Computed tomography–quantified body composition predicts short-term outcomes after gastrectomy in gastric cancer

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ABSTRACT

Background Malnutrition is a common and critical problem that influences outcome in cancer patients. Body composition reflects a patient’s metabolic profile and physiologic reserves, which might be the true determinant of prognosis. In the present study, which aimed to identify valuable new prognostic indicators, we investigated the association between computed tomography–quantified body composition and short-term outcomes after gastrectomy for gastric cancer.

Methods Skeletal muscle index, mean muscle attenuation, and ratio of visceral-to-subcutaneous adipose tissue area ($vsa$) were calculated from preoperative computed tomography images. Low skeletal muscle index, low mean muscle attenuation, and high $vsa$ were respectively termed “sarcopenia,” “myosteatosis,” and “visceral obesity.” The association of body composition with postoperative complications and serum markers of nutrition and inflammation after radical gastrectomy were analyzed.

Results The overall complication rate was significantly higher in the sarcopenia (62.5% vs. 27.3%, $p = 0.001$) and myosteatosis groups (38.2% vs. 4%, $p = 0.002$). Patients with visceral obesity had a higher incidence of inflammatory complications (20.3% vs. 6.5%, $p = 0.01$). Multivariate logistic regression analysis demonstrated that sarcopenia ($p = 0.013$), myosteatosis ($p = 0.017$), and low serum retinol-binding protein ($p = 0.019$) were independent risk factors for overall complications. Compared with control subjects, patients with sarcopenia had lower postoperative levels of serum retinol-binding protein ($p = 0.007$), and patients with visceral obesity had higher levels of C-reactive protein ($p = 0.026$).

Conclusions Sarcopenia, myosteatosis, and visceral obesity were significantly associated with increased rates of postoperative complications and affected the postoperative nutrition and inflammation status of patients with gastric cancer.

Key Words Body composition, sarcopenia, myosteatosis, visceral obesity, gastrectomy, complications

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INTRODUCTION

Globally, gastric cancer is one of the most commonly diagnosed cancers and a leading cause of cancer-related death. In 2013 in China, it was estimated that 427,000 new cases of gastric cancer and 301,000 deaths from the disease occurred worldwide, accounting for half the global incidence and deaths. The most effective therapy for potentially curable gastric cancer is surgical resection. However, radical surgery is associated with high rates of complications and operative mortality, severely negatively affecting prognosis in these patients. Objective and precise prognostic assessments before radical gastrectomy are therefore critical so that physicians can...
predict postoperative clinical outcomes and guide the therapeutic protocol.

Malnutrition and weight loss are common problems in cancer patients, the pathophysiology of which consists of a mixture of reduced food intake and disturbance of the metabolic and inflammatory responses. Those factors have been recognized to increase the risk for surgical complications and to be associated with longer hospital stays, increased health care costs, lower quality of life, and shorter survival. Assessing the nutrition status of these patients before surgery and rendering the appropriate nutrition support is therefore important to optimize status, decrease complications, and improve clinical outcomes.

Identification of patients who are at nutritional risk and who have malnutrition is the first step in the nutrition care pathway. Commonly used tools for nutrition assessment such as body mass index (BMI) or Nutritional Risk Screening (NRS) 2002 are limited because of their inability to assess individual components of body weight such as regional fat distribution and muscle volume and composition. On the other hand, nutrition assessments based on body composition measurements (BCMs) can reflect body shape and composition, metabolic profile, and physiologic reserve, which might affect the perioperative inflammatory response and nutrition metabolism and be a true determinant of prognosis

It has been reported that visceral obesity, rather than BMI, is an independent risk factor for recurrence of hepato-cellular carcinoma in patients with non-viral disease. Loss of muscle mass, called sarcopenia, has been found in 19%–74% of patients with solid tumors, and it is an independent risk factor for complications and survival after surgical resection. The mean muscle attenuation (MA), measured in mean Hounsfield units during routine computed tomography (CT) imaging, indicates muscle composition. Low MA, known as myosteatosis, indicates increased intramuscular lipid content that contributes to muscle weakness. Myosteatosis has previously been reported to be associated with postoperative mortality after hepatocellular carcinoma resection.

Thus, in the present study, we explored the association of body composition assessed by preoperative CT with postoperative complications and markers of nutrition and inflammation in patients undergoing radical surgery for gastric cancer. We aimed to identify prognostic BCMs that can predict short-term outcomes after gastrectomy and guide the therapeutic protocol.

**METHODS**

**Patients and Data Collection**

The study protocol was approved by the Ethics Committee of Jinling Hospital. All procedures involving human participants conformed to the ethics standards of the institutional or national research committee (or both) and the 1964 Helsinki Declaration and its later amendments. Written informed consent was obtained from all patients participating in the study.

The study included all consecutive patients with gastric cancer undergoing open radical gastrectomy at the Department of General Surgery at Jinling Hospital from September 2015 to March 2017. Inclusion criteria were age 18–80 years, histologically proven gastric adenocarcinoma before surgery, availability of digitally-stored CT imaging taken within 15 days before surgery, and no history of previous abdominal surgery. Patients with metastatic cancer and those undergoing laparoscopic-assisted surgery or combined organ resection were excluded. The operations were performed by a single group of specialized surgeons with extensive experience in radical resections for gastric cancer. All patients were managed according to the Japanese gastric cancer treatment guidelines (version 3, 2010).

The following data were collected by trained surgeons and maintained in a digital database: clinicopathologic features (age, sex, BMI, NRS 2002 score, presence of diabetes and other comorbidities, neoadjuvant chemotherapy, type of resection and reconstruction, histologic type, and TNM tumor stage); body composition variables and laboratory parameters associated with nutrition and inflammation status (albumin, prealbumin, transferrin, retinol-binding protein (RBP), C-reactive protein (CRP), procalcitonin, and interleukin 6); and postoperative outcomes (complications, time of intestinal exhaust, gastric drainage, abdominal drainage, albumin use, and postoperative hospital stay). Postoperative complications were graded using the Clavien–Dindo system. Overall complications were defined as those of Clavien–Dindo grade 2 or higher. Inflammatory complications such as infection at the surgical site, pneumonia, infection of the gastrointestinal system, and bloodstream infection were defined using the National Healthcare Safety Network criteria established by the U.S. Centers for Disease Control and Prevention. Cancer staging was based on the 7th edition of the TNM classification system published by the Union for International Cancer Control.

**Imaging Analysis**

The OsiriX open-source software (version 8.5.2: Pixmeo SARL, Geneva, Switzerland) was used to analyze the CT imaging according to a previously described protocol. A single slice at L3, with both transverse processes visible, was extracted to determine the skeletal muscle and abdominal adipose tissue area. These tissue-specific thresholds, as previously described, were used: −29 HU to 150 HU for skeletal muscle; −190 HU to −30 HU for subcutaneous adipose tissue; and −150 HU to −50 HU for visceral adipose tissue. Each specific tissue area was normalized to the square of the patient’s height (m²), resulting in a skeletal muscle index (SMI), a subcutaneous adipose tissue index, and a visceral adipose tissue index. We calculated the MA by averaging the Hounsfield units of the L3 skeletal muscle to assess skeletal muscle composition and the visceral-to-subcutaneous ratio of adipose tissue area (VSR) to explore abdominal adipose tissue distributions. Sarcopenia was accepted when the SMI was 34.9 cm²/m² or less for women and 40.8 cm²/m² or less for men (cut-off values determined in a very large cohort of Chinese patients). Myosteatosis was accepted when the MA was 44.4 HU or less in men and 39.3 HU or less in women, and visceral obesity was accepted when the VSR was 1.33 or greater in men and 0.93 or greater in women (based on a prior report from Japan).
Statistics
Quantitative variables are expressed as means and standard deviations (normally distributed data) or medians with interquartile ranges (non-normally distributed data). Categorical variables are expressed as numbers and percentages. Groups were compared using the Student t-test for normally distributed data, the Pearson chi-square test or Fisher exact test for categorical variables, and the Mann–Whitney U-test for non-normally distributed continuous data and ranked data. Univariate and multivariate analyses of postoperative complications were performed using logistic regression, and the results are presented as odds ratios (ors) with 95% confidence intervals (cIs). Variables significant in the univariate model were entered into the multivariate models. Repeated-measures linear regression models were used to account for the dependency of the observations over time and to analyze the effect of body composition over time on changes in markers of nutrition and inflammation. Values of \( p < 0.05 \) were considered statistically significant. All data were analyzed using the IBM SPSS Statistics software application (version 23.0: IBM, Armonk, NY, U.S.A.).

RESULTS

Patient Characteristics
Of the 187 patients who met the inclusion criteria, 31 (16.6%) were excluded (7 with metastatic cancer incurable by radical surgery, 10 who had undergone combined organ resection, and 14 who had undergone laparoscopic-assisted surgery), leaving 156 patients [115 men (73.7%), 41 women (26.3%)] available for analysis.

Table 1 summarizes the demographic and clinical characteristics of the patients. Mean age in the cohort was 59.1 years. The TNM stage distribution showed 48 patients with stage I disease (30.8%), 27 with stage II disease (17.3%), and 81 with stage III disease (51.9%). Neoadjuvant chemotherapy was administered to 35 patients (22.4%) with unresectable locally advanced gastric cancer. Although 31.7% of the patients were found to be at nutritional risk (NRS 2002 score \( \geq 3 \)), only 6.4% (10 patients) had a BMI less than 18.5. The mean preoperative values for serum markers of nutrition, inflammatory cytokines, and other laboratory parameters were within normal range.

Using the OsiriX software, body composition variables were calculated based on CT imaging (supplementary Figure 1). The mean SMI, MA, subcutaneous adipose tissue index, visceral adipose tissue index, and VSR were, respectively, 50.7 ± 7.9 cm²/m², 36.4 ± 5.8 HU, 32.6 ± 17.0 cm²/m², 43.9 ± 28.9 cm²/m², and 1.3 ± 0.6 in men, and 40.6 ± 6.6 cm²/m², 30.8 ± 6.4 HU, 55.5 ± 28.0 cm²/m², 37.4 ± 23.5 cm²/m², and 0.7 ± 0.6 in women.

We subsequently investigated the associations between body composition and clinicopathologic characteristics in the patients (Table 1). Patients were divided into groups with and without sarcopenia, myosteatosis, and visceral obesity based on the criteria previously discussed. According to those criteria, 24 patients (15.4%) had sarcopenia, 131 patients (84.0%) had myosteatosis, and 64 patients (41.0%) had visceral obesity. Visceral obesity was more frequently seen in men (\( p < 0.001 \)). Patients

| TABLE I Baseline characteristics of the study patients |
|------------------------------|------------------|
| Characteristic | Value |
|------------------------------|------------------|
| Patients (n) | 156 |
| Sex [n (%)] | |
| Men | 115 (73.7) |
| Women | 41 (26.3) |
| Mean age (years) | 59.1 ± 9.9 |
| Mean BMI (kg/m²) | 23.3 ± 3.3 |
| BMI group [n (%)] | |
| <18.5 | 10 (6.4) |
| 18.5–25 | 97 (62.2) |
| >25 | 49 (31.4) |
| NRS 2002 score [n (%)] | |
| <3 | 91 (58.3) |
| ≥3 | 65 (41.7) |
| Diabetes [n (%)] | |
| Yes | 10 (6.4) |
| No | 146 (93.6) |
| Other comorbidities [n (%)] | |
| Yes | 62 (39.7) |
| No | 94 (60.3) |
| Neoadjuvant chemotherapy [n (%)] | |
| Yes | 35 (22.4) |
| No | 121 (77.6) |
| Gastrectomy type [n (%)] | |
| Subtotal | 111 (71.2) |
| Total | 45 (28.8) |
| Histologic type [n (%)] | |
| Poorly differentiated | 100 (64.1) |
| Moderately differentiated | 50 (32.1) |
| Well differentiated | 6 (3.8) |
| TNM stage [n (%)] | |
| I | 48 (30.8) |
| II | 27 (17.3) |
| III | 81 (51.9) |
| Markers of nutrition in serum (mean) | |
| IGF-1 (µg/L) | 125.3 ± 59.7 |
| Albumin (g/L) | 42.5 ± 4.3 |
| Prealbumin (mg/L) | 213.0 ± 59.9 |
| Transferrin (g/L) | 3.1 ± 0.7 |
| Retinol-binding protein (mg/L) | 33.7 ± 17.9 |
| Inflammatory cytokines in serum [median (IQR)] | |
| C-Reactive protein (mg/L) | 0.7 (0.5–1.68) |
| Procalcitonin (µg/L) | 0.046 (0.034–0.064) |
| Interleukin 6 (ng/L) | 3.57 (1.5–6.32) |
| Other major laboratory indicators | |
| Mean hemoglobin (g/L) | 127.9 ± 21.5 |
| Mean platelets (×10⁹/L) | 185.3 ± 77.3 |
| Mean lymphocytes (×10⁹/L) | 1.5 ± 0.5 |
| Mean alanine transaminase (U/L) | 21.7 ± 14.3 |
| Mean creatinine (µmol/L) | 69.6 ± 16.0 |
with sarcopenia (p = 0.004), myosteatosis (p < 0.001), and visceral obesity (p = 0.003) were significantly older than patients without those conditions. Patients with sarcopenia had a significantly lower BMI (p = 0.002) and NRS 2002 score (p < 0.001). Serum markers of nutrition, including insulin-like growth factor 1 (p = 0.022), albumin (p = 0.003), prealbumin (p < 0.001), and hemoglobin (p = 0.013) were also significantly lower in the sarcopenia group. However, patients with visceral obesity had a significantly higher BMI (p < 0.001), serum CRP (p = 0.049), and serum creatinine (p = 0.005), and lower serum RBP (p = 0.048). Serum CRP and interleukin 6 were higher in patients with myosteatosis, but not significantly so (p = 0.058 and p = 0.062 respectively). Of sarcopenia, myosteatosis, and visceral obesity, none was significantly associated with tumour histologic type, TNM stage, or preoperative comorbidities.

**Short-Term Surgical Outcomes**

In terms of short-term surgical outcomes, 51 patients (32.7%) experienced postoperative complications, and 19 (12.2%) experienced inflammatory complications. The inflammatory complications included anastomotic leakage (n = 7), wound infection (n = 1), intra-abdominal infection (n = 3), pneumonia (n = 6), and bloodstream infection (n = 2). The median postoperative hospital stay was 8 days (Table III).

The associations between body composition parameters and clinical outcomes were also investigated (Table III). The results showed that the overall complication rate was significantly higher in the sarcopenia group (62.5% vs. 27.3%, p = 0.001) and in the myosteatosis group (38.2% vs. 4%, p = 0.002). Patients with visceral obesity had a higher

**FIGURE 1** Relationship between body composition and perioperative changes in markers of nutrition and inflammation. Serum retinol-binding protein (RBP) and C-reactive protein (CRP) were measured preoperatively (preop) and on postoperative days 1, 3, and 5 (post1d, post3d, post5d). The differences in serum RBP and CRP over time were compared for the patients with and without sarcopenia, myosteatosis, and visceral obesity. *p < 0.05.

### TABLE I

| Characteristic                  | Value  |
|--------------------------------|--------|
| Mean skeletal muscle index (cm²/m²) |        |
| Overall                        | 48.0±8.8 |
| In men                         | 50.7±7.9 |
| In women                       | 40.6±6.6 |
| Mean muscle attenuation (HU)   |        |
| Overall                        | 34.9±6.4 |
| In men                         | 36.4±5.8 |
| In women                       | 30.8±6.4 |
| Mean SATI (cm²/m²)             |        |
| Overall                        | 38.5±23.0 |
| In men                         | 32.6±17.0 |
| In women                       | 55.5±28.0 |
| Mean VATI (cm²/m²)             |        |
| Overall                        | 42.1±27.8 |
| In men                         | 43.9±28.9 |
| In women                       | 37.4±23.5 |
| Mean VSR                       | 1.16±0.7 |
| In men                         | 1.3±0.6  |
| In women                       | 0.7±0.6  |

BMI = body mass index; NRS = Nutritional Risk Screening; IGF-1 = insulin-like growth factor 1; SATI = subcutaneous adipose tissue index; VATI = visceral adipose tissue index; VSR = visceral-to-subcutaneous ratio of adipose area.
### TABLE II  Association between body composition and clinicopathologic characteristics in the study patients

| Characteristic | Sarcopenia | | Myosteatosis | | Visceral obesity | |
|---------------|-----------|-----------|--------------|-----------|--------------|-----------|
|               | Yes       | No        | p Value      | Yes       | No        | p Value      |
| Sex [n (%)]   |           |           |              |           |           | <0.001      |
| Men           | 17 (70.8) | 98 (74.2) | 0.727        | 96 (73.3) | 19 (76.0) | 0.777       |
| Women         | 7 (29.2)  | 34 (25.8) |              | 35 (26.7) | 6 (24.0)  |              |
| Mean age (years) | 64.5±9.4 | 58.1±9.7  | 0.004        | 61.0±8.0  | 49.0±12.6 | <0.001      |
| Mean BMI (kg/m²) | 21.5±3.4 | 23.6±3.1  | 0.002        | 23.39±3.31| 22.88±2.98| 0.474       |
| BMI group [n (%)] |           |           |              |           |           |             |
| <18.5         | 5 (20.8)  | 5 (3.8)   |              | 9 (6.9)   | 1 (4.0)   |            |
| 18.5–25       | 17 (70.8) | 80 (60.6) |              | 80 (61.1) | 17 (68.0) | 34 (53.1)   |
| >25           | 2 (8.3)   | 47 (35.6) |              | 42 (32.1) | 7 (28.0)  | 63 (68.5)   |
| NRS 2002 score group [n (%)] |           |           |              |           |           | 0.742       |
| <3            | 5 (20.8)  | 87 (65.9) | <0.001       | 76 (58.0) | 16 (64.0) | 0.577       |
| ≥3            | 19 (79.2) | 45 (34.1) |              | 55 (42.0) | 9 (36.0)  |              |
| Diabetes [n (%)] |           |           |              |           |           | 0.319       |
| Yes           | 1 (4.2)   | 9 (6.8)   | 0.972        | 10 (7.6)  | 0 (0.0)   | 0.367       |
| No            | 23 (95.8) | 123 (93.2) |              | 121 (92.4)| 25 (100.0)|             |
| Other comorbidities [n (%)] |           |           |              |           |           | 0.418       |
| Yes           | 12 (50)   | 50 (37.9) | 0.264        | 76 (58.0) | 7 (28.0)  | 0.19        |
| No            | 12 (50)   | 82 (62.1) |              | 55 (42.0) | 18 (72.0) | 23 (35.9)   |
| Neoadjuvant CTx [n (%)] |           |           |              |           |           | 0.596       |
| Yes           | 7 (29.2)  | 28 (21.1) | 0.39         | 30 (22.9)| 5 (20.0)  | 0.802       |
| No            | 17 (70.8) | 104 (78.8)|              | 101 (77.1)| 20 (80.0) | 13 (20.3)   |
| Gastrectomy type [n (%)] |           |           |              |           |           | 0.103       |
| Subtotal      | 17 (70.8) | 94 (71.2) | 0.97         | 91 (69.5)| 20 (80.0) | 41 (64.1)   |
| Total         | 7 (29.2)  | 38 (28.8) |              | 40 (30.5)| 5 (20.0)  | 23 (35.9)   |
| Histologic type [n (%)] |           |           |              |           |           | 0.797       |
| Poorly differentiated | 15 (62.5)| 85 (64.4) | 0.505        | 82 (62.6)| 18 (72.0) | 43 (67.2)   |
| Moderately differentiated | 9 (37.5)| 41 (31.1) |              | 45 (34.4)| 5 (20.0)  | 19 (29.7)   |
| Well differentiated | 0 (0)   | 6 (4.5)   |              | 4 (3.1)  | 2 (8.0)   | 2 (3.1)     |
| TNM stage [n (%)] |           |           |              |           |           | 0.106       |
| I             | 3 (12.5)  | 45 (34.1) | 0.107        | 38 (29.0)| 10 (40.0) | 14 (21.9)   |
| II            | 5 (20.8)  | 22 (16.7) |              | 25 (19.1)| 2 (8.0)   | 14 (21.9)   |
| III           | 16 (66.7)| 65 (49.2) |              | 68 (51.9)| 13 (52.0) | 36 (56.3)   |
| Characteristic | Sarcopenia | | | | Myosteatosis | | | | | | Visceral obesity | | | |
|---------------|------------|--------|--------|--------|------------|--------|--------|--------|--------|------------|--------|--------|
|               | Yes | No | p Value | Yes | No | p Value | Yes | No | p Value |
| Nutrition indicators in serum (mean) | | | | | | | | | | | | | | |
| IGF-1 (μg/L) | 104.7±66.2 | 134.8±57.2 | 0.022 | 129.0±57.4 | 136.1±70.1 | 0.585 | 139.0±63.2 | 123.9±56.3 | 0.12 |
| Albumin (g/L) | 40.1±4.9 | 42.9±4.1 | 0.003 | 42.4±4.4 | 42.9±4.2 | 0.599 | 42.6±4.7 | 42.4±4.1 | 0.802 |
| Prealbumin (mg/L) | 171.1±56.1 | 220.6±57.5 | <0.001 | 210.6±60.0 | 225.4±58.9 | 0.258 | 213.6±60.8 | 212.6±59.6 | 0.923 |
| Transferrin (g/L) | 2.9±0.5 | 3.1±0.8 | 0.109 | 3.1±0.8 | 2.9±0.5 | 0.246 | 3.2±1.0 | 3.1±0.4 | 0.384 |
| RBP (mg/L) | 28.3±16.9 | 34.6±18 | 0.112 | 33.5±19.0 | 34.6±11.6 | 0.785 | 30.3±12.8 | 36.0±20.5 | 0.048 |
| Serum inflammatory cytokines | | | | | | | | | | | | | | |
| C-Reactive protein (mg/L) | | 0.057 | 0.058 | 0.049 |
| Median | 1.15 | 0.6 | 0.8 | 0.5 | 0.85 | 0.65 |
| IQR | (0.5–8.5) | (0.5–1.5) | (0.5–1.95) | (0.5–0.9) | (0.5–2.75) | (0.5–1.28) |
| Procalcitonin (μg/L) | 0.487 | 0.752 | 0.481 |
| Median | 0.046 | 0.046 | 0.045 | 0.049 | 0.045 | 0.047 |
| IQR | (0.033–0.058) | (0.034–0.065) | (0.034–0.066) | (0.043–0.058) | (0.034–0.065) | (0.034–0.064) |
| Interleukin 6 (ng/L) | 0.235 | 0.062 | 0.445 |
| Median | 4.66 | 3.49 | 3.7 | 1.95 | 3.97 | 3.25 |
| IQR | (2.28–6.81) | (1.5–6.28) | (1.5–6.52) | (1.5–4.0) | (1.5–6.36) | (1.5–6.29) |
| Other major laboratory indicators (mean) | | | | | | | | | | | | | | |
| Hemoglobin (g/L) | 118±22.4 | 130±20.9 | 0.013 | 126.9±20.6 | 133.5±25.0 | 0.155 | 129.7±23.2 | 126.2±20.3 | 0.392 |
| Platelets (× 10^9/L) | 199±87 | 182.8±75.5 | 0.344 | 180.2±77.0 | 212.0±75.1 | 0.059 | 179.2±73.4 | 189.5±80.1 | 0.419 |
| Lymphocytes (× 10^9/L) | 1.5±0.7 | 1.5±0.5 | 0.974 | 1.5±0.6 | 1.7±0.4 | 0.17 | 1.5±0.5 | 1.5±0.5 | 0.537 |
| ALT (U/L) | 18.5±9.4 | 22.2±15 | 0.236 | 21.7±14.6 | 21.6±12.9 | 0.984 | 21.7±13.6 | 21.6±14.9 | 0.963 |
| Creatinine (μmol/L) | 66.7±15.1 | 70.2±16.2 | 0.328 | 69.2±15.2 | 71.6±19.8 | 0.494 | 73.9±15.7 | 66.7±15.6 | 0.005 |

BMI = body mass index; NRS = Nutritional Risk Screening; CTx = chemotherapy; IGF-1 = insulin-like growth factor 1; RBP = retinol-binding protein; IQR = interquartile range; ALT = alanine transaminase.
### TABLE III  Postoperative outcomes

| Characteristic | All patients (n=156) | Sarcopenia | Myosteatosis | Visceral obesity | p Value |
|----------------|----------------------|------------|--------------|-----------------|---------|
| Complications* [n (%)] | | | | | |
| All | 51 (32.7) | 15 (62.5) | 36 (27.3) | 0.001 | 50 (38.2) | 1 (4.0) | 0.002 | 23 (35.9) | 28 (30.4) | 0.471 |
| Stage 2 | 26 (16.7) | 9 (37.5) | 18 (13.6) | | 26 (19.8) | 0 (0.0) | | 13 (20.3) | 13 (14.1) | |
| Stage 3a | 17 (10.9) | 5 (20.8) | 12 (9.1) | | 16 (12.2) | 1 (4.0) | | 6 (9.4) | 11 (12.0) | |
| Stage 3b | 7 (4.5) | 1 (4.2) | 6 (4.5) | | 7 (5.3) | 0 (0.0) | | 3 (4.7) | 4 (4.3) | |
| Stage 4 | 1 (0.6) | 0 (0.0) | 1 (0.8) | | 1 (0.8) | 0 (0.0) | | 1 (1.6) | 0 (0.0) | |
| Inflammatory | 19 (12.2) | 14 (16.7) | 15 (11.4) | 0.695 | 19 (14.5) | 0 (0.0) | 0.089 | 13 (20.3) | 6 (6.5) | 0.01 |
| Exsufflation time (days) | | | | 0.136 | | 0.26 | | 0.574 | |
| Median | 3 | 3 | 3 | | 3 | 3 | | 3 | 3 | |
| IQR | (3–4) | (3–4) | (3–4) | | (3–4) | (2–4) | | (3–4) | (3–4) | |
| Gastric drainage (mL) | | | | 0.216 | | 0.209 | | 0.837 | |
| Median | 80 | 140 | 80 | | 70 | 130 | | 80 | 80 | |
| IQR | (25–247) | (36–408) | (21–215) | | (22–210) | (30–300) | | (30–290) | (22–232.5) | |
| Abdominal drainage (mL) | | | | 0.467 | | 0.003 | | 0.609 | |
| Median | 525 | 560 | 520 | | 580 | 275 | | 545 | 515 | |
| IQR | (275–1180) | (324–1545) | (267–1080) | | (300–1250) | (151–419) | | (270–1260) | (277–1045) | |
| Albumin use (g) | | | | 0.002 | | 0.037 | | 0.85 | |
| Median | 40 | 70 | 35 | | 40 | 0 | | 40 | 30 | |
| IQR | (0–60) | (23–70) | (0–60) | | (0–60) | (0–50) | | (0–75) | (0–60) | |
| Postoperative hospitalization (days) | | | | 0.065 | | 0.006 | | 0.135 | |
| Median | 8 | 11 | 8 | | 8.5 | 7 | | 9 | 8 | |
| IQR | (7–11.8) | (7–17) | (7–11) | | (7–12) | (6–8) | | (7–12) | (6–10.5) | |

*a Assessed by Clavien–Dindo grade.

IQR = interquartile range.
incidence of inflammatory complications (20.3% vs. 6.5%, \( p = 0.01 \)). Increased albumin infusions were needed postoperatively in both the sarcopenia and myosteatosis groups. The myosteatosis group had more abdominal drainage and a longer postoperative hospital stay. Other short-term postoperative outcomes were not significantly different in the body composition groups.

**Factors Associated with Postoperative Complications**

In univariate analysis (Table IV), the overall rate of postoperative complications was associated with a higher NRS 2002 score (\( p = 0.021 \)), more advanced tumour stage (stage II, \( p = 0.005 \); stage III, \( p = 0.017 \)), lower serum prealbumin (\( p = 0.044 \)) and serum rBP (\( p = 0.003 \)), sarcopenia (\( p = 0.001 \)), and myosteatosis (\( p = 0.009 \)). No significant associations between postoperative complications and the other variables were found.

The multivariate logistic regression analysis demonstrated that lower serum rBP (OR: 2.5; 95% CI: 1.2 to 5.5; \( p = 0.019 \)), sarcopenia (OR: 3.4; 95% CI: 1.3 to 8.8; \( p = 0.013 \)), and myosteatosis (OR: 12.7; 95% CI: 1.6 to 93.0; \( p = 0.017 \)) were independently associated with overall complications after surgery for gastric cancer. Among the various variables listed in Table V, only visceral obesity (OR: 3.7; 95% CI: 1.3 to 10.2; \( p = 0.013 \)) was associated with inflammatory complications.

**Relationship Between Body Composition and Perioperative Changes in Markers of Nutrition and Inflammation**

Serum rBP and CRP were measured preoperatively and on days 1, 3, and 5 postoperatively to estimate perioperative change in markers of nutrition and inflammation. In patients without sarcopenia, serum rBP declined sharply on postoperative day 1 and was lowest on day 3, after which it began to slowly recover. In patients with sarcopenia, serum rBP reached a lower level and recovered later (\( p = 0.007 \)). In patients with and without myosteatosis and visceral obesity, no differences in the change of serum rBP were observed. Postoperatively, serum CRP rose significantly on day 1, as expected, peaking on day 3; it declined thereafter. In the group with visceral obesity, serum CRP rose higher on day 3 and declined less than it did in the group without visceral obesity (\( p = 0.026 \)). A difference in the pattern of CRP change was not observed in other two groups (Figure 1).

**DISCUSSION**

In the present study, we prospectively analyzed the associations of three main RCSMs with postoperative outcomes in patients with operable gastric cancer. The results showed that sarcopenia, myosteatosis, and visceral obesity were poor prognostic factors for short-term outcomes. In particular, our study is, to the best of our knowledge, the first to find a significant association between visceral obesity and inflammatory complications after radical gastrectomy for gastric cancer. We also showed that body composition might affect markers of nutrition and inflammation, which means that it might influence the body’s response to operative stress.

Increasing modern evidence shows that body composition, rather than BMI, is the stronger prognostic indicator of patient outcomes. Several prior studies have found that loss of muscle (sarcopenia), defined as a low SMI, is independently associated with poor clinical outcomes in cancer patients, including excess chemotherapy toxicity\(^{23,24}\), increased risk of surgical complications\(^{25,29}\), and even poor long-term survival\(^{27,28}\). Several studies have investigated the effect of sarcopenia on outcomes in gastric cancer patients\(^{21,29,30}\). However, the results of these studies were inconsistent, possibly because of the different cut-off values used to define sarcopenia and the heterogeneity of the patient cohorts and study designs.

Our prospective study focused specifically on patients with operable disease, and all surgeries were performed by a single group of surgeons. To define sarcopenia, we adopted SMI cut-off values of 40.8 cm\(^2\)/m\(^2\) or less for men and 34.9 cm\(^2\)/m\(^2\) or less for women (obtained from a very large study about gastric cancer in patients from China\(^{22}\)). In our study, 24 patients (15.4%) were diagnosed with sarcopenia. It is well known that poor nutrition status is associated with an increased postoperative complication rate. Our results confirmed that sarcopenia serves as a reflection of poor nutrition status and is strongly associated with a lower BMI, a higher NRS 2002 score, and lower levels of other serum markers of nutrition, including insulin-like growth factor 1, albumin, prealbumin, and hemoglobin. Sarcopenia was also an independent risk factor for overall postoperative complications.

Based on work by the European Working Group on Sarcopenia in Older People\(^{31}\) and the Asian Working Group for Sarcopenia\(^{32}\), sarcopenia has been defined as low muscle mass plus low muscle strength or low physical performance (or both). Not only decreased muscle size, but also an increased proportion of intramuscular fat can contribute to reduction in muscle strength. Most earlier studies tended to focus exclusively on skeletal muscle size, but in the present study, we introduced MA. Determined by CT imaging, MA is a noninvasive measure of muscle density in which lower values reflect increased muscle lipid content. In prior studies, MA has been found to account for differences in muscle strength independent of muscle mass, making it an indicator of muscle strength\(^{15}\). A significant association between low MA and reduced overall or progression-free survival has been reported in patients with gastrointestinal or respiratory tract cancer\(^{14}\), renal cell carcinoma\(^{23}\), melanoma\(^{14}\), and epithelial ovarian cancer\(^{34}\). However, any associations of MA with the rate of postoperative complications in patients with gastric cancer had not been fully investigated. Given the lack of a large study of MA in gastric cancer patients, the low MA cut-off value adopted in our study was based on a large cohort of Japanese patients with hepatocellular carcinoma\(^{16}\). We found that both low SMI (sarcopenia) and low MA (myosteatosis) were independent predictors for more complications of Clavien–Dindo grade 2 or higher. Furthermore, we observed that patients with myosteatosis did not present with an obviously worse nutrition status as measured by BMI, NRS 2002 score, or the usual serum markers of nutrition. However, based on their elevated serum CRP (\( p = 0.058 \)) and interleukin 6 (\( p = 0.062 \)), they seemed to present in a state of systemic inflammation that was associated with a greater occurrence of postoperative
### TABLE IV  Univariate and multivariate logistic regression analysis of factors associated with total postoperative complications

| Variable                  | Patients [n (%)] | Univariate analysis | Multivariate analysis |
|---------------------------|-----------------|---------------------|-----------------------|
|                           | All With        | OR 95% CI p Value   | OR 95% CI p Value     |
|                           | complications<sup>a</sup> |                     |                       |
| Sex                       |                 |                     |                       |
| Women                     | 41 (34.1)       | Reference           |                       |
| Men                       | 115 (32.2)      | 0.9 0.4 to 1.9 0.817|                       |
| Age group                 |                 |                     |                       |
| <65 Years                 | 105 (29.6)      | Reference           |                       |
| ≥65 Years                 | 51 (43.1)       | 2.0 0.9 to 4.0 0.054|                       |
| BMI group                 |                 |                     |                       |
| 18.5–25                   | 97 (33.0)       | Reference           |                       |
| <18.5                     | 10 (60.0)       | 3.0 0.8 to 11.6 0.102|                       |
| >25                       | 49 (26.5)       | 0.7 0.3 to 1.6 0.426|                       |
| NRS 2002 score group      |                 |                     |                       |
| <3                        | 92 (26.1)       | Reference           |                       |
| ≥3                        | 64 (42.2)       | 1.6 1.1 to 2.5 0.021|                       |
| Diabetes                  |                 |                     |                       |
| No                        | 146 (33.6)      | Reference           |                       |
| Yes                       | 10 (20.0)       | 0.5 0.1 to 2.4 0.385|                       |
| Other comorbidities       |                 |                     |                       |
| No                        | 94 (30.9)       | Reference           |                       |
| Yes                       | 62 (35.5)       | 1.2 0.6 to 2.4 0.546|                       |
| Neoadjuvant CTx           |                 |                     |                       |
| No                        | 121 (29.8)      | Reference           |                       |
| Yes                       | 35 (42.9)       | 1.7 0.8 to 3.8 0.148|                       |
| Resection type            |                 |                     |                       |
| Subtotal                  | 111 (28.8)      | Reference           |                       |
| Total                     | 45 (42.2)       | 1.8 0.9 to 3.7 0.108|                       |
| Histologic type           |                 |                     |                       |
| Well differentiated       | 6 (16.7)        | Reference           |                       |
| Moderately differentiated | 50 (36.0)       | 2.4 0.3 to 21.0 0.443|                       |
| Poorly differentiated     | 100 (32.0)      | 2.8 0.3 to 26.0 0.362|                       |
| TNM stage                 |                 |                     |                       |
| I                         | 48 (16.7)       | 4.6 1.6 to 13.5 0.005|                       |
| II                        | 27 (48.1)       | 2.9 1.2 to 7.1 0.017|                       |
| III                       | 81 (37.0)       |                     |                       |
| IGF-1                     |                 |                     |                       |
| ≥75 μg/L                  | 128 (41.1)      | Reference           |                       |
| <75 μg/L                  | 28 (39.3)       | 1.4 0.6 to 3.3 0.413|                       |
| Albumin                   |                 |                     |                       |
| ≥35 g/L                   | 146 (31.5)      | Reference           |                       |
| <35 g/L                   | 10 (50.0)       | 2.2 0.6 to 7.9 0.237|                       |
| Prealbumin                |                 |                     |                       |
| ≥150 mg/L                 | 135 (29.6)      | Reference           |                       |
| <150 mg/L                 | 21 (52.4)       | 2.6 1.0 to 6.6 0.044|                       |
| Transferrin               |                 |                     |                       |
| ≥2.5 g/L                  | 146 (32.2)      | Reference           |                       |
| <2.5 g/L                  | 10 (40.0)       | 1.4 0.4 to 5.2 0.612|                       |
| Retinol-binding protein   |                 |                     |                       |
| ≥25 mg/L                  | 110 (25.5)      | Reference           |                       |
| <25 mg/L                  | 46 (50.0)       | 2.9 1.4 to 6.0 0.003| 2.5 1.2 to 5.5 0.019 |
| Hemoglobin                |                 |                     |                       |
| ≥110 g/L                  | 127 (32.3)      | Reference           |                       |
| <110 g/L                  | 29 (34.5)       | 1.1 0.5 to 2.6 0.82 |                       |
| Platelets                 |                 |                     |                       |
| ≥100×10<sup>9</sup>/L     | 135 (30.4)      | Reference           |                       |
| <100×10<sup>9</sup>/L     | 21 (47.6)       | 2.1 0.8 to 5.3 0.122|                       |
| Lymphocytes               |                 |                     |                       |
| ≥1.0×10<sup>9</sup>/L     | 132 (31.1)      | Reference           |                       |
| <1.0×10<sup>9</sup>/L     | 24 (41.7)       | 1.6 0.7 to 3.9 0.311|                       |
| Sarcopenia                |                 |                     |                       |
| No                        | 132 (27.3)      | Reference           |                       |
| Yes                       | 24 (62.5)       | 4.0 1.9 to 8.6 0.001| 3.4 1.3 to 8.8 0.013 |
| Myosteatosis              |                 |                     |                       |
| No                        | 25 (4.0)        | Reference           |                       |
| Yes                       | 131 (32.7)      | 14.8 1.9 to 112.9 0.009| 12.7 1.6 to 93.0 0.017|                       |
| Visceral obesity          |                 |                     |                       |
| No                        | 92 (30.4)       | Reference           |                       |
| Yes                       | 64 (35.9)       | 1.3 0.7 to 2.5 0.472|                       |

<sup>a</sup> Clavien-Dindo grade 2 or greater.

OR = odds ratio; CI = confidence interval; BMI = body mass index; NRS = Nutritional Risk Screening; CTx = chemotherapy; IGF-1 = insulin-like growth factor 1.
TABLE V  Univariate logistic regression analysis of factors associated with postoperative inflammatory complications

| Variable                           | Patients [n (%)] | OR      | 95% CI   | p Value |
|------------------------------------|-----------------|---------|----------|---------|
|                                    | All With        |         |          |         |
|                                    | complications*  |         |          |         |
| Sex                                | Women 41 2 (4.9) | Reference | 3.4 0.7 to 15.3 | 0.114   |
|                                    | Men 115 17 (14.8) | Reference | 1.2 0.5 to 3.3  | 0.681   |
| Age                                | <65 Years 105 12 (11.4) | Reference |          |         |
|                                    | ≥65 Years 51 7 (13.7) | Reference |          |         |
| BMI group                          | 18.5–25 97 10 (10.3) | Reference |          |         |
|                                    | <18.5 10 0 (0.0) | —       |          | 0.999   |
|                                    | ≥25 49 9 (18.4) | 2.0 0.7 to 5.2 | 0.177   |
| NRS 2002 score group              | <3 92 9 (9.8) | Reference |          |         |
|                                    | ≥3 64 10 (15.6) | 1.7 0.7 to 4.5 | 0.276   |
| Diabetes                           | No 146 18 (12.3) | Reference |          |         |
|                                    | Yes 10 1 (10.0) | 0.8 0.1 to 6.6 | 0.828   |
| Other comorbidities               | No 94 10 (10.6) | Reference |          |         |
|                                    | Yes 62 9 (14.5) | 1.4 0.6 to 3.7 | 0.47    |
| Neoadjuvant CTx                    | No 121 14 (11.6) | Reference |          |         |
|                                    | Yes 35 5 (14.3) | 1.3 0.4 to 3.8 | 0.666   |
| Resection type                     | Subtotal 111 15 (13.5) | Reference |          |         |
|                                    | Total 45 4 (8.9) | 0.6 0.2 to 2.0 | 0.427   |
| Histologic type                    | Well differentiated 6 1 (16.7) | Reference |          |         |
|                                    | Moderately differentiated 50 7 (14.0) | 0.8 0.1 to 8.0 | 0.86    |
|                                    | Poorly differentiated 100 11 (11.0) | 0.6 0.1 to 5.8 | 0.618   |
| TNM stage                          | I 48 5 (10.4) | Reference |          |         |
|                                    | II 27 3 (11.1) | 1.1 0.2 to 4.9 | 0.926   |
|                                    | III 81 11 (13.6) | 1.4 0.4 to 4.2 | 0.599   |
| IGF-1                              | ≥75 µg/L 128 16 (12.5) | Reference |          |         |
|                                    | <75 µg/L 28 3 (10.7) | 0.8 0.2 to 3.1 | 0.794   |
| Albumin                            | ≥35 g/L 146 18 (12.3) | Reference |          |         |
|                                    | <35 g/L 10 1 (10.0) | 0.8 0.1 to 6.6 | 0.828   |
| Prealbumin                         | ≥150 mg/L 135 15 (11.1) | Reference |          |         |
|                                    | <150 mg/L 21 4 (19.0) | 1.9 0.6 to 6.3 | 0.307   |
| Transferrin                         | ≥2.5 g/L 146 18 (12.3) | Reference |          |         |
|                                    | <2.5 g/L 10 1 (10.0) | 0.8 0.1 to 6.6 | 0.828   |
| Retinol-binding protein            | ≥25 mg/L 110 12 (10.9) | Reference |          |         |
|                                    | <25 mg/L 46 7 (15.2) | 1.5 0.5 to 4.0 | 0.455   |
| Hemoglobin                         | ≥110 g/L 127 15 (11.8) | Reference |          |         |
|                                    | <110 g/L 29 4 (13.8) | 1.2 0.4 to 3.9 | 0.769   |
| Platelets                          | ≥100×10^9/L 135 15 (11.1) | Reference |          |         |
|                                    | <100×10^9/L 21 4 (19.0) | 1.9 0.6 to 6.3 | 0.307   |
| Lymphocytes                        | ≥1.0×10^9/L 132 14 (10.6) | Reference |          |         |
|                                    | <1.0×10^9/L 24 5 (20.8) | 2.2 0.7 to 6.9 | 0.167   |
| Sarcopenia                         | No 132 15 (11.4) | Reference |          |         |
|                                    | Yes 24 4 (16.7) | 1.6 0.5 to 5.2 | 0.468   |
| Myosteatosis                       | No 25 0 (0.0) | Reference |          |         |
|                                    | Yes 131 19 (14.5) | —       |          | 0.998   |
| Visceral obesity                   | No 92 6 (6.5) | Reference |          |         |
|                                    | Yes 64 13 (20.3) | 3.6 1.3 to 10.2 | 0.013   |

*Inflammatory complications.

OR = odds ratio; CI = confidence interval; BMI = body mass index; NRS = Nutritional Risk Screening; CTx = chemotherapy; IGF-1 = insulin-like growth factor 1.
inflammatory complications ($p = 0.089$). However, that association did not reach statistical significance, possibly because of the limited sample size or lack of an optimal cut-off value for $\text{Ma}$.

In addition to sarcopenia and myosteatosis, our study focused on visceral obesity as another important body composition factor. Visceral adipose tissue is an important metabolic tissue that secretes factors that systemically alter the immunologic, metabolic, and endocrine milieu$^{35}$. Excess visceral adipose tissue gives rise to a state of chronic systemic inflammation with associated insulin resistance and dysmetabolism$^{35}$. Earlier studies have demonstrated associations between visceral obesity and an increased risk of breast cancer$^{36}$, colorectal cancer$^{37}$, and esophageal adenocarcinoma$^{38}$. A higher $\text{BMI}$ was found to be associated with increased tumour progression and reduced survival in cancer patients$^{11,16}$. Our study uncovered a significant relationship between visceral adipose tissue and inflammatory complications and a greater postoperative level of serum $\text{CRP}$. Those observations indicate that visceral adipose tissue might exacerbate the postoperative acute-phase inflammatory response, affect the immune response, and ultimately result in poorer outcomes.

Cancer cachexia results not only from reduced nutrient intake or availability, but also from metabolic abnormalities triggered by the cancer and the patient’s antineoplastic therapies. Those factors stimulate systemic inflammation and cytokine networks$^{39}$ that in turn result in significant loss of body weight, alterations in body composition, and declining physical function. Our findings showed that patients with sarcopenia had a lower postoperative level of serum $\text{ALP}$ and that $\text{ALP}$ recovery was slower in them than in patients without sarcopenia. Compared with patients not having visceral obesity, those with visceral obesity were observed to have a higher postoperative maximal level of serum $\text{CRP}$ and a prolonged systemic inflammatory response. Similar findings were reported in another study$^{40}$. Those findings suggested that $\text{BCM}$ could reflect variation in physiologic reserves, metabolic profile, and inflammatory and immune responses, and might consequently have a close association with clinical outcomes.

Limitations of our study include the small number of patients, the single-centre setting, and the lack of long-term survival data. Using long-term follow-up, we will continue to investigate this issue, combining various individual $\text{BCM}$ so as to obtain more accurate variables potentially reflecting body metabolism and clinical prognosis.

CONCLUSIONS

In the present study, we observed that sarcopenia, myosteatosis, and visceral obesity were not only significantly associated with increased postoperative complication rates, but that they were also associated with the pattern of change in perioperative serum markers of nutrition and inflammation in patients with primary operable gastric cancer.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood Current Oncology’s policy on disclosing conflicts of interest, and we declare that we have none.

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