症や腎症を有し，それぞれ病期も進行し，HbA1c 値が高く，eGFR 値が低く，虚弱を有していた（p < 0.05）。目的変数を転倒の有無とし，糖尿病関連項目を説明変数としたロジスティック回帰分析の結果から，年齢，低血糖が転倒の発生を予測する因子として抽出された（表 3）。

FRI においては，そのほとんどのリスク項目が，転倒群で高値であった。体力要因は，その中でもすべてのカテゴリにおいて有意に関連していた（p < 0.001）。疾病要因においては，「転ばないかと不安になる」が全体の約半数（49 %）において「はい」と答えていた（表 4）。

さらに糖尿病の因子と転倒との関連を調べるため，FRI の体力要因，疾病要因の各項目と糖尿病の臨床指標との関連をロジスティック回帰分析（年齢，性別，BMI，で調整）で検討した（表 5）。「つまずくことがある」の項目に対し低血糖が抽出され，「1km くらい歩くのが不可能」の項目に対し円背，年齢，BMI が抽出され，「片足で 5 秒くらい立っていることが不可能」の項目に対し治療法，年齢が抽出され，「目が見えにくい」の項目に対し，HbA1c が抽出され，「転ばないかと不安になる」の項目に対し治療法がそれぞれ抽出された。

表 3　転倒の予測因子

| | B | 95%CI | P |
|---|---|---|---|
| 年齢 | 1.063 | 1.019-1.108 | 0.004 |
| 女性 | 1.589 | 0.953-2.649 | 0.076 |
| BMI | 1.052 | 0.986-1.121 | 0.125 |
| 低血糖 | 2.395 | 1.244-4.613 | 0.009 |
| 骨粗鬆症 | 1.705 | 0.905-3.214 | 0.099 |

ステップワイズ法（変数増加法）によるロジスティック回帰分析でモデルに採択された変数
有意水準 P < 0.05

## Ⅳ　考察

本研究で，転倒の有無から高齢糖尿病患者の転倒要因を検討し，関連のある因子が明らかになった。今回の症例において，転倒と低血糖が関連し，血糖のコントロール不良も転倒に関与していた。多変量解析の結果，もっともオッズ比が高かったのが低血糖であり，このことから，高齢糖尿病患者の転倒を予防するためには，低血糖の回避が第一に重要と考える。荒木ら[6) 7)]の縦断研究において，160 名の糖尿病患者の転倒の要因を追跡調査した結果，低血糖が減少することにより，転倒・骨折・転倒予測スコアの減少がみられた。今回の研究は，横断研究であるため，さらに縦断的に介入研究を行う必要があるが，高齢糖尿病患者の転倒の要因としては，矛盾しない結果であった。糖尿病外来における血糖自己測定の結果をモニタリングし，低血糖の早期発見を行うとともに，低血糖を予防する指導が必要であると考える。SU 剤など内服中の患者においては，血糖のモニタリングが難しく，患者が気付かずに低血糖になっているケースも考えられる。そのため，低血糖が起こっていると考えられる患者に際しては，外来での血糖測定器の貸し出しなどにより，計画的に深夜，早朝の血糖の変動を確認する必要があるものと考えられた。Nelson らの研究におい

表 4　転倒の有無と転倒スコア 21 項目

| 項目 | 転倒あり（n = 95） | 転倒なし（n = 205） | p |
|---|---|---|---|
| 1　つまずくことがある | 72 (75.8) | 92 (44.4) | < 0.000 |
| 2　手すりにつかまらないと，階段の上り下りが不可能 | 58 (61.1) | 44 (21.6) | < 0.000 |
| 3　歩行速度が遅くなってきた | 69 (72.6) | 101 (49.3) | < 0.000 |
| 4　横断歩道を青のうちに渡りきることが不可能 | 37 (38.9) | 26 (12.7) | < 0.000 |
| 5　1km くらいを続けて歩くことが不可能 | 44 (46.3) | 40 (19.6) | < 0.000 |
| 6　片足で 5 秒くらい立っていることが不可能 | 44 (46.3) | 44 (21.5) | < 0.000 |
| 7　杖を使っている | 38 (40.0) | 20 ( 9.8 ) | < 0.000 |
| 8　タオルを固く絞ることが不可能 | 25 (26.3) | 15 ( 7.3 ) | < 0.000 |
| 9　めまい，ふらつきがある | 35 (36.8) | 49 (23.9) | 0.013 |
| 10　背中が丸くなってきた | 43 (45.3) | 68 (33.2) | 0.063 |
| 11　ひざが痛む | 41 (43.2) | 59 (28.8) | 0.011 |
| 12　目が見えにくい | 60 (63.2) | 100 (48.8) | 0.010 |
| 13　耳が聞こえにくい | 50 (52.6) | 75 (36.6) | 0.006 |
| 14　物忘れが気になる | 51 (54.7) | 82 (40.0) | 0.024 |
| 15　転ばないかと不安になる | 75 (78.9) | 74 (36.1) | < 0.000 |
| 16　毎日お薬を 5 種類以上飲んでいる | 63 (66.3) | 76 (37.1) | < 0.000 |
| 17　家の中で歩くと暗く感じる | 20 (20.1) | 13 ( 6.3 ) | < 0.000 |
| 18　廊下，居間，玄関によけて通る物が置いてある | 26 (27.4) | 42 (20.5) | 0.155 |
| 19　家の中に段差がある | 63 (66.3) | 116 (56.6) | 0.234 |
| 20　家で階段を使う | 39 (41.1) | 113 (55.1) | 0.013 |
| 21　生活上家の近くの急な坂道を歩く | 25 (26.3) | 62 (30.2) | 0.535 |

転倒あり群 vs 転倒なし群の FRI スコア（10.1 ± 4.5vs6.4 ± 3.5）
平均値（%）　有意水準 P < 0.05

表5　転倒スコアのカテゴリに関連する糖尿病の項目

| FRI 項目 | 糖尿病関連項目 | B | 95%CI | p |
|---|---|---|---|---|
| 1　つまずくことがある | 低血糖 | 2.048 | 1.060-3.956 | 0.033 |
| 5　1km くらい歩くのが不可能 | 円背 | 2.028 | 1.024-4.016 | 0.043 |
| | 年齢 | 1.112 | 1.063-1.163 | 0.000 |
| | BMI | 1.102 | 1.030-1.179 | 0.005 |
| 6　片足で5秒くらい立っていることが不可能 | 治療法 | 1.588 | 1.152-2.190 | 0.005 |
| | 年齢 | 1.139 | 1.085-1.196 | 0.000 |
| 12　目が見えにくい | HbA1c | 1.415 | 1.081-.1846 | 0.011 |
| 15　転ばないかと不安になる | 治療法 | 1.319 | 1.008-1.727 | 0.004 |

年齢，性別，BMI で調整したロジスティック回帰分析（ステップワイズ法）において選択された糖尿病関連項目
有意水準 P < 0.05

ては，75 歳以上の 111 人の高齢者において，虚弱と非虚弱間で HbA1c が7％以下であると転倒頻度が高くなり，厳格な血糖コントロールを行うと低血糖が誘発され転倒回数が高齢者では増えると報告している[11]。今回の症例においても，転倒と虚弱とは有意な関連を示しており（$p < 0.001$），Nelson らの研究と同様に，転倒の既往のある患者は，虚弱を有し低血糖が関与した結果であり，糖尿病が転倒の独立した危険因子と考えられる。薬剤（スルホニル尿素）により，低血糖が起きた場合は，ブドウ糖の摂取などの対処法を指導していく必要があり，高齢者において自覚に乏しい早朝，睡眠中の低血糖の調査を薬剤内服中の患者にも行う必要が考えられる。転倒スコアのカテゴリに関連する糖尿病関連項目における表5の結果から，高齢糖尿病患者は低血糖があるとつまずきやすく，円背があると1km くらい歩くのが不可能な状態であり，加齢と BMI の増加により，転倒リスクは上昇する。糖尿病の治療をしているとバランス感覚が悪く，転倒に対する不安を持っていた。HbA1c 値が高い人ほど，網膜症が進み，目が見えにくくなることで糖尿病による治療や合併症が転倒を引き起こしている可能性が高いと考えられる。今後も FRI の手帳を1回／年に配布し，糖尿病が転倒の危険因子であることを指導していく必要がある。

森田ら[5]の横断研究において，糖尿病患者の神経障害がバランスに影響し転倒の要因になっていると報告している。今回のわれわれの研究においては，神経障害が予測因子として抽出されなかったが，転倒の有無と糖尿病罹患歴が関連していることから，転倒ありの患者において，神経障害の診断がされていない者がいる可能性も否定できない。今後は外来において，しびれなどの自覚症状の問診も必要であると考える。今回，糖尿病罹患歴が転倒の予測因子として抽出されなかったのは，糖尿病罹患歴と治療法，腎症，神経障害，網膜症，虚血性心疾患，低血糖，HbA1c それぞれの関連が深かったためと考えられる（$p < 0.001$）。斉藤ら[12]は，1381 人の高齢者を対象として調査を行い，80 歳以上の高年齢，長座位立ち上がり時間，生活機能 10 点以下，もの忘れあり，糖尿病の既往が将来の要介護認定を予測する因子として示唆されたと報告している。また，2010 年の国民生活基礎調査のうち，要介護状態に至った原因として，「高齢による衰弱」の割合が増え，実質的に虚弱による介護保険の導入が余儀なくされている。多くの糖尿病患者は，HbA1c を7％以下でコントロールすることが望ましいが，虚弱な高齢者では，HbA1c8％とすることが提案されている[13]。すなわち，緩やかなコントロールが高齢糖尿病患者に適していると考えるが，血糖コントロールが不良な状態においても転倒が誘発することを視野に入れると，高齢糖尿病患者個々に合ったコントロールの指標が必要である。今回の症例においては，後期高齢者に入り「高齢による衰弱」に該当する時期にあり，虚弱の判定が必要な時期と考えられる。転倒あり群は網膜症，腎症，認知症，低血糖，円背の合併症と虚弱を有し，年齢と関連していた。本研究は，FRI と KCL の調査も行っており，転倒の有無と KCL25 項目中，24 項目と有意差があり，転倒の予測に KCL が有用であると考え，高齢糖尿病患者は，虚弱になる要因も多く有している。鳥羽らが開発した FRI を使用した先行研究において，糖尿病群，非糖尿病群で比較すると，糖尿病患者の FRI スコアは，対照と比較して高値であった（$10.2 \pm 3.1$ vs $8.5 \pm 3.7$，$p < 0.05$）[8]。FRI は，転倒リスク評価として作成されたものであるが，転倒の有無にかかわらず ADL 低下を予測することが報告されている[10]。糖尿病患者では，FRI が高値であり，さらに転倒群は要介護のリスク患者であると考えられる。

高齢糖尿病患者は，年間に 18 ～ 78％の割合で転倒し，糖尿病がない人と比較して 1.5 ～ 3 倍転倒しやすいと報告されている[15]。転倒の有無と虚弱を示す KCL24 項目の間に有意な関連が示され，本症例における転倒歴

のある高齢糖尿病患者は，虚弱の因子を多く有し，年齢や性別，BMI を調整しても年齢が抽出されたことから，高齢糖尿病患者への転倒予防介入が必要である。高齢糖尿病患者においては，糖尿病合併症，身体能力の低下，血糖コントロール，機能低下，薬物の増加や階段を使う環境などの要因を有しているため，適切な運動療法，栄養や心理サポート，個々に合わせた血糖管理，環境整備が必要であると考える。今回の研究の限界として，前向き観察研究ではないために，詳しい低血糖の状況が把握できていないことがある。低血糖を予防することで，転倒を回避することが今回の研究で示唆されているが，さらに高齢糖尿病患者への前向き転倒予防の介入の必要性が強く示唆された。

## V　結語

高齢糖尿病患者においては，加齢と低血糖が転倒との関連要因であった。

転倒予防の観点から，外来に通院する高齢糖尿患者への低血糖の聞き取りと予防指導の強化を行いたい。

## VI　利益相反

すべての著者において，申告すべき事項はない。

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Original

# Characteristics of Elderly Diabetic Patients with a History of Falls

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## Abstract

**[Purpose]** To provide the initial causes of falls among elderly diabetic patients.
**[Method]** Three hundred elderly outpatients this diabetes mellitus aged 65 or over were enrolled in this study. Fall risk index (FRI) and Kihon check list (KCL) were adopted to determine frailty based on KCL score (KCL $\geqq 8$ : with frailty ; KCL $< 8$ : without frailty), and the targeting patients were divided into these two groups. The difference of clinical components between these two groups were analyzed with a Mann-Whitney U test, then the correlation and relevance between falls and diabetes were examined by the multivariate logistic regression analysis.
**[Results]** Ninety four patients had a history of falls (fallers), while 206 were non-fallers. Statistically significant differences between these two groups were observed in age, height, retinopathy, kidney disease, hypoglycemia, dementia, Frailty, duration of diabetes, HbA1c value, eGFR value and Mini-mental state examination. Independent factors extracted as associated with fall were higher age and hypoglycemia.
**[Consideration]** In the elderly diabetic patients, avoiding hypoglycemia is crucial to prevent falls.
**[Conclusion]** Fall of elderly diabetic patients were significantly associated with higher age and hypoglycemia.

**Keywords** Falls, Diabetes, Fall risk index, Kihon check list, Frailty

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ORIGINAL ARTICLE

# Age-related changes in skeletal muscle mass among community-dwelling Japanese: A 12-year longitudinal study

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**Aim:** The present study aimed to evaluate age-related changes in skeletal muscle mass among community-dwelling middle-aged and elderly Japanese.

**Methods:** This 12-year longitudinal study of a community-dwelling population in Japan included 15 948 examinations of 1962 men and 1990 women. We assessed appendicular muscle mass (AMM) using dual X-ray absorptiometry and calculated the skeletal muscle index (SMI) using the AMM divided by height squared (kg/m$^2$). Low muscle mass was defined as muscle mass minus two standard deviations below the mean for young healthy adults. Leg extension power (watts) was measured as an index of muscle function. Longitudinal data of skeletal muscle mass were analyzed using a general linear mixed-effect model.

**Results:** The prevalence of low muscle mass at the first wave of examinations was 27.1% in men and 16.4% in women. Longitudinal analysis showed that skeletal muscle mass decreased with aging during the 12-year study period except in middle-aged men, and to a greater extent in elderly men (*P* for trend, <0.001). Skeletal muscle mass decreased slightly, but significantly, in women. Although a cross-sectional analysis showed that SMI did not differ with age in women, leg extension power per leg muscle mass and grip strength per arm muscle mass as indices of muscle quality were significantly lower in older women (*P* for trend, <0.001 for both).

**Conclusion:** Age-related decreases in muscle mass were trivial, especially in women, but the quality of muscle decreased with aging in both sexes. **Geriatr Gerontol Int 2014; 14 (Suppl. 1): 85–92.**

**Keywords:** aging, epidemiology, longitudinal study, sarcopenia, skeletal muscle.

## Introduction

Aging is associated with a progressive loss of neuromuscular function that often leads to progressive disability and loss of independence along with a reduced quality of life among the elderly.[1–6] The loss of skeletal muscle mass and strength with biological and pathological aging is now commonly described as sarcopenia.[1] This decline of skeletal muscle is thought to be inevitable even among healthy older adults. The European Working Group on Sarcopenia in Older People (EWGSOP) assumed that muscle loss is a required component for a diagnosis of sarcopenia, as well as low muscle strength and/or low physical performance.[6]

However, the rate at which community-dwelling populations lose skeletal muscle mass with aging is unclear, because accurate assessments of muscle mass can be challenging. Skeletal muscle mass can be determined by anthropometric measurements, bioelectrical impedance analysis and dual X-ray absorptiometry (DXA),[7,8] and DXA is the most effective method recommended for clinical practice.[7] However, DXA is usually impractical for epidemiological surveys, because it is costly and it involves exposure to radiation, although minimal.

The definition of low muscle mass (sarcopenia by muscle mass) proposed by Baumgartner in the Population of New Mexico Elder Health Survey has been widely applied.[9] This definition uses the ratio between appendicular skeletal muscle mass (ASM) of the upper and lower limbs (kg) and height squared (m$^2$; ASM/

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height[2]), which is known as the skeletal muscle mass index (SMI). Thus, low muscle mass is defined as SMI ≥2 standard deviations below the normal means for a reference group aged 18–40 years determined using DXA. Several cross-sectional studies have investigated the prevalence of low muscle mass using the same definition.[6,10–18] However, the prevalence of low muscle mass has not been investigated in a longitudinal study capable of demonstrating actual changes in skeletal muscle mass with aging by repeated DXA measurements in a community-dwelling population.

The present study evaluated age-related changes in skeletal muscle mass among middle-aged and elderly Japanese men and women. Muscle mass was measured biennially up to seven times by DXA over a period of 12 years to explore actual changes in skeletal muscle mass with aging.

## Methods

### *Participants*

The study participants were derived from the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA), which involves population-based biennial examinations of a dynamic cohort of approximately 2300 individuals.[19] The participants in the NILS-LSA were community-dwelling men and women aged 40–79 years at the time of the first wave of assessments who were randomly selected from resident registrations, and stratified by sex and decade of age. Age- and sex-matched random samples of the same number of dropouts were recruited, except for those aged >79 years. New male and female participants aged 40 years were also recruited annually. The NILS-LSA is a comprehensive and interdisciplinary observational study of age-related changes that includes various gerontological and geriatric assessments of medical status, blood chemistry, body composition, anthropometry, nutritional status, psychological status, physical function, and physical activity. The first wave of NILS-LSA assessments started in November 1997. The participants were assessed approximately every 2 years until the seventh wave of examinations. We excluded those with incomplete DXA information about muscle mass. The first wave examination included 1090 men and 1081 women, and the mean number of repeat visits and length of follow up ± standard deviation (SD) were 4.04 ± 2.25 and 6.56 ± 2.25 years, respectively. A total of 1962 men and 1990 women participated in the study that comprised 15 948 assessments (including repeats). We derived data from community dwellers aged 40–91 years who participated in the NILS-LSA between November 1997 (first wave) and July 2012 (seventh wave).

The Ethics Committee of the National Center for Geriatrics and Gerontology approved the study in which all included individuals provided written informed consent to participate.

### *Measurement of muscle mass*

Appendicular muscle mass (AMM; kg) was assessed using a QDR-4500 DXA (Hologic, Bedford, MA, USA). The AMM represents appendicular fat-free mass minus bone mineral content, and it is assumed to be an index of the amount of skeletal muscle mass.

We evaluated the SMI calculated as AMM divided by height squared (kg/m$^2$).[5] Low muscle mass was defined as muscle mass minus two SD below the mean for young healthy adults.[9] We set the cut-off as SMI <6.87 and <5.46 kg/m$^2$ for Japanese men and women, respectively, as described by Sanada *et al.*, who also measured appendicular muscle mass using the DXA apparatus as aforementioned.[15]

### *Other parameters*

Height and weight were measured using a digital scale. Body mass index (kg/m$^2$) was calculated as weight divided by height squared. Medical history was assessed using questionnaires, and responses were confirmed by a physician at the time of medical assessments. Smoking habit, years of education and annual income were also assessed using a questionnaire. Trained interviewers applied a questionnaire to analyze the frequency and intensity of exercise (metabolic equivalents [MET]) to determine how free time had been spent over the past 12 months.[20] The means per day for physical activity (metabolic equivalents; MET × h/day) during leisure time were calculated. Nutritional intake was assessed using 3-day diet records.[21] Foods were weighed separately on a scale before cooking or portion sizes were estimated. Participants photographed meals before and after eating using disposable cameras. Registered dietitians used the photographs to complete missing data and telephoned participants to resolve discrepancies or obtain further information when necessary. The average of over 119 nutrients consumed over 3-day periods was calculated. The means per day for total energy intake (kcal/day) were calculated from the 3-day dietary records. Leg extension power was measured using the T.K.K.4236 adjustable seat and foot plate (Takei, Niigata, Japan). The maximum values of eight tests were included in analyses. Grip strength was also measured using the T.K.K.4301 grip dynamometer (Takei). The maximum values of two tests using the dominant hand were included in analyses.

### *Statistical analysis*

Data were statistically analyzed using R version 3.0.1 (http://www.r-project.org/). $P < 0.05$ was considered significant. Differences in continuous and class variables between men and women were assessed using *t*-tests and $\chi^2$-tests, respectively.

Trends in the skeletal muscle index, leg extension power/leg skeletal muscle mass, and grip strength/arm skeletal muscle mass in men and women according to age decade at the first wave examination were assessed using a general linear model.

Longitudinal data of skeletal muscle mass were analyzed using the general linear mixed-effect model, which takes into account the dependence of repeated observations within participants, which is an important feature of longitudinal analyses.[22,23] An additional advantage of the general linear mixed-effect model is that participants are included regardless of missing values. Thus, participants who were lost to follow up after early wave assessments or those who were assessed in later waves were also included in the analyses. General linear mixed-effect (lme) models were fitted using the lme function in the nlme package of R version 3.1–111. The lme function fits general linear mixed-effect models. The intragroup correlation structure was specified as a compound symmetry structure that corresponded to a constant correlation.

The effects of birth year on the rate of change in appendicular skeletal muscle mass over time were evaluated using general LME models. We determined fixed effects, such as average effects for birth cohorts, and random effects, such as individual deviations from the fixed effects to model changes in the mass of individual muscles. Birth year was categorized as 1920s or before, the 1930s, 1940s and 1950s, and thereafter. Time is expressed as years from time 0 defined as 1 October 2005, to approximately the midpoint between the first and the last waves of assessments to reduce the influence of collinearity. Appendicular skeletal muscle mass was estimated from the fixed effects of time, birth cohort, time × birth cohort interaction, and random effects of the intercept (individual differences in basic values for muscle mass) and slope (individual changes in muscle mass over time). Smoking, alcohol consumption, years of education, annual income and comorbidities (hypertension, heart disease, dyslipidemia, diabetes mellitus and stroke) were controlled in the model. Data from 1869 men (7297 assessments) and 1868 women (7095 assessments) with no missing values in covariates were analyzed in the linear mixed effect model.

## Results

Table 1 shows the characteristics of the participants by sex at the first wave of assessments. Men were significantly taller and heavier than women (each, $P < 0.001$), but the body mass index was essentially the same. Among 1090 men and 1081 women, 295 (27.1%) and 177 (16.4%) were diagnosed with low muscle mass at the first wave of assessments, respectively. The ratio (%) was significantly higher in men than in women ($P < 0.001$ for both). AMM and SMI were also significantly higher in men than in women ($P < 0.001$ for both), with no difference in age between men and women. More men smoked and consumed alcohol than women ($P < 0.001$ for both). Men spent more years being educated than women, and had higher annual incomes ($P < 0.001$ for both). Grip strength and leg extension power were significantly stronger in men than in women ($P < 0.001$ for both). Men were more likely to have a history of diabetes and stroke than women ($P = 0.004$ and 0.007, respectively), but women were more likely to have a history of dyslipidemia than men ($P < 0.001$), although hypertension and heart disease did not differ between the sexes. Men consumed significantly more total energy, and participated in leisure-time physical activities more frequently and at a greater intensity than women ($P < 0.001$ for both).

Figure 1 shows SMI by age decade in men and women. The SMI was lower in older than in younger men (*P* for trend, < 0.001), but did not differ by age in women (*P* for trend, not significant). Leg extension power (watts) divided by leg skeletal muscle mass (kg) was used as an index of leg muscle performance. Leg extension power per leg skeletal muscle mass (watts/kg) by age decade was significantly lower in older men and women (*P* for trend, <0.001 for both; Figure 2a). Handgrip strength (kg) divided by arm skeletal muscle mass (kg) was used as an index of hand muscle performance. Handgrip strength per arm skeletal muscle mass (kg/kg) by age decade was also significantly lower in older men and women (*P* for trend, <0.001 for both; Figure 2b).

Figure 3 shows estimated 12-year changes in SMI by birth cohort between 1998 and 2010 in 1869 men (7297 assessments) and 1868 women (7095 assessments). Changes in SMI by birth cohort were estimated using the general linear mixed-effect model controlled for smoking, alcohol consumption, years of education, annual income and comorbidities (hypertension, heart disease, dyslipidemia, diabetes mellitus and stroke). The main effects of time ($P = 0.03$), birth cohort ($P < 0.001$), and interaction between time and birth ($P < 0.001$) in men were significant. However, only the main effects of time were significant in women ($P < 0.001$).

The estimated SMI values in men were larger in younger birth cohorts in 1998 and 2010 ($P < 0.001$ for both), and the trend in slope by birth cohort was also significant. The estimated SMI significantly decreased in the 1920s ($P < 0.001$), 1930s ($P < 0.001$) and 1940s ($P = 0.005$) birth cohorts. However, the estimated SMI slightly, but significantly, increased in the 1950s ($P < 0.001$) birth cohort. The estimated SMI values in women did not increase by birth cohort in 1998 and

**Table 1** Characteristics of study participants by sex at first wave of examinations

| Variable | Men ($n$ = 1090) | Women ($n$ = 1081) | $t$-test/$\chi^2$ test | |
|---|---|---|---|---|
| Age (years) | 59.3 ± 11.0 | 59.3 ± 10.9 | $t$ (2169) = 0.07 | NS |
| Height (cm) | 164.5 ± 6.4 | 151.3 ± 6.1 | $t$ (2169) = 49.45 | *** |
| Weight (kg) | 62.1 ± 9.1 | 52.4 ± 8.2 | $t$ (2169) = 26.02 | *** |
| BMI (kg/m²) | 22.9 ± 2.8 | 22.9 ± 3.3 | $t$ (2169) = 0.09 | NS |
| Smoking | | | | |
| Never smoker, $n$ (%) | 237 (21.7%) | 968 (89.7%) | $\chi^2$ (2) = 1023.51 | |
| Ex-smoker, $n$ (%) | 440 (40.4%) | 31 (2.9%) | | *** |
| Current smoker, $n$ (%) | 413 (37.9%) | 80 (7.4%) | | |
| Alcohol consumption (ethanol mL/day) | 16.0 ± 19.3 | 2.6 ± 5.6 | $t$ (2073) = 21.54 | *** |
| Education (year) | 12.1 ± 2.5 | 11.4 ± 2.1 | $t$ (2161) = 7.38 | *** |
| Annual income (yen) | | | | |
| <4 500 000 | 267 (24.8%) | 332 (32.9%) | $\chi^2$ (2) = 18.8 | |
| ≥4 000 000 and <7 5000 000 | 379 (35.2%) | 292 (28.9%) | | *** |
| ≥7 5000 000 | 432 (40.1%) | 385 (38.2%) | | |
| Grip strength (kg) | 41.6 ± 7.9 | 25.0 ± 5.2 | $t$ (2146) = 57.49 | *** |
| Leg extension power (watts) | 533.6 ± 184.4 | 301.4 ± 106.8 | $t$ (2058) = 34.80 | *** |
| Medical history | | | | |
| Hypertension, $n$ (%) | 191 (17.6%) | 210 (19.5%) | $\chi^2$ (1) = 1.33 | NS |
| Heart Disease, $n$ (%) | 71 (6.5%) | 65 (6.0%) | $\chi^2$ (1) = 0.23 | NS |
| Dyslipidemia, $n$ (%) | 55 (5.1%) | 98 (9.1%) | $\chi^2$ (1) = 13.40 | *** |
| Diabetes mellitus, $n$ (%) | 71 (6.5%) | 41 (3.8%) | $\chi^2$ (1) = 8.24 | ** |
| Stroke, $n$ (%) | 23 (2.1%) | 8 (0.7%) | $\chi^2$ (1) = 7.27 | * |
| AMM (kg) | 20.0 ± 2.8 | 14.0 ± 2.0 | $t$ (2169) = 57.76 | *** |
| SMI (kg/m²) | 7.36 ± 0.80 | 6.11 ± 0.70 | $t$ (2169) = 38.82 | *** |
| Prevalence of low muscle mass, $n$ (%) | 295 (27.1%) | 177 (16.4%) | $\chi^2$ (1) = 36.46 | *** |
| Total energy intake (kcal/day) | 2323.7 ± 420.5 | 1894.3 ± 322.2 | $t$ (2073) = 26.11 | *** |
| Leisure-time PA (MET × min / year / 1000) | 47.6 ± 59.9 | 30.8 ± 43.3 | $t$ (2135) = 7.44 | *** |

Data are shown as means ± standard deviation. *$P$ < 0.05, **$P$ < 0.01, ***$P$ < 0.001. Final sample comprised 2171 participants at first wave assessment. Missing data: Smoking, $n$ = 2; Alcohol (ethanol) consumption, $n$ = 96; Education, $n$ = 8; Annual income, $n$ = 101; Grip strength, $n$ = 23; Leg extension power, $n$ = 111; Hypertension, $n$ = 7; Heart disease, $n$ = 7; Dyslipidemia, $n$ = 14; Diabetes mellitus, $n$ = 11; stroke, $n$ = 10; Total energy intake, $n$ = 96; PA, $n$ = 34. Cut-offs for low muscle mass in men and women: SMI <6.87 and 5.46 kg/m², respectively. AMM, appendicular muscle mass; BMI, body mass index; NS, not significant; PA, physical activity during leisure time; SMI, skeletal muscle index calculated by appendicular muscle mass divided by height squared.

2010, and slightly but significantly decreased in all birth cohorts. No trends in the slopes by birth cohort were evident ($P$ for trend, not significant).

Table 2 shows the fixed effects of birth cohorts and of interactions between time and birth cohorts in the model without the intercept and the main effect of time in men and women. In this model, each fixed effect of birth cohort was an intercept of the birth cohort; that is, the estimated SMI at time 0 (1 October 2005) of each birth cohort, and the fixed effects of the interaction between time and birth cohort were slopes (annual changes) of the birth cohorts.

## Discussion

Older persons commonly lose bone and skeletal muscle mass, and gain a relative amount of fat mass. Sarcopenia is characterized by progressive and generalized loss of skeletal muscle mass and strength, and it increases the risk of disability and a poor quality of life.[1,2,24]

Primary sarcopenia is caused by normal aging, but the manner and speed of skeletal muscle mass decrease in community-dwelling populations remain unclear. Here, we confirmed a significant decrease in skeletal muscle mass with aging except among middle-aged men. The prevalence of low muscle mass in the present study was 27.1% in men and 16.6% in women. However, the prevalence varies from 8% to 40% of people aged >60 years depending on the study sample, age, definition and assessment tool.[11] Values obtained using DXA comprise the most accepted method of quantifying muscle mass in research and clinical practice.[7] The cut-off for low muscle mass ≥2 SD below the young adult mean (YAM) derived from individuals aged between 18

 

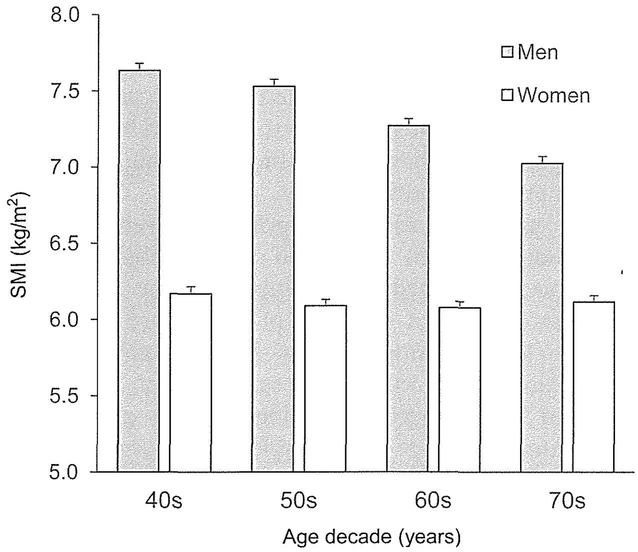


**Figure 1** Skeletal muscle index (SMI) of men and women according to age decade (mean ± standard error). SMI is lower in older than in younger men (*P* for trend, <0.001), but does not differ according to age among women (*P* for trend, not significant).

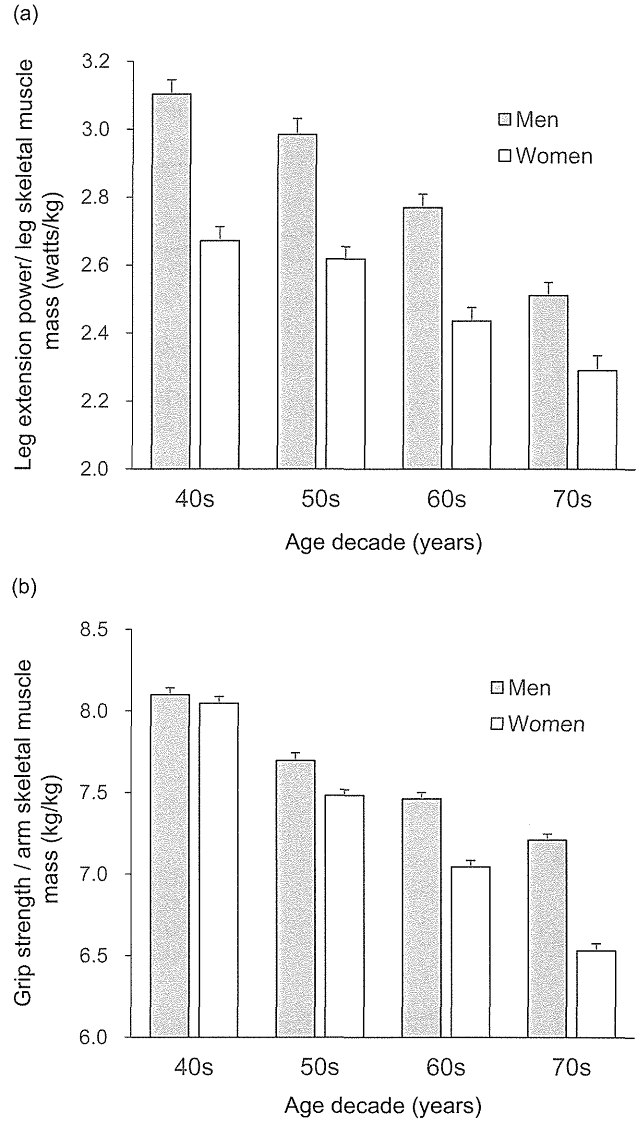


**Figure 2** (a) Leg extension power/leg skeletal muscle mass and (b) grip strength/arm muscle mass according to sex and age (mean ± standard error). Both values are significantly lower in older men and women (*P* for trend, <0.001 for both).

and 80 years, but obtaining reference values from relevant young, healthy, sex and ethnicity-matched populations can be challenging. Thus, some studies have used the lowest third of fat-free mass (FFM) to define low muscle mass.[16,25]

The New Mexico Elder Health Survey defined cut-offs for SMI as 7.26 and 5.45 kg/m$^2$ for men and women, respectively, based on ≥2 SD below the YAM.[9] They found that the prevalence of low muscle mass in persons aged <70 years increased from 13–24% to >50% in those aged >80 years. Although some cross-sectional studies have studied the prevalence of low muscle mass according to the same definition, the prevalence greatly differs depending on the cohort. The prevalence was 35.3% in men and 34.7% in women aged between 20 and 84 years in a Thai population,[10] and 8.9% and 10.9% in women aged 76–80 years and 86–95 years in the Epidemiologie de l'Osteoporose cohort, which was an observational, prospective and multicenter cohort study of French community-dwelling women aged ≥75 years.[11,12] The prevalence of low muscle mass had been reported to be 64.0% and 95.0% for female and male inpatients with hip fractures, respectively,[14] 6.7% and 6.3% among healthy male and female Japanese volunteers aged 70–85 years,[15] and 10.4% among female patients in an orthopedic outpatient clinic with normal lumbar spine bone mineral density.[17] A cross-sectional study of a Chinese population found the prevalence of low muscle mass of 13.2% for men and 4.8% for women aged ≥70 years.[18] The Korean National Health and Nutrition Examination Survey identified a 9.9% prevalence of low muscle mass among men age ≥60 years.[13]

Cooper *et al.* stated that assessments of sarcopenia should not depend only on muscle mass, but on a combination of measures of muscle mass and physical performance.[8] EWGSOP suggested an algorithm for sarcopenia case findings among older individuals based on measurements of gait speed, grip strength and muscle mass.[6] We found a rather small decrease in skeletal muscle mass; however, the muscle performance was greatly reduced, especially in women, which could cause frailty and disrupted daily activities among elderly women. The prevalence of sarcopenia was also determined according to the EWGSOP algorithm

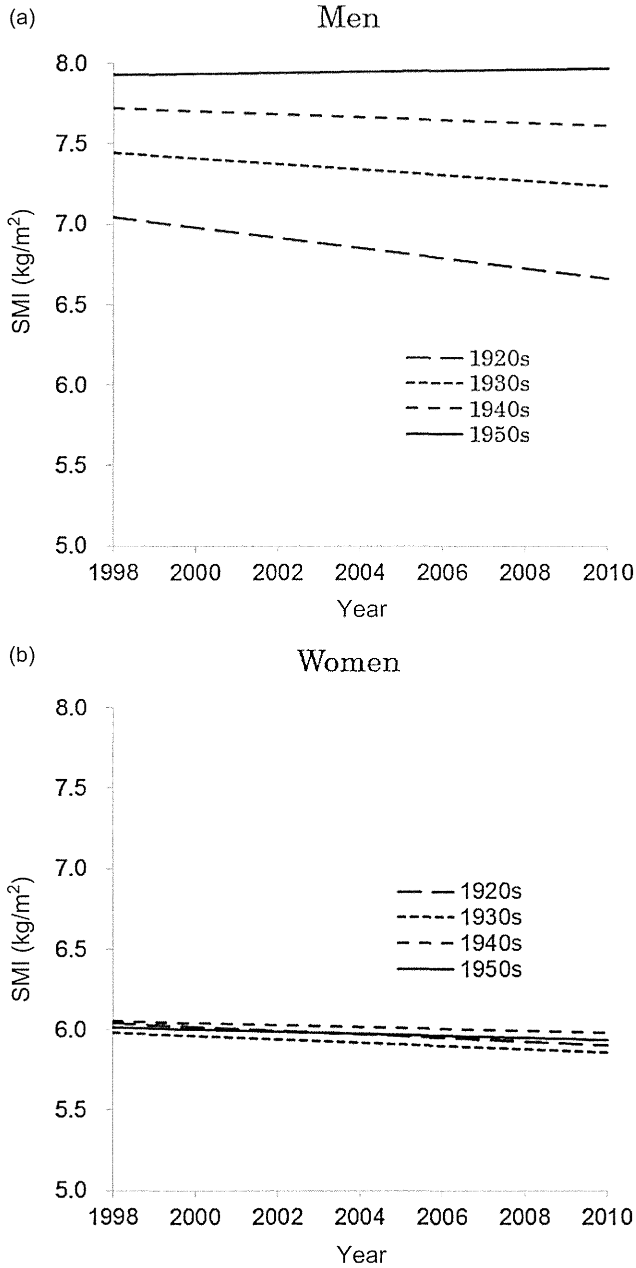


**Figure 3** Estimated 12-year changes in skeletal muscle index (SMI) by birth cohort between 1998 and 2010 determined using general linear mixed-effect model controlled for smoking, alcohol consumption, years of education, annual income, and comorbidities (hypertension, heart disease, dyslipidemia, diabetes mellitus, and stroke) among (a) men and (b) women.

in our participants aged ≥65 years in the first wave examination.[6] Among them, 38 (10.3%) men and 52 (14.5%) women, and 90 (12.4%) in total had sarcopenia.

The present study found that skeletal muscle mass decreased with age, except among men born in the 1950s. The examination was repeated every 2 years. Because the participants were informed about the results of their muscle strength, they often tried to improve it by training before the next examination. This trend was particularly prevalent among middle-aged men. Although muscle mass is supposed to decrease with age, it might have indeed increased among middle-aged men in the present study.

The present study had significant strengths. The longitudinal design supported the credibility of our inferences. Repeatedly assessing the same individuals over time provided evidence of a decrease in appendicular skeletal muscle mass in men and women. Approximately 15 000 assessments of randomly selected middle-aged and elderly male and female community dwellers over a period of 12 years avoided potential bias arising from the inclusion of patients with a specific disease or volunteers recruited by advertisements.

The present study also had several limitations. We could assess only appendicular muscle mass, as DXA cannot assess the skeletal muscle mass of the trunk. We were also unable to determine the quality of skeletal mass; for example, fat infiltration into muscle, and changes in muscle innervation and capillary density.[4,26] Another limitation was selection bias imposed by the longitudinal design of the study. Muscle mass data were obtained only from those who could be repeatedly examined, and these individuals tended to be healthier than those who dropped out of the study. Other factors besides aging that are associated with a decrease in muscle mass include nutrition and food consumption, frequency and intensity of physical activity, smoking habit, alcohol consumption, medical history, genotypes, and endocrine factors including sex hormones. However, the NILS-LSA has repeatedly examined most of these factors. Further studies of the NILS-LSA data should show associations between various factors and sarcopenia.

The present study mainly analyzed age-related changes in muscle mass. However, poor physical function among the elderly is more important as a geriatric syndrome, and the definition of sarcopenia has gradually shifted from a decrease in muscle mass alone to poor physical performance with low muscle mass. We plan to determine age-related changes in physical performance including walking speed and muscle strength using the NILS-LSA data in a future study.

In summary, we applied a longitudinal design to evaluate changes in skeletal muscle mass with aging among community-dwelling, middle-aged, and elderly Japanese men and women over a period of 12 years. Our data confirmed that skeletal muscle mass decreases with advancing age except in middle-age men. The decrease was large among elderly men and small, but significant, among women. Although a cross-sectional analysis showed that SMI did not differ according to age in

**Table 2** Fixed effects of birth cohort and interaction between time and birth cohort according to sex in general linear mixed-effect model of SMI

| | Fixed effect | Estimated parameter | SE | *P* |
|---|---|---|---|---|
| Men | BC 1920s | 6.842 | 0.057 | <0.001 |
| | BC 1930s | 7.195 | 0.056 | <0.001 |
| | BC 1940s | 7.465 | 0.061 | <0.001 |
| | BC 1950s | 7.658 | 0.058 | <0.001 |
| | Time × BC 1920s | −0.033 | 0.004 | <0.001 |
| | Time × BC 1930s | −0.015 | 0.002 | <0.001 |
| | Time × BC 1940s | −0.006 | 0.002 | <0.01 |
| | Time × BC 1950s | 0.008 | 0.002 | <0.001 |
| Women | BC 1920s | 6.080 | 0.054 | <0.001 |
| | BC 1930s | 6.061 | 0.053 | <0.001 |
| | BC 1940s | 6.148 | 0.059 | <0.001 |
| | BC 1950s | 6.115 | 0.058 | <0.001 |
| | Time × BC 1920s | −0.012 | 0.004 | <0.001 |
| | Time × BC 1930s | −0.011 | 0.002 | <0.001 |
| | Time × BC 1940s | −0.007 | 0.002 | <0.01 |
| | Time × BC 1950s | −0.007 | 0.002 | <0.01 |

Smoking, alcohol drinking, years of education, annual income and comorbidities (hypertension, heart disease, dyslipidemia, diabetes mellitus and stroke) were controlled in the model. BC, birth cohort; SMI, skeletal muscle index.

women, leg extension power per leg muscle mass, which is an index of muscle quality, was significantly lower in older women. The age-related decrease muscle mass was very small in women, but the muscle quality decreased with aging in both men and women. Our findings should provide useful basic data for assessments and the development of strategies to prevent sarcopenia.

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## Disclosure statement

The authors declare no conflict of interest.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

# Six-year longitudinal changes in body composition of middle-aged and elderly Japanese: Age and sex differences in appendicular skeletal muscle mass

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**Aim:** Little is known about longitudinal changes of body composition measured by dual-energy X-ray absorptiometry (DXA) in middle-aged and elderly individuals. We evaluated longitudinal changes of body composition, and age and sex differences in appendicular skeletal muscle mass.

**Methods:** Participants were 1454 community-dwelling Japanese men and women aged 40–79 years. Body composition at baseline and 6-year follow up was measured by DXA.

**Results:** Fat increased significantly in men of all ages, and in women aged in their 40s and 50s. Among men, arm lean tissue mass (LTM) changed by 0.9%, −0.5%, −1.4% and −3.7%, respectively, for the 40s to the 70s, and decreased significantly in the 60s and 70s. Leg LTM in men changed by −0.4%, −1.3%, −1.7% and −3.9%, respectively, and decreased significantly from the 50s to the 70s. Compared with the preceding age groups, significant differences were observed between the 60s and 70s in arm and leg LTM change in men. Among women, arm LTM changed by 0.7%, 0.2%, 1.6% and −1.5%, respectively, which was significant in the 60s and 70s. Leg LTM decreased significantly in all age groups of women by −2.0%, −2.8%, −2.4% and −3.9%, respectively. With respect to sex differences, leg LTM loss rates were significantly higher in women than men at the 40s and 50s.

**Conclusions:** Longitudinal data suggest that arm and leg LTM decreased markedly in men in their 70s, and leg LTM had already decreased in women in their 40s. **Geriatr Gerontol Int 2014; 14: 354–361.**

**Keywords:** aging, appendicular skeletal mass, body composition, longitudinal study.

## Introduction

Significant changes in body composition occur with aging, and these changes greatly affect health and physical function. Cross-sectional studies have suggested that skeletal muscle mass decreases with age,[1–3] and that fat mass increases linearly or curvilinearly with age.[4,5] Sarcopenia, age-associated loss of skeletal muscle mass,[6,7] is correlated with functional impairment and disability.[8,9] In advanced countries, where the elderly population is rapidly growing, the prevention of sarcopenia is important, and changes in appendicular skeletal muscle mass with aging need to be clarified to develop appropriate measures for sarcopenia.

Metter *et al.* reported that the relationship between muscle quality and age is dependent on how muscle is estimated, and on whether subjects are studied cross-sectionally or longitudinally.[10] Most studies dealing with body composition changes with aging have been cross-sectional, and their results might not reflect actual changes with aging. There have been some longitudinal reports of body composition using dual-energy X-ray absorptiometry (DXA)[11–14] or other methods,[15,16] but the number of participants and their age range were limited. With respect to evaluation, previous studies have reported that DXA is an accurate method for measuring body composition.[17–19] To date, there have been no

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This study was performed at National Institute for Longevity Sciences, National Center for Geriatrics and Gerontology, Aichi, Japan.

 

large-scale, population-based studies using DXA to evaluate longitudinal changes of body composition from middle age. In the present study, 6-year longitudinal changes in body composition measured by DXA were examined, and sex and age group differences in appendicular skeletal muscle mass changes were evaluated in middle-aged and elderly Japanese individuals.

## Methods

### *Study sample*

The data of the present study were collected as part of the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA). NILS-LSA is a population-based, prospective cohort study of aging and age-related diseases with follow up of the participants every 2 years. Participants in the NILS-LSA were randomly-selected age- and sex-stratified individuals selected from the pool of independent residents in the NILS neighborhood, Obu City and Higashiura Town, Aichi Prefecture, in central Japan. The age at the first wave ranged from 40 to 79 years. Details of the NILS-LSA have been given elsewhere.[20] A total of 2258 men and women took the examination by DXA at the first wave (from April 1998 to March 2000) of NILS-LSA. Among them, a total of 1469 participants (748 men and 706 women) underwent the evaluation by DXA in the fourth wave (from June 2004 to July 2006). We used the data of the participants who attended both investigations. There were various reasons why the participants could not be followed up; for example, transfer to another area, drop out for personal reasons, or death. Participants who used androgen and estrogen drugs were excluded. The study protocol was approved by the Committee of Ethics of Human Research of the National Center for Geriatrics and Gerontology. Written informed consent was obtained from all participants.

### *Anthropometric variables*

Bodyweight was measured to the nearest 0.1 kg using digital scales, height was measured to the nearest 0.1 cm using a stadiometer, and body mass index (BMI) was calculated as weight (kg) divided by height squared ($m^2$).

### *Body composition*

Body composition, fat mass, lean tissue mass (LTM), and bone mineral content (BMC) at baseline and 6-year follow up were assessed by DXA (QDR-4500; Hologic, Madison, OH, USA). LTM is equal to the fat-free mass minus BMC. Arm and leg LTM compartments were examined. Absolute change in each body composition measure was calculated as follow-up value minus baseline value. Percentage of change in each body composition measure was calculated as follows:

$$\text{Percent change} = (\text{absolute change value}/\text{baseline value}) \times 100$$

### *Total physical activity*

Participants responded to a self-administered questionnaire, and were interviewed according to an assessment method for leisure time and on-the-job physical activity within the last 12 months by trained interviewers.[21] Each activity was classified into four categories according to the intensity as determined by metabolic equivalent scores by duration in minutes. The total physical activity score was calculated by summing physical activity scores during leisure time, on the job, sleep and residual time.

### *Prevalence of diseases and smoking status*

Prevalence of diseases (cerebrovascular disease, heart disease and diabetes mellitus) and smoking status at baseline were determined by a questionnaire.

### *Statistical analysis*

Data were analyzed with the Statistical Analysis System (SAS) release 9.13 (SAS Institute, Cary, NC, USA). Differences between baseline and follow-up characteristics were tested using paired *t*-tests. The $\chi^2$-test was carried out to compare smoking status and disease prevalence between men and women. The participants were analyzed by age decade groups (40s, 40–49 years; 50s, 50–59 years; 60s, 60–69 years; 70s, 70–79 years at baseline). Changes in body composition over time in each age group were tested using paired *t*-tests. Sex and age group differences in arm and leg LTM were analyzed using the general linear model (GLM). Another GLM, with adjustment for confounding factors, the presence of diseases (cerebrovascular disease, heart disease and diabetes mellitus), smoking status and total physical activity at baseline, was also evaluated. Values of $P < 0.05$ were considered to show statistical significance.

## Results

Mean ages at baseline were 57.2 ± 9.9 years in men and 56.2 ± 9.9 years in women. The mean follow-up interval was 6.3 ± 0.3 years both in men and women. The participants' anthropometric variables, total physical activity, smoking status and prevalence of diseases at baseline are shown in Table 1.

Weight and height were significantly higher in men than women, and there was no difference in BMI. Total

**Table 1** Baseline anthropometric variables, total physical activity, and prevalence of smoking status and diseases

| | Men | Women |
|---|---|---|
| Weight (kg) | 63.4 ± 8.4** | 53.6 ± 7.5 |
| Height (cm) | 165.3 ± 6.0** | 152.3 ± 5.5 |
| BMI (kg/m$^2$) | 23.2 ± 2.5 | 23.1 ± 2.9 |
| Total physical activity (*10$^3$*METS*min/y) | 705.3 ± 93.5** | 736.5 ± 68.8 |
| Smoking status (%) | | |
| Never | 22.9** | 90.5 |
| Past | 41.0** | 2.6 |
| Current | 36.1** | 7.0 |
| Prevalence of disease (%) | | |
| Cerebrovascular disease | 2.0* | 0.7 |
| Heart disease | 9.9 | 7.8 |
| Diabetes mellitus | 7.1* | 3.1 |

Values for anthropometric variables and total physical activity are mean ± standard deviation. Differences between men and women were evaluated by *t*-test or $\chi^2$-test. Significantly different from women, **$P < 0.01$, *$P < 0.05$. METS, metabolic equivalents.

physical activity was significantly greater in women than in men. There were significant differences in smoking status, and prevalence of cerebrovascular disease and diabetes between men and women.

Table 2 shows changes in body composition by age groups in men. A significant weight increase was observed from the 40s to 60s age groups, but not for the 70s age group. There were significant increases in fat for all age groups. A significant decrease in BMC was observed in the 70s age group. Total LTM increased in the 40s and 50s age groups, and decreased in the 70s age group. Arm LTM increased in the 40s age group, and decreased in the 60s and 70s age groups. Leg LTM decreased significantly from the 50s to the 70s age group.

Table 3 shows changes in body composition by age groups in women. Significant increases in weight in the 40s and 60s age groups, and in fat in the 40s and 50s age groups were observed. There were significant decreases in BMC in all age groups. Total LTM increased significantly in the 60s age group. Arm LTM increased significantly in the 60s age group and decreased in the 70s age group. Leg LTM decreased significantly in all age groups.

Figure 1 presents the percentage change of arm (a) and leg (b) LTM in men. Percentage changes of arm LTM were 0.9%, –0.5%, –1.4% and –3.7%, respectively. Compared with the preceding age group, there were significant differences between the 40s and 50s age groups ($P < 0.05$), and between the 60s and 70s age groups ($P < 0.01$) in men. When adjusting for confounding factors, the significant difference between the 60s and 70s age groups continued, but that between the 40s and 50s age groups disappeared in men.

Percentage changes of leg LTM in men were –0.4%, –1.3%, –1.7% and –3.9%, respectively. Compared with the preceding age group, there were significant differences between the 60s and the 70s age groups ($P < 0.01$), and this did not change after adjustment for confounding factors.

Figure 2 presents percentage change of arm (a) and leg (a) LTM in women.

Percentage changes of arm LTM were 0.7%, 0.2%, 1.6% and –1.5%, respectively. Compared with the preceding age group, there was a significant difference between the 60s and the 70s age groups ($P < 0.01$) in women, and this did not change after adjustment for confounding factors.

Percentage changes of leg LTM in women were –2.0%, –2.8%, –2.4% and –3.9%, respectively. There were no differences between the adjacent age groups in women.

With respect to sex differences of arm LTM within the same age groups, men in the 60s and 70s age groups had a relatively greater percentage decrease change than women ($P < 0.01$), and when adjusting for confounding factors, the significant differences persisted. With respect to sex differences of leg LTM within the same age groups, women in the 40s and 50s age groups had a significantly greater percentage decrease change than men ($P < 0.01$), and after adjustment for the confounding factors, the significance of these differences did not change.

## Discussion

The present study showed the 6-year longitudinal changes in body composition measured by DXA in men

**Table 2** Changes in body composition by age group during the 6-year follow-up period in men

| | Age group | Baseline (kg) | Change (kg) | *P*-value | Percent change (%) |
|---|---|---|---|---|---|
| Weight | 40s | 66.8 ± 8.5 | 1.9 ± 3.4 | <0.0001 | 2.7 |
| | 50s | 64.4 ± 7.7 | 1.5 ± 3.2 | <0.0001 | 2.4 |
| | 60s | 61.5 ± 7.8 | 1.5 ± 3.7 | <0.0001 | 2.6 |
| | 70s | 58.7 ± 7.7 | 0.4 ± 3.2 | 0.15 | 0.6 |
| Fat | 40s | 14.1 ± 4.2 | 1.1 ± 2.2 | <0.0001 | 8.4 |
| | 50s | 13.4 ± 3.8 | 1.2 ± 2.2 | <0.0001 | 10.4 |
| | 60s | 13.5 ± 3.8 | 1.3 ± 2.4 | <0.0001 | 11.4 |
| | 70s | 13.0 ± 3.7 | 1.0 ± 2.1 | <0.0001 | 8.3 |
| BMC | 40s | 2.37 ± 0.29 | –0.01 ± 0.06 | 0.09 | –0.3 |
| | 50s | 2.31 ± 0.30 | –0.01 ± 0.06 | 0.07 | –0.4 |
| | 60s | 2.18 ± 0.30 | –0.01 ± 0.07 | 0.05 | –0.5 |
| | 70s | 2.08 ± 0.26 | –0.04 ± 0.08 | <0.0001 | –1.9 |
| LTM | 40s | 50.4 ± 5.4 | 0.8 ± 1.6 | <0.0001 | 1.6 |
| | 50s | 48.6 ± 4.8 | 0.3 ± 1.6 | 0.002 | 0.7 |
| | 60s | 45.8 ± 4.7 | 0.2 ± 1.8 | 0.08 | 0.5 |
| | 70s | 43.5 ± 4.8 | –0.5 ± 1.8 | 0.003 | –1.3 |
| Arm LTM | 40s | 5.97 ± 0.75 | 0.05 ± 0.34 | 0.03 | 0.9 |
| | 50s | 5.73 ± 0.69 | –0.04 ± 0.31 | 0.08 | –0.5 |
| | 60s | 5.35 ± 0.67 | –0.08 ± 0.29 | 0.0002 | –1.4 |
| | 70s | 5.01 ± 0.67 | –0.18 ± 0.30 | <0.0001 | –3.7 |
| Leg LTM | 40s | 15.89 ± 1.97 | –0.05 ± 0.74 | 0.32 | –0.4 |
| | 50s | 15.08 ± 1.82 | –0.21 ± 0.79 | <0.0001 | –1.3 |
| | 60s | 14.14 ± 1.69 | –0.25 ± 0.89 | <0.0001 | –1.7 |
| | 70s | 13.45 ± 1.81 | –0.52 ± 0.73 | <0.0001 | –3.9 |

$n = 204$ in age group 40s, $n = 234$ in age group 50s, $n = 196$ in age group 60s, $n = 114$ in age group 70s. Values of baseline and change are mean ± standard deviation). Significant changes from baseline were evaluated by paired *t*-test. BMC, bone mineral content; LTM, lean tissue mass.

and women aged 40–79 years. Weight and fat mass increased or did not change in both men and women in all age groups. Among men, marked decreases in both arm and leg LTM were found in the 70s age group. Among women, leg LTM decreased significantly in all age groups. The rates of loss in arm LTM were larger in men than in women in the 60s and 70s, the elderly age groups. In contrast, the rate of loss in leg LTM was larger in women than in men in the 40s and 50s, the early stage, middle-aged groups.

Previous cross-sectional studies suggested that appendicular skeletal muscle mass decreases with age in both sexes.[1,3,22] However, these cross-sectional studies show indirect evidence of age-related changes.[23] There have been several longitudinal studies of body composition measured by DXA. Gallagher *et al.* reported that there were significant decreases in leg skeletal muscle mass, and tendencies for a loss of arm skeletal muscle mass in healthy men and women aged over 60 years during an average 4.7-year follow up.[13] Visser *et al.* showed that, over a 2-year period, appendicular skeletal muscle mass decreased –0.8% in men, but not in women aged 70–79 years, and leg lean soft tissue mass decreased significantly in both sexes.[12] Zamboni *et al.* found that significant losses of leg skeletal muscle were observed in stable-weight, elderly (68–78 years) men and women over a 2-year period.[13] However, in most of these studies, the participants were aged over 60 years. In the present study, we showed the changes in body composition in participants of a wide age range, 40–79 years. In the 60s and 70s age groups, except for the arm LTM in the 60s age group in women, there were significant decreases of arm and leg LTM in men and women. Already in the 40s and 50s age group, there were significant decreases in leg LTM in women.

With respect to sex differences, previous cross-sectional[1,5] and longitudinal studies[11,13,14] reported that the rates of decrease in appendicular lean mass were greater for men than for women. The present study showed that the rates of loss in arm LTM were greater in men than in women in the 60s and 70s age groups. However, the rate of loss in leg LTM was greater in women than in men in the 40s and 50s age groups, and no significant sex difference was found in the 60s and 70s age groups. Previous longitudinal studies evaluated the differences using absolute change,[11,12,14] whereas the

 

**Table 3** Changes in body composition by age group during the 6-year follow-up period in women

| | Age group | Baseline (kg) | Change (kg) | *P*-value | Percent change (%) |
|---|---|---|---|---|---|
| Weight | 40s | 54.8 ± 7.9 | 1.2 ± 3.9 | <0.0001 | 2.1 |
| | 50s | 54.4 ± 6.9 | 0.3 ± 3.0 | 0.19 | 0.5 |
| | 60s | 53.3 ± 7.1 | 0.5 ± 2.8 | 0.02 | 0.9 |
| | 70s | 49.9 ± 7.8 | −0.2 ± 3.1 | 0.60 | −0.4 |
| Fat | 40s | 16.5 ± 4.6 | 1.2 ± 2.6 | <0.0001 | 8.0 |
| | 50s | 17.2 ± 4.4 | 0.5 ± 2.3 | 0.001 | 3.6 |
| | 60s | 17.7 ± 4.5 | 0.3 ± 2.0 | 0.06 | 2.1 |
| | 70s | 16.2 ± 4.7 | 0.02 ± 2.3 | 0.95 | 0.5 |
| BMC | 40s | 1.98 ± 0.25 | −0.11 ± 0.13 | <0.0001 | −5.6 |
| | 50s | 1.77 ± 0.26 | −0.13 ± 0.10 | <0.0001 | −3.7 |
| | 60s | 1.54 ± 0.23 | −0.06 ± 0.06 | <0.0001 | −3.7 |
| | 70s | 1.36 ± 0.23 | −0.06 ± 0.06 | <0.0001 | −4.4 |
| LTM | 40s | 36.3 ± 4.2 | 0.1 ± 1.8 | 0.24 | 0.3 |
| | 50s | 35.5 ± 3.4 | −0.1 ± 1.3 | 0.18 | −0.3 |
| | 60s | 34.0 ± 3.5 | 0.2 ± 1.2 | 0.008 | 0.7 |
| | 70s | 32.4 ± 3.8 | −0.1 ± 1.2 | 0.34 | −0.4 |
| Arm LTM | 40s | 3.56 ± 0.54 | 0.02 ± 0.28 | 0.22 | 0.7 |
| | 50s | 3.53 ± 0.44 | 0.003 ± 0.22 | 0.85 | 0.2 |
| | 60s | 3.43 ± 0.45 | 0.05 ± 0.23 | 0.003 | 1.6 |
| | 70s | 3.24 ± 0.47 | −0.05 ± 0.20 | 0.02 | −1.5 |
| Leg LTM | 40s | 11.19 ± 1.64 | −0.22 ± 0.63 | <0.0001 | −2.0 |
| | 50s | 10.88 ± 1.34 | −0.31 ± 0.57 | <0.0001 | −2.8 |
| | 60s | 10.42 ± 1.33 | −0.25 ± 0.48 | <0.0001 | −2.4 |
| | 70s | 9.91 ± 1.36 | −0.39 ± 0.51 | <0.0001 | −3.9 |

$n = 216$ in age group 40, $n = 218$ in age group 50, $n = 177$ in age group 60, $n = 95$ in age group 70. Values of baseline and change are mean ± SD (standard deviation). Significant changes from baseline were evaluated by paired t-test. BMC, bone mineral content; LTM, lean tissue mass.

present study used a relative index, the percent change. In the present study, comparisons using the absolute change in mass were also made, but the results for the sex differences showed almost the same tendency (data not shown). As there were many differences among the studies in the participants' characteristics, race, lifestyle and study design, further examination is required to clarify these differences.

The present study showed that there were significant decreases in leg LTM, but not in arm LTM, among women in the 40s to 60s age groups. Lynch *et al.* reported that, with increasing age, leg muscle quality declined ~20% more than arm muscle quality in women.[24] Based on these results, changes in muscle mass or function might differ between arms and leg muscles in women; decreases were apparent in the leg muscles. Leg muscle mass is closely associated with functional performance[14,25] and, in general, women have significantly less skeletal muscle mass than men.[1,2,23] There were several reports that frailty was higher in women than men in the elderly.[26,27] Therefore, it might be especially important for women to prevent the decrease of leg LTM from middle age. Some studies have suggested the relationship between menopause and loss of muscle mass,[28–30] and that estrone predicted loss of appendicular muscle mass.[31] The early onset of leg LTM decrease of women in the present study might be associated with the menopausal transition.

For evaluating sarcopenia, skeletal muscle mass index (SMI), obtained by dividing appendicular skeletal muscle mass by height squared, is often used.[8] Appendicular skeletal muscle mass was measured as the sum of the LTM for arms and legs. In the present study, both arm and leg LTM significantly decreased at the same time in the 70s age group in men. In contrast, in women, the time of LTM decrease differs in arms and legs. Therefore, in order to evaluate the decrease of muscle mass in women more clearly, it might be better to use leg LTM alone. Further detailed analyses of LTM in women would be necessary in future studies.

Regarding fat mass change, Hughes *et al.* reported that fat mass increased in the elderly, but the increase in women was attenuated with advancing age.[15] Other studies showed that fat mass increased significantly in elderly men and decreased non-significantly in elderly women.[11,12] As in these previous studies, the present

 

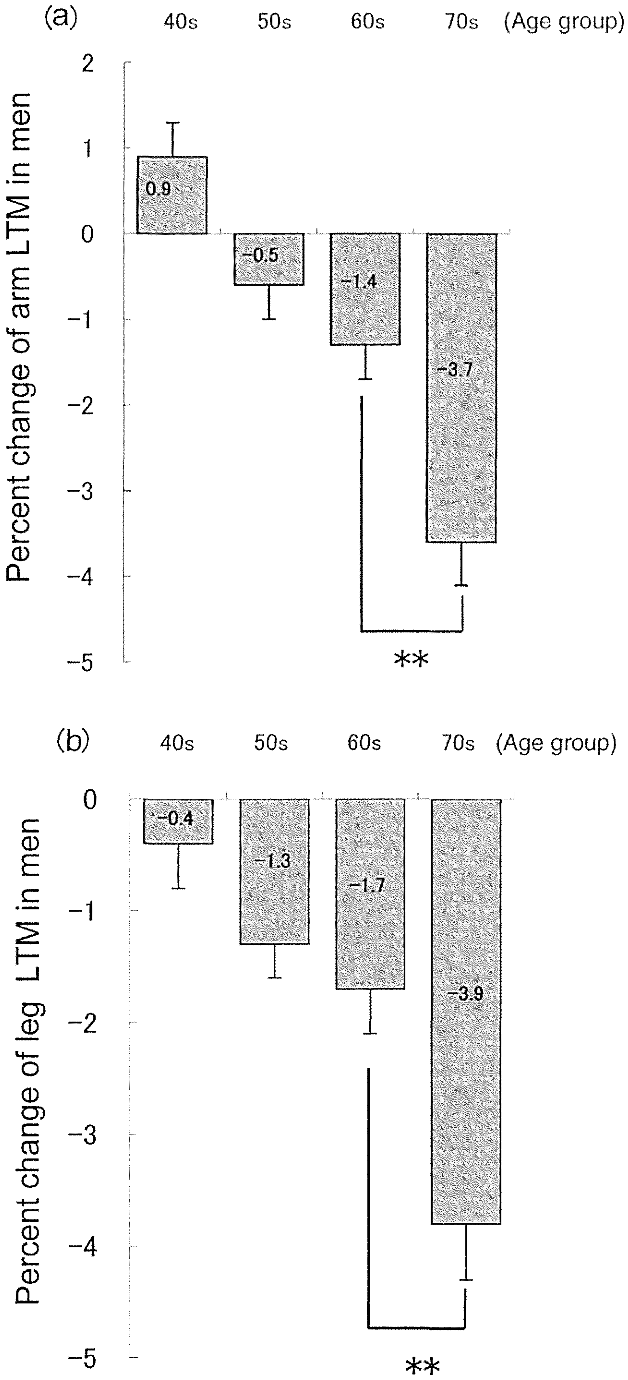


**Figure 1** Percentage change of (a) arm and (b) leg lean tissue mass (LTM) during the 6-year follow-up period by age group in men. Values are mean ± standard error of the mean. $^{**}P < 0.01$, compared with the preceding age group adjusting for confounding factors.

study showed that fat mass increased in all age groups in men and that, in women, it increased in the 40s and 50s, but it did not change thereafter.

The strengths of the present study are the large age- and sex-stratified sample size, the wide range of ages and the 6-year follow-up period. This is the first study to report the longitudinal changes of body composition,

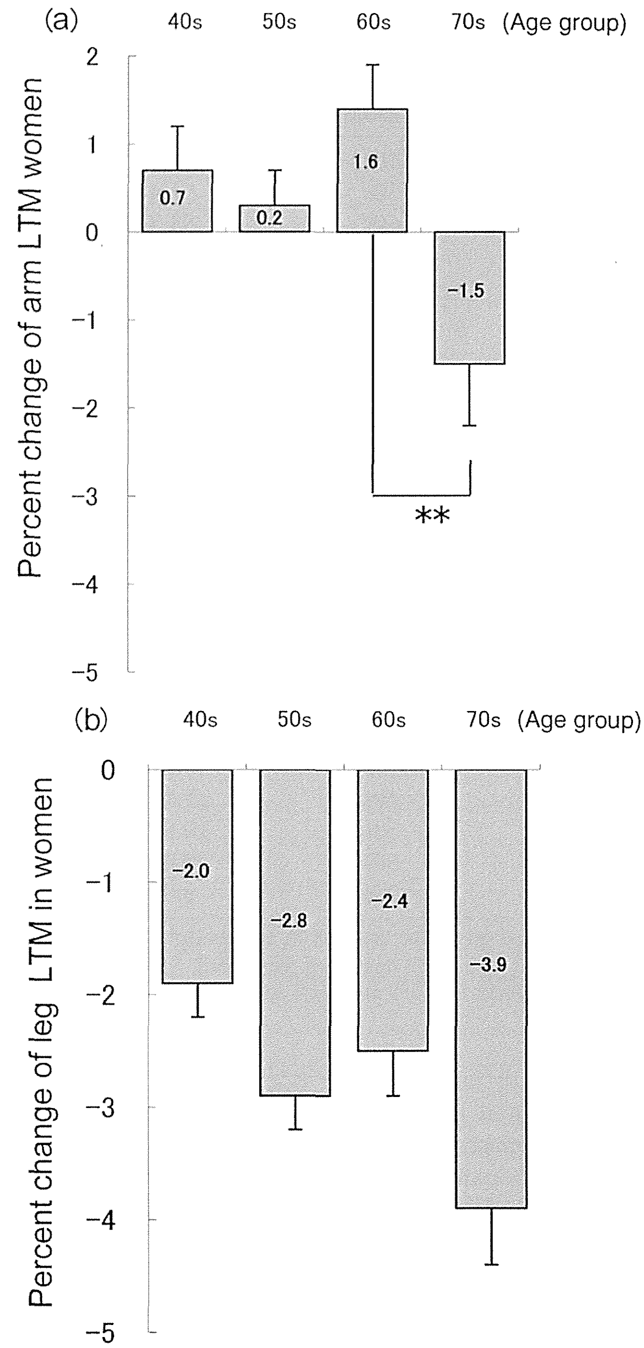


**Figure 2** Percentage change of (a) arm and (b) leg lean tissue mass (LTM) during the 6-year follow-up period by age group in women. Values are mean ± standard error of the mean. $^{**}P < 0.01$, compared with the preceding age group adjusting for confounding factors.

measured by DXA in 40- to 79-year-old Japanese subjects. With respect to race, so far, no longitudinal study of Asians has been reported, and there has not been sufficient research on racial differences. It will be necessary to clarify racial differences and consider various environmental factors in future studies.

Although loss of muscle mass is associated with decline in strength[32,33] and disability,[8] there were reports that strength decline in older adults is much more rapid than loss of muscle mass,[32] and that muscle strength is more important than muscle mass in estimating mortality risk.[9,34,35] Recently, the European Working Group on Sarcopenia in Older People recommended that the presence of both low muscle mass and low muscle function (strength or performance) be used.[36] Thus, to measure not only muscle mass, but also muscle strength, might be important for the evaluation of actual activity, especially in the elderly.

As several reports have suggested differences of bodyweight and the prevalence of obesity by birth cohort,[37,38] there might also be differences of changes in body composition by birth cohort. In addition, although the participants of the present study were randomly selected, they were relatively well-functioning men and women able to participate in the study. Therefore, the results might not accurately represent changes with aging in the general population.

In conclusion, we evaluated 6-year longitudinal changes of body composition in middle-aged and elderly participants. Remarkable decreases of arm and leg LTM in men in the 70s age group, and early decreases of leg skeletal muscle mass already in the 40s age group in women were found. We believe that these results might offer important information with respect to prevention of sarcopenia, and improving the health-related quality of life in older adults.

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## Disclosure statement

The authors declare no conflict of interest.

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