Citation: Clin Transl Sci (2021) 14, 837–846; doi:10.1111/cts.12940

ARTICLE

Sarcopenia in Patients With Normal Body Mass Index Is an Independent Predictor for Postoperative Complication and Long-Term Survival in Gastric Cancer

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Malnutrition in patients with gastric cancer (GC) with normal body mass index (BMI) is often ignored. This study aimed to explore the role of sarcopenia in predicting postoperative complication and long-term survival in patients with GC with normal BMI. We included patients with normal BMI (18.5 kg/m^2 ≤ BMI < 23 kg/m^2) who underwent radical gastrectomy between July 2014 and December 2016. Sarcopenia was assessed by muscle mass, handgrip strength, and gait speed. Kaplan–Meier survival analysis was used to analyze the association between sarcopenia and the prognosis of patients with GC. Univariate and multivariate analyses were used to identify risk factors contributing to postoperative complications and long-term survival. Overall, 267 patients with GC with normal BMI were included in this study; of which 49 (18.35%) patients were diagnosed with sarcopenia. Patients with sarcopenia had higher incidence of a major postoperative complication, longer postoperative hospital stays, and greater hospital costs. The Kaplan–Meier survival analysis showed that patients with sarcopenia had poorer overall survival than non-sarcopenia patients. Univariate and multivariate analyses showed that sarcopenia was an independent predictor for postoperative complication and long-term survival in such patients. Sarcopenia is an independent predictor for postoperative complications and long-term survival in patients with normal BMI after radical gastrectomy for GC. We recommend that patients with normal BMI should perform nutritional risk screening by sarcopenia.

Study Highlights

WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?

✔ Preoperative nutritional status has a significant impact on postoperative complications and long-term survival of patients with gastric cancer (GC). Body mass index (BMI) and various nutritional scores based on it were widely used for the assessment of nutritional status of patients with GC in clinical practice.

WHAT QUESTION DID THIS STUDY ADDRESS?

✔ Is there malnutrition in patients with GC with normal BMI? When can sarcopenia be used as a good nutritional indicator to predict the clinical outcome of patients with GC?

WHAT DOES THIS STUDY ADD TO OUR KNOWLEDGE?

✔ About 18% of patients with GC with normal BMI have sarcopenia. Sarcopenia was an independent predictor for postoperative complications and long-term survival in such patients.

HOW MIGHT THIS CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?

✔ In clinical practice, malnutrition in patients with normal BMI GC should not be ignored. Sarcopenia has high applicability as a nutrition screening tool for such patients, may serve as a target for therapeutic intervention to reduce complications, and improve prognosis.

Gastric cancer (GC) is the fifth most common cancer, causing > 783,000 annual deaths worldwide.[1] Approximately 42.5% of cases occur in China, and both morbidity and mortality from this cancer type rank third among China's malignant tumors, seriously threatening public health in China.[2] To date, gastrectomy with D2 lymph node dissection remains the primary treatment choice for GC,[3] although the postoperative complication mortality rate after gastrectomy was reportedly 4–16%.[4] With improvement on evidence-based medicine and precision medicine, establishing an accurate prediction model for clinical outcomes is crucial for improving the quality of GC surgery and reducing postoperative complications and mortality as well as the medical burden.

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Received: July 18, 2020; accepted: October 6, 2020. doi:10.1111/cts.12940

Due to cancer cachexia and digestion disorders, 36–43% of patients with GC have pre-operative nutritional risks.[5,6] Pre-operative nutritional status has a significant impact on postoperative clinical outcomes.[7] In clinical practice, the assessment of nutritional status generally relies on body mass index (BMI) and various nutritional scores based on it. Reportedly, lean body tissue composition is most closely related to the clinical outcome in patients with malignancy.[8] Lean body mass might be lost, whereas fat mass may be preserved or even increased in patients with malignancy, leading to either a normal BMI or obesity.[9] Therefore, traditional nutrition assessment indicators, such as BMI and Nutritional Risk Screening (NRS) 2002 score, have declined in sensitivity and specificity for predicting postoperative clinical outcomes of GC.[10]

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes, such as physical disability, poor quality of life, and death.[11] Examining sarcopenia can reportedly better evaluate the true nutritional status of patients with normal BMI or even obesity,[12] and was also closely related to the postoperative clinical outcomes of various malignancies, such as colorectal,[13] liver,[14] and pancreatic cancers.[15] Our previous study has reported that sarcopenia was associated with postoperative complication in GC in overweight and obese patients.[9] However, no research has focused on sarcopenia in patients with GC with normal BMI to date.

Therefore, this study aimed to explore the role of sarcopenia in predicting postoperative complications and long-term survival in patients with GC with normal BMI.

PATIENTS AND METHODS

Patients

This study included patients with GC who underwent radical gastrectomy at the Gastrointestinal Surgical Department, The First Affiliated Hospital of Wenzhou Medical University, between July 2014 and December 2016. The inclusion criteria were patients who (i) had a normal BMI (18.5 kg/m^2 ≤ BMI < 23 kg/m^2)[16]; (ii) were over 18 years old; (iii) with American Society of Anesthesiologists (ASA) grade ≤ III; (iv) had histologically proven gastric cancer; (v) had adequate quality abdominal computed tomography (CT); and (vi) agreed to participate in the study and signed the informed consent. The exclusion criteria were patients who (i) were unable to finish the measure for muscle strength or gait speed and (ii) underwent palliative operation. In order to avoid possible bias, all operations were conducted by special surgeons who had performed > 200 radical resections for GC according to Japanese GC treatment guidelines 2014 (version 4).[3] The study was approved by the Research Ethics Committee of The First Affiliated Hospital of Wenzhou Medical University.

Data collection

The following three part data were collected form each patient: (i) pre-operative date: clinicopathological features including age, sex, height, weight, BMI, pre-operative comorbidity, hemoglobin concentration, serum albumin, ASA grade, NRS 2002 scores, comorbidity, previous abdominal operation, tumor size, tumor location, tumor differentiation, tumor-node-metastasis (TNM) stage of tumor, muscle mass, handgrip strength, and gait speed; (ii) operative data: operative method and duration, the way of surgical resection and reconstruction, and anesthesia method; (iii) postoperative outcomes: postoperative complications, postoperative hospital stay, and hospital costs. Complications meeting the criterion of grade II or higher were calculated, according the Clavien–Dindo classification system.[17] Long-term survival data were obtained by postoperative follow-up assessment. The final follow-up evaluation was performed in October 2018. Overall survival (OS) time was calculated from the day of surgery to death or to the day of last follow-up.

Quantification of skeletal muscle mass

Because skeletal muscle mass in the cross-sectional of third lumbar vertebra (L3) was reportedly the most correlated with total body skeletal muscle mass,[18] a representative CT image at L3 was selected to quantify skeletal muscle mass, as described previously.[19] The identification and quantification of skeletal muscle mass were performed on a dedicated processing system (version 3.0.11.3; BN17 32 bit; INFINITT Healthcare, Seoul, South Korea). Hounsfield unit threshold range of –29 to 150 in the image was selected for skeletal muscle mass with tissue boundaries corrected manually. Muscle areas were normalized for stature (m^2) to carry out the L3 skeletal muscle index (SMI; cm^2/m^2).

Evaluation of muscle strength and physical performance

Grip strength and 6-meter usual gait speed were used to evaluate muscle strength and physical performance within 7 days pre-operatively. Grip strength was tested on the dominant hand by a hand dynamometer (EH101; Camry, Guangdong Province, China). A 6-meter usual gait speed indicates the speed of patients walking over 6 meters in normal gait.[20] Each experiment was performed in triplicate, and the maximal value was recorded.

Diagnosis of sarcopenia

According to the European Working Group on Sarcopenia in (EWGSOP)[11] and the Asian Working Group for Sarcopenia (AWGS),[21] patients with low skeletal muscle mass and low muscle strength and/or physical performance were diagnosed with sarcopenia. At the recommendation of AWGS, low muscle strength indicates patients with handgrip strength < 26 kg for men and < 18 kg for women; low physical performance was defined in patients with 6-meter usual gait speed < 0.8 m/second.[21] Our previous study reported suitable cutoff values (L3 SMI < 40.8 cm^2/m^2 for men and < 34.9 cm^2/m^2 for women) of low muscle mass for patients with GC.[22]

Statistical analysis

Statistical analysis was performed using EmpowerStats (X&Y Solutions, Boston, MA) and SPSS software (version 21; IBM, Armonk, NY). Student's *t*-test (or Mann–Whitney *U* test) was used to assess the difference between the continuous variables. The Pearson's χ^2 test (or Fisher's exact test) was used to assess the difference among categorical variables. Univariate and multivariate logistic analyses were performed to examine potential risk factors associated with complications. Survival analysis was performed using Kaplan–Meier curve, and statistical significance was determined by the log-rank test. Univariate and multivariate Cox proportional hazards regression analyses were performed to analyze the effects of prognostic factors on GC. $P < 0.05$ (two-tailed) was considered statistically significant.

RESULTS

Clinicopathological features

From July 2014 to December 2016, 267 consecutive patients overall who met the criteria were included in this study. Of them, the average age was 64.78 ± 10.27 years, 202 (75.66%) patients were men, and the mean BMI was 20.90 ± 1.25 kg/m^2. Based on the diagnostic criteria of sarcopenia, 49 (18.35%) patients were identified under the sarcopenia group, comprising 32 men and 17 women. According to the clinicopathological analysis shown in **Table 1**, as the sarcopenia features, L3 SMI ($P < 0.001$), handgrip strength ($P < 0.001$), and gait speed ($P < 0.001$) were all significantly lower in the sarcopenia group. Sarcopenia was significantly associated with older age ($P < 0.001$), lower BMI ($P = 0.004$), lower albumin level ($P < 0.001$), lower hemoglobin level ($P < 0.001$), higher NRS 2002 score ($P < 0.001$), and higher prevalence of diabetes ($P = 0.031$; **Table 1**).

Influence of sarcopenia on postoperative outcomes

The relationship between sarcopenia and postoperative outcomes is shown in **Table 2**. According to the Clavien–Dindo classification, 54 (20.22%) patients experienced grade II or higher complications. Pneumonia is the most frequent complication in both groups. Seven (2.62%) patients experienced grade III complications and underwent reoperation. Six (2.24%) patients experienced grade IV complications and received intensive care unit management. Patients in the sarcopenia group had a higher incidence of a major postoperative complications than patients in the non-sarcopenia group (44.90% vs. 14.68%, $P < 0.001$). The incidence of grade IV postoperative complication is much higher in the sarcopenia group ($n = 4$, 8.16%) than in the non-sarcopenia group ($n = 2$, 0.92%). Additionally, patients with sarcopenia had longer postoperative hospital stays (14 days vs. 13 days, $P = 0.016$) and greater hospital costs (¥63,341 vs. 55,576, $P = 0.004$).

Factors associated with postoperative complications

Univariate logistic analysis showed that sarcopenia ($P < 0.001$), age ≥ 75 years ($P = 0.010$), hypoproteinemia ($P = 0.018$), tumor size ≥ 4 cm ($P = 0.037$), open surgery ($P = 0.037$), reconstruction type ($P = 0.015$), and total gastrectomy ($P = 0.004$) were associated with postoperative complications (**Table 3**). Significant differences were not observed among other factors, such as sex, BMI, anemia, NRS 2002 scores, ASA, cardiopulmonary comorbidity, diabetes tumor differentiation, TNM stage, previous abdominal operation, epidural anesthesia, and surgical durations. After controlling the potential confounders by multivariate logistic analysis, sarcopenia (odds ratio (OR), 4.466, 95% confidence interval (CI), 2.240–8.907, $P < 0.001$) and Billroth I reconstruction (OR, 0.356, 95% CI, 0.165–0.768, $P = 0.008$) remained as the independent predictors for postoperative complications of GC (**Table 4**).

Prognostic significance of sarcopenia

For all patients, the median OS was 35 months. The Kaplan–Meier survival analysis showed that patients with sarcopenia had a shorter median OS than non-sarcopenia patients (31 months vs. 36 months, log rank $P = 0.012$; **Figure1**). Univariable Cox analysis showed that in addition to sarcopenia ($P = 0.014$), age ≥ 75 years ($P = 0.002$), NRS 2002 scores ≥ 3 ($P = 0.008$), ASA ≥ III ($P = 0.005$), tumor size ≥ 4 cm ($P < 0.001$), advanced TNM stage ($P < 0.001$), reconstruction type ($P < 0.001$), and total gastrectomy ($P < 0.001$) were significant prognostic factors for patients with GC with normal BMI (**Table 5**). Multivariable COX analysis further indicated that sarcopenia (OR, 1.784, 95% CI, 1.119–2.844, $P = 0.035$), NRS 2002 scores ≥ 3 (OR, 1.622, 95% CI, 1.009–2.609, $P = 0.046$), tumor size ≥ 4 cm (OR, 2.058, 95% CI, 1.097–3.860, $P = 0.025$), TNM stage III (OR, 6.394, 95% CI, 1.870–21.862, $P = 0.003$), and Billroth I reconstruction type (OR, 0.347, 95% CI, 0.160–0.752, $P = 0.007$) were independent prognostic factors for the shorter OS (**Table 5**).

DISCUSSION

To the best of our knowledge, this is the first study to focus on sarcopenia in patients with GC with normal BMI. There was 49.26% (267/562, data was not showed in this paper) of patients with GC who had normal BMI, of which 49 (18.35%) were diagnosed with sarcopenia. The incidence of sarcopenia was consistent with the overall incidence rate of patients with GC.[23] Patients with sarcopenia showed a higher incidence of postoperative complications and a lower OS rate. Sarcopenia was an independent risk factor for postoperative complications, although it was not an independent prognostic factor for the shorter OS in patients with GC.

A large number of patients with GC suffer from malnutrition due to cancer cachexia and digestion disorders. Pre-operative malnutrition has been reported to be closely related to postoperative complications[24] and long-term survival of patients with GC.[25] Therefore, increasing pre-operative nutrition risk screening indicators were used to predict the clinical outcome of such patients.

The diagnosis of malnutrition recommended by the European Society of Clinical Nutrition and Metabolism (ESPEN) should be based on either a low BMI (< 18.5 kg/m^2), or on the combined finding of weight loss together with either reduced BMI or a low fat free mass index.[26] Moreover, BMI plays a vital role in the diagnosis of malnutrition. Therefore, malnutrition in patients with normal BMI may often be misdiagnosed. BMI as a weight-basis nutritional indicator cannot distinguish the proportion of fat mass and lean body tissue composition, which have opposing effects on the occurrence of postoperative complications.[27,28]

Table 1 The relationship between sarcopenia and clinical characteristics of patients with gastric cancer

Factors	Total (*n* = 267)	Sarcopenia (*n* = 49)	Non-sarcopenia (n = 218)	*P* value
Age, mean (SD), years	64.78 (10.27)	72.31 (7.89)	63.08 (9.99)	< 0.001*
Sex				
Female	65 (24.34%)	17 (34.69%)	48 (22.02%)	0.062
Male	202 (75.66%)	32 (65.31%)	170 (77.98%)	
BMI, mean (SD), kg/m^2	20.90 (1.25)	20.43 (1.33)	21.00 (1.21)	0.004*
Albumin, mean (SD), g/L	37.53 (4.33)	35.47 (4.18)	37.98 (4.24)	< 0.001*
Hemoglobin, mean (SD), g/L	116.81 (22.22)	105.16 (22.32)	119.42 (21.39)	< 0.001*
NRS 2002 scores, median (IQR)	2.00 (2.00)	3.00 (1.00)	2.00 (2.00)	< 0.001*
ASA				
I, II	225 (84.27%)	37 (75.51%)	188 (86.24%)	0.062
III	42 (15.73%)	12 (24.49%)	30 (13.76%)	
Cardiopulmonary comorbidity				
No	214 (80.15%)	38 (77.55%)	176 (80.73%)	0.614
Yes	53 (19.85%)	11 (22.45%)	42 (19.27%)	
Diabetes				
No	248 (92.88%)	42 (85.71%)	206 (94.50%)	0.031*
Yes	19 (7.12%)	7 (14.29%)	12 (5.50%)	
L3 SMI, mean (SD), cm^2/m^2	40.30 (7.03)	32.89 (4.93)	41.97 (6.33)	<0.001*
Handgrip strength, mean (SD), kg	28.07 (8.38)	20.45 (6.45)	29.80 (7.79)	<0.001*
Gait speed, mean (SD), m/second	0.98 (0.23)	0.83 (0.24)	1.02 (0.21)	<0.001*
Surgical durations, mean (SD), minutes	198.65 (51.08)	209.02 (43.14)	196.32 (52.51)	0.116
Differentiation				
Undifferentiated	204 (76.40%)	39 (79.59%)	165 (75.69%)	0.561
Differentiated	63 (23.60%)	10 (20.41%)	53 (24.31%)	
Tumor location				
Not cardia	230 (86.14%)	40 (81.63%)	190 (87.16%)	0.312
Cardia	37 (13.86%)	9 (18.37%)	28 (12.84%)	
Tumor size				
< 4 cm	123 (46.07%)	18 (36.73%)	105 (48.17%)	0.147
≥ 4 cm	144 (53.93%)	31 (63.27%)	113 (51.83%)	
TNM stage				
I	76 (28.57%)	9 (18.37%)	67 (30.88%)	0.170
II	63 (23.68%)	15 (30.61%)	48 (22.12%)	
III	128 (47.94%)	25 (51.02%)	102 (47.00%)	
Previous abdominal operation				
No	232 (86.89%)	42 (85.7%)	190 (87.2%)	0.787
Yes	35 (13.11%)	7 (14.3%)	28 (12.8%)	
Operation method				
Open	197 (73.78%)	42 (85.71%)	155 (71.10%)	0.036
Laparoscopy	70 (26.22%)	7 (14.29%)	63 (28.90%)	
Epidural anesthesia				
No	61 (22.85%)	14 (28.57%)	47 (21.56%)	0.291
Yes	206 (77.15%)	35 (71.43%)	171 (78.44%)	
Type of reconstruction				
Roux-en-Y	122 (45.69%)	27 (55.10%)	95 (43.58%)	0.296
Billroth I	100 (37.45%)	14 (28.57%)	86 (39.45%)	
Billroth II	45 (16.85%)	8 (16.33%)	37 (16.97%)	
Type of resection				
Subtotal gastrectomy	160 (59.93%)	22 (44.90%)	138 (63.30%)	0.018*
Total gastrectomy	107 (40.07%)	27 (55.10%)	80 (36.70%)	

ASA, American Society of Anesthesiologists; BMI, body mass index; IQR, interquartile range; NRS, nutritional risk screening; L3 SMI, third lumbar vertebra skeletal muscle index; TNM, tumor–node–metastasis.
*Statistically significant ($P < 0.05$).

Table 2 The relationship between sarcopenia and postoperative outcomes of patients with gastric cancer

Postoperative complications[a]	All (*n* = 267)	Sarcopenia (*n* = 49)	Non-sarcopenia (*n* = 218)	*P* value[b]
Grade II				
Delayed gastric emptying	3	3	0	
Pneumonia	12	6	6	
Intra-abdominal infection	7	1	6	
Anastomotic leakage	4	0	4	
Intra-abdominal fluid collection	2	1	1	
Small bowel obstruction	3	0	3	
Malnutrition	2	2	0	
Wound infection	1	0	1	
Deep venous thrombosis	3	1	2	
Postoperative delirium	1	1	0	
Lymphatic fistulas	2	1	1	
Grade III				
Intra-abdominal hemorrhage	4	1	3	
Intussusception	1	0	1	
Anastomotic hemorrhage	1	0	1	
Intestinal fistula	1	0	1	
Grade IV				
Pulmonary embolism	1	0	1	
Hemorrhagic shock	2	2	0	
Septic shock	2	2	0	
Digestive tract perforation	1	0	1	
Grade V				
Multiple organ failure	1	1	0	
Total, %	54 (20.22%)	22 (44.90%)	32 (14.68%)	< 0.001*
Postoperative hospital stays, days (IQR)	13 (7)	14 (10)	13 (6)	0.016*
Costs, ￥(IQR)	56,688 (19,927)	63,341 (31,627)	55,576 (18,268)	0.004*

IQR, interquartile range.
[a]Patients who experienced more than one complication were classified as higher-grade complication. [b]Due to the limited number of patients with a specific complication, we did not perform statistical analysis for each of the postoperative complications.
*Statistically significant ($P < 0.05$).

Additionally, with the improvement of living standards, the average weight of patients with GC continues to increase as well as the proportion of patients with hidden malnutrition (BMI ≥ 18.5 kg/m^2). BMI and NRS 2002 score were insufficiently accurate to predict the occurrence of postoperative complications of GC (**Table 3**).

Sarcopenia was first proposed by Irwin Rosenberg to describe the age-related decrease of muscle mass in 1989.[29] In 2010, the EWGSOP redefined its diagnostic criteria as low skeletal muscle mass and low muscle strength and/or physical performance.[11] Further, sarcopenia is a new type of nutritional index that directly measures the amount and function of lean body tissue. Due to the huge difference in physical constitution between Asians and Europeans, its diagnostic criteria (handgrip strength and gait speed) in this study mainly refer to AWGS.[21] However, AWGS's assessment of the skeletal muscle mass is based on dual X-ray absorptiometry. This method's accuracy for muscle mass assessment is much lower than CT,[30] a routine examination item for patients with GC. Hence, we used the L3 index evaluated by CT image here, and its cutoff value for different sexes was carried out by our previous large sample research.[22] According to these diagnostic criteria, 49 (18.35%) patients with GC in normal BMI were diagnosed with sarcopenia. Patients with sarcopenia were also recorded worse on traditional nutritional indicators, such as lower BMI, lower albumin and hemoglobin levels, and higher NRS 2002 scores (**Table 1**).

Sarcopenia reportedly has a significant impact on postoperative complications in various kinds of malignancies.[14,31] Here, patients with sarcopenia with normal BMI have a higher incidence of complications, which can be serious, leading to longer postoperative hospital stays and greater hospital costs (**Table 2**). In the univariate logistic analysis, age, hypoproteinemia, sarcopenia, tumor location, tumor size, operation method, reconstruction type, and resection type were associated with postoperative complications. When within the normal range, BMI no longer had a decisive impact on postoperative complications. After adjusting by multivariate analysis, only sarcopenia (OR, 4.466, 95% CI, 2.240–8.907, $P < 0.001$) and Billroth I reconstruction type (OR, 0.356, 95% CI, 0.165–0.768, $P = 0.008$) were the independent risk factors for postoperative complications. Age and hypoproteinemia might be covered by sarcopenia because of the interactive effects among age, hypoproteinemia, and sarcopenia (**Table 1**). Tumor location, tumor size,

Table 3 Univariate logistic analysis of factors associated with postoperative complications

Factors	No complications (*n* = 213)	Complications (*n* = 54)	OR	95% CI	*P* value
Age					
< 70 years	147 (69.01%)	27 (50.00%)	1		0.010*
≥70 years	66 (30.99%)	27 (50.00%)	2.227	1.213–4.088	
Sex					
Female	48 (22.54%)	17 (31.48%)	1		0.174
Male	165 (77.47%)	37 (68.52%)	0.633	0.328–1.223	
BMI[a]					
< 20.57 kg/m^2	91 (42.72%)	19 (35.19%)	1		0.316
≥ 20.57 kg/m^2	122 (57.28%)	35 (64.81%)	1.374	0.738–2.557	
Hypoproteinemia					
No	157 (74.06%)	31 (57.41%)	1		0.018*
Yes	55 (25.94%)	23 (42.59%)	2.118	1.139–3.940	
Anemia					
No	170 (79.81%)	37 (68.52%)	1		0.078
Yes	43 (20.19%)	17 (31.48%)	1.816	0.935–3.531	
NRS 2002 scores					
< 3	126 (59.16%)	24 (44.44%)	1		0.053
≥ 3	87 (40.85%)	30 (55.56%)	1.810	0.991–3.306	
ASA					
I, II	183 (85.92%)	42 (77.78%)	1		0.146
III	30 (14.09%)	12 (22.22%)	1.743	0.824–3.685	
Cardiopulmonary comorbidity					
No	167 (78.40%)	47 (87.04%)	1		0.160
Yes	46 (21.60%)	7 (12.96%)	0.541	0.229–1.276	
Diabetes					
No	198 (92.96%)	50 (92.59%)	1		0.926
Yes	15 (7.04%)	4 (7.41%)	1.056	0.336–3.321	
Sarcopenia					
No	186 (87.32%)	32 (59.26%)	1		< 0.001*
Yes	27 (12.68%)	22 (40.74%)	4.736	2.408–9.316	
Differentiation					
Undifferentiated	164 (77.00%)	40 (74.07%)	1		0.652
Differentiated	49 (23.00%)	14 (25.93%)	1.171	0.589–2.329	
Tumor location					
Not cardia	188 (88.26%)	42 (77.78%)		1	0.050*
Cardia	25 (11.74%)	12 (22.22%)	2.149	0.999–4.619	
Tumor size					
< 4 cm	105 (49.30%)	18 (33.33%)		1	0.037*
≥ 4 cm	108 (50.70%)	36 (66.67%)	1.944	1.039–3.638	
TNM stage					
I	64 (30.19%)	12 (22.22%)		1	0.277
II	52 (24.53%)	11 (20.37%)	1.128	0.460–2.765	0.792
III	96 (45.28%)	31 (57.41%)	1.722	0.824–3.601	0.149
Previous abdominal operation					
No	184 (86.39%)	48 (88.89%)		1	0.627
Yes	29 (13.61%)	6 (11.11%)	0.793	0.311–2.020	
Operation method					
Open	151 (70.89%)	46 (85.19%)		1	0.037*
Laparoscopy	62 (29.11%)	8 (14.81%)	0.424	0.189–0.949	
Epidural anesthesia					
No	47 (22.07%)	14 (25.93%)		1	0.547
Yes	166 (77.93%)	40 (74.07%)	0.809	0.406–1.612	

(Continues)

Table 3 (Continued)

Factors	No complications (*n* = 213)	Complications (*n* = 54)	OR	95% CI	*P* value
Type of reconstruction					
Roux-en-Y	89 (41.78%)	33 (61.11%)		1	0.015*
Billroth I	89 (41.78%)	11 (20.37%)	0.333	0.159–0.701	0.004*
Billroth II	35 (16.44%)	10 (18.52%)	0.771	0.343–1.729	0.528
Type of resection					
Subtotal gastrectomy	137 (64.32%)	23 (42.59%)		1	0.004*
Total gastrectomy	76 (35.68%)	31 (57.41%)	2.430	1.323–4.462	
Surgical durations, minutes					
< 210	119 (56.94%)	30 (55.56%)		1	0.855
≥ 210	90 (43.06%)	24 (44.44%)	1.058	0.579–1.932	

ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; NRS, nutritional risk screening; OR, odds ratio; TNM, tumor–node–metastasis.
[a]The cutoff value was chosen at the maximal Youden index in the receiver operating characteristic analysis according to complications of patients.
*Statistically significant ($P < 0.05$).

operation method, and resection type all play an important role in selecting the reconstruction type.[32] Billroth I type of reconstruction reportedly have a significantly lower rate of postoperative complications than Billroth II and Roux-en-Y,[33,34] which was consistent with our research findings.

Furthermore, patients with sarcopenia had a worse prognosis in several cancer types.[35,36] Accordingly, sarcopenia was associated with the shorter OS in patients with GC with normal BMI. This may be because the risk of postoperative complications in patients with sarcopenia is nearly 4.5 times that of non-sarcopenia patients, and postoperative complications have a significant impact on their survival.[37] Multivariable COX analysis further indicated that sarcopenia (OR, 1.784, 95% CI, 1.119–2.844, $P = 0.035$), NRS 2002 scores ≥ 3 , tumor size ≥ 4 cm, TNM stage III, and Billroth I reconstruction type were independent prognostic factors for the shorter OS (**Table 5**). Our study suggested that the nutritional status of patients with GC in normal BMI should be further analyzed, and sarcopenia can serve as a target for therapeutic intervention to reduce complications and improve prognosis.

Some limitations of the present study should not be ignored. According to the definition of sarcopenia, there is a strong correlation between sarcopenia and age. It is difficult to decouple sarcopenia and age differences between groups. Therefore, we used COX regression analysis to exclude the synergistic effect of age on sarcopenia, and sarcopenia is still an independent risk factor for postoperative complications long-term survival of patients with GC. Moreover, this was a single-center study, limited by the number of patients with complications, we did not perform subgroup analyses of complications and sarcopenia stages according to the severity of sarcopenia, wherein the EWGSOP divided sarcopenia into four stages: "presarcopenia," "sarcopenia," and "severe sarcopenia."[11] Hence, further external, multicenter, evidence-based validation is necessary to confirm our findings.

In summary, our research demonstrated that sarcopenia existed in patients with GC with normal BMI and proved to be an independent predictor for postoperative complications and shorter OS. Therefore, with the improvement of living standards and nutritional status of patients with GC, sarcopenia plays an increasingly important role in the assessment of nutritional status and the prediction of short-term clinical outcomes and long-term prognosis of patients with GC with normal BMI.

Table 4 Multivariate logistic analysis of factors associated with postoperative complications

Factors	OR	95% CI	*P* value
Sarcopenia			
No	1		< 0.001
Yes	4.466	2.240–8.907	
Type of reconstruction			
Roux-en-Y	1		0.030*
Billroth I	0.356	0.165–0.768	0.008*
Billroth II	0.808	0.347–1.881	0.621

CI, confidence interval; OR, odds ratio.
*Statistically significant ($P < 0.05$).

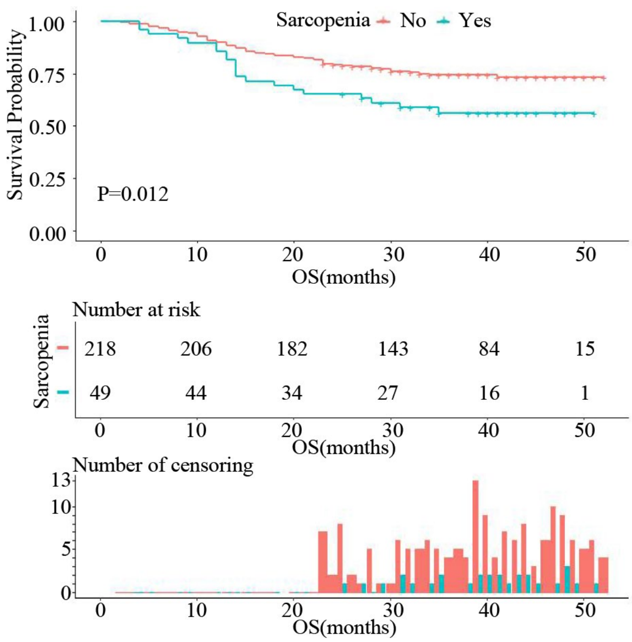

Figure 1 Kaplan–Meier survival analysis of overall survival (OS) according to sarcopenia in patients with gastric cancer with normal body mass index.

Table 5 Univariable and multivariable Cox analysis for the overall survival of patients with GC with normal BMI

	Univariate analysis			Multivariate analysis		
Factors	OR	95% CI	*P* value	OR	95% CI	*P* value
Age						
< 70 years	1					
≥ 70 years	2.062	1.315–3.234	0.002*			
Sex						
Female	1					
Male	1.663	0.915–3.022	0.095			
Hypoproteinemia						
No	1					
Yes	1.555	0.977–2.475	0.063			
Anemia						
No	1					
Yes	1.315	0.795–2.174	0.286			
NRS 2002 scores						
< 3	1			1		
≥ 3	1.852	1.176–2.915	0.008*	1.622	1.009–2.609	0.046*
ASA						
I, II	1					
III	2.078	1.247–3.463	0.005*			
Cardiopulmonary comorbidity						
No	1					
Yes	1.360	0.809–2.286	0.246			
Diabetes						
No	1					
Yes	1.100	0.478–2.531	0.823			
Sarcopenia						
No	1			1		
Yes	1.881	1.137–3.110	0.014*	1.784	1.119–2.844	0.035*
Differentiation						
Undifferentiated	1					
Differentiated	0.917	0.535–1.574	0.917			
Tumor location						
Not cardia	1					
Cardia	0.707	0.340–1.472	0.354			
Tumor size						
< 4 cm	1			1		
≥ 4 cm	4.550	2.546–8.132	< 0.001*	2.058	1.097–3.860	0.025*
TNM stage						
I	1		< 0.001*	1		< 0.001*
II	4.639	1.294–16.630	0.018*	1.859	0.481–7.181	0.368
III	15.912	4.990–50.747	< 0.001*	6.394	1.870–21.862	0.003*
Previous abdominal operation						
No	1					
Yes	1.390	0.765–2.525	0.280			
Operation method						
Open	1					
Laparoscopy	0.442	0.233–0.838	0.012*			
Epidural anesthesia						
No	1					
Yes	0.740	0.444–1.234	0.248			
Type of reconstruction						
Roux-en-Y	1		< 0.001*	1		0.006*

(Continues)

Table 5 (Continued)

Factors	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Billroth I	0.163	0.077–0.345	< 0.001*	0.347	0.160–0.752	0.007*
Billroth II	1.137	0.675–1.916	0.629	1.329	0.779–2.267	0.297
Type of resection						
Subtotal gastrectomy	1					
Total gastrectomy	2.241	1.423–3.530	< 0.001*			
Surgical durations, minutes						
< 210	1					
≥ 210	1.012	0.641–1.597	0.959			

ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; GC, gastric cancer; NRS, nutritional risk screening; OR, odds ratio; TNM, tumor–node–metastasis.
*Statistically significant ($P < 0.05$).

Funding. This work was supported by the National Natural Science Foundation of China (grant no. 31670922), the Natural Science Foundation of Zhejiang (grant no. LQ20C060003), the Health CommissIon of Zhejiang (grant no. 2019KY458), and the Municipal Science and Technology Bureau of Wenzhou (grant no. ZY202001-1).

Conflicts of Interest. The authors declared no competing interests for this work.

Author Contributions. X.Sun, J.X., X.C., X.Y., J.S., and Y.H. wrote the manuscript. X.Shen, Y.C., and Y.H. designed the research. X.Sun, J.X., X.C., W.Z, W.C., C.Z., and J.S. performed the research. X.Sun, J.X., X.C., X.Y., X.W., Y.H., and Y.C. analyzed the data.

Data Availability Statement. The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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