Introduction

Age-related changes in body composition are characterized by loss of skeletal muscle mass, termed sarcopenia, and gain in fat mass\(^1\). Sarcopenia is a geriatric syndrome, and its association with frailty has been a focus of research\(^2\). Obesity accompanied with aging is characterized by central adiposity and ectopic fat deposits. Because sarcopenia and obesity both are associated with adverse health outcomes in the elderly\(^3\), sarcopenic obesity (SO), which is coexistence of sarcopenia and obesity, seems to be a more serious condition because of its poor outcomes, such as higher risks of disability\(^4\), cardiovascular diseases\(^5\), metabolic disorders\(^6\), and mortality\(^7\).

Because of a lack of consensus, different definitions for SO have been used in various studies\(^8\). Recently, the Asian Working Group for Sarcopenia (AWGS) declared the regional consensus guidelines for sarcopenia in the Asian elderly, and the diagnostic cutoff points for height-adjusted skeletal muscle mass measured using dual-energy X-ray absorptiometry (DXA) were advocated\(^9\). Since then, many researches on sarcopenia from Asian countries have been reported\(^10\). However, research on SO using the AWGS consensus is lacking. In the present study, we evaluated the relationship between SO defined by the AWGS criteria and metabolic syndrome (MetS) among the Japanese elderly who underwent a comprehensive health checkup.

Materials and Methods

Subjects

Individuals aged 65 years or older who underwent comprehen-
sive health checkups at the Center for Preventive Medicine, Keio University Hospital, from August 1, 2012 to July 31, 2015 were enrolled. Those who did not undergo examination for body composition and visceral fat mass were excluded. In total, 235 subjects (95 men and 140 women; mean age, 73.2 ± 6.0 years) were eligible for inclusion in this study.

**Ethical consideration**

A written general informed consent was obtained from the participants. This study was performed with approval from the Ethics Committee of Keio University School of Medicine (approval number: 20160363).

**Anthropometry, blood pressure, and body composition measurements**

Body height and body weight were measured with the subjects wearing light clothes without shoes. Body mass index (BMI) was calculated as body weight (kg) divided by the squared body height (m^2). Blood pressure was measured on the right upper arm using an automatic device (BP-900; TANITA Corporation, Tokyo, Japan), which works on the combination of the Korotkoff sound method and oscillometric technique, after subjects had rested for at least 5 min in a sitting position at the hospital.

Appendicular skeletal muscle mass (ASM) and total-body fat mass (FM) were measured using DXA (LUNAR PRODIGY series X-ray bone densitometer; GE Healthcare Japan Corporation, Tokyo, Japan), and visceral fat area (VFA) and abdominal circumference (AC) was measured using computed tomography (Aquilion CXL; Toshiba Medical Systems Corporation, Tochigi, Japan) using a single slice at the umbilical level. Skeletal muscle mass index (SMI) was calculated as ASM (kg) divided by the squared body height (m^2). The percentage of FM was calculated as FM (kg) divided by the body weight (kg) multiplied by 100.

**Blood chemistry measurements**

Blood samples were collected after overnight fasting and immediately examined using an automatic biochemical analyzer (LABOSPECT008; Hitachi High-Technologies Corporation, Tokyo, Japan) at the central laboratory.

**Other clinical data**

Clinical data were extracted from the results of the comprehensive health checkups and included data related to age, sex, fasting plasma glucose (FPG) level, hemoglobin A1c (HbA1c) level, total cholesterol level, triglycerides (TG) level, high-density lipoprotein cholesterol (HDL-C) level, low-density lipoprotein cholesterol (LDL-C) level, and high-sensitivity C-reactive protein (hsCRP) level. Life-style habits, such as current smoking, current drinking, and regular exercise, and medical histories were obtained from self-reported questionnaires. Drinking habit was defined as “consumption of more than 40 g of alcohol at least three times a week,” and exercise habit as “daily walking activity for at least 1 h” or “performing daily exercise with mild sweating for more than 30 min at least twice a week.”

**Definition of sarcopenia, obesity, and sarcopenic obesity**

According to AWGS criteria \(^{12}\), we used SMI cutoff points of <7.0 kg/m\(^2\) for men and <5.4 kg/m\(^2\) for women to diagnose sarcopenia. Regarding obesity, we used %FM cutoff points of ≥25% for men and ≥30% for women \(^{14}\). Participants who met the criteria for both definitions were defined as SO. According to these definitions, participants were classified into four phenotypes of body composition: standard, sarcopenia (without obesity), obesity (without sarcopenia), and SO (Fig. 1).

**Definition of metabolic syndrome at-risk**

To identify MetS at-risk, we used the diagnostic criteria of MetS defined by the Japanese Society of Internal Medicine \(^{15}\). In addition to central obesity defined by VFA ≥ 100 cm\(^2\) in both sexes, the presence of at least one of the following three metabolic disorders indicated MetS at-risk: (1) systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg or taking antihypertensive medicines, (2) TG 150 ≥ mg/dL and/or HDL-C < 40 mg/dL, or taking lipid-lowering medicines, and (3) FPG ≥ 110 mg/dL, or taking hypoglycemic medicines.

**StatISTICS**

Continuous variables were expressed as mean ± standard deviations, and categorical variables were presented as counts and percentages. Comparisons between men and women were analyzed using the unpaired Student’s t-test; comparisons among four body composition phenotypes were analyzed using one-way analysis of variance, followed by the Scheffé test for multiple comparisons. Multivariate logistic regression analyses were performed to identify the risk for MetS associated with SO. The following explanatory variables were included in the models: age, sex, BMI, and smoking habits (0,1); drinking habits (0,1); and exercise habits (0,1). A value of \(p < 0.05\) (two sided) was considered significant. Data were analyzed using IBM SPSS Statistics version 22 for Windows (IBM Japan, Tokyo, Japan).

**Results**

**Characteristics of participants**

The baseline characteristics of the participants are shown in Table 1. Although BMI, VFA, and AC were higher in men than...
in women, almost all the participants fell within the standard range for BMI. Men had higher FPG, HbA1c, and TG levels and a lower HDL-C level than women. The prevalences of hypertension and dyslipidemia were 33% and 28%, respectively, and the prevalence of diabetes mellitus was 14%. None of the men or women had serious metabolic disorders. Regarding body composition, ASM and SMI were higher in men and %FM was higher in women.

Regarding body composition phenotypes, 31% of all the participants had a standard body composition, 20% of the participants had sarcopenia, 31% had obesity, and 18% had SO. The distributions of the four phenotypes of body composition were similar for both men and women.

The prevalence of MetS at-risk was 31% in all the participants, and it was significantly higher in men than in women (42% in men and 24% in women, \( p < 0.05 \)).

**Comparison of clinical parameters among the four phenotypes of body composition**

Compared with the standard phenotype, BMI was higher among obese subjects and lower among subjects with sarcopenia, whereas, no significant difference in BMI was observed between subjects with standard body composition and those with SO. AC was the lowest among subjects with sarcopenia and gradually increased in accordance with the body composition phenotypes. As expected, a higher amount of VFA was observed in the obese and SO groups, accompanied by a higher prevalence of MetS at-risk, higher homeostasis model assessment of insulin resistance (HOMA-R), and higher TG and lower HDL-C levels than the corresponding values seen the subjects with the standard phenotype or sarcopenia alone (Table 2).

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### Table 1 Characteristics of participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=235)</th>
<th>Men (n=95)</th>
<th>Women (n=140)</th>
<th>P value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73.2 ± 6.0</td>
<td>73.5 ± 6.7</td>
<td>72.9 ± 5.5</td>
<td>0.455</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.2 ± 3.5</td>
<td>23.2 ± 2.9</td>
<td>21.5 ± 3.8</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>VFA (cm²)</td>
<td>91.4 ± 51.1</td>
<td>108.7 ± 53.7</td>
<td>79.6 ± 45.7</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>AC (cm)</td>
<td>80.7 ± 10.1</td>
<td>82.2 ± 8.8</td>
<td>79.6 ± 10.8</td>
<td>0.049</td>
</tr>
<tr>
<td>Mets at-risk (n (%)) b</td>
<td>74 (31.5)</td>
<td>40 (42.1)</td>
<td>34 (24.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>124.9 ± 18.0</td>
<td>126.1 ± 14.5</td>
<td>124.1 ± 20.0</td>
<td>0.401</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>74.8 ± 10.2</td>
<td>75.2 ± 9.5</td>
<td>74.6 ± 10.7</td>
<td>0.637</td>
</tr>
<tr>
<td>FPG (mg/dL)</td>
<td>107.7 ± 19.6</td>
<td>113.8 ± 22.1</td>
<td>103.6 ± 16.4</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.9 ± 0.7</td>
<td>6.0 ± 0.9</td>
<td>5.8 ± 0.4</td>
<td>0.006</td>
</tr>
<tr>
<td>HOMA-R</td>
<td>1.5 ± 1.2</td>
<td>1.7 ± 1.2</td>
<td>1.4 ± 1.2</td>
<td>0.060</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>207.4 ± 34.6</td>
<td>196.3 ± 32.4</td>
<td>214.9 ± 34.2</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>93.7 ± 47.8</td>
<td>105.6 ± 56.1</td>
<td>85.6 ± 39.4</td>
<td>0.002</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>61.2 ± 14.4</td>
<td>54.2 ± 13.0</td>
<td>65.9 ± 13.4</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>113.4 ± 29.1</td>
<td>110.3 ± 28.8</td>
<td>85.6 ± 39.4</td>
<td>0.188</td>
</tr>
<tr>
<td>hsCRP (mg/dL)</td>
<td>0.12 ± 0.35</td>
<td>0.11 ± 0.31</td>
<td>0.12 ± 0.37</td>
<td>0.821</td>
</tr>
<tr>
<td>ASM (kg)</td>
<td>16.0 ± 3.8</td>
<td>19.8 ± 2.4</td>
<td>13.4 ± 1.7</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>SMI (kg/m²)</td>
<td>6.29 ± 0.94</td>
<td>7.14 ± 0.61</td>
<td>5.72 ± 0.63</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>Percentage of FM (%)</td>
<td>27.9 ± 8.1</td>
<td>24.1 ± 6.7</td>
<td>30.5 ± 8</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>15.9 ± 6.6</td>
<td>15.9 ± 6.2</td>
<td>15.9 ± 6.9</td>
<td>0.977</td>
</tr>
</tbody>
</table>

All data are expressed as mean ± standard deviation. *: \( p < 0.05 \).

* Unpaired Students’ t-test (men vs. women). \( \chi^2 \)-test.

Abbreviations: BMI, body mass index; VFA, visceral fat area; AC, abdominal circumference; FPG, fasting blood glucose; HbA1c, hemoglobin A1c; HOMA-R, homeostasis model assessment of insulin resistance; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hsCRP, high sensitivity C-reactive protein; ASM, appendicular skeletal muscle mass; SMI, skeletal muscle mass index; FM, total-body fat mass.
Multivariate logistic regression analyses

To determine the relationship between SO and MetS at-risk, multivariate logistic regression analyses were performed. As shown in Table 3, the subjects with obesity or SO were associated with increased risk for MetS at-risk (odds ratio [OR] and 95% confidence intervals [CI] for obesity: 9.69, 4.13–22.75; for SO: 3.12, 1.23–7.94) in the age- and sex-adjusted model (Model 1). Moreover, after additive adjustments for BMI and lifestyle parameters, the odds ratio for SO was further increased to 3.02 (95% CI: 0.99–9.22). The risk of MetS was significantly higher in the SO group compared to the standard group in both Model 1 and Model 2 adjusted for additional factors such as smoking, drinking, and regular exercise.
habits (Model 2), only the SO group showed a marginally positive association with the risk for MetS at-risk (OR and 95% CI for obesity: 1.88, 0.61–5.84; for SO: 3.02, 0.99–9.22).

Discussion

The present cross-sectional study assessed the relationship between SO and MetS among elderly subjects who had completed comprehensive health checkups. As a result, SO was found to be correlated with the risk for MetS, independently of the BMI and other confounders. To the best of our knowledge, this is the first report to evaluate the relationship between SO and MetS in elderly Japanese subjects.

Definition of sarcopenic obesity

Several definitions of sarcopenia and obesity have been reported previously. Baumgartner first proposed the use of height-adjusted muscle mass using DXA for the diagnosis of sarcopenia, and the total-body fat percentage for the diagnosis of obesity. They demonstrated the strongest association of SO with physical disabilities. Another study assessed skeletal muscle mass using bioelectrical impedance analysis and also assessed muscle strength using grip power to define sarcopenia, while waist circumference was used to assess abdominal obesity. It was found that SO, based on muscle strength but not muscle mass, was modestly associated with an increased risk of cardiovascular disease. Recently, the AWGS proposed diagnostic criteria of sarcopenia for elderly Asian population. According to the AWGS criteria, sarcopenia is diagnosed by not only low muscle mass (SMI <7.0 kg/m² for men and <5.4 kg/m² for women) but also low muscle strength (grip power <26 kg for men and <18 kg for women). Muscle strength is considered as an index of muscle quality, and cumulative evidence has supported the importance of evaluations of both muscle mass and muscle quality, and cumulative evidence has supported the importance of evaluations of both muscle mass and muscle quality, and cumulative evidence has supported the importance of evaluations of both muscle mass and muscle quality, and cumulative evidence has supported the importance of evaluations of both muscle mass and muscle quality, and cumulative evidence has supported the importance of evaluations of both muscle mass and muscle quality, and cumulative evidence has supported the importance of evaluations of both muscle mass and muscle quality,

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The underlying pathogenesis linking SO and MetS

It has been postulated that age-related intramuscular fat infiltration causes insulin resistance based on mitochondrial dysfunction. Chronic inflammation is another possible mechanism linking SO and MetS. It has been reported that obesity and inflammation are associated with the presence of MetS. Visceral adipose tissue is a source of inflammatory adipokines, such as interleukin (IL)-6 and tumor necrosis factor (TNF)-α, which are associated with both increased fat mass and decreased muscle mass, and the acceleration of muscle catabolism may exacerbate insulin resistance. In the present study, hsCRP was the only inflammatory biomarker that was examined. No significant differences in the hsCRP level were observed between the SO group and the other phenotypes of body composition. The positive association of SO to MetS at-risk remained after further adjustment with hsCRP in Model 2 (OR, 3.04; 95% CI, 0.99–9.24, p=0.05).

The underlying pathogenesis linking SO and MetS

It has been postulated that age-related changes of body composition, that is, reduced muscle mass and increased fat mass, are strongly connected each other, and multiple interactions between muscle and adipose tissue along with aging may exacerbate insulin resistance. For example, sedentaryism and lower physical activity seen in the elderly people may lead to muscle mass decline and muscle weakness, decreased endurance, reduced total energy expenditure, and fat gain. Increased adipose tissue, particularly visceral adipose tissue, may lead to increased secretion of pro-inflammatory cytokines and adipokines, such as IL-6, TNF-α, and leptin. Besides further increase of chronic low-grade inflammation, which may exacerbate insulin resistance as mentioned above, increased leptin may lead to leptin resistance, as a result of a reduction of fatty acid oxidation in muscles which contributes to ectopic fat deposition. Ectopic intramuscular fat infiltration may affect muscle quality. Therefore, a vicious circle between muscle loss and fat gain along with aging may lead to more SO and metabolic disorders in the elderly people. Interestingly, a recent study suggested that metabolic disorders linked to SO may appear in the early stages of aging process, and
that insulin resistance may act not only as a risk factor for cardiometabolic disorders but as an additional factor accelerating age-related muscle mass decline by interfering with protein metabolism\(^\text{12}\). Further researches are needed in order to explore underlying pathogenesis between SO and MetS.

**Limitations**

Several limitations of the present study must be mentioned. First, participants of this study were examinees from comprehensive health checkups who might be more health conscious. Therefore, our results may not be representative of the general population. Second, because of its cross-sectional, observational nature, causal relationships between SO and MetS cannot be determined. Third, in this study, we evaluated only muscle mass and did not examine physical performance or muscle strength, such as walking speed and grip power, which are important components for diagnosis of sarcopenia. Finally, we could not assess the biological pathway linking SO and MetS. Further studies should be prompted to evaluate mechanisms underlying age-related changes in body composition and metabolic disorders. Researches on ectopic adipose tissue, especially intramuscular fat, inflammatory biomarkers and adipokines, such as IL-6, TNF-\(\alpha\), and leptin, might benefit this issue.

**Conclusions**

In conclusion, the present study examined the relationship between age-related changes in body composition and the risk for MetS among the Japanese elderly who underwent comprehensive health checkups. As a result, SO had a greater association with MetS than obesity alone, independent of BMI and lifestyle factors. From a practical perspective, age-related changes in body composition might benefit this issue.

The authors state that they have no Conflict of Interest (COI).

**Acknowledgement**

This study was supported, in part, by a Grant-in Aid for Clinical Research 2016 from the Japan Society of Health Evaluation and Promotion.

An abstract of this article was presented at the 45\(^{\text{th}}\) Annual Meeting of Japan Society of Health Evaluation and Promotion in Chiba, Japan in 2017.

We would like to express our gratitude to Kazunari Ito, M.D., Suketaka Momoshima, M.D., and Yoshinori Sugino, M.D. for their advice on imaging diagnosis.

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