、Asian Working Group for Sarcopenia（AWGS）のアルゴリズムに従ってサルコペニア有症率を検証した。

【研究 2】

40-79 歳までの男性 16,379 名、女性 21,660 名を対象に、生体電気インピーダンス法によって計測した骨格筋量の加齢変化について検証した。

【研究 3】

地域在住高齢男性 385 名（74.3±5.9 歳）、女性 628 名（74.3±5.5 歳）を対象に、骨格筋量と関連するバイオマーカーの検証を行った。

結果

【研究 1】

男性では 94 名（16.5%）、女性では 262 名（19.9%）がサルコペニアに該当した。また、男女ともに年齢依存的にサルコペニア有症率が高まっており、特に 75 歳以上では有症率が急激に増加していた

【研究 2】

男性の SMI（骨格筋量）は 40-44 歳と比べて 75-79 歳では 10.8%減少していた。女性の SMI では、40-44 歳と比べて 75-79 歳では 6.4%減少していた。

【研究 3】

男女ともに SMI で関連性を示したのは IGF-1 であった（P<0.05）。

結論

地域在住高齢者のサルコペニアの割合は約 20%であった。骨格筋量は 40 歳頃から緩やかに減少が始まり、約 35 年間で男性で 10.8%、女性で 6.4%も減少していた。そして、この骨格筋量は IGF-1 と強く関連していた。

山田　実・京都大学大学院医学研究科　助教

## A. 目的

本邦でのサルコペニア（加齢に伴う筋量減少症）の有症率は約20%であり、自立した日常生活を阻害する要因となっている。

2013年、Asian Working Group for Sarcopenia（AWGS）においてアジア人におけるサルコペニアの診断基準が提案された。これまでは2010年にEuropean Working Group on Sarcopenia in older People（EWGSOP）によって報告されたアルゴリズムが一般的に使用されてきたが、AWGSによるアルゴリズムによりアジア人に適した基準で診断できるようになった。研究1の目的は、地域在住日本人高齢者（65歳以上）におけるサルコペニア有症率をAWGSの基準によって明らかにすることである。

また、欧米諸国の報告によると、骨格筋量は50歳から79歳にかけて6.6-23.3%減少するとされているが、アジア人を対象としたそのような骨格筋量の加齢変化を検討した報告はない。そこで研究2では、40歳から79歳までの38,039名の日本人を対象に、横断的に骨格筋量を計測しその加齢変化を検証した。

さらに研究3では、このような筋量減少と関連するバイオマーカーを検証することを目的とした。サルコペニアに関しては、バイオマーカーの検討が十分とは言えず、スタンダードなバイオマーカーは存在しない。

## B. 研究方法

研究1［サルコペニアの有症率の検討］

地域在住高齢者1,882名（74.9±5.5歳、女性率69.8%）を対象とした。バイオインピーダンス（BIA）法による体組成の計測を行い、得られた四肢筋量データを身長の2乗で除した値を骨格筋指数（SMI）と定義した。なお、AWGSではBIA法によるSMIの基準値を男性7.0kg/m2、女性5.7kg/m2と定めており、これらの値を下回る者を筋量低下者と定義している。加えて、AWGSでは握力が低下している場合（男性＜26kg、女性＜18kg）を筋力低下、歩行速度低下している場合（≦0.8m/秒）を運動パフォーマンス低下と定義している。そして、サルコペニアは筋力低下（かつ、または）運動パフォーマンス低下がある者と定義されている。なお、本研究は京都大学医の倫理委員会の承認を受けて実施した。

研究2［骨格筋量の加齢変化の検討］

対象はフィットネスセンターやコミュニティーセンター等に来場し、歩行が自立している40-79歳までの男性16,379名、女性21,660名であった。なお、正常な加齢変化を検証することが目的となるため、特筆すべき疾患を有する者は除外した。対象者には、バイオインピーダンス法による体組成計測を実施した（Inbody 720, Biospace製）。得られたデータより、四肢筋量を身長の二乗で除した値（SMI : skeletal muscle mass index, kg/m2）、上肢筋量を身長の二乗で除した値（arm-SMI, kg/m2）、それに下肢筋量を身長の二乗で除した値（leg-SMI, kg/m2）を算出した。対象者は男女別に40歳から5歳刻みに8つのカテゴリーの分類し、一元配置分散分析を用いてSMIの加齢変化を検証した。なお、本研究は京都大学医の倫理委員会の承認を受けて実施した。

研究3［バイオマーカーの検討］

対象は地域在住高齢男性385名（74.3±5.9歳）、女性628名（74.3±5.5歳）であった。バイオインピーダンス法による体組成計測よりSMIを算出した。さらに、体組成計測と同

日に採血を行い、25(OH)D (25-hydroxyvitamin D)、インスリン様成長因子(IGF-1 : insulin-like growth factor 1)、テストステロン、総コレステロール、それにアルブミン値を求めた。統計解析としては、男女それぞれで、SMIの4分位によって4群に分類し、一元配置分散分析を用いて各血清指標の差を検討した。なお、本研究は京都大学医の倫理委員会の承認を受けて実施した。

## C. 研究成果

研究1[サルコペニアの有症率の検討](図1)

男性では94名(16.5%)、女性では262名(19.9%)がサルコペニアに該当した。また、男女ともに年齢依存的にサルコペニア有症率が高まっており、特に75歳以上では有症率が急激に増加していた(65-89歳の5歳刻みのサルコペニア有症率、男性:5.3%、6.3%、15.1%、24.4%、66.7%、女性:13.7%、11.3%、24.6%、27.8%、42.9%)。

研究2[骨格筋量の加齢変化の検討] (図2)

各年代の対象者数は40-44歳(男性3,697名, 女性3,828名)、45-49歳(男性3,151名, 女性3,686名)、50-54歳(男性2,202名, 女性3,597名)、55-59歳(男性1,952名, 女性3,002名)、60-64歳(男性2,274名, 女性3,490名)、65-69歳(男性1,683名, 女性2,314名)、70-74歳(男性1,030名, 女性1,269名)、それに75-79歳(男性390名, 女性474名)であった。 男性のSMIは40-44歳で8.20 kg/m2、45-49歳で8.11 kg/m2、50-54歳で8.11 kg/m2、55-59歳で7.98 kg/m2、60-64歳で7.84 kg/m2、65-69歳で7.64 kg/m2、70-74歳で7.59 kg/m2、それに75-79歳で7.32 kg/m2と加齢に伴い筋量は減少し($P<0.001$)、40-44歳と比べて75-79歳ではSMIが10.8%減少していた。女性のSMIは40-44歳で6.41 kg/m2、45-49歳で6.39 kg/m2、50-54歳で6.33 kg/m2、55-59歳で6.23 kg/m2、60-64歳で6.14 kg/m2、65-69歳で6.08 kg/m2、70-74歳で6.09 kg/m2、それに75-79歳で6.00 kg/m2と男性と同様に加齢に伴い筋量は減少し($P<0.001$)、40-44歳と比べて75-79歳ではSMIが6.4%減少していた。なお、arm-SMIでは40-44歳から75-79歳にかけて男性で12.6%、女性で4.1%減少し、leg-SMIでは男性で10.1%、女性で7.1%減少していた($P<0.001$)。

研究3[バイオマーカーの検討](表1,2)

男性のSMIで関連性を示したのは、総コレステロール、IGF-1、TRAP-5b、テストステロンであった($P<0.05$)。女性のSMIでもIGF-1と関連していていた($P<0.05$)。

## D. 考察

AWGSアルゴリズムに従って地域在住高齢者のサルコペニア有症率を求めたところ、男性では16.5%、女性では19.9%がサルコペニアに該当した。この有症率は諸外国の先行研究と比較してもほぼ同等であった。

筋肉量の加齢変化では、男女ともに40歳以降緩やかにSMIは減少し、特に65歳以降に減少率が大きくなっていた。SMIは40-44歳から75-79歳にかけて男性で10.8%、女性で6.4%減少しており、男性の方が加齢に伴って骨格筋量が減少しやすいことが分かった。

筋肉量と関連するバイオマーカーの検証では、男女ともに筋量の増加とともに骨格筋同化ホルモンであるIGF-1レベルも上昇していた。IGF-1は加齢とともに減少することが知られていることから、サルコペニアと密接な関わりがあると考えられる。

## E. 結論

地域在住高齢者のサルコペニアの割合は約20%であった。骨格筋量は 40 歳頃から緩やかに減少が始まり、約 35 年間で男性で 10.8%、女性で 6.4%も減少していた。そして、この骨格筋量は IGF-1 と強く関連していた。

**F. 健康危険情報**

特筆すべき情報はない。

**G. 研究発表**

1. Yamada M, Moriguchi Y, Mitani T, Aoyama T, Arai H. Age-dependent changes in skeletal muscle mass and visceral fat area in Japanese adults from 40-79 years of age. Geriatr Gerontol Int 2014 Feb;14 Suppl 1:8-14 doi: 10.1111/ggi.12209.
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**H. 知的財産権の出願・登録状況**

なし

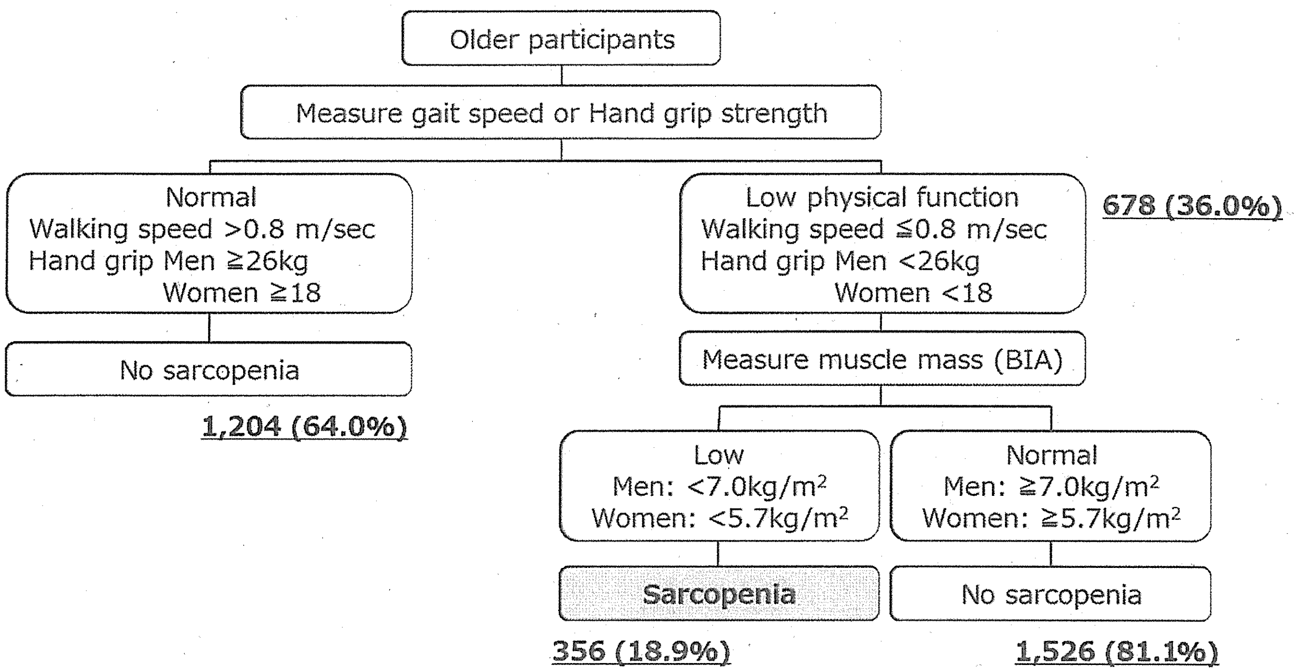


図 1　AWS のアルゴリズムに従って求めたサルコペニア有症率

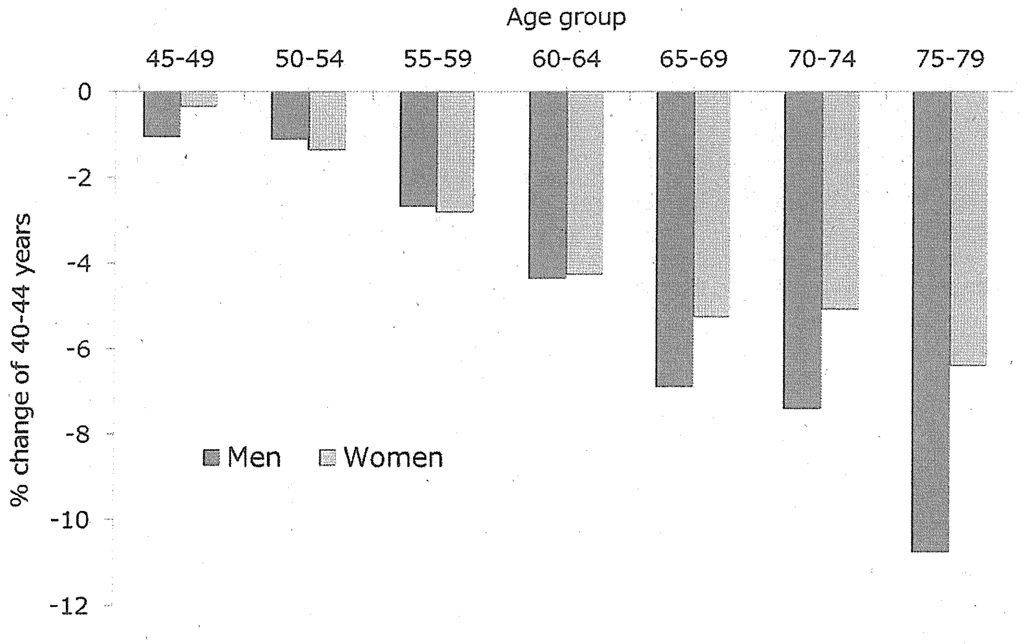


図 2　40-44 歳を基準に求めた SMI の変化率

表 1 男性における骨格筋量と各指標との関連

| | | Men n=385 Skeletal muscle mass index (kg/m2) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | <6.77 n=81 | | 6.77 - 7.22 n=102 | | 7.23 - 7.80 n=114 | | >7.80 n=88 | | F-value | P-value |
| | | Mean | SD | Mean | SD | Mean | SD | Mean | SD | | |
| Age | | 77.3 | 5.2 | 74.4 | 5.9 | 73.9 | 5.8 | 72.2 | 5.6 | 11.83 | .000 ** |
| Height | cm | 160.0 | 5.2 | 160.8 | 5.4 | 163.8 | 9.4 | 165.8 | 5.5 | 11.12 | .000 ** |
| Weight | kg | 52.9 | 5.9 | 58.5 | 5.3 | 64.4 | 5.3 | 70.7 | 7.3 | 106.32 | .000 ** |
| BMI | | 20.7 | 2.1 | 22.7 | 2.2 | 24.3 | 4.8 | 25.7 | 2.4 | 29.77 | .000 ** |
| Walking time | sec | 9.0 | 1.9 | 8.1 | 1.5 | 8.4 | 2.1 | 8.0 | 1.6 | 5.46 | .001 * |
| TUG | sec | 6.6 | 1.3 | 6.4 | 0.8 | 6.3 | 1.2 | 6.4 | 1.2 | .48 | .697 |
| FR | cm | 28.1 | 5.2 | 30.2 | 7.7 | 31.2 | 3.9 | 30.3 | 4.7 | .83 | .483 |
| 5CS | sec | 8.3 | 2.1 | 8.0 | 2.1 | 8.1 | 1.9 | 8.1 | 2.9 | .53 | .663 |
| Grip | kg | 30.5 | 5.5 | 33.6 | 7.0 | 35.9 | 6.7 | 37.5 | 7.5 | 17.71 | .000 ** |
| IGF-1 | ng/mL | 85.9 | 28.6 | 104.9 | 31.8 | 104.7 | 32.3 | 116.7 | 37.0 | 12.77 | .000 ** |
| 25OHD | ng/mL | 36.2 | 8.8 | 37.2 | 9.2 | 36.1 | 11.6 | 36.9 | 11.0 | .25 | .859 |
| Teststerone | ng/mL | 4.86 | 2.19 | 4.43 | 1.47 | 4.66 | 1.73 | 3.85 | 1.57 | 2.93 | .034 * |
| T-chol | mg/dL | 201.9 | 39.3 | 200.4 | 36.4 | 192.3 | 28.8 | 188.3 | 30.7 | 2.54 | .057 ** |
| Alb | g/dL | 4.45 | 0.22 | 4.46 | 0.31 | 4.43 | 0.30 | 4.40 | 0.29 | .63 | .599 |

表 2 女性における骨格筋量と各指標との関連

| | | Women n=628 Skeletal muscle mass index (kg/m2) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | <5.30 n=76 | | 5.30 - 5.85 n=185 | | 5.86 - 6.34 n=176 | | >6.34 n=191 | | F-value | P-value |
| | | Mean | SD | Mean | SD | Mean | SD | Mean | SD | | |
| Age | | 76.9 | 5.2 | 75.1 | 4.9 | 74.3 | 6.0 | 72.6 | 5.0 | 14.08 | .000 ** |
| Height | cm | 147.6 | 5.7 | 149.4 | 4.8 | 150.4 | 5.8 | 151.6 | 5.4 | 8.40 | .000 ** |
| Weight | kg | 42.5 | 4.9 | 47.9 | 4.6 | 52.5 | 5.2 | 58.1 | 7.4 | 125.22 | .000 ** |
| BMI | | 19.5 | 2.2 | 21.5 | 2.0 | 23.2 | 2.5 | 25.3 | 2.9 | 91.74 | .000 ** |
| Walking time | sec | 8.3 | 1.8 | 7.9 | 1.4 | 8.0 | 1.8 | 7.8 | 1.4 | 1.97 | .117 |
| TUG | sec | 7.2 | 1.1 | 6.6 | 1.0 | 6.7 | 1.3 | 6.4 | 1.2 | 4.16 | .007 ** |
| FR | cm | 27.1 | 6.5 | 27.4 | 5.4 | 26.5 | 4.9 | 28.5 | 6.7 | .51 | .677 |
| 5CS | sec | 8.6 | 2.3 | 8.1 | 2.1 | 8.3 | 2.7 | 7.8 | 1.8 | 3.44 | .017 |
| Grip | kg | 20.2 | 3.1 | 22.6 | 3.7 | 23.3 | 4.7 | 24.7 | 4.5 | 22.25 | .000 ** |
| IGF-1 | ng/mL | 82.3 | 25.4 | 86.0 | 29.9 | 86.3 | 27.4 | 93.2 | 28.8 | 3.69 | .012 ** |
| 25OHD | ng/mL | 28.8 | 8.8 | 29.7 | 8.9 | 29.2 | 7.8 | 29.4 | 7.7 | .27 | .844 |
| Teststerone | ng/mL | 0.08 | 0.07 | 0.13 | 0.54 | 0.09 | 0.07 | 0.26 | 0.87 | 2.25 | .082 |
| T-chol | mg/dL | 217.9 | 36.4 | 206.9 | 30.4 | 218.4 | 32.9 | 214.3 | 34.7 | 3.02 | .030 |
| Alb | g/dL | 4.45 | 0.21 | 4.46 | 0.29 | 4.48 | 0.27 | 4.50 | 0.26 | .79 | .503 |

研究成果の刊行に関する一覧表

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Geriatrics Gerontology International | Medline Indexed

*Geriatr Gerontol Int 2014;* **14 (Suppl. 1):** *8–14*

ORIGINAL ARTICLE

# Age-dependent changes in skeletal muscle mass and visceral fat area in Japanese adults from 40 to 79 years-of-age

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**Aim:** The age-dependent loss of skeletal muscle mass is highly concerning in diverse aging populations. However, age-dependent changes in muscle mass and the visceral fat area have not been well documented in Asian populations. The aim of the present study was to evaluate the age-dependent changes in skeletal muscle mass and the visceral fat area in Japanese adults from 40 to 79 years-of-age.

**Methods:** This was a cross-sectional study. Healthy men ($n$ = 16 379) and women ($n$ = 21 660) aged 40–79 years participated in the present study. The skeletal muscle mass and visceral fat area were measured in the study participants by bioelectrical impedance. The muscle mass data were converted into the skeletal muscle mass index (SMI) by dividing the weight by the height squared (kg/m$^2$).

**Results:** The SMI showed an age-dependent decrease in both sexes. Between 40 and 79 years, the total SMI decreased by 10.8% in men and by 6.4% in women. The arm SMI decreased by 12.6% in men and 4.1% in women, and the leg SMI decreased by 10.1% in men and by 7.1% in women in the same period. In contrast, the visceral fat area showed an age-dependent increase in both sexes. The visceral fat area increased by 42.9% in men and by 65.3% in women. The multiple regression analysis showed that the SMI was negatively associated with visceral obesity in both sexes.

**Conclusions:** In Japanese adults, sex-specific changes in skeletal muscle mass are more prominent in the arm than in the leg. Furthermore, the age-dependent increases in visceral adipose tissue might lead to loss of skeletal muscle mass. **Geriatr Gerontol Int 2014; 14 (Suppl. 1): 8–14.**

**Keywords:** age-dependent, Japanese, skeletal muscle mass, visceral fat area.

## Introduction

Sarcopenia is an age-dependent loss of skeletal muscle mass, and is a serious medical concern in older populations.[1,2] Sarcopenia is characterized by an impaired state of health associated with mobility disorders, an increased risk of falls and fractures, an impaired ability to carry out activities of daily living, disabilities, and a loss of independence.[3–5]

Previous epidemiological studies of sarcopenia in several countries have shown a disease prevalence of 5–40% in older men and 7–70% in older women.[6–18] In general, the prevalence of sarcopenia is approximately 25% in older men and 20% in older women. Notably, previous work from this laboratory has shown that sarcopenia is highly prevalent among Japanese adults aged 80 years and older.[18] Because older adults have a greater potential for health problems than young adults, it is very important to begin prevention of sarcopenia early, possibly before the age of 65 years. Two previous studies from the USA and Europe have shown that the age-dependent loss of skeletal muscle mass starts at approximately 50 years-of-age, and that skeletal muscle mass declines by 6.6–23.3% until 79 years-of-age.[19,20] However, age-dependent changes in muscle mass in Asians are not well documented.

Visceral adiposity, which is the basis of metabolic syndrome and cardiovascular disease, is aggravated with age.[21] The visceral adipose tissue produces many inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-$\alpha$) and interleukin (IL)-6,[22] and expression of these inflammatory cytokines can lead to increased skeletal muscle breakdown.[23] Furthermore, previous studies have shown that increased visceral fat area is associated with decreased skeletal muscle mass in a

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small sample of older adults.[24] However, the association of skeletal muscle mass with age-dependent changes in visceral fat in a large population has not previously been shown.

The primary aim of the present study was to evaluate the age-dependent changes in skeletal muscle mass and visceral fat area using a large cross-sectional cohort of Japanese adults between 40 and 79 years-of-age. We also evaluated sex differences in skeletal muscle loss in the arms and legs. The secondary aim of the present study was to evaluate the association between the skeletal muscle mass and visceral fat area.

## Methods

### *Participants*

Participants were recruited by advertisements at several fitness and community centers. The participants in the present study were limited to visitors to these centers in the Kyoto, Osaka, and Hyogo prefectures in Japan. The inclusion criteria were an age of 40–79 years, living in the community and the ability to walk independently (including with a cane). The exclusion criteria were a certification of frailty status by the long-term care insurance service in Japan and artificial implants, such as cardiac pacemakers and replacement joints, which would interfere with accurate bioimpedance measurements. An interview was also used to identify those with the following exclusion criteria: severe cognitive impairment; severe cardiac, pulmonary, or musculoskeletal disorders; and comorbidities associated with greater risk of falls, such as Parkinson's disease or stroke. Because the purpose of the present study was to address physiological age-dependent changes in body composition, we excluded frail elderly and adults with those comorbidities. The present study was carried out in accordance with the guidelines of the Declaration of Helsinki, and the study protocol was reviewed and approved by the Ethics Committee of the Kyoto University Graduate School of Medicine.

Healthy men ($n$ = 16 379) and women ($n$ = 21 660) aged 40–79 years participated in the present study. The male participants were divided into eight groups according to age: 40–44 ($n$ = 3697), 45–49 ($n$ = 3151), 50–54 ($n$ = 2202), 55–59 ($n$ = 1952), 60–64 ($n$ = 2274), 65–69 ($n$ = 1683), 70–74 ($n$ = 1030), and 75–79 ($n$ = 390) years. The female participants were similarly divided into eight groups according to age: 40–44 ($n$ = 3828), 45–49 ($n$ = 3686), 50–54 ($n$ = 3597), 55–59 ($n$ = 3002), 60–64 ($n$ = 3490), 65–69 ($n$ = 2314), 70–74 ($n$ = 1269), and 75–79 ($n$ = 474) years.

### *Skeletal muscle mass index and visceral fat area*

A bioelectrical impedance data acquisition system (Inbody 720; Biospace, Seoul, Korea) was used to determine bioelectrical impedance.[25] This system uses an electrical current at different frequencies (5, 50, 250, 500, and 1000 kHz) to directly measure the amount of extracellular and intracellular water in the body. The study participants stood on two metallic electrodes and held metallic grip electrodes. Using segmental body composition and muscle mass, a value for the appendicular skeletal muscle mass was determined and used for further analysis. The muscle mass was converted into the skeletal muscle mass index (SMI) by dividing the weight by the height squared (kg/m$^2$). This index has been used in several epidemiological studies.[6,26] Additionally, the SMI of the arms and legs was calculated. The visceral fat area was determined by evaluating a transverse cross-section of the fourth and fifth abdominal lumbar area.

### *Statistical analysis*

Differences in the total SMI, arm SMI, leg SMI, and visceral fat area among the eight age groups were examined using an analysis of variance. Multiple regression models were applied to determine the relationship between the visceral fat area and the SMI, adjusted for age and weight in each sex. The data were managed and analyzed using SPSS (Windows version 18.0; SPSS, Chicago, IL, USA). A $P$-value of <0.05 was considered to show statistical significance for all analyses.

## Results

The mean age of the study participants was 54.5 ± 9.9 years, and 21 660 (56.9%) of the participants were women. The total SMI showed an age-dependent decrease in both sexes (men, $F = 251.1$, $P < 0.001$; women, $F = 135.6$, $P < 0.001$; Table 1). The percentage change in the total SMI at 40–44 years showed an age-dependent decrease in both sexes (Fig. 1, Table 1). In those aged over 65 years, the percentage change in the total SMI was greater in men than in women. In addition, the 20th percentile of total SMI in men and women aged 65–79 years was 7.02 kg/m$^2$ and 5.61 kg/m$^2$, respectively (Table 2).

To compare the age-dependent changes in muscle mass in the upper and lower limbs in this cohort, we analyzed the arm and leg SMI. The arm SMI showed an age-dependent decrease in both sexes (men, $F = 132.1$, $P < 0.001$; women, $F = 24.1$, $P < 0.001$; Table 1). The percentage change in the arm SMI using the 40–44 years group as a reference also showed an age-dependent decrease in both sexes (Fig. 2, Table 1).

Similarly to the arm SMI, the leg SMI also showed an age-dependent decrease in both sexes (men, $F = 273.2$, $P < 0.001$; women, $F = 192.2$, $P < 0.001$; Table 1). The percentage change in the leg SMI also showed an

**Table 1** Participant characteristics by age half decade

| | | Overall Men ($n$ = 16 379) Women ($n$ = 21 660) | | | 40–44 years Men ($n$ = 3697) Women ($n$ = 3828) | | | 45–49 years Men ($n$ = 3151) Women ($n$ = 3686) | | | 50–54 years Men ($n$ = 2202) Women ($n$ = 3597) | | | 55–59 Men ($n$ = 1952) Women ($n$ = 3002) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | % change over 40–44 years | Mean | SD | % change over 40–44 years | Mean | SD | % change over 40–44 years | Mean | SD | % change over 40–44 years | Mean | SD | % change over 40–44 years |
| Total SMI (kg/m²) | Men | 7.97 | 0.73 | – | 8.20 | 0.78 | – | 8.11 | 0.66 | −1.0 | 8.11 | 0.67 | −1.1 | 7.98 | 0.64 | −2.7 |
| | Women | 6.26 | 0.64 | – | 6.41 | 0.67 | – | 6.39 | 0.64 | −0.3 | 6.33 | 0.64 | −1.3 | 6.23 | 0.59 | −2.8 |
| Arm SMI (kg/m²) | Men | 2.08 | 0.28 | – | 2.14 | 0.31 | – | 2.11 | 0.26 | −1.4 | 2.11 | 0.26 | −1.2 | 2.08 | 0.24 | −3.0 |
| | Women | 1.47 | 0.22 | – | 1.49 | 0.24 | – | 1.49 | 0.23 | −0.5 | 1.47 | 0.22 | −1.4 | 1.46 | 0.21 | −2.3 |
| Leg SMI (kg/m²) | Men | 7.98 | 0.73 | – | 6.06 | 0.51 | – | 6.00 | 0.46 | −0.9 | 5.99 | 0.46 | −1.1 | 5.91 | 0.45 | −2.5 |
| | Women | 6.26 | 0.64 | – | 4.92 | 0.48 | – | 4.91 | 0.45 | −0.3 | 4.85 | 0.46 | −1.3 | 4.77 | 0.42 | −3.0 |
| Visceral fat area (cm²) | Men | 100.6 | 29.2 | – | 88.4 | 28.8 | – | 91.9 | 27.1 | 4.0 | 98.9 | 28.8 | 11.9 | 103.5 | 25.7 | 17.1 |
| | Women | 84.7 | 27.4 | – | 68.0 | 25.3 | – | 72.1 | 23.9 | 6.0 | 79.3 | 23.6 | 16.5 | 89.4 | 23.0 | 31.5 |

| | | 60–64 years Men ($n$ = 2274) Women ($n$ = 3490) | | | 65–69 years Men ($n$ = 1683) Women ($n$ = 2314) | | | 70–74 years Men ($n$ = 1030) Women ($n$ = 1269) | | | 75–79 years Men ($n$ = 390) Women ($n$ = 474) | | | ANOVA | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | % change over 40–44 years | Mean | SD | % change over 40–44 years | Mean | SD | % change over 40–44 years | Mean | SD | % change over 40–44 years | *F*-value | *P*-value |
| Total SMI (kg/m²) | Men | 7.84 | 0.68 | −4.3 | 7.64 | 0.67 | −6.9 | 7.59 | 0.66 | −7.4 | 7.32 | 0.62 | −10.8 | 251.1 | <0.001 |
| | Women | 6.14 | 0.61 | −4.2 | 6.08 | 0.60 | −5.2 | 6.09 | 0.55 | −5.1 | 6.00 | 0.60 | −6.4 | 135.6 | <0.001 |
| Arm SMI (kg/m²) | Men | 2.05 | 0.25 | −4.4 | 1.99 | 0.25 | −6.9 | 1.96 | 0.24 | −8.5 | 1.87 | 0.26 | −12.6 | 132.1 | <0.001 |
| | Women | 1.45 | 0.22 | −3.1 | 1.44 | 0.21 | −3.6 | 1.46 | 0.20 | −2.5 | 1.43 | 0.21 | −4.1 | 24.1 | <0.001 |
| Leg SMI (kg/m²) | Men | 5.80 | 0.48 | −4.3 | 5.64 | 0.46 | −6.9 | 5.64 | 0.51 | −7.0 | 5.45 | 0.45 | −10.1 | 273.2 | <0.001 |
| | Women | 4.69 | 0.43 | −4.6 | 4.64 | 0.44 | −5.7 | 4.63 | 0.41 | −5.9 | 4.57 | 0.45 | −7.1 | 192.2 | <0.001 |
| Visceral fat area (cm²) | Men | 108.3 | 26.2 | 22.5 | 113.0 | 25.7 | 27.8 | 122.3 | 25.1 | 38.3 | 126.4 | 25.2 | 42.9 | 376.9 | <0.001 |
| | Women | 94.0 | 23.3 | 38.2 | 101.6 | 23.0 | 49.4 | 108.5 | 24.1 | 59.5 | 112.4 | 29.3 | 65.3 | 966.7 | <0.001 |

Percentage change of 40–44 years = (absolute change value / 40–44 years value) × 100. SMI, skeletal muscle mass index.

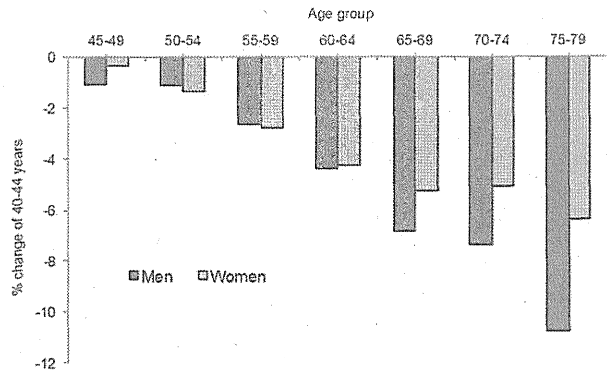


**Figure 1** The percentage of change in the total skeletal muscle mass index in each sex and each age group, using 40–44 years-of-age as a reference.

**Table 2** 20th percentile of total skeletal muscle mass index (kg/m$^2$) in both sexes

| Age group (years) | 20th percentile of SMI Men | Women |
|---|---|---|
| 65–69 | 7.06 | 5.61 |
| 70–74 | 7.09 | 5.63 |
| 75–79 | 6.83 | 5.54 |
| 65–79 | 7.02 | 5.61 |

SMI, skeletal muscle mass index.

age-dependent decrease in both sexes (Fig. 2, Table 1). The age-dependent changes in the leg SMI were similar in men and women. However, the age-dependent changes in the arm SMI were greater in men than in women.

Next, we examined the age-dependent changes in visceral obesity. The visceral fat area showed an age-dependent increase in both sexes (men, $F = 376.9$, $P < 0.001$; women, $F = 966.7$, $P < 0.001$; Table 1). The percentage change from 40–44 years in the visceral fat area showed an age-dependent increase in both sexes (Fig. 3, Table 1).

To examine the association between skeletal muscle mass and visceral obesity, we carried out a multiple regression analysis using the SMI as an outcome. We found that the visceral fat area, age, and weight were significant and independent determinants of the SMI in both men ($\beta = -0.586$) and women ($\beta = -0.627$; Table 3). Therefore, the age-dependent change in the SMI was negatively associated with the visceral-fat area in both sexes.

## Discussion

The current cross-sectional study was carried out to evaluate the SMI in Japanese adults aged between 40 and 79 years. Our data show that the SMI decreased age-dependently in both sexes. Notably, regarding the age-dependent decreases in the total SMI and in those aged over 65 years, the percentage change in the total SMI was greater in men than in women. From 40 to 79 years, the total SMI decreased by 10.8% in men and by 6.4% in women. Previous epidemiological studies of body composition have shown that between 40 and 79 years, the fat-free mass decreases by 6.6–23.3% in both sexes.[19,20] The age-dependent increases in inflammatory cytokines, such as IL-6 and TNF-α, can result in increased skeletal muscle breakdown.[23] In contrast, the age-dependent decrease in anabolic hormones, such as testosterone, growth hormone, and insulin-like growth factor-1 (IGF-1), might lead to a loss of skeletal muscle

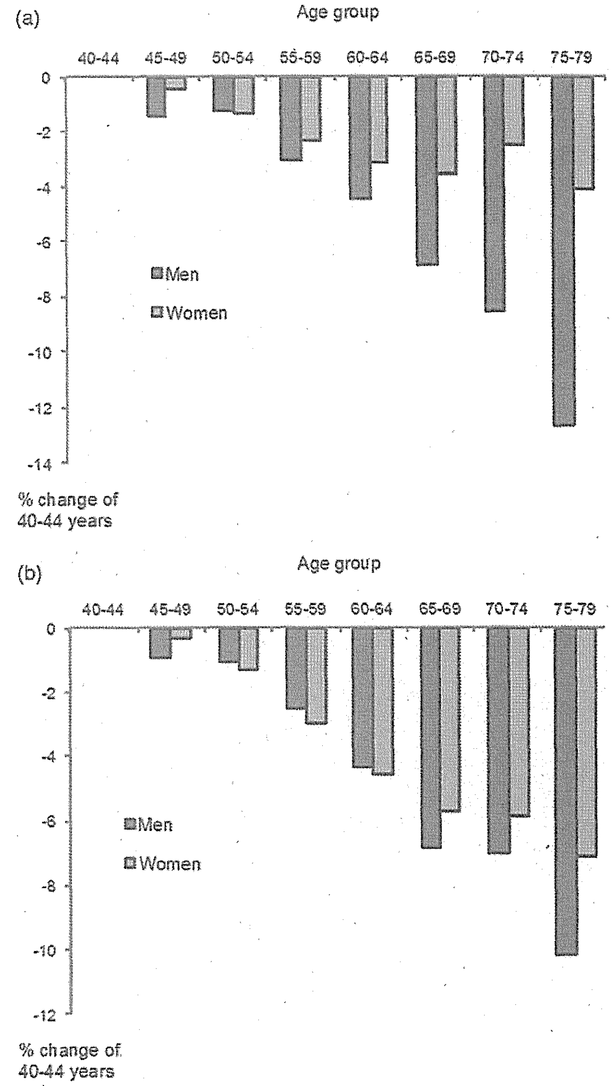


**Figure 2** The percentage of change in the (a) arm and (b) leg skeletal muscle mass index (SMI) in each sex and each age group using 40–44 years-of-age as a reference.

mass.[27,28] In addition, there is also an age-dependent decrease in the amount of physical activity and energy intake. These behavioral changes can enhance the age-dependent reduction in skeletal muscle mass.

Interestingly, in those aged over 65 years, age-dependent decreases in total SMI were greater in men than in women. Furthermore, this age-dependent sex difference was more prominent in the arm than in the leg. From 40 to 79 years, the arm SMI decreased by 12.6% in men and by 4.1% in women. This is consistent to the previous studies in Japanese older adults. Kitamura *et al.* reported that the arm lean tissue mass was 5.97 ± 0.75 and 5.01 ± 0.67 in men, and 3.56 ± 0.54 and 3.24 in women aged in their 40s and 70s, respectively.[29] Based on their data, the percentage change in the arm lean tissue mass in men is –16.0% and is –8.9% in women. However, there is no sex difference in the percentage change in the leg lean tissue mass. The mechanism of this sex difference in the arm and leg lean tissue mass change is not clear. In general, older Japanese women frequently use the upper limbs, such as when washing and cooking. However, older Japanese men usually do not carry out such work. Therefore, it is possible that these behavioral differences lead to greater age-dependent decreases in the arm SMI in men than in women. As another possibility, Baumgartner reported that the sex hormone signal is an important factor for muscle mass in men, but not in women; however, physical activity is an important factor for muscle mass in both sexes.[30] Furthermore, previous studies have shown that 20% of men older than 60 years, 30% of men older than 70 years, and 50% of men older than 80 years have serum testosterone levels below the normal range.[31] Thus, it is also possible that the sex hormone-dependent changes in muscle mass are greater in men than in women. Therefore, age-dependent gender differences in the SMI might be influenced by daily activity or alterations in sex hormone levels.

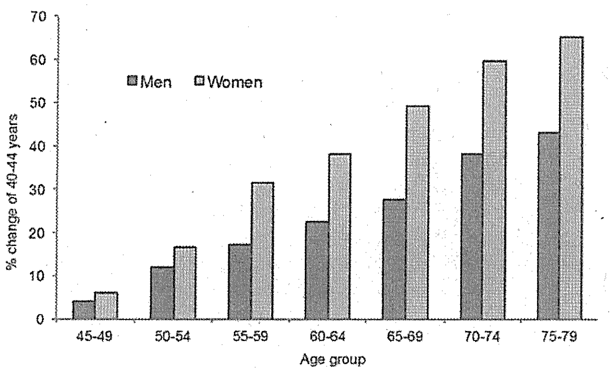


**Figure 3** The percentage of change in the visceral fat area in each sex and each age group using 40–44 years-of-age as a reference.

The present data show that aging is associated with a progressive increase in visceral fat area in both sexes. From 40 to 79 years of age, the visceral fat area increased by 42.9% in men and by 65.3% in women. Furthermore, the SMI was negatively associated with the visceral fat area when adjusted for age and body weight in both sexes. The visceral adipose tissue produces many catabolic factors, such as TNF-α and IL-6.[22] Therefore, the age-dependent increases in both visceral adipose tissue and inflammatory cytokines might lead to a loss of skeletal muscle mass. Recently, sarcopenic obesity has been defined as both low muscle mass and high adipose tissue in older adults, and the health-related risk is higher in sarcopenic obesity than in sarcopenia.[32] The current data show that the age-dependent changes in body composition can accelerate sarcopenic obesity. These results suggest that it is very important to begin prevention of sarcopenia and sarcopenic obesity as early as possible.

According to our analysis of this cohort, we found that the 20th percentile of total SMI in men and women aged 65–79 years was 7.02 kg/m$^2$ and 5.61 kg/m$^2$, respectively. These values were slightly higher than those determined by the young adult mean in our database (men 6.75 kg/m$^2$; women 5.07 kg/m$^2$).[18] That these values were lower than the 20th percentile of total SMI

**Table 3** Multiple regression analysis for the association with skeletal muscle mass index in both sexes

| Independent variables | Men Adjusted $R^2$ value = 0.781** standard regression value | Women Adjusted $R^2$ value = 0.627** standard regression value |
|---|---|---|
| Visceral fat area (cm$^2$) | –0.586** | –0.627** |
| Age (year) | 0.212** | 0.252** |
| Weight (kg) | 1.180** | 1.169** |

**$P < 0.01$.

 

is probably because we did not use the data of SMI in participants aged 80 years and older. Other studies on sarcopenia in Asia also show that the cut-off of SMI is 6.08–7.27 kg/m$^2$ in men and 4.79–5.80 kg/m$^2$ in women,[13,33–35] which is quite consistent with the present results. Thus, the 20th percentile of total SMI in men and women in our data can be used for the cut-off of SMI in Asians; however, further studies are required to address whether these cut-off points are associated with adverse health outcomes in Asian older adults.

There were several limitations to the present study that warrant mention. First, physical performance data were not measured. The European Working Group on Sarcopenia in Older People (EWGSOP) has recommended using the presence of both low muscle function (low physical performance or muscle strength) and low muscle mass to diagnose sarcopenia.[36] Therefore, the prevalence of sarcopenia could not be determined. Second, the study design was cross-sectional, and no outcome data are available. Further research with a longitudinal design will be required to clarify whether low muscle mass can predict adverse health outcomes in older Japanese adults. Third, the SMI measurement was estimated using BIA, which is not a method that is recommended by the EWGSOP for assessing muscle mass. However, it is very challenging to measure muscle mass in community-dwelling older adults using dual-energy X-ray absorptiometry (DXA); thus, BIA is a more practical screening method to use in large samples, especially in a community setting. However, to determine the specific effect of an intervention, a more accurate measurement, such as DXA, computed tomography, or magnetic resonance imaging, should be used in future studies. Serum outcomes were not measured. Therefore, the relationship between the SMI and hormone signals could not be determined. Finally, the participants in the present study were limited to visitors to fitness and community centers. Therefore, the participants of this study might not be a representative sample of community-dwelling adults.

In conclusion, the SMI showed an age-dependent decrease in both sexes, and the total SMI decreased by 10.8% in men and by 6.4% in women aged 40–79 years. Notably, age-dependent sex differences were more pronounced in the arm SMI; from 40 to 79 years, the arm SMI decreased by 12.6% in men and 4.1% in women. These results suggest that the age-dependent loss of skeletal muscle mass begins at approximately 40 years-of-age, and becomes prominent after 50 years-of-age in Japanese adults. Furthermore, the visceral fat area showed an age-dependent increase in both sexes, and the visceral fat area increased by 42.9% in men and by 65.3% in women of 40–79 years-of-age. Finally, the SMI was negatively associated with the visceral fat area in both sexes. Thus far, no studies have reported age-dependent changes and the association of muscle mass and visceral fat in Asian populations. Therefore, the current data could be used as the reference value for Asian adults.

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## Disclosure statement

The authors declare no conflict of interest.

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Original Study

# Prevalence of Sarcopenia in Community-Dwelling Japanese Older Adults

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*Keywords:*
Prevalence of sarcopenia
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Japanese

ABSTRACT

*Background:* Sarcopenia, the age-dependent loss of skeletal muscle mass, is highly prevalent among older adults in many countries; however, the prevalence of sarcopenia in healthy Japanese community-dwelling older adults is not well characterized.
*Objective:* The aim of this study was to evaluate the prevalence of sarcopenia and to examine the association of sarcopenia with falls and fear of falling in community-dwelling Japanese older adults.
*Design:* This is a cross-sectional study.
*Setting and Subjects:* Healthy men (568) and women (1314) aged 65 to 89 years participated in this research.
*Measurements:* For all participants, 3 measurements were taken: skeletal muscle mass measurement using bioelectrical impedance, 10 m at a usual walking speed, and handgrip strength. Sarcopenia was defined as the presence of both poor muscle function (low physical performance or low muscle strength) and low muscle mass.
*Results:* The prevalence of sarcopenia, determined using the European Working Group on Sarcopenia in Older People—suggested algorithm, in men and women aged 65 to 89 years was 21.8% and 22.1%, respectively. The prevalence of sarcopenia increased age-dependently, especially in those older than 75 years in both genders. In the young old, the prevalence of sarcopenia was higher in women than in men; however, in those older than 85 years, the prevalence of sarcopenia was lower in women than in men ($P < .05$). In addition, fall incidents and fear of falling were more prevalent in sarcopenic older adults than in nonsarcopenic older adults ($P < .05$).
*Conclusions:* These results suggest that sarcopenia is highly prevalent in community-dwelling Japanese older adults and is related to falls and fear of falling.


In 1989, Rosenberg[1] proposed the term sarcopenia to describe the age-dependent loss of skeletal muscle mass. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) recommended using the presence of both low muscle function (low physical performance or muscle strength) and low muscle mass to diagnose sarcopenia.[2] Numerous epidemiological studies showed that sarcopenia is highly prevalent and is a serious problem in older adults.[3,4] Sarcopenia is considered to be characterized by an impaired state of health with mobility disorders, increased risk of falls and fractures, impaired ability to perform activities of daily living, disabilities, and loss of independence.[5–7]

The mechanism of sarcopenia remains unclear; however, it may be related to the age-dependent loss of skeletal muscle mass due to multifactorial processes, such as physical inactivity, malnutrition, oxidative stress, and changes in endocrine function.[2] Additionally, age-dependent increases in inflammatory cytokines, such as interleukin-6 and tumor necrosis factor alpha, can result in increased skeletal muscle breakdown.[8] In contrast, the age-dependent decrease in anabolic hormones, such as testosterone, estrogen, growth hormone, and insulinlike growth factor-1 (IGF-1), may lead to loss of skeletal muscle mass.[9,10]

The aged population in Japan is increasing faster than in any other country. Frailty in older adults is a serious problem in aging countries, such as Japan. A recent cross-sectional study showed that sarcopenia is highly prevalent in Japanese older adults with hip fracture (men, 81.1%; women, 44.7%).[11] Especially in older adults with hip fracture, the prevalence of sarcopenia increased with age. However, age-dependent changes in the prevalence of sarcopenia in Japanese community-dwelling healthy older adults are not well established.

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The authors declare no conflicts of interest.

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The primary aim of this study was to evaluate the prevalence of sarcopenia in community-dwelling Japanese older adults by gender and age. The secondary aim was to determine the prevalence of falls and fear of falling in sarcopenic older adults and to compare these with nonsarcopenic older adults.

## Methods

### *Participants*

Participants were recruited by an advertisement in the local press and by public ads. We recruited community-dwelling older adults in the Kyoto prefecture and the Hyogo prefecture in Japan. The inclusion criteria were an age of 65 to 89 years, living in the community, and the ability to walk independently (including with a cane). The exclusion criteria were certification of frailty status by the long term care insurance service in Japan and artificial implants, such as cardiac pacemakers and joints, which did not allow the potential subject to receive bioimpedance. An interview was also used to identify those with the following exclusion criteria: severe cognitive impairment; severe cardiac, pulmonary, or musculoskeletal disorders; and comorbidities associated with greater risk of falls, such as Parkinson disease or stroke. This study was conducted in accordance with the guidelines of the Declaration of Helsinki, and the study protocol was reviewed and approved by the Ethics Committee of the Kyoto University Graduate School of Medicine.

Healthy men (n = 568) and women (n = 1314) aged 65 to 89 years participated in this study. The male participants were divided into 5 groups according to age: 65 to 69 (n = 76), 70 to 74 (n = 190), 75 to 79 (n = 172), 80 to 84 (n = 82), and 85 to 89 (n = 48) years. The female participants were also divided into 5 groups according to age: 65 to 69 (n = 278), 70 to 74 (n = 372), 75 to 79 (n = 414), 80 to 84 (n = 180), and 85 to 89 (n = 70) years. The prevalence of sarcopenia in each age and gender group was then determined.

### *Skeletal Muscle Mass Index*

A bioelectrical impedance data acquisition system (Inbody 720; Biospace Co, Ltd, Seoul, Korea) was used to determine bioelectrical impedance.[12] This system uses electrical current at different frequencies (5, 50, 250, 500, and 1000 kHz) to directly measure the amount of extracellular and intracellular water in the body. Participants stood on 2 metallic electrodes and held metallic grip electrodes. Using segmental body composition and muscle mass, a value for the appendicular skeletal muscle mass was determined and used for further analysis. Muscle mass was converted into the skeletal muscle mass index (SMI) by dividing by weight by height squared ($kg/m^2$). This index has been used in several epidemiological studies.[13,14] Reference value (SMI) for low muscle mass in each gender was defined as a value 2 SDs below the gender-specific means of the study reference data for young adults aged 18 to 40 years.[15] The study population included young adults (19,797 men and 18,302 women) aged 18 to 40 years, to determine the reference values. The SMIs in young men and women aged 18 to 40 years old were $8.11 \pm 0.68$ $kg/m^2$ and $6.35 \pm 0.64$ $kg/m^2$, respectively. Therefore, the reference values for low muscle mass in Japanese men and women using bioelectrical impedance analysis (BIA) were 6.75 $kg/m^2$ and 5.07 $kg/m^2$, respectively.

### *Measurement of Physical Performances*

For all participants, the following 2 measures of physical performance were obtained: 10 m usual walking speed[16] and handgrip strength (HGS).[17] If a walking aid was normally used at home, this aid was used during the 10-m walking speed test.

In the walking speed test, participants were asked to walk 15 m at a comfortable pace. A stopwatch was used to record the time required to reach the 10-m point (marked in the course). The time recorded in 2 trials was averaged to obtain the data for the present analyses. A cutoff point of less than 0.8 m/s identified participants with low physical performance.[2]

In the HGS test, participants used a handheld dynamometer. Participants kept their arms by the sides of their body. The participant squeezed the dynamometer with the dominant hand using maximum isometric effort. No other body movement was allowed. The HGS score was defined as the better performance of 2 trials. Low muscle strength was defined as handgrip strength less than 30 kg in men and 20 kg in women.[2]

### *Definition of Sarcopenia*

We defined sarcopenia using the EWGSOP-suggested diagnostic algorithm to assess the presence of both low muscle function (low physical performance or low muscle strength) and low muscle mass.[2]

### *Fall Incidents and Fear of Falling*

Fall events in the previous year were recorded based on an interview with family members. A fall was defined as "an event that results in a person coming to rest inadvertently on the ground or other lower level regardless of whether an injury was sustained, and not as a result of a major intrinsic event or overwhelming hazard."[18] The date, number, characteristics (eg, while rising from a lying or sitting position, while turning in the opposite direction, while tripping over an obstacle), and consequences (eg, bruise, fracture) of the falls were recorded using a standardized questionnaire. Fear of falling was assessed by asking the yes-or-no question, "Are you afraid of falling?"

### *Statistical Analysis*

Differences in the prevalence of sarcopenia, muscle mass, strength, and physical performance among 5 age groups by gender were evaluated using the chi-square test. The prevalence of sarcopenia and the corresponding 95% confidence intervals (CIs) were calculated for men and women and compared using the chi-square test in each age group. The results were presented as odds ratios (ORs) with 95% CIs.

The incidence of falls and the prevalence of fear of falling were calculated for participants with or without sarcopenia and were compared using the chi-square test. The results were presented using ORs with 95% CIs. The physical performances of sarcopenic and nonsarcopenic older adults were compared by gender using the Student *t* test. The data were managed and analyzed using SPSS (Statistical Package for the Social Sciences, Windows version 18.0; SPSS, Inc., Chicago, IL). A $P$ value less than .05 was considered to indicate statistical significance for all analyses.

## Results

The mean age of study participants was $74.9 \pm 5.5$ years, and 1314 (69.8%) participants were women. According to the EWGSOP-suggested algorithm, the prevalence of low physical performance in older adults aged 65 to 89 years was 4.1% in this cohort. The prevalence of low muscle strength in older adults with normal physical performance was 31.9%. The prevalence of low muscle mass with low physical performance or muscle strength was 22.0%. Thus, the prevalence of sarcopenia using the EWGSOP-suggested algorithm for