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ORIGINAL ARTICLE

# Sarcopenia is associated with severe postoperative complications in elderly gastric cancer patients undergoing gastrectomy

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**Abstract**
*Background* Malignancy is a secondary cause of sarcopenia, which is associated with impaired cancer treatment outcomes. The aim of this study was to investigate the prevalence of preoperative sarcopenia among elderly gastric cancer patients undergoing gastrectomy and the differences in preoperative dietary intake and postoperative complications between sarcopenic and non-sarcopenic patients.
*Methods* Ninety-nine patients over 65 years of age who underwent gastrectomy for gastric cancer were analyzed. All patients underwent gait and handgrip strength testing, and whole-body skeletal muscle mass was measured using a bioimpedance analysis technique based on the European Working Group on Sarcopenia in Older People (EWGSOP) algorithm for the evaluation of sarcopenia before surgery. Preoperative dietary intake was assessed using a food frequency questionnaire.
*Results* Of these patients, 21 (21.2 %) were diagnosed with sarcopenia. Sarcopenic patients consumed fewer calories and less protein preoperatively (23.9 vs. 27.8 kcal/kg ideal weight/day and 0.86 vs. 1.04 g/kg ideal weight/day; $P = 0.001$ and 0.0005, respectively). Although the overall incidence of postoperative complications was similar in the two groups (57.1 % vs. 35.9 %; $P = 0.08$), the incidence of severe (Clavien–Dindo grade $\geq$ IIIa) complications was significantly higher in the sarcopenic group than in the non-sarcopenic group (28.6 % vs. 9.0 %; $P = 0.029$). In the multivariate analysis, sarcopenia alone was identified as a risk factor for severe postoperative complications (odds ratio, 4.76; 95 % confidence interval, 1.03–24.30; $P = 0.046$).
*Conclusions* Preoperative sarcopenia as defined by the EWGSOP algorithm is a risk factor for severe postoperative complications in elderly gastric cancer patients undergoing gastrectomy.

**Keywords** Sarcopenia · Postoperative complication · Gastric cancer · Gastrectomy

## Introduction

With aging, there are gradual changes in body composition and progressive, systematic loss of skeletal muscle mass (SM). Since Rosenberg [1] referred to this inevitable age-related phenomenon as sarcopenia in 1989, this term has gained widespread acceptance as a new disease concept. Recently, the European Working Group on Sarcopenia in Older People (EWGSOP) [2] and the Asian Working Group for Sarcopenia [3] recommended adding both loss of muscle strength and functional compromise to loss of muscle mass in the definition of sarcopenia. These working groups have designed a new algorithm for assessing sarcopenia. The prevalence of age-related sarcopenia based on the EWGSOP algorithm in elderly community-dwelling residents in Japan ($n = 4811$) was reported to be 8.2 % for men and 6.8 % for women [4]. Sarcopenia can be also

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caused by malnutrition, low levels of physical activity, and various diseases [5, 6]. Particularly in cancer patients, an excessive systemic inflammatory response can induce insulin resistance, protein hypercatabolism, and metabolic changes [7, 8]. Therefore, the prevalence of sarcopenia in cancer patients is predicted to be higher than in the general elderly population. Furthermore, various studies have shown that inadequate energy and protein intake are independent risk factors for sarcopenia [9, 10] among community-dwelling elderly adults. In gastric cancer patients, insufficient oral intake related to disease-specific symptoms can induce more severe nutritional depletion than in other cancer patients, which may result in an increased prevalence of sarcopenia.

Although sarcopenia is widely recognized as a risk factor for functional limitation, physical disability, decreased quality of life, and ultimately death [2], it remains unclear how greatly sarcopenia affects cancer patients. Recently, the influence of sarcopenia on treatment outcomes in cancer patients has been intensively investigated; sarcopenia was demonstrated to be independently associated with negative short-term [11–18] and long-term [11, 18–20] outcomes after surgery and an increased rate of chemotherapy-related toxicity [21–23].

However, few studies have explored the preoperative nutritional intake of gastric cancer patients with sarcopenia and the influence of sarcopenia on clinical outcomes after gastrectomy, although sarcopenia should be evaluated as a part of risk assessment during planning for gastric surgery.

The purpose of this study was to investigate the prevalence of sarcopenia according to the EWGSOP algorithm [2] and the relationship between sarcopenia and preoperative food intake and postoperative complications among elderly gastric cancer patients undergoing gastrectomy.

## Methods

### Patients and perioperative observations

Between July 2012 and January 2015, a total of 101 gastric cancer patients more than 65 years of age underwent gastrectomy at Osaka National Hospital (ONH). We excluded 2 patients who underwent combined resection of gastric and colorectal cancer; the remaining 99 patients were included in this analysis.

We investigated the preoperative prevalence of sarcopenia and differences in clinicopathological factors, nutrient intake, and postoperative complications between sarcopenic and non-sarcopenic patients.

Among clinical factors, weight loss was defined as a decrease in body weight greater than 5 % in the past 6 months. Preoperative nutritional intake was calculated using a food frequency questionnaire by registered dietitians at ONH on admission before surgery. Not all patients analyzed received intravenous nutrition before surgery, and for patients who received oral nutritional supplements (ONS) at an outpatient clinic, registered dietitians carefully asked them about the amount of ONS taken at home in addition to the amount of dairy diet. Ideal body weight (IBW, kg) was calculated as height$^2$ (m$^2$) × 22 (kg/m$^2$). The total amount of dietary energy (kcal) and protein (g) intake was normalized by IBW. Postoperative complications were graded according to the Clavien–Dindo (CD) classification system [24]. Complications were defined as those that were CD grade II or higher. Complications that were grade IIIa or higher were considered severe complications. Cancer staging was based on the 7th edition of the Union for International Cancer Control (UICC) TNM classification system [25]. All data were extracted from our database and individual patient medical records.

### Screening for sarcopenia

Preoperative screening for sarcopenia was based on diagnostic criteria from the EWGSOP algorithm (Fig. 1) [2]. Gait speed was calculated by dividing the distance of 4 m by the time required (m/s) to walk this distance. A cutoff >0.8 m/s was used to identify the risk for sarcopenia. Handgrip strength was tested twice in each hand using a hand dynamometer, and the average of four values (kg) was analyzed. A cutoff <30 kg for men and <20 kg for women was used to indicate risk of sarcopenia [26]. Subsequently, whole-body SM was measured using a bioimpedance analysis (BIA) measurement technique with a multifrequency body composition analyzer, InBody720 (Biospace) [27]. The skeletal muscle mass index (SMI, kg/m$^2$) was calculated by dividing absolute SM (kg) by height$^2$. Based on EWGSOP recommendations, SMI 8.87 kg/m$^2$ was considered the cutoff for men, compared to 6.42 kg/m$^2$ for women.

### Statistical analysis

Statistical analysis was conducted using JMP software (SAS Institute, Cary, NC, USA). Continuous variables were expressed as medians (range). The $\chi^2$ test or Fisher's exact test was used to compare categorical variables, and the Mann–Whitney *U* test was used to compare continuous variables. Univariate and multivariate logistic regression was performed. *P* values <0.05 were considered statistically significant.

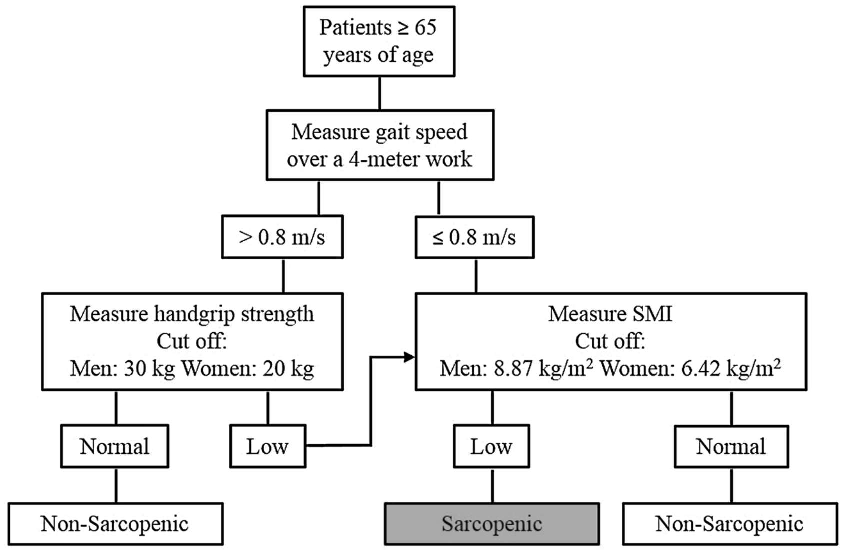


**Fig. 1** European Working Group on Sarcopenia in Older People (*EWGSOP*) algorithm assessing sarcopenia. *SMI* skeletal muscle mass index

## Results

### Patient characteristics

Among the 99 consecutive patients assessed using the EWGSOP algorithm [2], 21 patients (21.2 %) were diagnosed as sarcopenic and the remaining 78 patients (78.8 %) as non-sarcopenic. The prevalence of sarcopenia by age category was 9.1 % of patients aged 65–69 years (2/22 patients), 8.7 % of those aged 70–74 years (2/23 patients), 24.1 % of those aged 75–79 years (7/29 patients), and 40.0 % of those over 80 years (10/25 patients). The prevalence of sarcopenia was remarkably higher among patients more than 75 years of age.

Clinicopathological features and preoperative nutritional intake of the two groups are shown in Table 1. There was no significant difference in age between the two groups (sarcopenic, 78 years, vs. non-sarcopenic, 75 years; $P = 0.10$). Regarding gender, the proportion of men was higher in the sarcopenic group than in the non-sarcopenic group (90.5 % vs. 60.3 %; $P = 0.009$). Of body weight and composition, body mass index (BMI) and lean body mass were lower in the sarcopenic group than in the non-sarcopenic group (19.2 vs. 22.8 kg/m$^2$ and 39.7 vs. 42.7 kg; $P = 0.001$ and 0.03, respectively), and weight loss was more frequently observed in the sarcopenic group than in the non-sarcopenic group (33.3 % vs. 16.7 %; $P = 0.08$), whereas body fat mass was comparable between the two groups (sarcopenic, 13.1, vs. non-sarcopenic, 13.5 kg; $P = 0.40$). Nutritional parameters such as serum albumin and total lymphocyte count were similar (sarcopenic, 4.3 vs. non-sarcopenic, 4.1 g/dl; sarcopenic, 1568 vs. non-sarcopenic, 1793/mm$^3$; $P = 0.40$ and 0.43, respectively). C-reactive protein, a marker of systemic inflammatory reaction, was similar between the two groups (sarcopenic, 0.09, vs. non-sarcopenic, 0.08 mg/dl; $P = 0.74$). On pulmonary function testing, vital capacity and forced expiratory volume in 1.0 s were worse in the sarcopenic group than in the non-sarcopenic group (98.0 % vs. 104.0 % of predicted and 71.9 % vs. 78.0 % of predicted; $P = 0.051$ and 0.045, respectively). With regard to preoperative dietary intake, the sarcopenic group consumed fewer calories and less protein than the non-sarcopenic group [23.9 vs. 27.8 kcal/IBW (kg)/day; 0.86 vs. 1.04 g/IBW (kg)/day; $P = 0.001$ and 0.0005, respectively]. There were no significant differences in surgical procedure type between the two groups, but operative blood loss was higher in the sarcopenic group than in the non-sarcopenic group (210 vs. 163 l; $P = 0.02$). Pathological stage was more advanced in the sarcopenic group than in the non-sarcopenic group ($P = 0.03$). The duration of postoperative hospitalization was comparable between the two groups (sarcopenic, 18 days, vs. non-sarcopenic, 16 days; $P = 0.10$).

### Impact of sarcopenia on postoperative complications

Of 99 patients who underwent gastrectomy, 40 patients developed postoperative complications with morbidity of 40.4 %. Two patients in the sarcopenic group died postoperatively of renal dysfunction and pneumonia, respectively. Figure 2 shows the incidence of postoperative complications in the two groups. Although there was no significant difference in the overall complication rate (sarcopenic, 57.1 %, vs. non-sarcopenic, 35.9 %; $P = 0.08$), severe complications (CD grade IIIa or higher) requiring interventional management or intensive treatment were more frequently observed in the sarcopenic group

**Table 1** Clinicopathological features and nutrient intakes of sarcopenic and non-sarcopenic patients

| | Sarcopenic ($n = 21$) | Non-sarcopenic ($n = 78$) | $P$ value |
|---|---|---|---|
| Age (years) | 78 (67–85) | 75 (66–91) | 0.10 |
| Gender, $n$ (%) | | | 0.009 |
| Men | 19 (90.5) | 47 (60.3) | |
| Women | 2 (9.5) | 31 (39.7) | |
| BMI (kg/m$^2$) | 19.2 (15.6–26.9) | 22.8 (16.8–32.2) | 0.001 |
| Weight loss, $n$ (%) | | | 0.08 |
| Yes | 7 (33.3) | 13 (16.7) | |
| No | 14 (66.7) | 65 (83.3) | |
| Body fat mass (kg)[a] | 13.1 (5.5–28.2) | 13.5 (1.6–32.4) | 0.28 |
| Lean body mass (kg)[a] | 39.7 (23.1–49.8) | 42.7 (30.3–55.9) | 0.03 |
| Serum albumin (g/dl) | 4.3 (2.3–4.9) | 4.1 (2.5–4.9) | 0.40 |
| Total lymphocyte count (/mm$^3$) | 1568 (388–2995) | 1793 (440–3422) | 0.43 |
| CRP (mg/dl) | 0.09 (0.01–4.06) | 0.08 (0.01–12.11) | 0.74 |
| ASA-PS, $n$ (%) | | | 0.85 |
| 1 | 2 (9.5) | 10 (12.8) | |
| 2 | 14 (66.7) | 47 (60.3) | |
| 3 | 5 (23.8) | 21 (26.9) | |
| Vital capacity (%) | 98.0 (59.7–138.4) | 104.0 (55.3–153.6) | 0.051 |
| Forced expiratory volume in 1.0 s (%) | 71.9 (37.6–89.2) | 78.0 (54.0–100.0) | 0.045 |
| Neoadjuvant chemotherapy, $n$ (%) | | | 0.85 |
| Yes | 1 (4.8) | 3 (3.8 %) | |
| No | 20 (95.2) | 75 (96.2 %) | |
| Total caloric intake, kcal/IBW (kg) | 23.9 (15.3–32.3) | 27.8 (12.6–46.0) | 0.001 |
| Protein intake, g/IBW (kg) | 0.86 (0.51–1.56) | 1.04 (0.43–1.94) | 0.0005 |
| Type of surgery, $n$ (%) | | | 0.91 |
| Total gastrectomy | 7 (33.3) | 27 (34.6) | |
| Partial gastrectomy[b] | 14 (66.7) | 51 (65.4) | |
| Lymph node dissection, $n$ (%) | | | 0.14 |
| D0/1 | 9 (42.9) | 32 (41.0) | |
| D2 or higher | 16 (57.1) | 46 (59.0) | |
| Operative time (min) | 291 (172–530) | 279 (120–561) | 0.34 |
| Operative blood loss (ml) | 210 (60–2900) | 163 (10–1450) | 0.02 |
| UICC pathological stage, $n$ (%) | | | 0.03 |
| I | 7 (33.3) | 41 (52.6) | |
| II | 2 (9.5) | 19 (24.4) | |
| III | 9 (42.9) | 14 (17.9) | |
| IV | 3 (14.3) | 4 (5.1) | |
| Postoperative hospital stay (days) | 18 (4–104) | 16 (9–152) | 0.10 |

*BMI* body mass index, *CRP* C-reactive protein, *ASA-PS* American Society of Anesthesiologists physical status, *IBW* ideal body weight, *UICC* Union for International Cancer Control

[a] Body composition was measured using a multifrequency body composition analyzer, InBody720 (Biospace) [27]

[b] Partial gastrectomy includes distal gastrectomy and proximal gastrectomy

than in the non-sarcopenic group (28.6 % vs. 9.0 %; $P = 0.029$). Severe complications included intraabdominal abscess ($n = 1$), anastomotic leakage ($n = 1$), pneumonia ($n = 3$), and renal dysfunction ($n = 1$) in the sarcopenic group, and intraabdominal abscess ($n = 1$), anastomotic leakage ($n = 1$), deep incisional surgical site infection (SSI) ($n = 2$), pneumonia ($n = 2$), and arrhythmia ($n = 1$) in the non-sarcopenic group. Additionally, we divided postoperative complications into SSIs and non-SSIs. The occurrence of SSI was similar in the two groups, but the

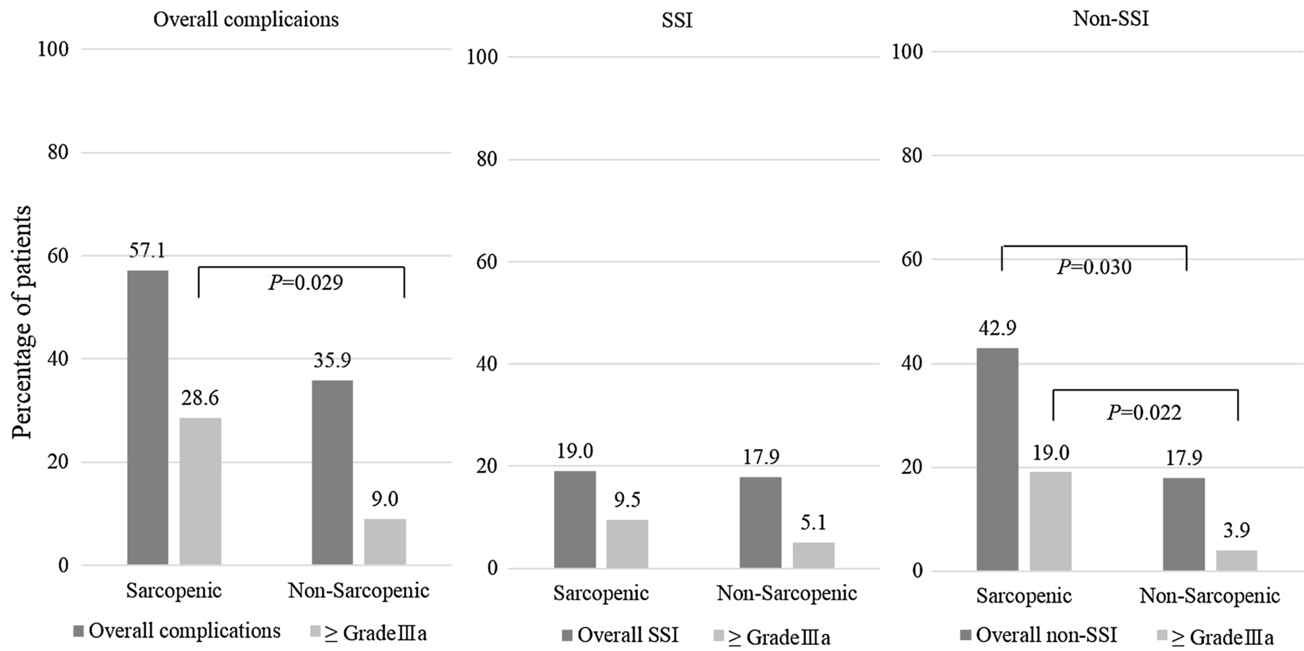


**Fig. 2** Incidence of postoperative complications in sarcopenic and non-sarcopenic patients. *SSI* surgical site infection. Complications were graded according to the Clavien–Dindo classification system [24]

**Table 2** Risk factors for severe postoperative complications in patients with gastric cancer

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95 % CI | *P* value | Odds ratio | 95 % CI | *P* value |
| Age (≥75 vs. <75 years) | 2.9 | 0.82–13.59 | 0.10 | 1.92 | 0.43–10.86 | 0.40 |
| Gender (men vs. women) | 1.79 | 0.50–8.41 | 0.39 | 1.16 | 0.25–6.39 | 0.86 |
| Serum albumin (<4 vs. ≥4 g/dl) | 1.78 | 0.53–5.84 | 0.34 | 2.03 | 0.50–8.32 | 0.31 |
| ASA PS (3 vs. 1 or 2) | 2.83 | 0.83–9.50 | 0.096 | 2.81 | 0.69–11.70 | 0.15 |
| Neoadjuvant chemotherapy (yes vs. no) | 2.31 | 0.11–19.75 | 0.51 | 5.74 | 0.21–88.11 | 0.25 |
| Type of surgery (total gastrectomy vs. partial gastrectomy) | 1.23 | 0.34–4.02 | 0.74 | 1.13 | 0.25–4.86 | 0.87 |
| Lymph node dissection (D2 or higher vs. D0 or D1) | 1.40 | 0.42–5.50 | 0.59 | 1.30 | 0.31–6.24 | 0.72 |
| Operative blood loss (≥400 vs. <400 ml) | 2.29 | 0.56–8.15 | 0.23 | 1.55 | 0.27–8.01 | 0.61 |
| Operative time (≥240 vs. <240 min) | 1.37 | 0.38–6.47 | 0.65 | 1.13 | 0.21–7.18 | 0.89 |
| UICC pathological stage (III or IV vs. I or II) | 1.02 | 0.26–3.46 | 0.97 | 0.56 | 0.10–2.50 | 0.46 |
| Sarcopenia (yes vs. no) | 4.06 | 1.16–14.00 | 0.029 | 4.76 | 1.03–24.30 | 0.046 |

*CI* confidence interval, *ASA-PS* American Society of Anesthesiologists physical status, *UICC* Union for International Cancer Control

overall non-SSI rate and the severe non-SSI rate were significantly higher in the sarcopenic group than in the non-sarcopenic group (42.9 % vs. 18.0 %, $P = 0.022$; 19.1 % vs. 3.9 %, $P = 0.030$; respectively). In particular, pneumonia was the most frequently observed severe non-SSI complication in both groups, at 14.3 % in the sarcopenic group and 2.6 % in the non-sarcopenic group ($P = 0.030$).

Risk factors for severe postoperative complications are shown in Table 2. The overall risk of a severe complication was analyzed considering various background factors, including the presence of sarcopenia. In the multivariate analysis, the presence of sarcopenia was the only significant risk factor for severe postoperative complications (odds ratio, 4.76; 95 % confidence interval, 1.03–24.30; $P = 0.046$).

## Discussion

Surgery remains the most prominent curative treatment for gastrointestinal malignancies. Postoperative complications may not only impair healthy lifestyles and increase healthcare costs, but also diminish adherence to postoperative treatment, which results in poorer oncological outcomes [29]. In this respect, stratification of surgical candidates by the risk of postoperative complications is important, but doing so remains challenging. Moreover, understanding what causes geriatric disorders is essential in a rapidly aging society. Sarcopenia, an important contributor to frailty in aging individuals, is a decline in muscle mass and physical function primarily induced by aging [5] and secondarily caused by malignancy [6]. It has previously been found to be associated with adverse postoperative outcomes after resection of colorectal cancer [12, 13], pancreatic cancer [17], hepatocellular carcinoma [11, 15], metastatic liver cancer [14], and perihilar cholangiocarcinoma [16]. In the current study, we demonstrated that sarcopenia is prevalent among elderly gastric cancer patients before surgery; calories and protein from food intake were insufficient in sarcopenic patients, and they had a higher incidence of severe postoperative complications.

Mourtzakis and colleagues [30] reported that the cross-sectional area of skeletal muscle at the level of the third lumbar vertebra was directly correlated with whole-body SM in cancer patients. Computed tomography (CT) imaging has been most frequently used to predict preoperative sarcopenia and investigate the relationship between sarcopenia and postoperative outcomes. However, methods for evaluating total mass of the psoas [14–17], SM [11–13, 31], or total volume of the psoas major [15] and cutoff points for sarcopenia differ across studies because of the difficulty in comparing sarcopenic candidates to healthy young adults in term of radiation exposure. How to best characterize sarcopenia remains to be elucidated. On the other hand, BIA measurement is inexpensive and does not involve radiation exposure. Since prediction equations with age, gender, physical status, and race have been developed, this technique has high reliability in healthy adults, comparable to CT or magnetic resonance imaging (MRI) [32]. In addition, it was reported that this technique could provide accurate estimate of SM for hospitalized elderly patients with clinical disorders [33]. When we adopted this method to identify sarcopenia, cutoffs of 8.87 kg/m$^2$ for men and 6.42 kg/m$^2$ for women were chosen based on data from community-dwelling residents in Taiwan [28], which are considered applicable to Japanese patients.

The presence of both low SM and low muscle function are essential to the definition of sarcopenia. It had been reported that decline of SM alone does not affect the incidence of postoperative complications [11, 17, 31]. Muscle density (quality), but not muscle mass, is a significant predictor of severe postoperative complications in pancreatic cancer [17]. In our study, five patients whose SMI was lower than the cutoff but who had normal gait speed and handgrip strength (defined as non-sarcopenic according to the EWGSOP algorithm [2]) did not develop severe postoperative complications, indicating that both muscle function and SM influence the occurrence of postoperative complications.

Sarcopenia in cancer is conceptionally similar to cancerous cachexia, which is associated with cancer progression and sequential dystrophy. Fearon et al. [34] classified cancerous cachexia as precachexia, cachexia, and refractory cachexia, with the presence of sarcopenia as a key component of cachexia. In addition, involuntary weight loss and low BMI are frequently the first symptoms observed in cancer patients [35]; these symptoms place them in the first phase of cachexia [34]. In fact, preoperative sarcopenia was associated with lower BMI in previous studies [11–14, 16] as well as in the current study, and weight loss was more frequently observed in the sarcopenic patients with gastric cancer in our series; it might be associated with more advanced disease stage and decreased food intake in our study. In contrast, serum albumin, routinely monitored as a nutritional parameter, was similar in the sarcopenic and non-sarcopenic groups. Although few studies have demonstrated a relationship between preoperative sarcopenia and serum albumin levels, we speculated that decreases in serum albumin are observed as patients move closer to the stage of refractory cachexia and that this decrease may not be observed early in cachexia.

Several studies have reported that sarcopenia is independently associated with severe postoperative complications (CD grade IIIa or higher) [14, 16, 17], consistent with our findings in this study. In addition, we examined postoperative complications in more detail. Sarcopenia is not a predictor of anastomotic leakage [31], which is often a fatal SSI after resection of colorectal cancer. We showed that sarcopenia is not associated with SSIs including anastomotic leakage, pancreatic fistula, and intraabdominal abscess, but sarcopenia is associated with non-SSI complications, particularly pneumonia. Sarcopenia had been reported as a risk factor for pneumonia because of decline in the ability to perform activities of daily living and poor chewing and swallowing function in the elderly general populations [36]. The high incidence of pneumonia in sarcopenic patients may be caused by delayed mobilization, sequential paralytic ileus, dysphagia, or difficulty with clearing the airway after gastrointestinal surgery. Sarcopenia was found to be an independent predictor of postoperative respiratory complications in esophageal cancer patients [37]. In this study, preoperative respiratory function was worse in the sarcopenic group, which might have adverse effects on postoperative respiratory complications.

Preoperative intervention is important for treating sarcopenia and preventing severe postoperative complications. Provision of adequate energy and protein intake and resistance training are key components in the management of sarcopenia that have been studied in community-dwelling elderly adults [38, 39]. Based on our finding that elderly gastric cancer patients with sarcopenia received significantly fewer dietary calories and less protein, sarcopenic patients should be provided appropriate nutritional support with adequate energy and protein intake preoperatively in addition to resistance training.

The current study has several limitations. Regarding measurement of skeletal muscle, reliability of the BIA technique has not completely established because limited studies have showed the appropriateness of BIA technique for patients with cancer who are regulated by a number of cancer-related pathological conditions. Further investigation is required to accommodate the BIA technique for cancer patients. Additionally, this was a single-center retrospective observational study and the sample size was small. A validation study with large sample size will be necessary to confirm the impact of preoperative sarcopenia on postoperative complications.

In conclusion, sarcopenia, as assessed by the EWGSOP algorithm, is prevalent among elderly gastric cancer patients. Sarcopenia is associated with lower preoperative dietary intake of calories and protein as well as the development of severe postoperative complications.

**Compliance with ethical standards**

**Ethical standards** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients for inclusion in the study.

**Conflict of interest** We declare that we have no conflicts of interest.

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