Original Study

Fat-Free Mass Index as a Surrogate Marker of Appendicular Skeletal Muscle Mass Index for Low Muscle Mass Screening in Sarcopenia

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\textbf{Abstract}

\textbf{Objectives:} We aimed to examine the relationship between the fat-free mass index (FFMI; FFM/height\textsuperscript{2}) and appendicular skeletal muscle mass index (ASMI; ASM/height\textsuperscript{2}), measured using both bioelectrical impedance analysis (BIA) and dual-energy X-ray absorptiometry (DXA), and investigate the effects of age and obesity. We also evaluated the suitability of BIA-measured FFMI as a simple surrogate marker of the ASMI and calculated the optimal FFMI cutoff value for low muscle mass screening to diagnose sarcopenia.

\textbf{Design:} Cross-sectional study.

\textbf{Setting and Participants:} This study included 1313 adults (women, 33.6\%) aged 40-87 years (mean age, 55 ± 10 years) from the WASEDA'S Health Study.

\textbf{Methods:} Body composition was measured using multifrequency BIA and DXA. Low muscle mass was defined according to the criteria of the Asian Working Group for Sarcopenia 2019.

\textbf{Results:} BIA-measured FFMI showed strong positive correlations with both BIA- (\(r = 0.96\)) and DXA-measured (\(r = 0.95\)) ASMIs. Similarly, in the subgroup analysis according to age and obesity, the FFMI was correlated with the ASMI. The areas under the receiver operating characteristic curve for screening low muscle mass defined by DXA-measured ASMI using BIA-measured FFMI values were 0.95 (95\% CI 0.93-0.97) for men and 0.91 (95\% CI 0.87-0.94) for women. The optimal BIA-measured FFMI cutoff values for screening low muscle mass defined by DXA-measured ASMI were 17.5 kg/m\textsuperscript{2} (sensitivity 89\%, specificity 88\%) for men and 14.6 kg/m\textsuperscript{2} (sensitivity 80\%, specificity 86\%) for women.

\textbf{Conclusions and Implications:} The FFMI showed a strong positive correlation with BIA- and DXA-measured ASMIs, regardless of age and obesity. The FFMI could be a useful simple surrogate marker of the ASMI for the low muscle mass screening in sarcopenia in community settings. The suggested FFMI cutoff values for predicting low muscle mass are <18 kg/m\textsuperscript{2} in men and <15 kg/m\textsuperscript{2} in women.

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Sarcopenia, defined as a progressive and generalized skeletal muscle disorder that involves accelerated loss of muscle mass and function, is associated with adverse health outcomes such as hospitalization, functional decline, fractures, falls, and mortality. Population screening for sarcopenia should be performed at an early stage, especially from the perspective of primary health care and community-based health promotion, given that muscle mass and strength loss begins in early adulthood.

There are several international diagnostic criteria for sarcopenia, including those developed by the Asian Working Group for Sarcopenia, European Working Group on Sarcopenia in Older People, Foundation for the National Institutes of Health Sarcopenia Project, and International Working Group on Sarcopenia. For most of these criteria, appendicular skeletal muscle mass (ASM) normalized by the body size (eg, ASM/height$^2$ and ASM/body mass index (BMI)) is used as an indicator of muscle mass. Therefore, evaluating ASM is essential for determining low muscle mass in sarcopenia. Dual-energy X-ray absorptiometry (DXA) is currently the most effective method for assessing ASM when diagnosing sarcopenia. However, the high cost, immobility, and exposure to X-ray radiation of the DXA system are potential limitations to its use for muscle mass assessment in community settings. Bioelectrical impedance analysis (BIA) is another muscle mass assessment method that is widely used worldwide and is applicable to community settings because of its simplicity and relative affordability. However, while most BIA devices for general consumer use (ie, 2-compartment models) can estimate whole-body fat mass and fat-free mass (FFM), only a few advanced devices can estimate ASM. Therefore, there may be difficulties in using BIA devices for general consumer use, which are widely used in community settings, to estimate ASM for low muscle mass screening in sarcopenia.

Vannitallie et al proposed the concept of the FFMI index (FFMI; whole-body FFM/height$^2$) and fat mass index, which classifies BMI into fat and other, as indicators of nutritional status. Lower FFMI is related to increased length of hospital stay, frailty, and all-cause mortality. As muscle mass is a primary component of FFM, the FFMI may act as a simple surrogate marker for low muscle mass screening when diagnosing sarcopenia. It is easy and relatively inexpensive to evaluate FFMI in community settings, even using widely available BIA devices for general consumer use. Although ASM, which does not include bone and organ mass, has long been internationally used as a skeletal muscle mass indicator for diagnosing sarcopenia, existing literature has revealed that the FFMI has a strong positive correlation with the ASM index (ASM; ASM/height$^2$) ($r \geq 0.87$). If the FFMI can estimate the ASM without advanced equipment or facilities, population screening of low muscle mass using the FFMI would be widely and easily available to primary health care and community prevention services, including regular health checkups and counseling, as well as for epidemiologic research. However, to our knowledge, whether BIA-measured FFMI can be used as a simple surrogate marker of the ASM (ie, via an equation for estimating the ASM using the FFMI), as well as the optimal FFMI cutoff values for low muscle mass screening for diagnosing sarcopenia, has not been studied.

This study aimed to examine the relationship between the FFMI and ASMI measured using both BIA and DXA and investigate the effects of age and obesity. Furthermore, the suitability of BIA-measured FFMI as a simple surrogate marker of the ASMI for low muscle mass screening when diagnosing sarcopenia was evaluated. Additionally, because the calf circumference is known as another simple screening tool for low muscle mass, we compared its prediction accuracy with that of the FFMI.

### Methods

#### Participants

This cross-sectional study used a baseline survey from Waseda Alumni’s Sports, Exercise, Daily Activity, Sedentariness and Health Study (WASEDA’S Health Study). The WASEDA’S Health Study is a prospective cohort study of graduates of Waseda University, a private university in Japan, and their spouses aged 40 years or older. Participants selected one of 4 courses (cohorts A to D) with different measurement items. Body composition was assessed using DXA only in cohort D.

Study participants comprised 1375 middle-aged and older adults who underwent body composition measurements using both BIA and DXA in cohort D between March 2015 and February 2020. Of the 1375 participants, those with metal implants or fragments in their body, those who were unable to remove metal worn at the time of measurement ($n = 55$), and foreign nationals ($n = 7$) were excluded. Finally, 1313 Japanese adults (672 men and 441 women) were included in the analysis.

The study was approved by the Research Ethics Committee of Waseda University (approval numbers: 2014-G002 and 2018-G001) and was conducted in accordance with the Declaration of Helsinki. All participants received an explanation of the study prior to measurements and provided written informed consent for participation.

#### Muscle Mass Measurements

All measurements were obtained in the morning, after fasting for at least 12 hours, by trained researchers. Height and body composition were measured with participants wearing light clothing and no shoes. BMI was calculated by dividing the weight (in kilograms) by the height squared (in meters).

Body weight, fat, and ASM were measured using a multifrequency BIA analyzer (MC-980A, Tanita Corp, Tokyo, Japan) with 6 electric frequencies (1, 5, 50, 250, 500, and 1000 kHz). Previous studies have found a strong correlation between ASM measured with this analyzer and that measured with DXA ($r = 0.88$ for men and $r = 0.84$ for women). The interinstrument reliability for ASM between this analyzer and DXA was good [intra-class correlation coefficient (ICC) = 0.88 for men and 0.76 for women].

The DXA [Delphi A (until December 2016) or Horizon A (after January 2017); Hologic Inc] was used to measure body fat and lean soft tissue mass. The interinstrument reliability for ASM between the 2 DXA devices was excellent (ICC = 0.97). Participants lay in the supine position on a DXA table for whole-body scanning according to the manufacturer’s protocol. ASM was estimated by summing the lean soft tissue mass of the arms and legs.

BIA- and DXA-measured FFMs were calculated as the whole-body weight minus whole-body fat mass. To adjust for individual physique, ASM (kg) or whole-body FFM (kg) was divided by the height squared ($m^2$). Supplementary Figure 1 shows an explanation drawing of the body compartments, including FFM and ASM.

#### Definition of Low Muscle Mass

Low muscle mass was defined based on the Asian Working Group for Sarcopenia 2019 recommended cutoffs for muscle mass assessments. The cutoffs for BIA-measured ASMI were 7.0 and 5.7 kg/m$^2$. The cutoffs for DXA-measured ASMI were 7.0 and 5.7 kg/m$^2$. The cutoffs for DXA-measured FFM were 15% and 20% of body weight.
Average of the maximum values for each hand was calculated. Dynamometer (T.K.K.5401; Takei Scientific Corp., Kyoto, Japan), with the participant in a neutral standing position. The mean age of participants was 55 ± 10 years (range, 40-87 years) (Table 1). The prevalence rates of low muscle mass defined by BIA and DXA were 5.2% and 9.9%, respectively. The proportion of older adults was 39.4% in men and 20.9% in women. The prevalence rates of obesity were 15.6% in men and 30.6% in women. Strong correlations between BIA- and DXA-measured ASMIs (r = 0.94; Supplementary Figure 2) and between BIA- and DXA-measured FFMIs (r = 0.94; Supplementary Figure 3) were observed.

Table 1
Characteristics of Study Participants in Men and Women

|                       | Overall | Men          | Women         |
|-----------------------|---------|--------------|---------------|
| n                     | 1313    | 872          | 441           |
| Age, years            | 55 ± 10 | 57 ± 10      | 52 ± 9        |
| Height, cm            | 166.4 ± 7.9 | 170.3 ± 5.8 | 158.7 ± 5.3   |
| Body weight, kg        | 63.9 ± 11.5 | 69.0 ± 9.7   | 53.9 ± 7.5    |
| BMI                   | 23.0 ± 3.1 | 23.8 ± 3.0   | 21.4 ± 2.9    |
| Body fat by DXA, %     | 22.7 ± 5.9 | 20.4 ± 4.7   | 27.3 ± 5.1    |
| FFM by BIA, kg         | 48.9 ± 8.8 | 54.3 ± 5.3   | 38.4 ± 3.0    |
| FFM by DXA, kg         | 49.2 ± 9.3 | 54.5 ± 6.3   | 38.8 ± 4.3    |
| ASM by BIA, kg         | 21.4 ± 4.6 | 24.0 ± 3.1   | 16.1 ± 1.7    |
| ASM by DXA, kg         | 20.5 ± 4.5 | 23.1 ± 3.0   | 15.4 ± 2.0    |
| FFMI by BIA, kg/m²     | 17.5 ± 2.1 | 18.7 ± 1.4   | 15.2 ± 0.9    |
| FFMI by DXA, kg/m²     | 17.6 ± 2.3 | 18.8 ± 1.8   | 15.4 ± 1.4    |
| ASM by BIA, kg/m²      | 7.6 ± 1.2  | 8.3 ± 0.9    | 6.4 ± 0.6     |
| ASM by DXA, kg/m²      | 7.3 ± 1.2  | 7.9 ± 0.8    | 6.1 ± 0.7     |
| Low muscle mass by BIA, n (%) | 68 (5.2) | 74 (4.2)     | 31 (7.0)      |
| Low muscle mass by DXA, n (%) | 130 (9.9) | 74 (8.5)     | 56 (12.7)     |
| Calf circumference, cm | 36.5 ± 2.9 | 37.6 ± 2.6   | 34.4 ± 2.2    |
| Hand-grip strength, kg | 33.4 ± 8.1 | 37.9 ± 5.7   | 245 ± 3.6     |
| Osteoporosis, n (%)    | 8 (0.6)  | 1 (0.1)      | 7 (1.6)       |
| Knee osteoarthritis, n (%) | 39 (3.0) | 18 (2.1)    | 21 (4.8)      |
| Hip osteoarthritis, n (%) | 9 (0.7)  | 0 (0.3)      | 6 (1.4)       |
| Rheumatoid arthritis, n (%) | 9 (0.7)  | 1 (0.1)      | 8 (1.8)       |

Data are expressed as mean ± SD or n (%).

*Low muscle mass was defined based on the Asian Working Group for Sarcopenia 2019 criteria. The recommended cutoffs for ASMI measured by BIA were <7.0 kg/m² for men and <5.7 kg/m² for women.

†Low muscle mass was defined based on the Asian Working Group for Sarcopenia 2019 criteria. The recommended cutoffs for ASMI measured by DXA were <7.0 kg/m² for men and <5.4 kg/m² for women.

‡The number of participants was 1262 (837 men and 425 women).

§The number of participants was 1304 (868 men and 436 women).

and those for DXA-measured ASMI were 7.0 and 5.4 kg/m², for men and women, respectively.

Other Variable Assessments

A physician-diagnosed medical history including osteoporosis, knee and hip osteoarthritis, and rheumatoid arthritis was obtained using a self-reported questionnaire. The maximal calf circumference was measured using a steel measuring tape (F10-02DM, Muratec-KDS Corp., Kyoto, Japan), with the participant in a neutral standing position. The left and right legs were each measured twice, and the final value was derived from the mean of these measurements. Hand-grip strength was measured twice for each hand using a digital grip dynamometer (T.K.K.5401; Takei Scientific Instruments Co, Ltd). The average of the maximum values for each hand was calculated.

Statistical Analysis

Continuous variables are shown as mean ± SD, whereas categorical variables are presented as numbers (%). Pearson correlation coefficients were calculated to evaluate the correlation of BIA-measured FFMI with BIA- and DXA-measured ASMIs. To formulate the ASMI prediction equation using the FFMI, we conducted a linear regression in which the BIA- and DXA-measured ASMIs were set as development variables. We assessed the equation-fitting performance using the coefficient of determination (R²) and standard error of the estimate (SEE). To examine the effects of obesity and age on the correlation, participants were divided into 2 groups based on body fat percentage (nonobese and obese) and age (middle-aged, <60 years and older, ≥60 years) for subgroup analyses. Obesity was defined as a DXA-measured body fat percentage ≥25.0% for men and ≥30.0% for women.

We conducted a paired t test to assess the differences between DXA-measured and predicted ASMIs. Absolute error was calculated as [predicted ASMI - DXA-measured ASMI]. Total error was calculated as \( \sqrt{\sum_{i=1}^{n} (\text{predicted ASMI} - \text{DXA measured ASMI})^2/n} \). Agreement between the DXA-measured and predicted ASMIs was assessed using the ICC. The kappa coefficient was calculated to assess the agreement in the determination of low muscle mass defined using DXA-measured and predicted ASMIs. Pearson correlation coefficients were compared using the method described by Meng et al. A receiver operating characteristic (ROC) analysis was performed to identify the optimal BIA-measured FFMI cutoffs for screening low muscle mass defined by BIA- and DXA-measured ASMIs in men and women. The ROC curve and 95% CI were determined, and the optimal cutoff values were calculated by determining the shortest distance between the ROC curve and the upper left corner of the graph.

Distribution normality was confirmed using histogram plots. A 2-tailed P value < .05 was considered statistically significant. All P values were unadjusted for multiple testing. All statistical analyses were performed using SPSS Statistics, version 28 (IBM Corp).

Results

The mean age of participants was 55 ± 10 years (range, 40-87 years) (Table 1). The prevalence rates of low muscle mass defined by BIA and DXA were 5.2% and 9.9%, respectively. The proportion of older adults was 39.4% in men and 20.9% in women. The prevalence rates of obesity were 15.6% in men and 30.6% in women. Strong correlations between BIA- and DXA-measured ASMIs (r = 0.94; Supplementary Figure 2) and between BIA- and DXA-measured FFMIs (r = 0.94; Supplementary Figure 3) were observed.

DXA-measured FFMI was strongly correlated with DXA-measured ASM (r = 0.96; Supplementary Figure 4). BIA-measured FFMI showed a strong positive correlation with both BIA- (r = 0.96) and DXA-measured (r = 0.95) ASMIs (Figure 1). The observed prediction equations were as follows: BIA-measured ASM (kg/m²) = 0.549 × BIA-measured FFMI (kg/m²) - 1.998 (R² = 0.92, SEE = 0.3 kg/m²); and DXA-measured ASM (kg/m²) = 0.542 × BIA-measured FFMI (kg/m²) - 2.173 (R² = 0.89, SEE = 0.4 kg/m²). In the subgroup analysis based on obesity and age, correlations between BIA-measured FFMI and DXA-measured ASM (kg/m²) were similar to those in the main analysis (Figure 2). The correlation between DXA-measured ASM and BIA-measured FFMI (r = 0.95) was significantly stronger than that between DXA-measured ASM and the calf circumference (r = 0.83), but did not differ from the correlation between DXA-measured ASM and BIA-measured ASM (r = 0.94) (Supplementary Table 1).

Supplementary Table 2 shows the DXA- and BIA-measured ASMIs and predicted DXA-measured ASM based on the derived equation using BIA-measured FFMI values. The mean predicted ASMI was not significantly different from the mean DXA-measured ASMI (mean difference = 0.01 ± 0.4 kg/m², P = .49). The total error and ICC between DXA-measured and predicted ASMIs using the equation were 0.4 kg/m² and 0.94, respectively.

The areas under the ROC curve for screening low muscle mass defined by DXA-measured ASMI using BIA-measured ASMI were 0.92 (95% CI 0.89-0.95) for men and 0.89 (95% CI 0.85-0.93) for women. The optimal BIA-measured ASMI cutoffs for screening low muscle mass defined by DXA-measured ASMI were 7.7 kg/m² (sensitivity 87%, specificity 83%) for men and 6.1 kg/m² (sensitivity 84%, specificity 80%) for women. The areas under the ROC curve for screening low muscle mass defined by BIA- and DXA-measured ASMI using BIA-measured FFMI values were 0.98 (95% CI 0.97-0.99) and 0.95 (95% CI 0.93-0.97) for men and 0.94 (95% CI 0.92-0.97) and 0.91 (95% CI 0.87-0.94) for women, respectively (Figure 3). The optimal FFMI cutoff values for screening low muscle mass defined by BIA- and DXA-measured ASMIs were 17.2 kg/m² (sensitivity 97%, specificity 92%) and 17.5 kg/m² (sensitivity 89%, specificity 88%) for men and
14.4 kg/m² (sensitivity 87%, specificity 91%) and 14.6 kg/m² (sensitivity 80%, specificity 86%) for women, respectively. Additionally, FFMI cutoff values with maximum sensitivity or specificity (≥90%) were calculated. The FFMI cutoff values for screening low muscle mass defined by BIA- and DXA-measured ASMs with maximum sensitivity without excessively reducing specificity were 17.3 kg/m² (sensitivity 100%, specificity 88%) and 17.6 kg/m² (sensitivity 91%, specificity 86%) for men and 14.6 (sensitivity 90%, specificity 82%) and 14.9 kg/m² (sensitivity 91%, specificity 72%) for women, respectively. The cutoff values defined by BIA- and DXA-measured ASMs with maximum specificity without excessively reducing sensitivity were 17.1 kg/m² (sensitivity 92%, specificity 93%) and 17.4 kg/m² (sensitivity 88%, specificity 90%) for men and 14.3 (sensitivity 84%, specificity 92%) and 14.5 kg/m² (sensitivity 68%, specificity 90%) for women, respectively. Comparison of the ROC curves for screening low muscle mass defined by DXA-measured ASM using BIA-measured ASMI, BIA-measured FFMI, and calf circumference values is shown in Supplementary Figure 5.

Discussion

In this study, the relationship between the FFMI and ASMI measured using both BIA and DXA was examined, and the effects of age and obesity were investigated. Furthermore, the suitability of the BIA-measured FFMI as a simple surrogate marker of the ASMI for low muscle mass screening when diagnosing sarcopenia was evaluated. We found that BIA-measured FFMI had a strong positive correlation with both BIA- (r = 0.96) and DXA-measured (r = 0.95) ASMIs. In the subgroup analysis based on obesity and age, correlations between BIA-measured FFMI and DXA-measured ASMI were also positive and similar to those in the main analysis. Further, the correlation between DXA-measured ASMI and BIA-measured FFMI was stronger than that between DXA-measured ASMI and the calf circumference, but did not differ from the correlation between DXA-measured ASMI and BIA-measured ASMI. Overall, our results suggest that the predicted ASMI using BIA-measured FFMI has similar or better accuracy compared with that of BIA-measured ASMI.

A study involving 1977 community-dwelling Japanese older adults aged 65 years or older showed a strong correlation between the FFMI and ASMI using multifrequency BIA (r = 0.93 in men and r = 0.87 in women). A study involving 56 hospitalized patients in geriatric care aged 65 years or older in Sweden showed a strong correlation between the FFMI and ASMI using DXA (r = 0.92). Another study involving 49 older patients undergoing maintenance hemodialysis in Brazil reported a strong correlation between the FFMI and ASMI using single-frequency BIA and DXA, respectively (r = 0.87). A study involving 46 patients with advanced non–small-cell lung cancer in Israel found that the FFMI was strongly correlated with the skeletal muscle index [skeletal muscle area (cm²)/height (m²)], which has been reported to correlate with the ASMI using computed tomography images at the level of the third lumbar vertebrae (r = 0.97). These previous findings support our results, suggesting that the FFMI has a strong positive correlation with the ASMI and could be employed as a simple surrogate marker of the ASMI for low muscle mass screening in sarcopenia.

In our ROC analysis, the areas under the curve for screening low muscle mass defined by DXA-measured ASMI using BIA-measured FFMI values were 0.95 in men and 0.91 in women, and high accuracy was observed. The optimal FFMI cutoff values for screening low muscle mass defined by DXA-measured ASMI were 17.5 kg/m² (sensitivity 89%, specificity 88%) for men and 14.6 kg/m² (sensitivity 80%, specificity 86%) for women. Studies from different countries, such as Japan, China, the United Kingdom, Switzerland, Italy, and the United States, have reported age- and sex-specific reference values (eg, mean and percentile values) for the FFMI measured using BIA and DXA. The consensus statement of the European Society of Clinical Nutrition and Metabolism and Global Leadership Initiative on Malnutrition proposed reference values for the FFMI (<17 kg/m² in men and <15 kg/m² in women) as one of the criteria to evaluate reduced body weight or muscle mass for the diagnosis of malnutrition. These reference values for the FFMI were determined using single-frequency BIA in 5635 apparently healthy Caucasians in Switzerland aged 24-98 years. A regression analysis of the BMI and FFMI showed that the FFMI corresponding to a BMI of 18.5 kg/m² was 16.7 kg/m² for men and 14.6 kg/m² for women. In the same sample, the 5th percentile values of the FFMI for young adults (18-34 years) were 16.8 kg/m² for men and 13.8 kg/m² for women. Although the method of calculating the FFMI cutoff values and aims were differed, the FFMI cutoff values for low muscle mass screening in both men and women in the present study were similar to the reference values for the diagnosis of malnutrition.

The calf circumference is considered a simple screening tool for determining low muscle mass. The Asian Working Group for Sarcopenia 2019 proposed using the calf circumference as a case-finding tool for primary health care and community preventive services to facilitate the early identification of people at risk for sarcopenia and...
implementation of early lifestyle interventions. Our results suggest that the FFMI is more accurate than the calf circumference as a surrogate marker of the ASMI. Therefore, in community settings without advanced diagnostic equipment (ie, DXA and multifrequency BIA), low muscle mass could be simply screened using the FFMI if a BIA device for general consumer use is available and the calf circumference if no such device is available. Individuals detected with low muscle mass on screening should then be recommended for confirmatory final diagnosis using advanced diagnostic equipment.

This study has several limitations. First, the study participants were Waseda University alumni and their spouses who opted to participate, and were not randomly selected from the population. Moreover, the participants were apparently healthy Japanese adults without serious illnesses, although a few had severe obesity. The mean BMI of our participants was 23.0 ± 3.1 (range, 15.2-45.4 kg/m²), and relatively few participants had a BMI above 30 kg/m² (n = 37, 2.8%) or below 18.5 kg/m² (n = 62, 4.7%). Furthermore, all participants were able to walk without assistance. However, several studies with older adults, geriatric inpatients, and older patients on maintenance hemodialysis have also reported a strong correlation between the FFMI and ASMI. Calculation of the predicted ASMI by the FFMI is possible even among older adults with chronic conditions and activity limitations. Because of racial differences in body size, caution should be taken when applying cutoff values for low muscle mass screening by the FFMI based on our findings, especially in non-Asian populations. Second, this study used only 1 type of BIA device, although the accuracy of FFM estimates made with BIA is dependent on the device and equation used. Further confirmatory studies using different BIA devices are warranted. Third, the FFMI estimated using BIA is affected by fluid retention. Measurements were made in the morning after fasting for at least 12 hours (with unrestricted water intake), the effect of fluid accumulation, such as ascites and edema, was not considered. A study that examined patients with chronic liver diseases reported that DXA-measured FFMI correlated with DXA-measured ASMI in patients without ascites (r = 0.50) but not in patients with ascites (r = 0.25). Especially in patients with severe ascites and edema, the FFMI measured using BIA with a 2-compartment model may

![Fig. 2. Correlation between BIA-measured FFMI and DXA-measured ASMI according to (A) age and (B) obesity.](image-url)
overestimate the predicted ASMI. Thus, further studies with various sample populations (different races, ages, body compositions, and health conditions) and using various BIA devices are recommended.

Conclusion and Implications

The FFMI has a strong positive correlation with BIA- and DXA-measured ASMIs, regardless of age and obesity. The FFMI could be a useful simple surrogate marker of the ASMI for the screening of low muscle mass in sarcopenia in community settings. The suggested FFMI cutoff values for predicting low muscle mass are <18 kg/m² in men and <15 kg/m² in women.

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References

1. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. Lancet. 2019;393:2636–2646.
2. Beaudart C, Zaaria M, Pasleau F, et al. Health outcomes of sarcopenia: a systematic review and meta-analysis. PLoS One. 2017;12:e0169548.
3. Xia L, Zhao R, Wan Q, et al. Sarcopenia and adverse health-related outcomes: an umbrella review of meta-analyses of observational studies. Cancer Med. 2020;9:7964–7978.
4. Sayer AA, Syddall H, Martin H, et al. The developmental origins of sarcopenia. J Nutr Health Aging. 2008;12:427–432.
5. Chen LK, Woo J, Assantachai P, et al. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. J Am Med Dir Assoc. 2020;21:300–307.
6. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48:16–31.
7. Studenski SA, Peters KW, Alley DE, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci. 2014;69:547–558.
8. Fielding RA, Velas B, Evans WJ, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International Working Group on Sarcopenia. J Am Med Dir Assoc. 2011;12:249–256.
9. Yilmaz O, Bahat G. Suggestions for assessment of muscle mass in primary care setting. Aging Mol. 2017;20:168–169.
VanItallie TB, Yang MU, Heymsfield SB, et al. Height-normalized indices of the body's fat-free mass and fat mass: potentially useful indicators of nutritional status. *Am J Clin Nutr.* 1990;52:953–959.

Pichard C, Kyle UC, Morabia A, et al. Nutritional assessment: lean body mass depletion at hospital admission is associated with an increased length of stay. *Am J Clin Nutr.* 2004;79:613–618.

Soh Y, Won CW. Sex differences in association between body composition and frailty or physical performance in community-dwelling older adults. *Medicine (Baltimore).* 2021;100:e24400.

Saito S, Kitamura A, Abe T, et al. Dose-response relationships between body composition indices and all-cause mortality in older Japanese adults. *J Am Med Dir Assoc.* 2020;21:726–733.e4.

Sørensen TIA, Frederiksen P, Heitmann BL. Levels and changes in body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. *Int J Obes (Lond).* 2010;34:791–799.

Franssen FM, Rutten EP, Groenen MT, et al. New reference values for body composition by bioelectrical impedance analysis: a consideration of the pros and cons. *Clin Nutr ESPEN.* 2021;45:442–448.

Kawakami R, Carrero JJ, Rodrigues JC, et al. Prevalence of sarcopenia in elderly maintenance hemodialysis patients: the impact of different diagnostic criteria. *J Nutr Health Aging.* 2014;18:710–717.

Kawakami R, Miyachi M, Sawada SS, et al. Cut-offs for calf circumference as a screening tool for low muscle mass: WASEDA'S Health Study. *Geriatr Gerontol Int.* 2020;20:943–950.

Heymsfield SB, Gonzalez MC, Lu J, et al. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. *Proc Nutr Soc.* 2015;74:355–366.

Kawakami R, Miyachi M, Tanisawa K, et al. Development and validation of a simple anthropometric equation to predict appendicular skeletal muscle mass. *Clin Nutr.* 2021;40:5523–5530.

Okorodudu DO, Jumane MF, Montori VM, et al. Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. *Int J Obes (Lond).* 2010;34:791–799.

Meng X-L, Rosenthal R, Rubin DB. Comparing correlated correlation coefficients. *Psychol Bull.* 1992;111:172–175.

Mourtzakis M, Prado CM, Lieffers JR, et al. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. *Appl Physiol Nutr Metab.* 2008;33:907–909.

Magri V, Gottfried T, Di Segni M, et al. Correlation of body composition by computerized tomography and metabolic parameters with survival of nivolumab-treated lung cancer patients. *Cancer Manag Res.* 2019;11:8201–8207.

Seino S, Shinkai S, Iijima K, et al. Reference values and age differences in body composition of community-dwelling older Japanese men and women: a pooled analysis of four cohort studies. *PLoS One.* 2015;10:e0131975.

Jin M, Du H, Zhang Y, et al. Characteristics and reference values of fat mass index and fat free mass index by bioelectrical impedance analysis in an adult population. *Clin Nutr.* 2019;38:2325–2332.

Franssen FM, Rutten EP, Groenen MT, et al. New reference values for body composition by bioelectrical impedance analysis in the general population: results from the UK Biobank. *J Am Med Dir Assoc.* 2014;15:e1–e6.

Schutz Y, Kyle UU, Pichard C. Fat-free mass index and fat mass index percentiles in Caucasians aged 18-98 y. *Int J Obes Relat Metab Disord.* 2002;26:953–960.

Coi A, Sergi C, Minucci N, et al. Fat-free mass and fat mass reference values by dual-energy X-ray absorptiometry (DEXA) in a 20-80 year-old Italian population. *Clin Nutr.* 2008;27:87–94.

Kelly TL, Wilson KE, Heymsfield SB. Dual energy X-ray absorptiometry body composition reference values from NHANES. *PLoS One.* 2009;4:e7038.

Cederholm T, Bosaeus I, Barazzoni R, et al. Diagnostic criteria for malnutrition – an ESPEN Consensus Statement. *Clin Nutr.* 2015;34:335–340.

Cederholm T, Jensen GL, Correia M, et al. GLIM criteria for the diagnosis of malnutrition – a consensus report from the global clinical nutrition community. *J Cachexia Sarcopenia Muscle.* 2019;10:e0131975.

Segi G, De Rui M, Stubbs B, et al. Measurement of lean body mass using bioelectrical impedance analysis: a consideration of the pros and cons. *Aging Clin Exp Res.* 2017;29:591–597.

Kyle UC, Bosaeus I, De Lorenzo AD, et al. Bioelectrical impedance analysis—part I: review of principles and methods. *Clin Nutr.* 2004;23:1226–1243.

Lindqvist C, Brismar TB, Majeed A, et al. Assessment of muscle mass depletion in chronic liver disease: dual-energy x-ray absorptiometry compared with computed tomography. *Nutrition.* 2019;61:93–98.
**Supplementary Data**

**Supplementary Fig. 1.** Body compartments (Modified Buckinx et al’s Figure). Reference: Buckinx F, Landi F, Cesari M, et al. Pitfalls in the measurement of muscle mass: a need for a reference standard. *J Cachexia Sarcopenia Muscle*. 2018;9:269-278.

**Supplementary Fig. 2.** Correlation between BIA-measured ASMI and DXA-measured ASMI. ASMI, appendicular skeletal muscle mass index; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry.

**Supplementary Fig. 3.** Correlation between BIA-measured FFMI and DXA-measured FFMI. BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; FFMI, fat-free mass index.

**Supplementary Fig. 4.** Correlation between DXA-measured FFMI and DXA-measured ASMI. ASMI, appendicular skeletal muscle mass index; DXA, dual-energy X-ray absorptiometry; FFMI, fat-free mass index.
Supplementary Fig. 5. Receiver operating characteristic curves for screening low muscle mass defined by DXA-measured ASMI using BIA-measured ASMI, BIA-measured FFMI, and the calf circumference in men and women. The number of participants was 1262 (837 men and 425 women). ASMI, appendicular skeletal muscle mass index; BIA, bioelectrical impedance analysis; CC, calf circumference; DXA, dual-energy X-ray absorptiometry; FFMI, fat-free mass index.
**Supplementary Table 1**
Comparisons in the Coefficient of Correlation With DXA-Measured ASMI

|                      | BIA-Measured ASMI | BIA-Measured FFMI | Calf Circumference |
|----------------------|-------------------|-------------------|-------------------|
| r with DXA-measured ASMI | 0.94              | 0.95              | 0.83              |
| BIA-measured ASMI     |                   |                   |                   |
| BIA-measured FFMI, P value | .11              |                   |                   |
| Calf circumference, P value | <.001            |                   | <.001             |

ASMI, appendicular skeletal muscle mass index; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; FFMI, fat-free mass index. The number of participants was 1262 (837 men and 425 women).

**Supplementary Table 2**
DXA- and BIA-Measured ASMIs and Predicted DXA-Measured ASMI by the Equation Using BIA-Measured FFMI

|                      | ASMI*          | Mean Difference* | P Value for Difference | Mean Absolute Error* | Total Error | R²** | ICC† | k† |
|----------------------|----------------|------------------|------------------------|----------------------|-------------|------|------|----|
| DXA                  | 7.3 ± 1.2      | 0                 | 0                      | 0.4 ± 0.3            | 0.5         | 0.89 | 0.91 | 0.39 |
| BIA                  | 7.6 ± 1.2      | 0.3 ± 0.4        | <.001                  | 0.3 ± 0.2            | 0.4         | 0.89 | 0.94 | 0.54 |
| Prediction equation by FFMI" | 7.3 ± 1.1      | 0.01 ± 0.4       | .49                    | 0.3 ± 0.2            | 0.4         | 0.89 | 0.94 | 0.54 |

ASMI, appendicular skeletal muscle mass index; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; FFMI, fat-free mass index; ICC, intraclass correlation coefficient.

*Data are expressed as mean ± SD.

"Calculated the average of predicted ASMI – DXA-measured ASMI.

"Calculated as \( \frac{1}{n} \sum (\text{predicted ASMI} – \text{DXA measured ASMI})^2 \).

"Coefficient of determination with DXA-measured ASMI.

"ICC with DXA-measured ASMI.

"Kappa coefficient with low muscle mass determined by DXA. The cutoffs for DXA-measured ASMI and predicted ASMI by the equation by FFMI were <7.0 for men and <5.4 for women. The cutoffs for BIA-measured ASMI were <7.0 for men and <5.7 for women.

"ASMI = 0.542 × BIA-measured FFMI – 2.173.