Original article

Prognostic value of sarcopenic obesity estimated by computed tomography in patients with cardiovascular disease and undergoing surgery

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A B S T R A C T

Background: Sarcopenic obesity is a health condition involving a combination of excess adipose tissue and loss of muscle mass. Although sarcopenic obesity is known to contribute to the morbidity and mortality of chronic diseases, limited data are available in patients with cardiovascular disease. The present study was performed to examine whether sarcopenic obesity determined by preoperative computed tomography (CT) is a useful predictor of postoperative mortality in patients undergoing cardiovascular surgery.

Methods: We reviewed the findings in 664 consecutive cardiovascular surgery patients (mean age, 65.8 ± 12.7 years; male, 66.6%) who underwent preoperative CT including the level of the third lumbar vertebra for clinical purposes. Psoas muscle attenuation (MA) and visceral adipose tissue (VAT) were measured as metrics of sarcopenia and obesity, respectively. Sarcopenia was defined as low MA (below median), while obesity was defined as high VAT (>103 cm\(^2\) for males and >69 cm\(^2\) for females). The endpoint was all-cause mortality and secondary outcomes were muscle function.

Results: After adjusting for age and sex, sarcopenic obesity showed significant associations with lower grip strength and quadriceps strength, slower gait speed, and shorter 6-min walking distance compared to the normal group (p < 0.05). On multivariate Cox regression analysis, sarcopenic obesity was associated with increased risk of mortality after adjusting for EuroSCORE (hazard ratio, 3.04; 95% confidence interval, 1.25–7.40).

Conclusions: Sarcopenic obesity is associated with poor muscle function and all-cause mortality in patients undergoing cardiovascular surgery.

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Introduction

The incidence of sarcopenia is increasing as the world’s population is aging [1,2], and the prevalence rates are especially high in patients with cardiovascular disease [3]. Sarcopenia is accompanied by loss of muscle mass, which is a powerful predictor of mortality in aging cardiovascular disease patients [3]. Diagnosis of sarcopenia in the elderly is important because of its close relation to adverse outcomes following cardiovascular surgery [4].

Sarcopenia identified by computed tomography (CT) was reported to be a useful predictor of mortality in patients with cancer [5], cardiovascular disease [6], and transcatheter aortic valve implantation (TAVI) [7]. There have been a number of studies regarding the utility of skeletal muscle density as a prognostic
predictor [5,8]. Previously, we reported that low skeletal muscle density, determined by mean radiation attenuation in Hounsfield Units (HU) on CT, predicted poorer muscle function and mortality in patients undergoing cardiac surgery [9].

Moreover, sarcopenic obesity, defined as the presence of both obesity and sarcopenia, has attracted a great deal of attention because it is related to poorer outcome compared to sarcopenia alone [10,11]. Most studies regarding sarcopenic obesity used body mass index (BMI) as a surrogate maker for obesity [12]. However, BMI cannot discriminate between fat and lean muscle. Indeed, several recent studies underlined the importance of evaluating body composition using BMI in combination with fat mass or muscle mass [13,14]. However, limited data are available regarding the impact of sarcopenic obesity determined by CT in patients with cardiovascular disease. Accordingly, the present study was performed to examine whether sarcopenic obesity determined by preoperative CT is a useful predictor of postoperative mortality in patients undergoing cardiovascular surgery.

Methods

Study population

A total of 664 consecutive cardiovascular surgery patients who were admitted to the Cardiovascular Center of Kitasato University Hospital between January 2008 and July 2016 were enrolled in this study. All patients underwent preoperative transverse CT including the third lumbar vertebral level. Chest and abdominal CT are performed as routine preoperative examinations before cardiovascular surgery in Japan [9]. Patients who underwent surgery for tumors, thrombosis, or congenital diseases were excluded. In addition, we also excluded patients with a prior history of cancer. The study was performed in accordance with the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Kitasato University Hospital.

Clinical data collection

The data for all variables evaluated before surgery, including height (measured to the nearest 0.1 cm with a stadiometer), body weight (determined to the nearest 0.1 kg), type of surgery, left ventricular ejection fraction (LVEF), and additive EuroSCORE were obtained from the electronic medical records. BMI was calculated as: body weight (kg)/height (m)^2. LVEF was estimated using Simpson's method based on the results of two-dimensional echocardiography. The presence or absence of complications was determined with reference to electronic medical records. Operative risk was evaluated in each patient using the additive EuroSCORE [15]. Cases with multiple surgeries were defined as those with simultaneous coronary artery bypass graft (CABG), valve, and/or aortic surgery. The study endpoint was all-cause mortality, and the time to reach the endpoint was calculated as the number of days from the date of surgery to the date of the event.

Muscle function measurements

We measured a number of indicators of muscle function before hospital discharge, i.e. grip strength measured using a digital dynamometer (TKK 5101 Grip-D; Takei, Tokyo, Japan), with the patient squeezing gradually and continuously for 3 s, taking the average of the highest values on the right and left sides and expressed in kg averaged by BMI (kg/m^2) [16,17]; quadriceps isometric strength (QIS) measured using a hand-held dynamometer (μ.Tas MT-1; ANIMA, Tokyo, Japan) with the highest values on the right and left sides (kg) averaged by BMI (kg/m^2); usual gait speed determined by timing the patients walking over the middle 10 m of a 16-m walkway at their usual speed; and 6-min walking distance (6MWD) determined according to the guidelines of the American Thoracic Society [18], with the patients instructed to cover as much distance as possible within the allotted time. The use of assistive devices was permitted for the walking test.

Body composition measurements

Measurements were obtained from the most recent preoperative CT transverse abdominal images for each patient and used two consecutive slices at the level of the third lumbar vertebra including both transverse processes. Body composition, including cross-sectional area of psoas muscle (range −29 to 150 HU), VAT area (range −150 to −50 HU), and subcutaneous adipose tissue area (SAT area; range −190 to −30 HU), were assessed by a single observer using a Slice-O-Matic (version 5.0; Tomovision, Magog, QC, Canada) with reference to previous studies (Fig. 1) [19,20]. Skeletal muscle density was quantified as the mean muscle attenuation (MA) of the psoas cross-sectional area based on two consecutive images for each patient.

The degrees of interobserver and intraobserver agreement were determined based on the intraclass correlation coefficients (ICC) in analysis of 10 different patients chosen at random by 2 independent investigators. Both psoas cross-sectional area (0.988, 0.972) and psoas MA (0.994, 0.997) showed excellent interobserver and intraobserver ICC [9].

Statistical analysis

Continuous variables are expressed as the means ± standard deviation (SD), while categorical variables are expressed as numbers and percentages. The cut-off points for VAT area were ≥103.0 cm^2 for males and ≥69.0 cm^2 for females [21], and high VAT area was defined as an indicator of obesity. The median was taken as the cut-off point of sarcopenia for MA [9]. Baseline characteristics were compared between the non-sarcopenia (non-sarcopenic obesity) and the sarcopenia (sarcopenic obesity) groups by t test or Fisher’s exact test where appropriate. The patients were divided into normal (non-obesity with non-sarcopenia), obesity
### Results

**Study population**

The baseline characteristics for all subjects and comparisons between those with and without sarcopenia or sarcopenic obesity are shown in Table 1. The study population had a mean age of 65.8 ± 12.7 years, and 66.6% were male. With regard to type of surgery, CABG was performed in 38.6% of the patients, cardiac valve surgery in 31.9%, and aortic surgery in 11.0%. The mean BMI and EuroSCORE were 22.4 kg/m² and 6.41, respectively. Sarcopenia and sarcopenic obesity were associated with higher rates of hypertension and chronic kidney disease, and poorer muscle function as determined by grip strength, Q5, gait speed, and 6MWd. In addition, sarcopenia was associated with higher rate of prior heart failure and lower hemoglobin, albumin, and low-density lipoprotein cholesterol (LDL-C) levels. On the other hand, sarcopenic obesity was associated with higher rates of dyslipidemia and diabetes mellitus, and lower high-density lipoprotein cholesterol (HDL-C) level.

**Associations between sarcopenic obesity and muscle functions**

Fig. 2 shows the results of ANCOVA to verify the association between body composition and muscle function. After adjusting

### Table 1

Patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Overall n = 664</th>
<th>Non-sarcopenic obesity n = 332</th>
<th>Sarcopenic obesity n = 332</th>
<th>p-Value</th>
<th>Non-sarcopenic obesity n = 491</th>
<th>Sarcopenic obesity n = 173</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Male (%)</td>
<td>442 (66.6)</td>
<td>231 (69.6)</td>
<td>211 (63.8)</td>
<td>&lt;0.001</td>
<td>330 (67.2)</td>
<td>112 (64.7)</td>
<td>0.574</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.4 ± 3.8</td>
<td>22.1 ± 3.4</td>
<td>22.6 ± 4.0</td>
<td>0.073</td>
<td>21.5 ± 3.3</td>
<td>25.0 ± 3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>EuroSCORE</strong></td>
<td>6.41 ± 2.96</td>
<td>5.52 ± 2.66</td>
<td>7.30 ± 2.99</td>
<td>&lt;0.001</td>
<td>6.13 ± 2.87</td>
<td>7.21 ± 3.09</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are means ± SD (standard deviation) or numbers (%), p-values calculated by t-test or Fisher's exact test.

BMI, body mass index; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CSAs, cross-sectional area; MA, muscle attenuation; HU, Hounsfield units; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; Q5, quadriceps isokinetic strength; 6MWd, 6-min walking distance.

(obesity with non-sarcopenia), sarcopenic (non-obesity with sarcopenia), and sarcopenic obesity (obesity with sarcopenia) groups, and the independent associations between body composition and muscle function (handgrip strength, Q5, usual gait speed, and 6MWd) were assessed by analysis of covariance (ANCOVA) with adjustment for age and sex. Kaplan–Meier analysis was performed to assess surgery, and the log-rank test was used to assess the prognostic significance of sarcopenia and sarcopenic obesity. Cox regression analysis was performed to estimate the hazard ratio (HR) and 95% confidence interval (CI) for the prognostic capability of sarcopenic obesity by constructing univariate and multivariate models adjusted for EuroSCORE. To assess sensitivity, we constructed a logistic model for calculating the propensity score (PS) for each individual based on age and sex. PS matching was performed in a one-to-one manner between the non-sarcopenia (non-sarcopenic obesity) group and the sarcopenia (sarcopenic obesity) group with the use of calipers of width equal to 0.2 SD of the logit of the PS [22]. After PS matching, we also performed Kaplan–Meier analysis and the log-rank test to assess the prognostic significance of sarcopenia and sarcopenic obesity. Analyses were performed using R version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria) and JMP version 13.2.1 (SAS Institute, Cary, NC, USA) as appropriate. In all analyses, two-tailed p < 0.05 was taken to indicate statistical significance.
for age and sex, sarcopenic obesity showed significant associations with lower grip strength and QIS, slower gait speed, and shorter 6MWD compared to the normal group. In addition, the sarcopenic obesity group tended to have poorer muscle function than the sarcopenic group.

**Associations of sarcopenia and sarcopenic obesity with all-cause mortality**

Forty-five deaths occurred over a median follow-up period of 1.87 years (6.8%, interquartile range: 0.84–4.04). Kaplan–Meier survival curves and multivariate Cox regression analysis for all-cause mortality of sarcopenia and sarcopenic obesity are shown in Fig. 3. After adjusting by EuroSCORE, both sarcopenia and sarcopenic obesity were significantly associated with increased all-cause mortality. In sensitivity analysis, both sarcopenia and sarcopenic obesity were also shown to significantly increase all-cause mortality after PS matching (Supplemental Table T1 and Supplemental Fig. S1).

Fig. 4 shows the results of Kaplan–Meier survival curves for all-cause mortality of the four groups. The results indicated poorer survival only in the sarcopenic obesity group compared to the normal control group (p = 0.019). Table 2 shows the results of

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**Fig. 2.** Associations of body composition with muscle function determined by analysis of covariance (ANCOVA) adjusted for age and sex. Black dots represent adjusted mean values, with error bars representing 95% confidence intervals. N, normal group; O, obesity group; S, sarcopenic group; SO, sarcopenic obesity group; BMI, body mass index; QIS, quadriceps isometric strength; 6MWD, 6-min walking distance. *Significant difference vs. normal group (p < 0.05).

**Fig. 3.** Kaplan–Meier curves of overall survival rate and multivariable Cox regression analysis after adjusting by EuroSCORE according to sarcopenia (left) and sarcopenic obesity (right). Both sarcopenia (log-rank, p < 0.001; adjusted hazard ratio, 2.48; 95% confidence interval, 1.25–4.93) and sarcopenic obesity (log-rank, p = 0.002; adjusted hazard ratio, 2.21; 95% confidence interval, 1.21–4.03) were significantly associated with all-cause mortality. HR, hazard ratio.

**Fig. 4.** Kaplan–Meier curves of overall survival rate according to body composition. The sarcopenic obesity group showed a significantly poorer survival rate than the normal control group (p = 0.021).
univariate and multivariate Cox regression analyses for all-cause mortality. Sarcopenic obesity was a significant predictor of all-cause mortality after adjusting for EuroSCORE (HR, 3.04; 95% CI, 1.25–7.40).

### Discussion

This study performed in a cohort of 664 cardiovascular surgery patients who underwent preoperative CT indicated that sarcopenic obesity, defined by high VAT area with low MA, was associated with reduced levels of muscle function and poorer prognosis. To our knowledge, this is the first report of the utility of sarcopenic obesity determined based on VAT area and muscle density as a predictor of muscle function and prognosis in patients undergoing cardiovascular surgery. In cancer patients, sarcopenic obesity determined by CT was reported to be associated with reduced survival rate [10] and increased rates of postoperative complications [11]. However, there have been few such reports regarding outcomes in patients with cardiovascular disease. Mok et al. [7] reported that cumulative mortality rate was higher in TAVI patients with than without sarcopenic obesity defined based on psoas muscle area and body fat mass, although the difference was not significant. Recently, we reported that psoas MA was a predictor of poorer muscle function and mortality regardless of psoas muscle area in patients undergoing cardiac surgery [9]. Consistent with our previous report, we defined sarcopenic obesity based on psoas MA and VAT in this study, and our results indicated significant associations of sarcopenic obesity with poorer muscle function and poorer prognosis in patients undergoing cardiovascular surgery. To our knowledge, this is the largest study to evaluate sarcopenic obesity using CT imaging in cardiovascular disease patients performed to date.

Kim reported that sarcopenic obesity is more complicated than either sarcopenia or obesity alone, because it is not just the simple combination of sarcopenia and obesity [23]. In our cohort, sarcopenia was related to higher rate of prior heart failure and lower levels of hemoglobin and albumin. Malnutrition and cachexia, caused by chronic diseases, such as heart failure, are considered to be among the causes of sarcopenia [24,25]. On the other hand, sarcopenic obesity was related to higher rates of hypertension, dyslipidemia, diabetes mellitus, and chronic kidney disease. Several previous studies showed that sarcopenic obesity is significantly associated with lower moderate-to-vigorous physical activity [26], sedentary time [26], and number of chronic diseases [26,27]. Lifestyle-related diseases, such as obesity, hypertension, dyslipidemia, and diabetes mellitus, are known to be associated with reduced levels of physical activity. These results suggest that although cachexic symptoms have a similar presentation to sarcopenia, sarcopenic obesity is more complicated.

Both adipose and skeletal muscle tissue are considered as secretory organs [28], with adipocytes and myocytes producing cytokines and myokines, respectively. Insulin resistance and increased levels of inflammatory cytokines are related to VAT [29–31] in patients with myocardial infarction [32]. Skeletal muscle loss is known to produce insulin resistance [33,34], and has also been reported to be associated with major complications following cardiac surgery [35]. This relation may be reflected by the observed association between adipose tissue and skeletal muscle, as dysregulation of cytokine and myokine secretion and production could be involved in the development of excess adiposity, which is a factor in whole-body insulin resistance [36]. In addition, sarcopenic obesity has been reported to be related to reduced levels of vitamin D and elevated risk of hypertension [37,38]. Advanced age is closely associated with poor prognosis in cardiovascular disease, which may be related to reduced nutritional status, including low vitamin D levels [39], low prealbumin level [24], and low serum amino acid concentration [25]. The results of the present study are supported by these previous reports, and these findings may at least partially correspond to the underlying reasons for the association between sarcopenic obesity and poorer survival rate.

This study had several limitations. First, although this study had a larger sample size than in previous studies, it was limited by its single-center observational nature. Second, the overall age of our study population was relatively young. Sarcopenia can be considered a “secondary” finding in cases with one or more other comorbidities, including heart disease [2]. Further studies are required to clarify the external validity of our results in older populations. Finally, we did not have data regarding potential confounding factors, including preoperative physical activity, exercise capacity, and socioeconomic status.

In conclusion, sarcopenic obesity was associated with poorer muscle function and increased mortality rate after cardiovascular surgery. Further studies are required to evaluate the utility of body composition measurement by CT to assess prognosis in patients undergoing cardiovascular surgery. This will allow us to elucidate the clinical roles of preoperative CT and cardiac rehabilitation in these patients.

### Funding

None declared.

### Conflict of interest

The authors have no conflicts of interest to disclose.

### Acknowledgments

We would like to thank the patients and the study team for their participation in this study.

### Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted</th>
<th>Adjusted by EuroSCORE</th>
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</thead>
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<tr>
<td></td>
<td>HR, 95% CI</td>
<td>p-Value</td>
</tr>
<tr>
<td>Normal</td>
<td>1.00</td>
<td>[Reference]</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.00</td>
<td>0.32–3.15</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>2.38</td>
<td>0.96–5.91</td>
</tr>
<tr>
<td>Sarcopenic obesity</td>
<td>3.60</td>
<td>1.50–8.61</td>
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CI, confidence intervals; HR, hazard ratio.
Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi: 10.1016/j.jjcc.2019.02.010.

References


