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ORIGINAL ARTICLE

Role of frailty and nutritional status in predicting complications following total gastrectomy with D2 lymphadenectomy in patients with gastric cancer: a prospective study

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Abstract
Purpose This study was performed to determine the association of frailty and nutritional status with postoperative complications after total gastrectomy (TG) with D2 lymphadenectomy in patients with gastric cancer.
Methods Patients undergoing TG with D2 lymphadenectomy for gastric cancer between August 2014 and February 2016 were enrolled. Frailty was evaluated by sarcopenia which was diagnosed by a combination of third lumbar vertebra muscle index (L3 MI), handgrip strength, and 6-m usual gait speed. Nutritional status was evaluated by the nutritional risk screening 2002 (NRS 2002) score. Univariate and multivariate analyses evaluating the risk factors for postoperative complications were performed.
Results A total of 158 patients were analyzed, and 27.2 % developed complications within 30 days of surgery. One patient died within 30 days of the operation. In the univariate analyses, NRS 2002 score ≥3 (OR = 2.468, P = 0.012), sarcopenia (OR = 2.764, P = 0.008), and tumor located at the cardia (OR = 2.072, P = 0.046) were associated with the postoperative complications. Multivariable analysis revealed that sarcopenia (OR = 3.084, P = 0.005) and tumor located at the cardia (OR = 2.347, P = 0.026) were independent predictors of postoperative complications.
Conclusions This study showed a significant relationship between postoperative complications and geriatric frailty using sarcopenia in patients with gastric cancer after TG with D2 lymphadenectomy. Frailty should be integrated into preoperative risk assessment and may have implications in preoperative decisionmaking.

Keywords Total gastrectomy · D2 lymphadenectomy · Morbidity · Frailty · Nutritional status · Sarcopenia

Introduction

Despite a decrease in its incidence, gastric cancer is still the fifth most common malignancy and the third leading cause of cancer-related death worldwide [1]. In Eastern Asian countries, particularly Japan, Korea, and China, gastric cancer is one of the most prevalent types of malignancy [2]. Although treatment of gastric cancer is multidisciplinary nowadays, optimal surgery remains the cornerstone of improved survival [3]. According to the Japanese treatment guidelines for gastric cancer [4], total gastrectomy (TG) with a proper extent of lymphadenectomy should be adopted for upper and middle-third gastric carcinoma, advanced esophagogastric junction tumor, or huge gastric tumors. Compared with subtotal gastrectomy (STG), TG is considered to have a worse short-term outcome [5, 6]. The value of extended surgical dissection to remove the draining lymph nodes is controversial. In Eastern countries, especially in high-volume countries like Japan and

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South Korea [7], surgeons routinely perform an extended (D2) lymphadenectomy. However, for fear of the increased postoperative morbidity and mortality, Western surgeons usually perform more limited lymph node dissection, such as D1 and modified D2 (D1+) lymphadenectomy [8]. Recently, a multicenter trial in the USA demonstrated that D2 lymphadenectomy did not increase morbidity or mortality in patients undergoing gastrectomy for cancer [9]. Performing D2 lymphadenectomy in patients undergoing gastrectomy is gradually reaching a consensus worldwide. Therefore, finding out the predictors for postoperative outcomes after TG with D2 is extremely urgent and significant.

Several previous studies have demonstrated the risk factors for postoperative outcomes after TG for gastric cancer [10–12]. While it remains difficult to select patients solely focusing on age, the American Society of Anesthesiologists (ASA) classification, body mass index (BMI), and weight loss at most is not sensitive and inadequate for high-risk patient selection [13–15]. Frailty and nutritional status, which can help to accurately identify elderly patients who are at risk of an adverse postoperative outcome and play a more important role in patient selection [16–19], were failed to be incorporated into risk analysis for postoperative complication in patients after TG for gastric cancer [10–12], especially in TG with D2 lymphadenectomy, making the scoring systems incomplete and inaccurate.

Recent studies have evaluated the relationship between frailty and postoperative mortality in gastric cancer surgery [20]. Frailty has been demonstrated to be a significant predictor of postoperative complications in the surgical patient [21]. A widely investigated aspect of frailty is sarcopenia. Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength [22]. Patients who had a concomitant decrease in muscle mass were more likely to suffer from disabilities and a worsening in their mobility. Sarcopenia, different from ordinary weight loss or cachexia, can occur in normal-weight, overweight, and obese patients and therefore relates to muscle mass rather than simply weight. In patients with upper gastrointestinal tract tumor, nutritional status is another important aspect as their intake is often compromised by mechanical obstruction. Nutritional risk is a key factor that is associated with poor clinical outcomes. However, despite preoperative malnutrition is common and has its high predictive values in patients with cancer, malnutrition remains unappreciated and neglected by clinicians. Several studies have shown the value of nutritional evaluation by the NRS 2002 score in surgical patients [19, 23] but not in patients after TG with D2 lymphadenectomy.

The aim of our study was to investigate if preoperative assessment of frailty using sarcopenia and assessment nutritional status using the NRS 2002 score could be a helpful tool in the preoperative risk assessment of the patients undergoing TG with D2 lymphadenectomy for gastric cancer.

Patients and methods

Patient selection

From August 2014 and February 2016, consecutive patients who underwent TG with D2 lymphadenectomy for gastric cancer at the Gastrointestinal Surgical Department, The First Affiliated Hospital of Wenzhou Medical University, were included in this prospective study. Inclusion criteria were patients over 18 years of age who had an ASA grade of III or less and histologically proven gastric adenocarcinoma before surgery. Exclusion criteria included patients with recurrent gastric cancer and patients with a presence of motor dysfunction or cancer metastasis that could not be cured by radical surgery. All operations were performed by nine surgeons whose operation quality was considered to be satisfactory after assessment by two professors in our department. Patients with distal esophagus cancer and patients who received extended resections (e.g., transhiatal gastrectomy and transthoracic esophagectomy) were also excluded in this study. TG with D2 lymphadenectomy for gastric cancer was performed in accordance with the Japanese Gastric Cancer Treatment Guidelines [4].

Preoperative investigations

All data were collected prospectively and maintained in a digital database. Preoperative assessment includes the following: (1) clinicopathological features, including age, gender, ASA grade, and BMI; NRS 2002 scores (recorded within 24 h of admission, and patients with a total score of 3 or more were considered at nutritional risk [24]); plasma albumin concentration (a plasma albumin concentration <35 g/L was defined as hypoproteinemia); hemoglobin concentration (a hemoglobin concentration <120 g/L in men and <110 g/L in women was defined as anemia); sarcopenia; Charlson comorbidity index score [25]; cardiopulmonary comorbidities (the presence of cardiopulmonary disease(s) before surgery, including hypertension, cardiac disease (myocardial infarction or stenocardia), pneumonia, bronchitis, tuberculosis, chronic obstructive pulmonary disease (COPD), and pleural effusion and asthma); previous abdominal surgery; Lauren's histology type; tumor location; tumor size; tumor node metastasis (TNM) stage; and combined resection and (2) postoperative outcomes, including the postoperative morbidities (complications that occurred within 30 days of the operation and those classified as grade II or above according to the Clavien-Dindo classification [26] were included in the univariate and multivariate analyses); surgical mortality (defined as death within 30 days after surgical resection); length of postoperative hospital stay; hospital costs; and readmissions within 30 days of discharge.

Measurement of muscle strength and physical performance

Muscle strength was evaluated by measuring handgrip strength, which was measured by hand using an electronic hand dynamometer (EH101; Camry, Guangdong Province, China) with all their strength. Three trials for the dominant hand were performed, with a 1-min rest interval between tests, and the best result was used for the present analyses. Low handgrip strength was defined as <26 kg for men and <18 kg for women [27].

Physical performance was evaluated by measuring the 6-m usual gait speed. Participants stood with their feet behind a starting line and started walking following the examiner's command. Timing was started with the first foot fall and stopped when the patient's first foot completely crossed the 6-m end line [28]. Low gait speed was defined as <0.8 m/s [27].

The two tests were conducted once patients were hospitalized within 7 days before surgery. The maximal value of three consecutive tests was recorded.

Image analysis

A cross-sectional computed tomography (CT) image at the inferior aspect of the third lumbar vertebra (L3) was selected for estimating muscle mass as described previously [29]. A Hounsfield units threshold range of −29 to +150 was used for skeletal muscle [30]. Hand adjustment of the selected areas was performed if necessary, and the muscle area was calculated automatically. To minimize measurement bias, one trained investigator, who was blinded for all anthropometric and surgical characteristics, identified and measured the muscle area on a dedicated processing system (version 3.0.11.3 BN17 32 bits; INFINITT Healthcare Co., Ltd.). Muscle areas computed from each image were normalized for stature (m^2) to obtain the L3 skeletal muscle index (SMI, cm^2/m^2). The cut-off values for low muscle mass were L3 SMI <34.9 cm^2/m^2 for women and L3 SMI <40.8 cm^2/m^2 for men, which was concluded from a large sample study in our department [31].

Assessment of sarcopenia

Sarcopenia was defined as low muscle mass plus low muscle strength and/or low physical performance according to the European Working Group on Sarcopenia in Older People (EWGSOP) [32] and the Asian Working Group for Sarcopenia (AWGS) [27].

Follow-up strategies

Information on complications was obtained by telephone interview every 10 days after discharge. For patients who had complications within 30 days after discharge, complications were assessed and recorded once they came back to our hospital.

Statistical analysis

The statistical analyses were performed using the SPSS statistics version 22.0 (IBM, Armonk, NY, USA) software programs. Continuous variables were presented as the mean and standard deviation (normally distributed variables) or median and interquartile range (non-normally distributed variables). Categorical variables were presented as numbers and percentages. Clinical variables were compared using Student's t test (normally distributed data), Pearson's chi-square test or Fisher's exact test (categorical data), and the Mann-Whitney U test (non-normally distributed continuous data and ranked data) as appropriate. Variables with a value of $P < 0.10$ in the univariate analyses were included in the subsequent multivariate forward logistic regression analysis. All tests were two-sided, and differences were considered to be statistically significant at $P < 0.05$.

Results

Patient population

The clinicopathological characteristics are summarized in Table 1. The recruited population was composed by 158 patients, with a mean age of 66.9 ± 8.7 years, predominantly males (79.7 %). Patients with a diagnosis of sarcopenia were 39 (24.7 %), while 119 (75.3 %) had no sarcopenia. The mean BMI of the study population was 22.8 kg/m^2. The distribution of the TNM stages in the patients was 33 (20.9 %), 37 (23.4 %), and 88 (55.7 %) for TNM stages I, II, and III, respectively. The most common comorbidities were cardiopulmonary comorbidities (27.8 %, $n = 44$), obesity (15.8 %, $n = 25$), and diabetes (10.1 %, $n = 16$). Nineteen operations were performed laparoscopically. Patients were divided into two groups: sarcopenia and non-sarcopenia. Among the preoperative factors analyzed, sex, Charlson score, ASA score, and diabetes did not differ significantly between sarcopenic and non-sarcopenic patients. However, sarcopenic patients were older ($P < 0.001$) and had lower BMI ($P < 0.001$), preoperative serum albumin ($P = 0.001$), and hemoglobin ($P = 0.002$) and higher NRS 2002 score ($P < 0.001$). The sarcopenia features, including L3 SMI ($P < 0.001$), handgrip strength ($P < 0.001$), and gait speed ($P < 0.001$), were all significantly lower among those with sarcopenia. No pathological characteristics differed between sarcopenic and non-sarcopenic patients.

Table 1 Patient demographic and clinical characteristics

Factors	Total ($n = 158$)	Sarcopenic ($n = 39$)	Non-sarcopenic ($n = 119$)	P value
Age, mean (SD), years	66.9 (8.7)	72.9 (6.5)	64.9 (8.5)	<0.001*
Gender				0.963
Female	32	8	24	
Male	126	31	95	
BMI, mean (SD), kg/m^2	22.8 (2.8)	20.5 (2.5)	22.8 (2.7)	<0.001*
Albumin, mean (SD), g/L	37.4 (4.1)	35.3 (4.5)	37.9 (4.1)	0.001*
Hemoglobin, mean (SD), g/L	115.3 (24.6)	108.7 (21.2)	121.1 (22.2)	0.002*
Median no. of retrieved lymph nodes, range	24 (18–52)	24 (19–49)	27 (18–52)	
BMI				0.004*
<18.5	12	32	87	
18.5–25	121	6	6	
>25	25	1	26	
ASA grade				0.105
I	7	0	7	
II	117	27	90	
III	34	12	22	
Charlson score				0.137
0	120	25	95	
1	27	10	17	
≥2	11	4	7	
NRS 2002 score				<0.001*
<3	91	12	79	
≥3	67	27	40	
Diabetes				0.736
No	142	34	108	
Yes	16	5	11	
SMI (cm^2/m^2; mean (SD))	41.8 (7.8)	34.5 (3.8)	44.2 (7.3)	<0.001*
Handgrip strength (kg; mean (SD))	28.6 (8.9)	20.8 (6.5)	31.2 (8.0)	<0.001*
Gait speed (m/s; mean (SD))	0.98 (0.21)	0.77 (0.17)	1.02 (0.18)	<0.001*
Cardiopulmonary comorbidities				0.639
No	114	27	87	
Yes	44	12	32	
Previous abdominal surgery				1.000
No	141	35	106	
Yes	17	4	13	
Histologic type				0.578
Differentiated[a]	51	14	37	
Undifferentiated[b]	107	25	82	
T category				0.595
T1	17	4	13	
T2	17	2	15	
T3	46	13	33	
T4	78	20	58	
N category				0.325
N0	59	10	49	
N1	27	9	18	
N2	31	8	23	
N3	41	12	29	
Tumor location				0.365
Not cardia	104	28	76	
Cardia	54	11	43	

Table 1 (continued)

Factors	Total ($n = 158$)	Sarcopenic ($n = 39$)	Non-sarcopenic ($n = 119$)	*P* value
TNM stage				0.282
I	33	6	27	
II	37	7	30	
III	88	26	62	
Laparoscopic surgery				0.214
No	139	37	102	
Yes	19	2	17	
Any additional organ resection[c]				0.038*
No	137	30	107	
Yes	21	9	12	

BMI body mass index, *ASA* American Society of Anesthesiologists, *NRS* nutritional risk screening, *SMI* skeletal muscle index, *SD* standard deviation, *IQR* interquartile range

[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

[c] Splenectomy and/or pancreatectomy

Short-term surgical outcomes

As shown in Table 2, the complications classified as grade II or above were observed in 27.2 % of the patients. The median postoperative hospital stay was 16.3 days (range, 11.0–18.0 days). The most common complications were pneumonia (7.0 %, $n = 11$) and wound infection (5.7 %, $n = 9$). Only one patient died within 30 days of the operation. The cause of death was cardiac failure. Eleven patients were readmitted within 30 days of discharge for a readmission rate of 7.0 %.

The results of the univariate and multivariate analyses of factors associated with postoperative complications (grade II or above) are shown in Tables 3 and 4, respectively. In the univariate analyses, NRS 2002 score ≥3 (OR = 2.468, $P = 0.012$), sarcopenia (OR = 2.764, $P = 0.008$), and tumor located at the cardia (OR = 2.072, $P = 0.046$) were associated with the postoperative complications. The results of the multivariate analysis revealed that the independent risk factors for postoperative complications were sarcopenia (OR = 3.084, $P = 0.005$) and tumor located at the cardia (OR = 2.347, $P = 0.026$).

Discussion

As TG should be adopted for tumors located in the upper third of the stomach or advanced gastric cancer extending to the cardia, selection of surgical procedure is mainly decided by the physical indexes of the tumor such as size and location. Although the Japanese treatment guidelines for gastric cancer issued by the Japanese Gastric Cancer Association (JGCA) have detailed the excision extension selection in different locations and sizes of the tumor, there still has an overlap between operation indication for TG and STG. Several previous studies have reported a higher complication rate after TG compared with subtotal gastrectomy [5, 6], leading to TG being considered a more invasive surgical procedure. On the other hand, with regard to lymph node dissection, D2 lymphadenectomy is widely accepted as the standard procedure for advanced gastric cancer, especially in Eastern countries. On the contrary, Western surgeons usually perform D1 or modified D2 (D1+) lymphadenectomy due to fears about increasing the short-term morbidity and mortality by D2 lymphadenectomy [33, 34]. With the emergence of the latest results based on a multicenter trial in the USA, D2 lymphadenectomy did not increase morbidity or mortality in patients undergoing gastrectomy for cancer, making the surgeons more confident in D2 lymphadenectomy [9]. Not long in the future, with the increase in the volume of surgery and improvement of surgical specialization, performing D2 lymphadenectomy in patients undergoing gastrectomy may gradually reach a consensus worldwide. Therefore, identifying the predictors for postoperative outcomes after TG with D2 lymphadenectomy is extremely urgent and significant.

Recently, factors such as age, ASA classification, BMI, and weight loss were found to be associated with postoperative outcomes in patients after gastrectomy for gastric cancer, while to identify high-risk patients, solely focusing on those factors is not sensitive and inadequate. Currently, frailty and nutritional status were suggested to be incorporated into risk analysis for postoperative outcomes in patients after surgery [13]. However, whether frailty and nutritional status were associated with postoperative complications in patients after TG with D2 lymphadenectomy for gastric cancer was unclear. To further improve and complete the prediction system, frailty and nutritional status were incorporated in this study.

Table 2 Short-term outcomes

Factors	Frequency, *n*	Patients, %
Major postoperative complications[a]		
Grade II or above	46	27.2
Grade III or above	10	6.3
Grade I	8	5.1
Grade II	33	20.9
Grade III	4	2.5
Grade IV	5	3.2
Grade V	1	0.6
Detail of complications		
Wound infection	9	5.7
Bleeding	5	3.2
Intra-abdominal abscess	2	1.3
Anastomotic leakage	4	2.5
Bowel obstruction or ileus	3	1.9
Pancreatic fistula	2	1.3
Pneumonia	11	7.0
Respiratory failure	2	0.9
Thoracic cavity fluid collection or abscess	4	2.5
Cardiac	3	1.9
Others	3	1.9
30-day mortality	1	0.6
Postoperative hospital stays, median (IQR), days	16.3 (11.0–18.0)	
30-day readmissions	11	7.0
Costs, median (IQR), ¥	58680 (50819–72942)	

[a] Patients who experienced more than one complication were classified as higher-grade complication

Frailty is associated with a decline in physiologic reserve and function across multiple physiologic systems [16]. The association of frailty and poor postoperative outcome has been described in gastric cancer surgery before [20], while a consensus on which method should be used to measure frailty has proved difficult to achieve [17]. Recently, sarcopenia has been proposed as an accurate and quantitative global marker of frailty [35]. Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength [22]. We choose sarcopenia for frailty assessment for several reasons. First, cross-sectional abdominal scanning by CT is routinely available for many gastric cancer patients, generally used to assess tumor location and size and to look for abdominal metastases. Thus, quantification of skeletal muscle mass is a precise, neither expensive nor time-consuming approach and could be included in the preoperative assessment of all patients in an objective way by radiologists. Second, we choose handgrip strength and 6-m usual gait speed test for muscle strength and physical performance assessment for these tests are quite simple and not time consuming. Several studies have highlighted the importance of sarcopenia to predict perioperative outcomes among patients undergoing surgery for gastrointestinal cancer [36–39]. Consistent with these findings, we demonstrated that sarcopenia was a predictor of postoperative complications in patients after TG with D2 lymphadenectomy for gastric cancer. However, the study by Tegels et al. [40] did not confirm a significant correlation between sarcopenia and postoperative morbidity or mortality. The difference in the results may be due to the different diagnostic methods and criteria for sarcopenia and demographic and clinical characteristics of patients. Due to the retrospective design of the study by Tegels et al., only skeletal muscle mass was included, as the unique parameter for diagnosing sarcopenia. However, in our prospective study, sarcopenia was defined as reduced muscle mass plus low muscle strength and/or low physical performance. Current consensus statements recommend to not use muscle mass measurement alone because of a non-linear relationship between muscle mass and function [27, 32]. Thus, defining sarcopenia solely by muscle mass measurement, as was done in the study by Tegels et al., is not an optimal method for classification of sarcopenia. Besides, in the study by Tegels et al., the diagnostic criteria of sarcopenia were based on the characteristics of the Western population. The study by Van Vugt et al. emphasized the cut-off values should be adjusted for ethnicity and tumor type [41]. Thus, considering the

Table 3 Univariate logistic regression analysis of risk factors for complications

Factors	Complications[a] (n = 43)	No complications (n = 115)	OR	95 % CI	P
Age					
<75	31	98	1		
≥75	12	17	2.231	0.961–5.180	0.058
Gender					
Female	7	25	1		
Male	36	90	1.429	0.568–3.595	0.447
BMI					0.216
<18.5	6	6			
18.5–25	30	89			
>25	7	20			
Hypoproteinemia					
No	24	78	1		
Yes	19	37	1.669	0.814–3.421	
Anemia					
No	23	64	1		
Yes	20	51	1.669	0.814–3.421	0.160
ASA grade					
I–II	29	94	1		
III	14	21	2.161	0.977–4.781	0.054
Charlson score					0.068
0	27	93			
1	11	16			
≥2	5	6			
NRS 2002 score					0.012*
<3	27	71	1		
≥3	26	44	2.468	1.204–5.059	
Sarcopenia					0.008*
No	26	93	1		
Yes	17	22	2.764	1.282–5.957	
Diabetes					
No	37	105	1		
Yes	6	10	1.703	0.579–5.010	0.497
Cardiopulmonary comorbidities					
No	27	87	1		
Yes	16	28	1.841	0.869–3.901	0.108
Previous abdominal surgery					
No	37	104	1		
Yes	6	11	1.533	0.530–4.439	0.614
Histologic type					
Differentiated[b]	14	37	1		
Undifferentiated[c]	29	78	0.983	0.465–2.077	0.963
Tumor location					
Not cardia	23	81	1		
Cardia	20	34	2.072	1.008–4.259	0.046*
TNM stage					0.660
I	11	22			
II	9	28			
III	23	65			
Laparoscopic surgery					
No	41	98	1		0.081
Yes	2	17	0.281	0.062–1.273	
Any additional organ resection[d]					
No	34	103	1		
Yes	9	12	2.272	0.881–5.859	0.085

Values in parentheses are percentages unless indicated otherwise

BMI body mass index, *ASA* American Society of Anesthesiologists, *NRS* nutritional risk screening, *SD* standard deviation, *IQR* interquartile range

[a] Grade II or above

[b] Undifferentiated carcinomas include poorly differentiated adenocarcinomas, signet-ring cell carcinomas, and mucinous carcinomas.

[c] Differentiated carcinomas include well- or moderately differentiated, tubular, or papillary adenocarcinomas.

[d] Splenectomy and/or pancreatectomy

*Statistically significant ($P < 0.05$)

Table 4 Multivariate logistic regression analysis of risk factors for complications

Factors	OR	95 % CI	P
Sarcopenia	3.084	1.395–6.820	0.005*
Tumor located at the cardia	2.347	1.107–4.976	0.026*

*Statistically significant ($P < 0.05$)

different patient characteristics in Asia and the West, we adopted the cut-off values of 34.9 cm^2/m^2 for women and 40.8 cm^2/m^2 for men to define low muscle mass, which were obtained from a large sample study in our department [31]. In addition, there were 47 (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.

Malnutrition is a common geriatric syndrome which has been recognized as a risk factor for sarcopenia and frequently coexists with it [42, 43]. Besides, commonly used methods for nutritional status assessment such as weight loss, BMI, and serum albumin are not sensitive and a normal or high BMI might mask malnutrition. These support a new strategy for the screening of malnutrition, in which body composition evaluation takes a greater role. The European Society for Clinical Nutrition and Metabolism (ESPEN) guideline recommendation for nutrition screening in the hospital setting is the NRS 2002 score [24], while the NRS 2002 score has not yet been validated in cohorts of patients after TG with D2 lymphadenectomy for gastric cancer. Another reason for choosing the NRS 2002 score for nutritional status assessment is that it can be completed in only a few minutes and therefore is easy to perform once patients are admitted to hospital. Without accounting for sarcopenia, we found nutritional risk (NRS 2002 score ≥3) and tumor located at the cardia were correlated with postoperative complications in multivariate analysis. However, after adjusting for sarcopenia, nutritional risk (NRS 2002 score ≥3) ceased to be significant predictors of postoperative complications. As mentioned earlier, our results also showed that patients with sarcopenia had higher NRS 2002 scores (Table 1). The analysis showed that the impact of sarcopenia on postoperative complications exceeded the NRS 2002 score in this study, which perhaps explained the fact that nutritional risk (NRS 2002 score ≥3) was not preserved in multivariate analysis.

In our further analysis, patients with tumor located at the cardia were found to have a significant high morbidity rate. Previous study have revealed that the clinicopathological features of esophagogastric junctional cancer (EGJC) were strikingly different from distal gastric cancer (DGC) [44] and patients with EGJC showed worse short- and long-term outcomes when compared with DGC [45]. Patients with tumor located at the cardia are more likely to suffer intake disorder and malnutrition due to cardinal stricture or obstruction and result in a poorer postoperative outcome. In consistency with this viewpoint, our data also showed that tumor located at the cardia was closely related to a higher nutritional risk (NRS 2002 scores ≥3) ($P = 0.025$, data not shown). In addition, patients with an upper gastric carcinoma may need an extended resection of the esophagus to achieve a negative resection margin which may increase the operation time, the extent of surgery, and complication rate.

Furthermore, early detection and treatment of sarcopenia by different strategies could improve the postoperative outcome in such frail patients. Among these strategies, specific nutritional intervention such as omega-3 fatty acid supplements could potentially provide a safe, simple, and low-cost intervention to counteract muscle loss and its complications in clinical conditions associated with sarcopenia [46, 47]. However, it has not been established whether a general or a specific (omega-3 fatty acids) supplement intervention is preferable and a prospective clinical trial is needed. In addition, to promote the increase of muscle mass rather than fat mass, this nutritional supplementation must be associated with exercise combining resistance and aerobic muscle training. Some studies already demonstrated that pre-habilitation, a multimodal approach before surgery, is effective in reducing postoperative complication in surgical patients [48–50], while its effects on sarcopenia and its efficiency to improve outcome after TG with D2 lymphadenectomy for gastric cancer have yet to be established.

There are several limitations associated with the present study. This study was conducted in a single center, which may limit the generalization of its conclusions. However, our department is one of the largest gastric cancer centers in China, so our data remain representative. Additionally, long-term outcomes were not well defined in this study. Long-term follow-up will be needed to further demonstrate whether preoperative assessment of frailty using sarcopenia and assessment nutritional status using the NRS 2002 score could have an effect on survival.

Conclusion

This study showed that frailty, reflected by sarcopenia, is associated with adverse postoperative complications in patients undergoing TG with D2 lymphadenectomy for gastric cancer. Evaluation of skeletal muscle mass by CT and evaluation of performance by measuring the handgrip strength and gait speed represents an interesting tool to identify patients with high risk of morbidity after TG with D2 lymphadenectomy for gastric cancer and should be integrated into scoring systems and therapeutic algorithm for gastric cancer treated by TG with D2 lymphadenectomy.

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Authors' contributions Study conception and design: Cheng-Le Zhuang, Zhen Yu

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Compliance with ethical standards All participants provided their written informed consent, and the protocol for this study was approved by the ethics committee of The First Affiliated Hospital of Wenzhou Medical University and in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of interest The authors declare that they have no conflict of interest.

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