# Appendicular skeletal muscle mass to truncal fat mass ratio as a new index for osteosarcopenic obesity syndrome in older adults: emphasizing the role of central obesity

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# Abstract

**Background** The relationship between obesity and low bone mineral density (BMD) in older adults is still unclear. Most of the previous study did not account the factor of sarcopenia which is the progressive loss of skeletal muscle mass due to aging, and distribution of fat in obesity. Thus, this study was aimed to explore the correlation between appendicular skeletal muscle mass (ASMM), total fat mass (FM), and truncal fat mass (TrFM) as well as indexes (ASMM/FM and ASMM/TrFM ratio) with BMD in older adults.

**Methods** This was an analytic cross-sectional study. Dual x-ray absorptiometry (DXA) and bioelectric impedance analysis (BIA) were used to assess BMD and body composition, respectively. Appendicular Skeletal Muscle Mass (ASMM) were used in the analysis to reflect sarcopenia, Fat Mass (FM) and Trunkal Fat Mass (TrFM) were used to reflect general and central obesity, respectively. All data were obtained from medical records of Geriatric Clinic of Hasan Sadikin General Hospital Bandung Indonesia from January 2014 to December 2018. The correlation between body compositions variable with BMD were analyzed using Spearman's test. We also conducted a comparison analysis of body composition variables between low and normal BMD using Mann-Whitney test.

**Results** A total of 112 subjects were enrolled in the study. ASMM and TrFM were positive ($r_s$=0.517, p<0.001) and negative ($r_S$=-0.22, p=0.02) correlated with BMD, respectively. FM were not correlated with BMD, $r_S$=-0.113 (p=0.234). As indexes, ASMM/FM and ASMM/TrFM had positive correlation with BMD, $r_S$=0.277 (p<0.001), and $r_S$=0.391 (p<0.001), respectively. The ASMM, TrFM, and ASMM/TrFM ratio between normal and low BMD also significantly different (p<0.001), meanwhile FM were not (p=0.204).

**Conclusion** ASMM and TrFM have a positive and negative correlation with BMD, respectively. ASMM/TrFM ratio as new sarcopenia-central obesity index has a positive correlation with BMD.


# Background

As life expectancy increases globally including in developing countries, more health problems were also found increases in the aging population. Low bone mineral density (BMD) is one of the pivotal problems that threaten the quality of life and risk of disability in the older adult population. Low BMD increases the risk of vertebral and neck femur bone fractures and approximately a quarter of older adults experienced vertebral bone fractures. The risk increases along with aging and it may reach up to 40% in the elderly over 80 years old. Vertebral fractures increased the risk of mortality and the health costs spent were more expensive than other bone fractures in older adults.[1,2]

One of the factors that affect BMD is obesity. However, the relationship between obesity and BMD is still debatable. Some studies showed that a high body mass index (BMI) is an independent risk factor for low BMD.[3,4] In contrast, other studies conclude that older adult with high BMI is a protective factor for low BMD.[5–7] Although this discrepancy of results occurred, these findings suggested that BMI *per se* may not be suitable to explain comprehensively the relationship of obesity and BMD. Therefore, instead of

BMI, body composition analysis consisting of skeletal muscle and fat mass is a more suitable and reliable way. The distribution of fat and muscle mass are also considered as essential factors for BMD.[8–10] In fact, there is a third of older adults population has a normal BMI or total fat mass percentage but also has central obesity which is called by normal-weight central obesity.[11] Furthermore, building evidence showed that central obesity which produces inflammatory cytokine might have deterious effects on muscle and bone metabolism. Central obesity is hypothesized as an associated factor that influences lower bone formation and microarchitecture of the bone due to visceral fat secretes inflammatory mediators and adipokines as well as serves to metabolize steroid hormone, hereby attenuates the bone metabolism.[12,13]

Sarcopenia is a common condition in older adults of a progressive loss of skeletal muscle mass and function due to the aging process and various other factors. It is associated with low BMD and has been known to increase the risk of osteoporosis.[14,15] It is usually accompanied by an increased fat mass percentage, and this condition is known as sarcopenic obesity (SO) syndrome. The presence of those three which is called as osteosarcopenic obesity (OSO) syndrome is commonly occurred in older adults.[16] However, previous studies defined obesity on SO according to BMI only or total fat mass (FM), which were considered as general obesity but not considering the importance of central obesity, showed an uncertain association between SO and BMD status.[17,18] Thus, the relationship between sarcopenia, central obesity, and low BMD as a distinctive syndrome is still unclear.

Considering and emphasizing the important role of both decreased skeletal mass and central obesity in the developing of OSO, we proposed to explore the role of appendicular skeletal muscle mass (ASMM), FM, and truncal fat mass (TrFM) on BMD. ASMM is approved as a representative measurement of sarcopenia.[19] Meanwhile, FM and TrFM could reflect the condition of general and central obesity, respectively.[20,21] The study was aimed to explore the correlation between ASMM, FM, and TrFM as well as indexes ASMM/FM and ASMM/TrFM ratio with BMD in older adults.

# Methods

### Study Design and Subjects

This was a cross-sectional study. We obtained the necessary data such as the lat est body composition analysis and vertebral BMD results for this study from the medical records of older adult outpatient in the Geriatric Clinic of Hasan Sadikin General Hospital. Patients who regularly took vitamin D supplementation,[22] immunosuppressant drugs,[23] hormone replacement therapy,[24] and chronic renal failure[25] were excluded in this study. All information relating to the characteristics of the subject was recorded in the form of self-identity data, anthropometry, body composition, vertebral BMD, nutritional status, and daily physical activity status.

The data was obtained from the medical record in the period of January 2014 to December 2018. A total of 112 of 256 patients was eligible as subjects in this part of the study. The study was approved by Ethics Committee at Sadikin General Hospital (LB.02.01/X.6.5/49/2019).

### Assessment of body composition and BMD

Body height was estimated according to knee height measurement. Body composition was measured using Tanita BC-418 (Tanita corp., Tokyo, Japan). It provides a complete measurement of weight, body mass index, body fat, and fat mass percentage, and fat-free mass, including segmental analysis of each body parts for muscle mass and fat mass necessary for this study. Geriatric Clinic of Hasan Sadikin General Hospital has a standard procedure of body composition examination. For each BIA, sex, age, and height were directly inputted into the instrument before the impedance measurement. Testing was scheduled to allow for a 10–12 h fasting window, avoid to strenuous exercise for 4 hours or more, avoid to drink for 1 hour, and patients were asked to void their bladder before testing to optimize the accuracy. Any metal items were removed from the patients. Then subject's feet were guided onto the BIA foot sensors by the examiner to ensure optimal contact and centralized the placement of heel. All BIA measurements were completed by a trained examiner according to the device manufacturers' instructions.

Vertebral BMD was examined using DXA Lunar Prodigy Oracle Bone Densitometer (GE corps., Madison, WI, USA) according to standard protocol. BMD measurements were performed at by trained radiology technician one point of the spine. The patient lay supine on the imaging table, the legs raised by support for the lower legs.

We analyzed the ASMM in the form of ASMM divided by squares of body height, and called as appendicular skeletal muscle mass index (ASMI). The fat mass and truncal fat also analyzed as fat mass index (FMI) and truncal fat mass index (TrFMI), respectively. ASMI, FMI, and TrFMI were presented as $kg/m^2$ unit. Dividing between ASMI by TrFMI yields ASMM/TrFM as an index. Likewise, ASMI per FMI yields ASMM/FM ratio.

### Data Processes and Statistical Analyses

All data were analyzed using IBM SPSS Statistics 25.0 for Windows (IBM Corp., Armonk, NY, USA). ASMI, TrFM, FMI, ASMM/FM ratio, ASM/TrFM ratio, and BMD were presented as continuous data and expressed as mean ± standard deviation (SD) or median (minimum-maximum value). In order to determine correlation coefficient, Spearman correlation test was performed. To confirm the relationship, we compared ASMI, FMI, TrFMI, ASMM/FM ratio and ASMM/TrFM ratio between normal and low BMD subjects. For this purpose, Mann-Whitney test was used to. Low BMD was defined as T-score <-1 SD. A p-value less than 0.05 was considered as statistically significant.

## Results

### Baseline Characteristics

We obtain secondary data from the medical records of Geriatric Clinic of Hasan Sadikin General Hospital outpatients. There were total of 256 older adult patients the that met the inclusion criteria from January

2014 to December 2018. The ones that were eligible were 133 patients. Chronic kidney disease (CKD) patients and vitamin D users were excluded. Thus, total of 113 patients were enrolled in this study (Fig.1).

**Table 1. Baseline characteristics**

| Variables | n (%) | Mean ± SD or Median (min-max) |
|---|---|---|
| Gender | | |
| - Female | 85 (75.9) | |
| - Male | 27 (24.1) | |
| Age (years) | | 72 ± 6 |
| Height (cm) | | 154.8 ± 7.5 |
| Weight (kg) | | 59.8 ± 11.8 |
| Body mass index (kg/m$^2$) | | 25.13 ± 4,28 |
| ASMI (kg/m$^2$) | | 7.05 ( 4.4–10.90) |
| FMI (kg/m$^2$) | | 7.68 (3.09–19.95) |
| TrFMI (kg/m$^2$) | | 4.17 (2.15–11.26) |
| ASMM/FM ratio | | 0.89 (0.39–2.46) |
| ASMM/TrFM ratio | | 1.62 (0.56–3.67) |
| BMD (gr/cm$^2$) | | 0.88 (0.55–1.58) |
| T-Score | | -1.8 (-4.3–3.3) |

ASMI: appendicular skeletal muscle index; ASMM/FM: appendicular skeletal muscle mass to fat mass ratio; ASMM/TrFM: appendicular skeletal muscle mass to fat mass ratio; BMD: bone mineral density; FMI: fat mass index; TrFMI: truncal fat mass index.

Baseline characteristics of this study were presented on Table 1. The mean age of subjects was 72 ± 6 years. The averages of body height, body weight, and body mass index were 154.8 ± 7.5 cm, 59.8 ± 11.8 kg, and 25.13 ± 4.28 kg/m$^2$, respectively. The results of body composition measurements using BIA showed that the median ASMI was 7.05 (4.4–10.90) kg. The median TrFMI was 4.17 (2.15–11.26) kg. The characteristic of subjects according to BMD status is presented on Table 2. Low BMD was diagnosed in 82 patients. The characteristic of ages and BMI were similar between normal and low BMD subjects.

**Table 2. Subject characteristics according to BMD status**

| Variables | Bone mass density status | |
|---|---|---|
| | Normal | Low |
| | n=30 | n=82 |
| Gender | | |
| - Female, n(%) | 12 (10.7) | 73 (65.2) |
| - Male, n(%) | 18 (16.1) | 9 (8.0) |
| Age (years) | 71.5 ± 6 | 71.9 ± 7 |
| Height (cm) | 160.73 ± 6.32 | 152.66 ± 6.70 |
| Weight (kg) | 67.13 ± 11.27 | 57.10±10.83 |
| Body mass index (kg/m$^2$) | 25.75(18.0–37.7) | 24.81 (17.1–36.3) |
| Vertebral bone mineral density (g/cm$^2$) | 1.19±0.21 | 0.81±0.14 |
| T-score | 0.4(-1.0–3.3) | -2.1(-4.3 – -1) |

### Correlation of ASMI, FMI, TrFMI, ASMM/FM ratio and ASMM/TrFM ratio with vertebral BMD

First, correlations between ASMI, TrFMI, and FMI, separately, with BMD were assessed and presented on Fig.2. The correlations of those three components to BMD are presented on Fig.2A-C. Among those components, ASMI has the strongest correlation with BMD (r=0.517, p<0.001). TrFMI also has a significant negative correlation with BMD (r=-0.220, p=0.02). FMI was not correlated with BMD (r=-0.113, p=0.234). As an index, ASMM/TrFM ratio had a stronger correlation with BMD compared with ASMM/FM ratio.

In addition to a correlative analysis, according to BMD examination using DXA, we compare the difference of ASMI, FMI, TrFMI, ASMM/FM ratio and ASMM/TrFM ratio between normal and low BMD. Comparison results were presented on Fig.3. ASMI, ASMM/FM ratio, and ASMM/TrFM ratio were significantly higher in normal BMD subjects. In contrast, normal BMD subjects had lower TrFMI compared to the low BMD one.  The FMI among those was not different.

## Discussion

In our study both ASMM and TrFM in the form of indexes (ASMI and TrFMI) showed significant correlations with BMD. However, ASMM had more significant association with BMD than TrFM. These findings were consistent with the results of ASMM/TrFM and ASMM/FM which both were correlated with BMD, but in fact, in this study it showed that FM (FMI) alone had no correlation with BMD. As far as we know, this is the first study that used ASMM, TrFM and both of them as an index to reflect the important condition of central obesity in SO. Those correlation results were consistent with the comparison test results between normal versus low BMD. Both in correlation and comparison tests, TrFMI (central obesity index) had positive associations with BMD, meanwhile FMI (general obesity index) had no association with BMD. These findings confirmed the interdependency between sarcopenia, central obesity, and low BMD. These three problems might occur, either alone or together as an osteosarcopenic-obesity syndrome, even though they may appear in the different onset. Sarcopenia is defined by the European Working Group on Sarcopenia in Older People (EWGSOP) as a syndrome characterized by progressive

and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death. The EWGSOP also classified sarcopenia into three stages as pre-sarcopenia (low muscle mass, without any decrease in muscle strength or physical performance); sarcopenia (reduction in muscle mass accompanied by a deterioration of strength or physical performance); and severe sarcopenia (the combination of low muscle mass, physical performance, and muscle strength).[19] Both pre-sarcopenia and sarcopenia are considered as a risk factor for decreased BMD.[14,15]

Some previous studies that investigate relationship between obesity and BMD yielded inconsistent results. Some studies showed that BMI has a negative correlation with BMD.[3,4] Meanwhile, other studies concluded that high BMI among older adults is a protective factor for low BMD. They reported that obese patients had a lower prevalence of osteoporosis and osteopenia. It might be explained by mechanically, a high BMI gives a greater mechanical load to the bone.[5,6] These miscellaneous findings suggested that BMI as single parameter for obesity assessment may not be a suitable method to explain comprehensively the relationship between obesity and BMD.[8–10] The distribution of fat and muscle mass are also essential factors for BMD and in our study showed that appendicular skeletal muscle and central obesity may have more significant role. In a previous studies, low skeletal muscle mass associated with low neck femoral BMD in older adults.[26–28] Another study also confirmed, the skeletal muscle mass is associated with BMD and trabecular microstructures.[29] Meanwhile, the accumulation of visceral adipose tissue, which measured using DXA, was significantly associated with high risk of fracture in non-obese subjects. It means central obesity has more significant role than general obesity to bone metabolism. [20,30] This fact also consistent with our results that showed no difference in BMI and FMI between normal versus low BMD subjects. Our study results emphasized the negative effect of central obesity on bone health rather than general obesity.

Previous studies used different methods to determine sarcopenic obesity by using a separated assessment on each low skeletal muscle mass and obesity based on ASMM and fat mass percentage or BMI. Our study revealed and emphasized more on the important role central obesity on the development of OSO. This is important since there are specific older adult populations characterized by a normal BMI or total fat mass percentage but has central obesity which is called by normal-weight central obesity. [11,31]

Abundant visceral fat in central obesity is a crucial for IL-6 secretion and provide a potential mechanistic link between visceral fat and systemic inflammation.[32] The adipocyte in the central obesity which produces pro-inflammatory cytokine known as adipokine has a deterious effect on the BMD. The common precursor for both adipocytes and osteoblast are bone marrow mesenchymal stromal cells (MSCs). The differentiation of bone marrow MSCs are affected by several factors including metabolism and aging. Aging processes shift the differentiation to become more adipogenic. It increases adipocytes and osteoclast, as well as decreased osteoblast activities. Adipocytes release the adiponectin, the pro-osteoclast and anti-osteoblast activities cytokine. In addition, central obesity also linked with high inflammatory cytokines such as interleukin-6 (IL-6), C-reactive protein (CRP) and tumor necrosis factor α

(TNFα). Consequently, these propagate osteoclast differentiation and bone resorption. Other studies also stated the decrease mitochondrial metabolism activity, as occur in metabolic syndrome, is associated with adipogenic bone marrows MSCs differentiation. Thus, the result of our study which showed a significant correlation of ASMM/TrFM with BMD further supports the condition of OSO as an important condition in the older adult population to be recognized.[33,34]

Similarly, the harmful effect central obesity has been proved on various inflammatory-related outcomes. Central obesity without general obesity had a greater risk for major adverse cardiovascular event than the condition of general obesity without central obesity.[35] Central body fatness also found as a stronger predictor for all-cancer risk than overall body size. These findings support that the central obesity could not be seen as the condition which is similar with general obesity. Moreover, compared to general obesity, central obesity has distinct level of undesirable outcomes.[36]

On the other hand, DXA has been used as a standardized diagnostic tool to measure BMD and it is also recommended by the National Osteoporosis Foundation for early detection of low BMD.[37–39] Nevertheless, the utilization of DXA as a detection method to detect low BMD still faces several problems in developing countries such as Indonesia. The problems among others are the availability of the device is still scarce and not well distributed due to its relatively high-cost, not mentioning that it still not yet covered by Indonesian universal health coverage. Hence, other modalities are needed that might help to screen certain groups of older adults with a high risk of low BMD. BIA is a more suitable procedure and relatively affordable and has been prioritized by Indonesian Health Ministry to be one of the supporting facilities for Geriatric clinic in the hospital. It is used to assess body composition, including ASMM and TrFM. Based on our study results, ASMM/TrFM could be a potential candidate as a screening tool to detect low BMD in more affordable way. However, a further diagnostic study is needed to determine whether the ASMM/TrFM could be used as a screening tool to detect low BMD.

Limitation of study is that we didn’t include other parts of the bone such as hip (femur) and wrist that is commonly assessed in osteoporosis examination by DXA, therefore this index maybe not be applied in other conditions beside vertebral low BMD. Our study also did not analyze and classify the subjects as sarcopenia, categorically, due to the incidence of sarcopenia is very low in our study which is similar with previous study by Darwita et al.[40] Hence it didn’t meet minimal requirement sample size to do the statistical analysis. However, our study is the first study that analyzed the relationship of BMD, skeletal muscle mass, and central obesity using ASMM/TrFM ratio as a new index.

# Conclusion

In conclusion, ASMM and TrFM has a positive and negative association with BMD, respectively. ASMM/TrFM ratio as sarcopenia-central obesity index has a positive association with BMD. It confirmed the crucial role of central obesity on the development of OSO syndrome.

# List Of Abbreviations

ASMI: appendicular skeletal muscle index;

ASMM/FM: appendicular skeletal muscle mass to fat mass ratio;

ASMM/TrFM: appendicular skeletal muscle mass to fat mass ratio;

BMD: bone mineral density;

BMI: body mass index;

FMI: fat mass index;

TrFMI: truncal fat mass index

OSO: osteosarcopeic-obesity

SO: sarcopenic obesity

# Declarations

### Ethics approval and consent to participate

The study was approved by Ethics Committee at Sadikin General Hospital (LB.02.01/X.6.5/49/2019).

### *Consent for publication*

Not applicable

### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interests

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### Author's Contribution

The corresponding author of this manuscript is Lazuardhi Dwipa, MD, Geriatrician, and contribution of the authors as mentioned below with their responsibility in the study.

1. Study concept and design: Lazuardhi Dwipa
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4. Drafting of the manuscript: Lazuardhi Dwipa, Alif Bagus Rakhimullah, Rini Widiastuti.
5. Critical revision of the manuscript for important intellectual content: Muhammad Apandi, Yuni Susanti Pratiwi.

All authors read and approved the final manuscript, as well as fulfill the International Committee of Medical Journal Editors (2008) criteria for authorship.

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# Figures

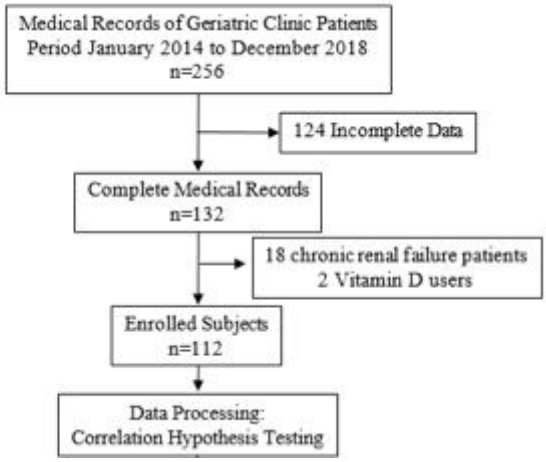
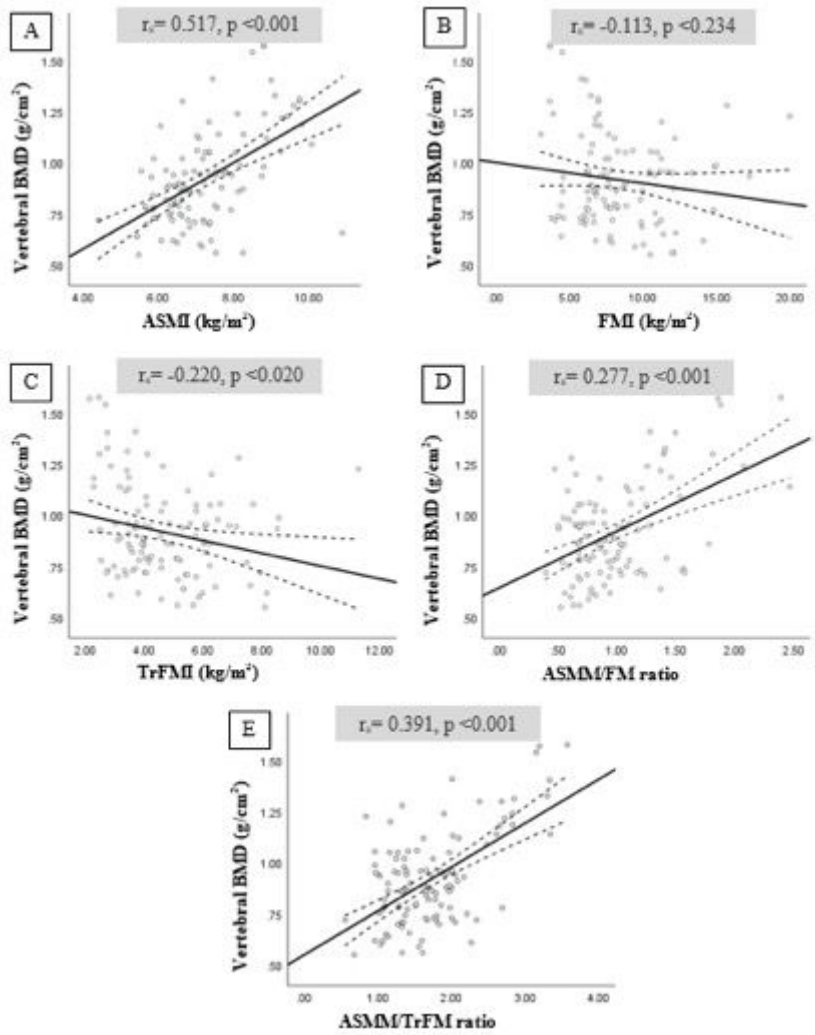


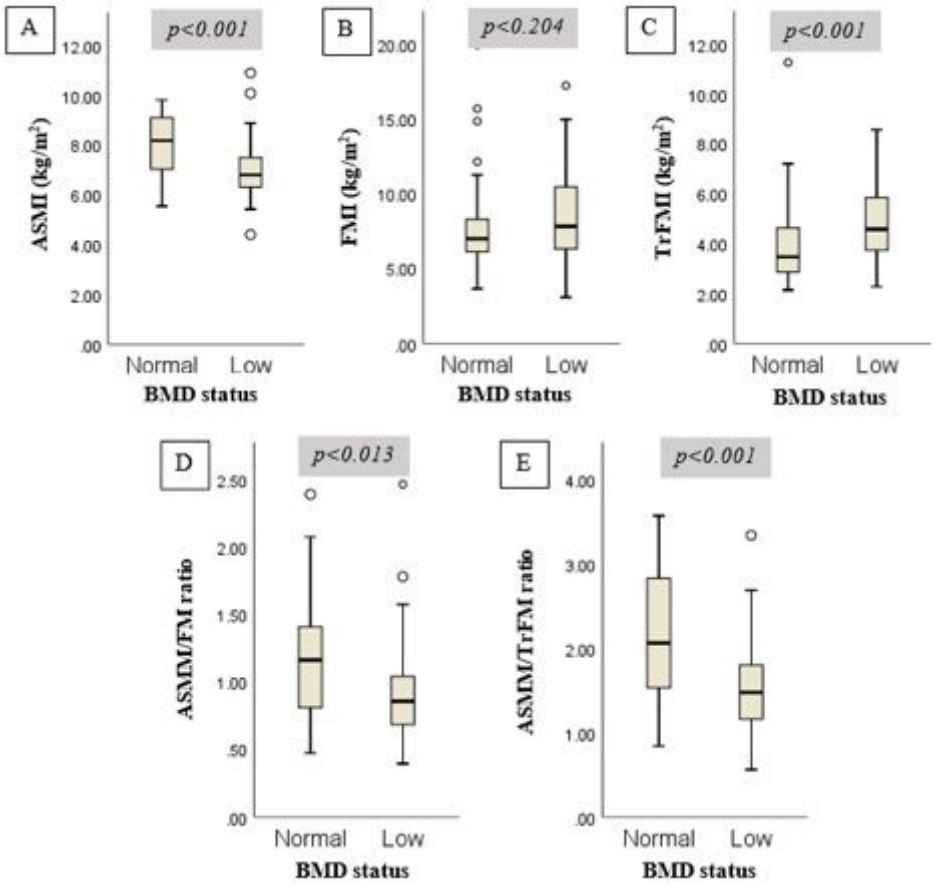

**Figure 1**

Study flowchart. Subjects who met the inclusion and did not meet exclusion criteria for the study population.




## Figure 2

Correlation between ASMI, FMI, TrFMI, ASMM/FM ratio, and ASMM/TrFM ratio with BMD Notes: rs were analyzed using Spearman Correlation test. ASMI: appendicular skeletal muscle index; ASMM/FM: appendicular skeletal muscle mass to fat mass ratio; ASMM/TrFM: appendicular skeletal muscle mass to fat mass ratio; BMD: bone mineral density; FMI: fat mass index; TrFMI: truncal fat mass index.




## Figure 3

Comparison of ASMI, FMI, TrFMI, ASMM/FM ratio, and ASMM/TrFM ratio between normal and low BMD
Notes: The differences between groups were analyzed using Mann-Whitney rank test. ASMI: appendicular skeletal muscle index; ASMM/FM: appendicular skeletal muscle mass to fat mass ratio; ASMM/TrFM: appendicular skeletal muscle mass to fat mass ratio; BMD: bone mineral density; FMI: fat mass index; TrFMI: truncal fat mass index.