European Journal of Surgical Oncology 45 (2019) 1092–1098

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Sarcopenia is an effective prognostic indicator of postoperative outcomes in laparoscopic-assisted gastrectomy

Xi-Yi Chen [a, 1], Bo Li [b, 1], Bing-Wei Ma [c], Xian-Zhong Zhang [c], Wei-Zhe Chen [a], Lie-Sheng Lu [c], Xian Shen [d], Cheng-Le Zhuang [a, c, **], Zhen Yu [a, c, *]

[a] Department of Gastrointestinal Surgery, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China
[b] Department of Endocrinology, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[c] Department of Gastrointestinal Surgery, Shanghai Tenth People's Hospital Affiliated to Tongji University, Shanghai, China
[d] Department of Gastrointestinal Surgery, The Second Affiliated Hospital of Wenzhou Medical University, Wenzhou, China

ARTICLE INFO

Article history:
Received 24 May 2018
Received in revised form
16 August 2018
Accepted 29 September 2018
Available online 6 February 2019

Keywords:
Sarcopenia
Laparoscopic-assisted
Gastrectomy
Gastric cancer
Postoperative complications

ABSTRACT

Background: The association between sarcopenia and postoperative outcomes in patients who undergo laparoscopic-assisted gastrectomy is unclear. We aimed to determine the predictive value of sarcopenia for adverse postoperative outcomes after laparoscopic-assisted gastrectomy for gastric cancer.

Materials and methods: We prospectively collected the clinical data of patients who underwent elective radical laparoscopic-assisted gastrectomy for gastric cancer in two large centers from August 2014 to October 2017. The third lumbar vertebra skeletal muscle index, handgrip strength, and 6-m usual gait speed were measured to diagnose sarcopenia. Subsequently, we aimed to identify the risk factors for postoperative complications.

Results: The study included 313 patients and 37 (11.8%) patients were classified as sarcopenic. Compared with non-sarcopenic patients, sarcopenic patients were significantly older ($P < 0.001$), had higher nutritional risk screening 2002 scores ($P = 0.013$), Charlson comorbidity index (CCI) scores ($P = 0.033$), and neutrophil to lymphocyte ratio ($P = 0.004$), and lower body mass index ($P < 0.001$), preoperative serum albumin ($P < 0.001$), and hemoglobin ($P < 0.001$). Sarcopenic patients had higher postoperative complication rate ($P = 0.002$), longer postoperative hospital stays ($P = 0.020$) and higher total cost of hospitalization ($P = 0.001$). Multivariate analysis revealed that CCI score ≥ 1 (odds ratio [OR]: 2.424, 95% confidence interval [CI]: 1.309–4.487; $P = 0.005$) and sarcopenia (OR: 2.752, 95% CI: 1.274–5.944; $P = 0.010$) were independent risk factors for short-term postoperative complications.

Conclusion: Sarcopenia is an independent clinical predictor of short-term postoperative complications after laparoscopic-assisted gastrectomy.

Introduction

Gastric cancer is the fifth most common cancer and the third leading cause of cancer-related deaths in the world [1]. Especially in China, the prevalence and mortality of gastric cancer are second only to those of lung cancer, with approximately 679,100 new diagnoses and an estimated 498,000 deaths occurring in 2015 [2]. Despite advances in treatment modalities, radical gastrectomy with lymphadenectomy remains the cornerstone therapy for gastric cancer [3]. Curative gastrectomy is usually accompanied by high morbidity and mortality rates because it is a complicated surgical procedure [4]. As an emerging therapy for gastric cancer, laparoscopic gastrectomy has been increasingly proven to be better than conventional open gastrectomy in many aspects, including lower complication rates, less pain, less operative bleeding, earlier bowel movement, and shorter hospitalization periods [5,6]. Because of the abovementioned advantages, laparoscopic gastrectomy is

* Corresponding author. Department of Gastrointestinal Surgery, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, 325000, Zhejiang Province, China.
** Corresponding author. Department of Gastrointestinal Surgery, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, 325000, Zhejiang Province, China.
E-mail addresses: zhuangchengle@126.com (C.-L. Zhuang), yuzhen0577@gmail.com (Z. Yu).
[1] Xi-Yi Chen and Bo Li contributed equally to this study.

https://doi.org/10.1016/j.ejso.2018.09.030

becoming widely accepted as a viable treatment option for gastric cancer. Moreover, according to the latest Japanese gastric cancer treatment guidelines, laparoscopic distal gastrectomy has become the routine treatment for stage I gastric cancer [7].

Sarcopenia is an age-related syndrome described as a progressive and generalized decline in muscle mass (with or without a loss of fat mass) and strength [8]. The postoperative morbidity and mortality rates of elderly patients are higher than those of younger persons despite advancements in surgical treatment [9]. Recent reports have demonstrated that patients with sarcopenia are at risk for postoperative complications [10]. However, to date, the subjects of most previous studies predominantly underwent open surgery. The impact of sarcopenia on postoperative outcomes after laparoscopic-assisted gastrectomy for gastric cancer has not been investigated. Therefore, it is necessary to identify the relationship between sarcopenia and postoperative outcomes after laparoscopic-assisted gastrectomy in the laparoscopic era.

This prospective study aimed to clarify whether sarcopenia is an effective predictor of postoperative outcomes after laparoscopic-assisted gastrectomy for gastric cancer.

Materials and methods

Selection of patients

The study included patients who underwent laparoscopic-assisted gastrectomy for curable gastric cancer, from August 2014 to October 2017, at the Gastrointestinal Surgical Department of the First Affiliated Hospital of Wenzhou Medical University and Tenth People's Hospital Affiliated to TongJi University. The primary inclusion criteria were as follows: (1) age $\geq$ 18 years; (2) American Society of Anesthesiology (ASA) grade $\leq$ 3; (3) abdominal computed tomography (CT) scans available within a month before surgery; and (4) estimated tumor size $\leq$ 5 cm, estimated T stage $\leq$ 4a, and estimated N stage $\leq$ 1. Patients who (1) underwent palliative gastrectomy or emergency surgery; (2) were converted to open gastrectomy; (3) received neoadjuvant chemotherapy or radiotherapy; and (4) were unable to complete the 6-m usual gait speed test or handgrip strength test were excluded. All of the surgeries were performed by four experienced surgeons who had performed more than 50 radical laparoscopic-assisted gastrectomies for gastric cancer. In order to control for possible bias, the Japanese gastric cancer treatment guidelines 2010 (version 3) were strictly applied to all patients [11]. Each participant provided written informed consent and the ethics committee of The First Affiliated Hospital of Wenzhou Medical University and The Tenth People's Hospital Affiliated to TongJi University approved the data collection protocol for this study.

Data collection

For each patient, data on the following parameters were collected: 1) clinicopathological features, including age, gender, body mass index (BMI), ASA grade, hemoglobin concentration (anemia was defined as hemoglobin concentration < 120 g/L for men and <110 g/L for women), neutrophil to lymphocyte ratio (NLR) (preoperative NLR represented the degree of systemic inflammatory response, high NLR: $\geq$ 2.7 [12]), plasma albumin concentration (hypoalbuminemia was defined as plasma albumin concentration < 35 g/L) (blood examination data was available within 2 weeks before surgery), Charlson comorbidity index (CCI) score [13], preoperative nutritional risk screening 2002 (NRS 2002) score (NRS 2002 score was assessed within 24 h after admission and NRS 2002 score $\geq$ 3 was considered being at risk for malnutrition) [14], sarcopenia, tumor location, tumor node metastasis (TNM) stage [15], history of abdominal surgery, and histologic type; 2) operative details, including resection type, digestive reconstruction style, combined organ resection and duration of surgery; and 3) postoperative short-term outcomes, including postoperative complications within 30 days after surgery (complication was defined as grade $\geq$ II according to the Clavien-Dindo classification [16,17], if a patient had more than one type of complication, the complication with the highest grade was used for the analysis), mortality within 30 days after surgery, postoperative length of hospital stay, total cost of hospitalization, and readmission within 30 days after discharge from hospital. All patients were followed-up within 30 days of discharge.

Quantification of skeletal muscle mass

Skeletal muscle mass was measured with INFINITT PACS software version 3.0.11.3 (Seoul, Korea) using a cross-sectional CT image at the third lumbar vertebra (L3) level [18] in the inferior direction by a trained investigator who was blinded to the surgical outcomes in order to minimize measurement bias. The total skeletal muscles at the L3 level comprise the rectus abdominis, internal obliques, external obliques, transversus abdominis, quadratus lumborum, erector spinae, and psoas. Any tissue demonstrating −29 to +150 Hounsfield units (HU) was identified as skeletal muscle [19] and the boundary of the skeletal muscle was outlined for quantification. Ultimately, skeletal muscle mass (cm^2) was corrected by the square of the stature (m^2) to obtain the L3 skeletal muscle index (L3 SMI) (cm^2/m^2).

Measurement of muscle strength and physical performance

The maximal handgrip strength of the patient's dominant hand was measured by an electronic hand dynamometer (EH101; Camry, Guangdong Province, China) and was considered to represent muscle strength.

The 6-m usual gait speed was measured to represent physical performance and was performed as follows. The patient started to walk, following the examiner's instructions until he/she walked 6 m, and the time was recorded. The first foot of patients went completely over the starting and finishing lines as the beginning and end of the timer, respectively. The 6-m usual gait speed was the ratio of the 6 m to the time.

The two foregoing tests were performed three times when patients were hospitalized and the average value was recorded.

Definition and diagnosis of sarcopenia

Sarcopenia was defined as the presence of both low muscle mass and low muscle function (physical performance or muscle strength) in this study, conforming to the definition of sarcopenia of the European Working Group on Sarcopenia in Older People (EWGSOP) [8] and the Asian Working Group for Sarcopenia (AWGS) [20].

Considering the racial differences in muscle mass [21], L3 SMI $\leq$ 40.8 cm^2/m^2 for men and $\leq$34.9 cm^2/m^2 for women was defined as low muscle mass, according to our research group's large sample study [10].

Following the AWGS recommendation, a maximum handgrip strength <26 kg for men and <18 kg for women was defined as low muscle strength and a 6-m usual gait speed <0.8 m/s was defined as low physical performance [20].

Statistical analysis

Continuous variables are expressed as the mean and standard

deviation (SD) or as median and the interquartile range (IQR), applying the Student *t*-test and Mann-Whitney *U* test respectively, for comparison. Categorical variables are expressed as the number of patients and proportions and were compared using Pearson's chi-square test or Fisher's exact test. Univariate analysis of clinically relevant parameters was performed to identify potential risk factors for postoperative complications. Factors with $P < 0.10$ in the univariate analysis were further analyzed in a subsequent multivariate logistic regression analysis. Two-sided values of $P < 0.05$ were considered statistically significant. All data were analyzed with SPSS software for Windows (version 21.0 IBM, Armonk, NY, USA).

Results

Patient characteristics

From August 2014 to October 2017, a total of 313 consecutive patients were recruited in this study. The demographic and clinical characteristics of patients are summarized in Table 1. The median age of the study population was 62 years. The recruited patients were composed of 229 (73.2%) male and 84 (26.8%) female patients. The mean BMI of the total population was 22.83 kg/m^2. There were 145 (46.3%) patients in TNM stage I, 74 (23.6%) patients in TNM stage II, and 94 (30.1%) patients in TNM stage III. According to the

Table 1
Patient demographic and clinical characteristics.

Factors	Total (n = 313)	Sarcopenic (n = 37)	Non-sarcopenic (n = 276)	*P*
Age, median (IQR), years	62 (12)	74 (14)	61 (12)	<0.001*
<65	136 (43.5)	6 (16.2)	130 (47.1)	<0.001*
≥65	177 (56.5)	31 (83.8)	146 (52.9)	
Gender				0.108
Male	229 (73.2)	23 (62.2)	206 (74.6)	
Female	84 (26.8)	14 (37.8)	70 (25.4)	
BMI, mean (SD), kg/m^2	22.83 (3.12)	20.28 (2.55)	23.17 (3.03)	<0.001*
<18.5	24 (7.7)	9 (24.3)	15 (5.4)	<0.001*
18.5–23.9	184 (58.8)	25 (67.6)	159 (57.6)	
≥24	105 (33.5)	3 (8.1)	102 (37.0)	
Albumin, mean (SD), g/L	39.47 (4.31)	36.52 (4.73)	39.87 (4.10)	<0.001*
Hemoglobin, median (IQR), g/L	128 (31)	110 (27)	130.5 (29)	<0.001*
NLR, median (IQR)	2.17 (1.24)	2.54 (1.18)	2.10 (1.17)	0.004*
SMI, mean (SD), cm^2/m^2	43.87 (8.12)	32.78 (4.41)	45.39 (7.31)	<0.001*
Handgrip strength, mean (SD), kg	29.83 (9.87)	20.00 (5.63)	31.15 (9.57)	<0.001*
Gait speed, mean (SD), m/s	1.01 (0.22)	0.81 (0.23)	1.04 (0.20)	<0.001*
ASA grade				0.067
I	83 (26.5)	7 (18.9)	76 (27.5)	
II	207 (66.2)	24 (64.9)	183 (66.3)	
III	23 (7.3)	6 (16.2)	17 (6.2)	
Charlson comorbidity index score				0.033*
0	224 (71.6)	21 (56.8)	203 (73.6)	
≥1	89 (28.4)	16 (43.2)	73 (26.4)	
Previous abdominal surgery				0.158
Yes	35 (11.2)	7 (18.9)	28 (10.1)	
No	278 (88.8)	30 (81.1)	248 (89.9)	
NRS 2002 score				0.013*
<3	216 (69.0)	19 (51.4)	197 (71.4)	
≥3	97 (31.0)	18 (48.6)	79 (28.6)	
Histologic type				0.438
Undifferentiated[a]	111 (35.5)	26 (70.3)	176 (63.8)	
Differentiate[b]	202 (64.5)	11 (29.7)	100 (36.2)	
Tumor location				0.520
Upper 1/3	39 (12.5)	2 (5.4)	37 (13.5)	
Middle 1/3	63 (20.1)	8 (21.6)	55 (19.9)	
lower 1/3	198 (63.3)	26 (70.3)	172 (62.3)	
2/3 or more	13 (4.2)	1 (2.7)	12 (4.3)	
TNM stage				0.916
I	145 (46.3)	16 (43.3)	129 (46.7)	
II	74 (23.6)	9 (24.3)	65 (23.6)	
III	94 (30.1)	12 (32.4)	82 (29.7)	
Type of resection				0.889
Subtotal gastrectomy	223 (71.2)	26 (70.3)	197 (71.4)	
Total gastrectomy	90 (28.8)	11 (29.7)	79 (28.6)	
Type of reconstruction				0.319
Billroth I	145 (46.4)	14 (37.8)	131 (47.5)	
Billroth II	58 (18.5)	10 (27.0)	48 (17.4)	
Roux-en-Y	110 (35.1)	13 (35.2)	97 (35.1)	
Combined organ resection				0.158
Yes	12 (3.8)	3 (8.1)	9 (3.3)	
No	301 (96.2)	34 (91.9)	267 (96.7)	
Surgical duration, median (IQR), minutes	209 (66)	202 (55)	210 (62)	0.362

Values in parentheses are percentages unless indicated otherwise.
*Statistically significant ($P < 0.05$).
SD, Standard Deviation; IQR, Interquartile Range; BMI, Body Mass Index; ASA, American Society of Anesthesiologists; TNM, Tumor Node Metastasis.
[a] Undifferentiated carcinomas include poorly differentiated adenocarcinomas, signet ring cell carcinomas, and mucinous carcinomas.
[b] Differentiated carcinomas include well or moderately differentiated, tubular or papillary adenocarcinomas.

predefined diagnostic criteria, the prevalence of sarcopenia was 11.8% (37/317).

Postoperative outcomes

As shown in Table 2, 17.3% (54/313) of patients experienced postoperative complications. The most common complications were anastomotic leakage (3.5%, n = 11), bleeding (2.9%, n = 9), and intra-abdominal abscess (2.9%, n = 9). The postoperative major complication rate was significantly higher in the sarcopenic patients than in the non-sarcopenic patients (35.1% versus 14.8%, P = 0.002). However, the postoperative severe complication rate shown no significant differences between both groups (P = 0.626). We found that sarcopenia is associated with medical complications (18.9% versus 4.7%, P = 0.005) but not with surgical complications (16.2% versus 10.1%, P = 0.263) in the subsequent analysis. There were no significant differences between both groups in terms of mortality (P = 0.223) and readmission (P = 0.181). According to the Clavien-Dindo complication classification, there were 2.9%, 13.7%, 2.2%, and 0.6% of patients classified as Grade I, II, III, and IV, respectively. Only 3 patients (1.0%) underwent re-operation after laparoscopic-assisted gastrectomy, because of intra-abdominal bleeding. The median postoperative length of hospital stay was 11 days. Compared with non-sarcopenic patients, sarcopenic patients had a significantly longer postoperative hospital stay (P = 0.020) and higher total cost of hospitalization (P = 0.001).

Risk factors for postoperative complications

Table 3 shows the results of the univariate and multivariate analysis of preoperative characteristics for postoperative complications after laparoscopic-assisted gastrectomy for gastric cancer. In the univariate analyses, age ≥65 years (P = 0.024), hypoalbuminemia (P = 0.022), CCI (P = 0.001), and sarcopenia (P = 0.002) were associated with postoperative complications. In the subsequent multivariate logistic regression analysis, CCI score ≥1 (odds ratio [OR]: 2.424, 95% confidence interval [CI]: 1.309–4.487; P = 0.005) and sarcopenia (OR: 2.752, 95% CI: 1.274–5.944; P = 0.010) remained independent risk factors for postoperative complications after laparoscopic-assisted gastrectomy.

Discussion

Over the past several years, the effect of sarcopenia on the prediction of adverse postoperative outcomes has been well investigated. Previous studies have indicated that sarcopenia is associated with adverse postoperative short-term and long-term outcomes [10,22], and the increasing toxicity of chemotherapy-related drugs [23]. Sarcopenia has been described as a negative prognostic factor in patients with various malignancies, including colorectal cancer [24], hepatocellular carcinoma [22], pancreatic cancer [25], endometrial cancer [26] and gastric cancer.

In the present study, we demonstrated that the prevalence of sarcopenia was 11.8% and sarcopenia was an independent risk factor for short-term postoperative complications after laparoscopic-assisted gastrectomy. More precisely, there was a threefold increased risk of having postoperative complications in the sarcopenic patients than in the non-sarcopenic patients. The results demonstrated an evident negative impact of sarcopenia resulting in a longer length of stay but not in mortality and hospital readmissions. These findings were consistent with previous researches [27,28], but inconsistent with the study by Tegels et al. [29]. The

Table 2
Postoperative outcomes.

Factors	Total (n = 313)	Sarcopenic (n = 37)	Non- Sarcopenic (n = 276)	*P*
Total major complications[a]	54 (17.3)	13 (35.1)	41 (14.8)	0.002*
Severe complications	11 (3.5)	2 (5.4)	9 (3.3)	0.626
Detail of complications				
Surgical complications	34 (10.9)	6 (16.2)	28 (10.1)	0.263
Delayed gastric emptying	1 (0.3)	0	1 (0.4)	1.000
Wound infection	1 (0.3)	0	1 (0.4)	1.000
Bleeding	9 (2.9)	1 (2.7)	8 (2.9)	1.000
Intra-abdominal abscess	9 (2.9)	2 (5.4)	7 (2.5)	0.288
Anastomotic leakage	11 (3.5)	2 (5.4)	9 (3.3)	0.626
Bowel obstruction or ileus	1 (0.3)	1 (2.7)	0	0.118
Others	2 (0.6)	0	2 (0.7)	1.000
Medical complications	20 (6.4)	7 (18.9)	13 (4.7)	0.005*
Pneumonia	4 (1.3)	2 (5.4)	2 (0.7)	0.070
Pleural effusion	5 (1.6)	2 (5.4)	3 (1.1)	0.108
Persistent hypoalbuminemia	2 (0.6)	1 (2.7)	1 (0.4)	0.223
Cardiac complications	2 (0.6)	0	2 (0.7)	1.000
Cerebral infarction	1 (0.3)	0	1 (0.4)	1.000
Deep venous thrombosis	2 (0.6)	0	2 (0.7)	1.000
Urinary infection	2 (0.6)	1 (2.7)	1 (0.4)	0.223
Others	2 (0.6)	1 (2.7)	1 (0.4)	0.223
Postoperative Clavien-Dindo Grading				
Grade I	9 (2.9)	1 (2.7)	8 (2.9)	1.000
Grade II	43 (13.7)	11 (29.7)	32 (11.6)	0.003*
Grade III	7 (2.2)	1 (2.7)	6 (2.2)	0.589
Grade IV	2 (0.6)	0	2 (0.7)	1.000
30-day mortality	2 (0.6)	1 (2.7)	1 (0.4)	0.223
Re-operation	3 (1.0)	0	3 (1.1)	1.000
Postoperative hospital stays, median (IQR), days	11 (4)	12 (9)	10 (5)	0.020*
Costs, median (IQR), yuan	59864.96 (16993.32)	69055.83 (26851.92)	59102.01 (15931.66)	0.001*
Readmissions within 30 days of discharge	24 (7.7)	5 (13.5)	19 (6.9)	0.181

Values in parentheses are percentages unless indicated otherwise.
* Statistically significant ($P < 0.05$).
[a] Postoperative complications in this study were defined as any adverse event corresponding to Clavien–Dindo classification grade II or greater, occurring within 30 days of surgery. If a patient had more than one type of complication, the complication with the highest grade was used for the analysis.

Table 3
Univariate and multivariate logistic regression analysis of risk factors for total complications.

Factors	Univariate analysis		Multivariate analysis	
	Case with complication (%)	*P*	OR (95% CI)	*P*
Age		0.024*		
≥65/<65	38 (21.5)/16 (11.8)			
Gender		0.238		
Male/Female	43 (18.8)/11 (13.1)			
BMI		0.751		
<18.5	5 (20.8)			
18.5–23.9	33 (17.9)			
≥24	16 (15.2)			
Hypoalbuminemia		0.022*		
Yes/No	14 (28.6)/40 (15.2)			
Anemia		0.051		
Yes/No	22 (23.7)/32 (14.5)			
NLR		0.653		
≥2.7/<2.7	16 (18.8)/38 (16.7)			
NRS 2002 score		0.168		
≥3/<3	21 (21.6)/33 (15.3)			
ASA grade		0.777		
III/II,I	3 (13.0)/51 (17.6)			
Charlson comorbidity index score		0.001*		0.005*
≥1/0	29 (12.9)/25(28.1)		2.424 (1.309–4.487)	
Sarcopenia		0.002*		
Yes/No	13 (35.1)/41 (14.9)		2.752 (1.274–5.944)	0.010*
Previous abdominal surgery		0.160		
Yes/No	10 (27.0)/45 (16.2)			
Histologic type		0.563		
Undifferentiated/Differentiated	33 (16.3)/21 (18.9)			
Tumor location		0.508		
Upper 1/3/Not upper 1/3	8 (21.1)/46 (16.7)			
TNM stage		0.370		
I	27 (18.6)			
II	15 (20.3)			
III	12 (12.8)			
Type of reconstruction		0.344		
Roux-en-Y/Not Roux-en-Y	22 (20.0)/32 (15.8)			
Type of resection		0.414		
Total/Subtotal	18 (20.0)/36 (16.1)			
Combined organ resection		0.134		
Yes/No	4 (33.3)/50 (16.6)			
Surgical durations ≥ 210 min		0.631		
Yes/No	28 (18.3)/26 (16.3)			

*Statistically significant ($P < 0.05$). [a] OR, Odds Ratio; CI, Confidence Interval.

difference in the results may be due to the different diagnostic methods and criteria for sarcopenia and demographic and clinical characteristics of the patients. The definition of sarcopenia comprised low skeletal muscle mass and low muscle function was used in our study and two former researches [27,28] rather than low skeletal muscle mass alone [29]. In the study of Tegels et al., the diagnostic criteria of sarcopenia were based on the characteristics of the Western population, which were different from the cutoff values we used in this study. Therefore, it is highly desirable to determine the CT cutoff values of sarcopenia for different populations. In addition, there were 30.9% patients with TNM stage IV included in the study by Tegels et al., while patients with TNM stage IV were not included in our study, which may partially explain the inconsistency of the study by Tegels et al. and our study.

Nevertheless, previous studies have shown that patients with sarcopenia did not demonstrate increased postoperative complications in laparoscopic colorectal resection [30,31]. The following may explain this inconsistent conclusion. First, laparoscopic gastrectomy is more complex than laparoscopic colorectal resection and leads to a distinctly longer surgical duration. Second, malnutrition might be one of the most important contributors to this difference. Because of the high incidence of dysphagia, nausea or mechanical obstruction, gastric cancer patients are at a higher risk for malnutrition [32]. Third, none of the two studies incorporated muscle function in their definition of sarcopenia. Skeletal muscle strength does not depend on skeletal muscle mass alone; hence, the relationship between skeletal muscle strength and muscle mass is not linear. Thus, it is insufficient and of limited clinical value to define sarcopenia only in terms of skeletal muscle mass. Combining low skeletal muscle mass with reduced muscle function might optimize the diagnosis of sarcopenia and should predict postoperative clinical outcomes more accurately [8]. In the present study, we identified that a low skeletal muscle mass was not associated with higher postoperative complication rates (Supplementary Table 1). Fourth, the enhanced recovery after surgery (ERAS) protocol was implemented in the colorectal cancer patients [30] but was not implemented in our study, which might have improved the patients' postoperative situation and counterbalanced the negative postoperative effects of sarcopenia.

Although the specific mechanisms behind the higher risk for postoperative complications in sarcopenic patients are ambiguous, the following reasons can be proffered. First, lower BMI, lower serum albumin level, and higher NRS 2002 scores were associated with sarcopenia in the present study, and all of these parameters reflected a poor nutritional status. It is well known that malnutrition leads to a higher postoperative complication rate [33]. Second, the low respiratory muscle strength caused by sarcopenia may lead to a high rate of pulmonary complications [34]. Finally, sarcopenia

has been reported to be closely connected with host immunity. Sarcopenic patients might have a lower natural killer cell activity due to the decreased expression of myokines [35], which would lead to an increased risk for infectious complications.

There are many different preoperative strategies that could be employed to modify sarcopenia. Physical exercise, adequate nutritional protein intake [36], and certain nutritional supplements (such as leucine and omega-3 polyunsaturated fatty acids) [37] are all effective interventions to counteract sarcopenia. Yamamoto et al. reported that preoperative exercise and nutritional support program can reduce sarcopenia and improve postoperative outcomes in elderly sarcopenic patients with gastric cancer [38].

The present study demonstrated that age and hypoalbuminemia were significantly associated with postoperative complications in the univariate analysis but these two factors did not remain significant in the multivariate analysis. Sarcopenia is strongly related to advanced age and lower plasma albumin concentration. Therefore, unsurprising, these two confounding factors did not retain their significance in the multivariate analysis. Consistent with previous report [39], we found the CCI score is another independent risk factor for postoperative complications in the current study.

There are several limitations in this study that should be noted. First, this is a nonrandomized controlled study from two centers. However, the data in our study conducted in two large centers of gastric cancer in China remains representative. Second, the data in this study only included outcomes within the first 30 days postoperatively, which may have limited our conclusions regarding the correlation between laparoscopic-assisted gastrectomy and early morbidity. Long-term follow-up data are needed in future studies to investigate whether sarcopenia has an effect on survival and quality of life in patients who undergo laparoscopic-assisted gastrectomy.

Conclusions

This prospective study showed that sarcopenia is an effective clinical indicator of adverse postoperative complications in patients undergoing laparoscopic-assisted gastrectomy for gastric cancer. The evaluation for sarcopenia should be integrated into the preoperative risk assessments for gastric cancer treated with laparoscopic-assisted gastrectomy.

Conflict of interest statement

The authors declare that they have no conflict of interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2018.09.030.

Disclosures

The authors declare that they have no competing interests.

Funding source

This work was supported by the National Natural Science Foundation of China (No. 81500663).

References

[1] Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics. CA A Cancer J Clin 2012;65(2):87–108. https://doi.org/10.3322/caac.21262. 2015.
[2] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, et al. Cancer statistics in China, 2015. CA A Cancer J Clin 2016;66(2):115–32. https://doi.org/10.3322/caac.21338.
[3] Thrumurthy SG, Chaudry MA, Hochhauser D, Mughal M. The diagnosis and management of gastric cancer. BMJ 2013;347:f6367. https://doi.org/10.1136/bmj.f6367.
[4] Papenfuss WA, Kukar M, Oxenberg J, Attwood K, Nurkin S, Malhotra U, et al. Morbidity and mortality associated with gastrectomy for gastric cancer. Ann Surg Oncol 2014;21(9):3008–14. https://doi.org/10.1245/s10434-014-3664-z.
[5] Kim W, Kim HH, Han SU, Kim MC, Hyung WJ, Ryu SW, et al. Decreased morbidity of laparoscopic distal gastrectomy compared with open distal gastrectomy for stage I gastric cancer: short-term outcomes from a multicenter randomized controlled trial (KLASS-01). Ann Surg 2016;263(1):28–35. https://doi.org/10.1097/SLA.0000000000001346.
[6] Hu Y, Huang C, Sun Y, Su X, Cao H, Hu J, et al. Morbidity and mortality of laparoscopic versus open D2 distal gastrectomy for advanced gastric cancer: a randomized controlled trial. J Clin Oncol: official journal of the American Society of Clinical Oncology 2016;34(12):1350–7. https://doi.org/10.1200/JCO.2015.63.7215.
[7] Japanese Gastric Cancer A Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer: official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association 2017;20(1):1–19. https://doi.org/10.1007/s10120-016-0622-4.
[8] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older People. Age Ageing 2010;39(4):412–23. https://doi.org/10.1093/ageing/afq034.
[9] Zhou CJ, Chen FF, Zhuang CL, Pang WY, Zhang FY, Huang DD, et al. Feasibility of radical gastrectomy for elderly patients with gastric cancer. Eur J Surg Oncol: the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 2016;42(2):303–11. https://doi.org/10.1016/j.ejso.2015.11.013.
[10] Zhuang CL, Huang DD, Pang WY, Zhou CJ, Wang SL, Lou N, et al. Sarcopenia is an independent predictor of severe postoperative complications and long-term survival after radical gastrectomy for gastric cancer: analysis from a large-scale cohort. Medicine 2016;95(13). https://doi.org/10.1097/MD.0000000000003164. e3164.
[11] Japanese Gastric Cancer A Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric Cancer: official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association 2011;14(2):113–23. https://doi.org/10.1007/s10120-011-0042-4.
[12] Miyatani K, Saito H, Kono Y, Murakami Y, Kuroda H, Matsunaga T, et al. Combined analysis of the pre- and postoperative neutrophil-lymphocyte ratio predicts the outcomes of patients with gastric cancer. Surg Today 2017. https://doi.org/10.1007/s00595-017-1587-6.
[13] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 1987;40(5):373–83.
[14] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M, Educational, et al. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003;22(4):415–21.
[15] Biondi A, Hyung WJ. Seventh edition of TNM classification for gastric cancer. J Clin Oncol: official journal of the American Society of Clinical Oncology 2011;29(32):4338–9. https://doi.org/10.1200/JCO.2011.36.9900. author reply 4340-4332.
[16] Dindo D, Demartines N, Clavien P-A. Classification of surgical complications. Ann Surg 2004;240(2):205–13. https://doi.org/10.1097/01.sla.0000133083.54934.ae.
[17] Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250(2):187–96. https://doi.org/10.1097/SLA.0b013e3181b13ca2.
[18] Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme 2008;33(5):997–1006. https://doi.org/10.1139/H08-075.
[19] Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol 1998;85(1):115–22.
[20] Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. J Am Med Dir Assoc 2014;15(2):95–101. https://doi.org/10.1016/j.jamda.2013.11.025.
[21] Silva AM, Shen W, Heo M, Gallagher D, Wang Z, Sardinha LB, et al. Ethnicity-related skeletal muscle differences across the lifespan. Am J Hum Biol: the official journal of the Human Biology Council 2010;22(1):76–82. https://doi.org/10.1002/ajhb.20956.
[22] Voron T, Tselikas L, Pietrasz D, Pigneur F, Laurent A, Compagnon P, et al. Sarcopenia impacts on short- and long-term results of hepatectomy for hepatocellular carcinoma. Ann Surg 2015;261(6):1173–83. https://doi.org/10.1097/SLA.0000000000000743.
[23] Tan BHL, Brammer K, Randhawa N, Welch NT, Parsons SL, James EJ, et al.

Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophago-gastric cancer. Ejso-Eur J Surg Onc 2015;41(3):333–8. https://doi.org/10.1016/j.ejso.2014.11.040.
[24] Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Canc 2012;107(6):931–6. https://doi.org/10.1038/bjc.2012.350.
[25] Joglekar S, Asghar A, Mott SL, Johnson BE, Button AM, Clark E, et al. Sarcopenia is an independent predictor of complications following pancreatectomy for adenocarcinoma. J Surg Oncol 2015;111(6):771–5. https://doi.org/10.1002/jso.23862.
[26] Kuroki LM, Mangano M, Allsworth JE, Menias CO, Massad LS, Powell MA, et al. Pre-operative assessment of muscle mass to predict surgical complications and prognosis in patients with endometrial cancer. Ann Surg Oncol 2015;22(3):972–9. https://doi.org/10.1245/s10434-014-4040-8.
[27] Wang SL, Zhuang CL, Huang DD, Pang WY, Lou N, Chen FF, et al. Sarcopenia adversely impacts postoperative clinical outcomes following gastrectomy in patients with gastric cancer: a prospective study. Ann Surg Oncol 2016;23(2):556–64. https://doi.org/10.1245/s10434-015-4887-3.
[28] Fukuda Y, Yamamoto K, Hirao M, Nishikawa K, Nagatsuma Y, Nakayama T, et al. Sarcopenia is associated with severe postoperative complications in elderly gastric cancer patients undergoing gastrectomy. Gastric Cancer: official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association 2016;19(3):986–93. https://doi.org/10.1007/s10120-015-0546-4.
[29] Tegels JJ, van Vugt JL, Reisinger KW, Hulsewe KW, Hoofwijk AG, Derikx JP, et al. Sarcopenia is highly prevalent in patients undergoing surgery for gastric cancer but not associated with worse outcomes. J Surg Oncol 2015;112(4):403–7. https://doi.org/10.1002/jso.24015.
[30] Pedziwiatr M, Pisarska M, Major P, Grochowska A, Matlok M, Przeczek K, et al. Laparoscopic colorectal cancer surgery combined with enhanced recovery after surgery protocol (ERAS) reduces the negative impact of sarcopenia on short-term outcomes. Eur J Surg Oncol: the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 2016;42(6):779–87. https://doi.org/10.1016/j.ejso.2016.03.037.
[31] Ouchi A, Asano M, Aono K, Watanabe T, Oya S. Laparoscopic colorectal resection in patients with sarcopenia: a retrospective case-control study. J Laparoendosc Adv Surg Tech Part A 2016;26(5):366–70. https://doi.org/10.1089/lap.2015.0494.
[32] Mariette C, De Botton ML, Piessen G. Surgery in esophageal and gastric cancer patients: what is the role for nutrition support in your daily practice? Ann Surg Oncol 2012;19(7):2128–34. https://doi.org/10.1245/s10434-012-2225-6.
[33] Cao XL, Zhao G, Yu T, An Q, Yang H, Xiao G. Preoperative prognostic nutritional index correlates with severe complications and poor survival in patients with colorectal cancer undergoing curative laparoscopic surgery: a retrospective study in a single Chinese institution. Nutrition And Cancer-an International Journal 2017;69(3):454–63. https://doi.org/10.1080/01635581.2017.1285038.
[34] Makiura D, Ono R, Inoue J, Kashiwa M, Oshikiri T, Nakamura T, et al. Preoperative sarcopenia is a predictor of postoperative pulmonary complications in esophageal cancer following esophagectomy: a retrospective cohort study. Journal of geriatric oncology 2016;7(6):430–6. https://doi.org/10.1016/j.jgo.2016.07.003.
[35] Lutz CT, Quinn LS. Sarcopenia, obesity, and natural killer cell immune senescence in aging: Altered cytokine levels as a common mechanism. Aging-Us 2012;4(8):535–46. https://doi.org/10.18632/Aging.100482.
[36] Deutz NE, Bauer JM, Barazzoni R, Biolo G, Boirie Y, Bosy-Westphal A, et al. Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. Clin Nutr 2014;33(6):929–36. https://doi.org/10.1016/j.clnu.2014.04.007.
[37] Phillips SM. Nutritional supplements in support of resistance exercise to counter age-related sarcopenia. Advances in nutrition 2015;6(4):452–60. https://doi.org/10.3945/an.115.008367.
[38] Yamamoto K, Nagatsuma Y, Fukuda Y, Hirao M, Nishikawa K, Miyamoto A, et al. Effectiveness of a preoperative exercise and nutritional support program for elderly sarcopenic patients with gastric cancer. Gastric Cancer: official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association 2016. https://doi.org/10.1007/s10120-016-0683-4.
[39] Huang CM, Tu RH, Lin JX, Zheng CH, Li P, Xie JW, et al. A scoring system to predict the risk of postoperative complications after laparoscopic gastrectomy for gastric cancer based on a large-scale retrospective study. Medicine 2015;94(17). https://doi.org/10.1097/MD.0000000000000812. e812.