*Original Article*

# The role of fat indices as factors leading to sarcopenia in older adults residing in underpopulated areas

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**Simplifying the diagnostic criteria for sarcopenia is key to establishing effective interventions. Herein, we aimed to clarify novel diagnostic factors. We calculated novel fat indices [total fat index (TFI) and limb fat index (LFI)] and clarified factors leading to pre-sarcopenia and sarcopenia in 594 enrolled older adults. Physical measurements [height, weight, body mass index (BMI), gait speed, grip strength, and skeletal muscle mass] were performed. Sarcopenia was determined using established diagnostic criteria (pre-sarcopenia, *n* = 102; sarcopenia, *n* = 42). Age was associated with sarcopenia status. BMI, TFI, and LFI were lower in patients with pre-sarcopenia and sarcopenia. Logistic regression analysis showed the following odds ratios (ORs) for pre-sarcopenia: BMI [OR: 0.787, 95% confidence interval (CI): 0.7–0.885], LFI (OR: 0.589, 95% CI: 0.402–0.863), and age (OR: 1.06, 95% CI: 1.02–1.1). ORs for sarcopenia (vs pre-sarcopenia) were as follows: LFI (OR: 50.6, 95% CI: 10.2–250.0), age (OR: 1.1, 95% CI: 1.0–1.2), and BMI (OR: 0.418, 95% CI: 0.28–0.608). Our findings contribute to informing medical guidelines.**

*Key Words*: **aging, body fat, risk factor, skeletal muscle index, sarcopenia**

The population of older adults in Japan is increasing. It is common for older adults living in community settings to exhibit skeletal muscle loss, muscle weakness, and a decline in physical function.[1] A topical research question in recent years has been how older adults can avoid requiring nursing care through nursing care prevention programs and comprehensive programs for older adults residing in the community. For example, an exercise-based long-term care prevention program is currently in place, and the intervention group showed significant improvement in total frailty checklist scores after one year.[2] Against this background, sarcopenia (considered a geriatric syndrome) has been attracting much attention. Sarcopenia was first proposed by Rosenberg in 1989.[3] All diagnostic definitions of sarcopenia are based on skeletal muscle reduction and resulting declines in physical function, and skeletal muscle mass is an essential item within each definition. We note that loss of skeletal muscle mass is an essential component in the Asian Working Group for Sarcopenia (AWGS) diagnostic criteria, wherein sarcopenia is defined according to a decrease in muscle strength and/or physical function.[4] Moreover, sarcopenia is said to be related to activities of daily living (ADL). Instrumental ADL and its prevention are critically important to allow community-dwelling older adults to lead healthy and fulfilling lives. Currently, according to a large survey conducted in Japan, sarcopenia prevalence is reported to range between 7.5% and 8.2%. On applying the AWGS criteria, sarcopenia prevalence is 9.9% [95% confidence interval (CI), 6.2–15.4%] overall and has previously been reported as 9.8% (95% CI, 6.2–15.2%) in men and 10.1% (95% CI, 6.4–15.5%) in women.[1,5,6] From the perspective of preventing or suppressing the onset of sarcopenia, Tanimoto *et al.*[7] evaluated the diversity of food intake in 1,074 Japanese participants aged ≥65 years and reported that the diversity of food intake was inversely associated with the onset of sarcopenia in men on multivariate analysis. Pre-sarcopenia is defined as the stage before sarcopenia, and it is important to recognize the signs of age-related loss of skeletal muscle mass to prevent it. Although established diagnostic criteria for sarcopenia are currently in use in the Asia Pacific region,[4] we hypothesized that there might be other factors besides the established criteria that could lead to sarcopenia.[8] This study aimed to calculate a novel fat index and determine whether it could be a factor in diagnosing pre-sarcopenia and sarcopenia.

## Methods

**Participants.** The enrolled participants were 594 older adults (186 men and 408 women; mean age: 77.1 ± 7.5 years) who responded to an open recruitment campaign in Wakasa Town, Japan (Fig. 1). The recruitment was publicized by Wakasa Town staff using flyers and telephone calls. This study was approved by the Medical Ethics Review Committee of our medical center (approval no. 20190014) and conducted in accordance with the ethical standards set forth in the Declaration of Helsinki. This research complies with the respective ethical statements pertaining to ethical issues related to scientific discovery in exercise science.[9] Written informed consent was obtained from all participants before participation.

**Protocol.** A basic study questionnaire (checklist questionnaire) and physical function measurements (walking speed, grip strength, skeletal muscle mass, total fat mass, and limb fat mass) were conducted, and the results were explained to all participants. In the basic study questionnaire, participants were asked about their age, sex, height, weight, medical history (diabetes,

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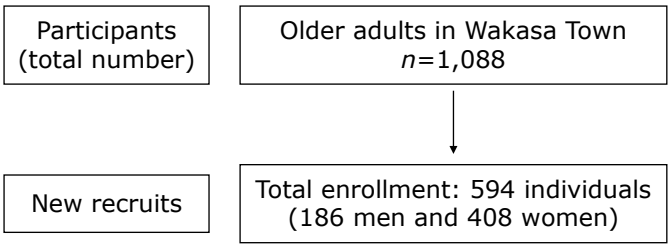


**Fig. 1.** Of 1,088 participants, 594 met the requirements of the measurement items and were included in the study.

hypertension, heart disease, and dyslipidemia), and lifestyle (exercise habits, smoking, and alcohol intake). Sarcopenia was determined according to the AWGS 2019 criteria.[4] Specifically, sarcopenia was defined according to grip strength and/or a walking speed below the reference range, besides a skeletal muscle mass index below the reference range (Table 1). The reference values for grip strength were 28.0 kg for men and 18.0 kg for women. A Smedley-type digital hand dynamometer (TTM; Tsutsumi Seisakusho, Tokyo, Japan) was used to measure grip strength. While in an upright posture with legs naturally open and arms naturally lowered, the participant was instructed to 1. grip the dynamometer with the display on the outside, 2. adjust the width of the grip so that the second joint of the index finger was almost at a right angle, 3. take care not to let the meter touch his/her body or clothing, and 4. clench his or her grip with all of their strength. Grip strength was measured on both sides, and the maximum value was applied in statistical analyses.[7] Walking speed was measured in the corridor using a 7 m interval, with a runway distance of 1 m each at the start and end of this interval. Walking time was measured when the participant started walking at a normal walking speed and passed through the middle 5 m without slowing down, after which the walking speed was calculated.[7] Walking speed was measured at least twice, and the fastest time was applied in statistical analyses. The reference value for walking speed was set to <1.0 m/s. Skeletal muscle mass, total fat mass, and limb fat mass were measured using bioelectrical impedance analysis (BIA) via a multi-frequency body composition analyzer (MC-780A; Tanita Inc., Tokyo, Japan). The skeletal muscle mass index (SMI) was calculated as the sum of the limb skeletal muscle mass divided by the participant's height squared. The reference values for SMI were 7.0 kg/m$^2$ for men and 5.7 kg/m$^2$ for women.[4] The total fat index (TFI) was calculated as the participant's whole body fat mass divided by height squared. The limb fat index (LFI) was calculated as the participant's total fat mass minus body fat mass divided by height squared (Fig. 2).

**Statistical analysis.** According to the derived information, 594 participants were classified into three groups (normal/healthy, pre-sarcopenia, and sarcopenia), and the participant's interview data and physical function measurement data were compared. More specifically, one-way analysis of variance with post hoc Bonferroni correction was used to evaluate participant

**Table 1.** Baseline characteristics of the study population according to disability status

| Demographic data | Total ($n$ = 594) | Normal[a] ($n$ = 450) | Presarcopenia[b] ($n$ = 102) | Sarcopenia[c] ($n$ = 42) | *post-hoc* | | | $p$ value |
|---|---|---|---|---|---|---|---|---|
| | | | | | a vs b $p$ value | a vs c $p$ value | b vs c $p$ value | |
| *Age (years) | 77.1 ± 7.5 | 75.9 ± 7.2 | 78.7 ± 7.1 | 86.5 ± 4.5 | <.001 | <.001 | <.001 | <.001 |
| *Height (cm) | 153.1 ± 9.3 | 153.5 ± 9.2 | 152.9 ± 8.6 | 148.1 ± 10.8 | 1 | <.001 | 0.013 | 0.001 |
| *Body weight (kg) | 53.2 ± 10.2 | 55.0 ± 10.0 | 48.0 ± 8.6 | 46.6 ± 9.6 | <.001 | <.001 | 1 | <.001 |
| *Body mass | 14.7 ± 5.8 | 15.5 ± 5.7 | 11.7 ± 5.1 | 12.5 ± 5.3 | <.001 | 0.003 | 1 | <.001 |
| *BMI | 22.6 ± 3.2 | 23.2 ± 3.1 | 20.5 ± 2.7 | 20.9 ± 2.8 | <.001 | <.001 | 1 | <.001 |
| *SMI | 6.6 ± 1.0 | 6.9 ± 0.9 | 5.9 ± 0.7 | 5.6 ± 0.8 | <.001 | <.001 | 0.16 | <.001 |
| **Hypertension (%) | 278 (46.8%) | 212 (47.1%) | 43 (42.2%) | 23 (54.8%) | 1 | 1 | 0.6 | 0.383 |
| **Diabetes (%) | 63 (10.6%) | 52 (11.6%) | 5 (4.9%) | 7 (16.7%) | 0.14 | 0.97 | 0.12 | 0.05 |
| **Hyperlipidemia (%) | 197 (33.2%) | 151 (33.6%) | 36 (35.3%) | 10 (23.8%) | 1 | 0.79 | 0.75 | 0.401 |
| **Smoking (%) | 41 (7.0%) | 31 (6.9%) | 7 (6.9%) | 3 (7.1%) | 1 | 1 | 1 | 1 |
| **Alcohol habit (%) | 157 (26.4%) | 124 (27.6%) | 24 (23.5%) | 9 (21.4%) | 1 | 1 | 1 | 0.582 |
| *5 m walking (s) | 3.8 ± 1.8 | 3.6 ± 1.7 | 3.7 ± 1.3 | 5.9 ± 2.1 | 1 | <.001 | <.001 | <.001 |
| *Grip strength (kg) | 27.7 ± 8.4 | 28.6 ± 8.6 | 27.1 ± 6.4 | 19.9 ± 5.2 | 0.25 | <.001 | <.001 | <.001 |
| ***TFI (total fat index) | 6.3 ± 2.6 | 6.6 ± 2.5 | 5.1 ± 2.2 | 5.8 ± 2.9 | <.001 | 0.043 | 0.504 | <.001 |
| ***LFI (limb fat index) | 2.7 ± 1.0 | 2.9 ± 1.0 | 2.1 ± 0.8 | 2.3 ± 0.9 | <.001 | <.001 | 1 | <.001 |

BMI, body mass index; LFI, limb fat index; SMI, skeletal muscle mass index; TFI, total fat index. *One-way analysis of variance (ANOVA) with post hoc Bonferroni correction. **$\chi^2$ test. ***Kruskal–Wallis test (Bonferroni).

$$\text{Total fat index (TFI)} = \frac{\text{amount of total body fat}}{\text{height}^2}$$

$$\text{Limb fat index (LFI)} = \frac{\text{limb fat mass (total fat mass} - \text{trunk fat mass)}}{\text{height}^2}$$

**Fig. 2.** Formulas for calculating total fat index and limb fat index for new indicators.

characteristics and conduct intergroup comparisons of physical function assessment findings, and the Kruskal–Wallis test with post hoc Bonferroni correction was used to evaluate findings for the TFI and LFI. After univariate analysis, we extracted age, BMI, and LFI that were significantly different, except for AWGS 2019 diagnostic criteria items. Binomial logistic regression analysis was then performed with the presence of sarcopenia as the dependent variable and age, BMI, and LFI as independent variables. All statistical data were analyzed using EZR statistical software (ver. 1.41; Saitama Medical Center, Jichi Medical University, Saitama, Japan). Statistical interpretation is indicated by *p* value.

## Results

Results for 594 older adults (186 men and 408 women) residing in Wakasa Town were as follows. First, 450 participants had neither sarcopenia nor pre-sarcopenia (i.e., were categorized into the normal/healthy group), 102 had pre-sarcopenia, and 42 had sarcopenia. We found a higher mean age in those with pre-sarcopenia than in normal/healthy individuals and in participants with sarcopenia than in participants with pre-sarcopenia. Moreover, the mean values of BMI, TFI, and LFI were lower in the pre-sarcopenia and sarcopenia participants, respectively, than in normal/healthy participants. ($p$<.001) (Table 1).

Binomial logistic regression analysis was performed, and the odds ratios (ORs) for pre-sarcopenia were as follows: BMI (OR: 0.787, 95% CI: 0.7–0.885), LFI (OR: 0.589, 95% CI: 0.402–0.863), and age (OR: 1.06, 95% CI: 1.02–1.1). The ORs for sarcopenia (vs pre-sarcopenia) were as follows: LFI (OR: 50.6, 95% CI: 10.2–250.0), age (OR: 1.1, 95% CI: 1.0–1.2), and BMI (OR: 0.418, 95% CI: 0.288–0.608) (Table 2).

## Discussion

The older adults who responded to the open recruitment campaign in Wakasa Town were categorized into the following study groups: normal/healthy individuals, those with pre-sarcopenia, and those with sarcopenia. Participants were classified according to the AWGS 2019 diagnostic algorithm.[4] Besides applying the diagnostic algorithm, age, BMI, TFI, and LFI were also examined for their relevance as factors in the transition to sarcopenia. Age, BMI, TFI, and LFI showed statistically significant differences among the three groups. Moreover, binomial logistic regression analysis revealed age, BMI, and LFI as factors affecting the risk of pre-sarcopenia and sarcopenia. Specifically, the likelihood of progression to pre-sarcopenia and sarcopenia was shown to increase with increasing age and with decreasing BMI. Conversely, findings for LFI differed in the transition from normal health to pre-sarcopenia and from pre-sarcopenia to sarcopenia, with the risk of progression to pre-sarcopenia increasing with a decrease in the LFI index and the risk of progression from pre-sarcopenia to sarcopenia increasing with an increase in the LFI index. Akima *et al.*[8] previously reported that intramuscular fat, called ectopic fat, is closely related to sarcopenia.

Moreover, as previously described by Chao *et al.*,[9] older adults with pre-sarcopenia tended to have a lower muscle mass, lower body fat, and better muscle function than healthy/normal participants in the present study. Conversely, Seino *et al.*[10] cited low body fat as a risk factor for mortality in women, and Sternfield *et al.*[11] suggested that excess fat mass predicts lower physical performance compared to the loss of muscle mass. The results of the current study suggest that, in pre-sarcopenia, fat mass may play an important role in muscle mass and muscle quality. We also found that progression from pre-sarcopenia to sarcopenia was associated with further loss of muscle mass, increased fat mass, and decreased muscle function. Fat mass also tended to increase with age and was associated with decreased muscle strength and motor function in the present study. These findings are similar to those of previous investigations.[12–17] In prior work, Guillet *et al.*[18] and Nilsson *et al.*[12] described how fat infiltration into muscle could cause muscle inflammation. Although the effect of myositis is unknown in the present study, a response similar to that described by Sakuma *et al.*[19]and Woodrow[20] may be occurring. Shida *et al.*[21] reported that non-obese NAFLD, besides previous increases in visceral fat, is primarily due to decreased skeletal muscle mass and strength, worsened muscle composition (pre-sarcopenia), and abnormal glucose metabolism. They report that this is primarily due to abnormal glucose metabolism.

Kusunoki *et al.*[22] showed that CysC is increased in patients with presarcopenia and sarcopenia compared to healthy controls; in some cases, muscle mass and strength are decreased and negatively correlated. Mikami *et al.*[23] also showed that participants with low SMI had lower BMI and grip strength, which correlated with the serum Cre/CysC ratio. The Cre/CysC ratio in non-obese NAFLD was not considered in this study. Whether similar results can be obtained for the relationship between lipid and glucose metabolism using the data from the participants in this study remains open for further study.

Despite the substantial strengths of this investigation, we acknowledge several limitations of the current work. First, we conducted a cross-sectional study, thereby precluding causal inferences. Although the number of participants enrolled in the present study is limited, we would like to conduct additional analyses on this group of participants following longitudinal tracking (i.e., future study surveys and physical assessments). Second, our data are limited to older adults residing within a limited geographical area, and the generalization of our findings may therefore be limited. Hence, we aim to conduct similar studies on older adults residing in different geographic areas to allow for the generalization of our findings. Third, since the estimation of body composition using the BIA method relies on certain assumptions and the presence of edema may overestimate skeletal muscle mass, we would like to continue the study in a manner that eliminates as much bias as possible. Fourth, the role of inflammation and other participants' characteristics or physiological processes on fat infiltration is presently unknown and requires additional investigation in future research.

**Table 2.** Risk factors associated with sarcopenia

| Variable | Non-sarcopenia vs pre-sarcopenia | | | Pre-sarcopenia vs sarcopenia | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | *p* value | OR | 95% CI | *p* value |
| Age | 1.06 | 1.020–1.100 | <.001 | 1.1 | 1.000–1.200 | 0.041 |
| BMI | 0.787 | 0.700–0.885 | <.001 | 0.418 | 0.288–0.608 | <.001 |
| LFI | 0.589 | 0.402–0.863 | 0.007 | 50.6 | 10.200–250.000 | <.001 |

BMI, body mass index; CI, confidence interval; LFI, limb fat index; OR, odds ratio. The ORs and 95% CIs were derived using multivariate logistic regression analysis (specifically, binomial logistic regression analysis).


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In the current study, we found that the LFI, a novel index, is lower during the progression to pre-sarcopenia. Conversely, LFI was found to be higher during the progression from pre-sarcopenia to sarcopenia. We determined several other characteristics, including age, BMI, and potentially the TFI, that were also associated with the progression to sarcopenia and pre-sarcopenia. We recommend that our findings be substantiated through mechanistic studies and longitudinal investigations. Our findings, if confirmed in future longitudinal studies, will serve to directly inform medical guidelines.

## Author Contributions

OY and HO contributed significantly to the conceptualization of the study; YM, YM, MK, RI, HO, HH, and OY contributed significantly to data acquisition; YM, HO, and OY contributed significantly to data analysis and interpretation; and YM, HO, HH, and OY contributed to manuscript preparation. All authors critically reviewed and revised the manuscript and approved and submitted the final version.


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## Conflict of Interest

No potential conflicts of interest were disclosed.

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