

Research Paper

Value of Sarcopenia defined by the new EWGSOP2 consensus for the prediction of Postoperative Complications and Long-term Survival after Radical Gastrectomy for Gastric Cancer: A comparison with four common nutritional screening tools

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Abstract

Background: Nutritional risk and sarcopenia are both associated with increased postoperative morbidity and mortality following elective surgery. This study aimed to investigate whether sarcopenia has additional predictive value for postoperative complications and long-term survival besides nutritional screening tools.

Methods: Clinical data of patients underwent radical gastrectomy for gastric cancer was prospectively collected. Sarcopenia was diagnosed by grip strength plus muscle quantity/quality based on preoperative abdominal CT scans. Nutritional screening was performed using 4 common nutritional screening tools, including Malnutrition Universal Screening Tool (MUST), Nutritional Risk Screening (NRS)-2002, Malnutrition Screening Tool (MST), and Short Nutritional Assessment Questionnaire (SNAQ).

Results: A total of 880 patients were analyzed, in which 167 (18.98%) were diagnosed with sarcopenia. The incidence of nutritional risk identified by the 4 tools were 44.66% (MUST ≥ 1), 35.23% (NRS-2002 ≥ 3), 29.89% (MST ≥ 2), and 20.34% (SNAQ ≥ 2). Multivariate analyses showed that nutritional risk identified by the 4 nutritional screening tools were not independently associated with postoperative complications, overall survival (OS) or disease-free survival (DFS), except for NRS-2002 ≥ 3 as an independent risk factor of OS. Sarcopenia was always an independent risk factor for postoperative complications, OS, and DFS after adjusting for nutritional risk and the other covariates in the multivariate analyses.

Conclusions: MUST, NRS-2002, MST, and SNAQ had low predictive power for postoperative complications and long-term survival in patients underwent radical gastrectomy for gastric cancer. Sarcopenia had additional predictive value for postoperative complications and long-term survival besides these nutritional screening tools and should be implemented in the preoperative assessments.

Key words: Sarcopenia; Malnutrition; Gastrectomy; Postoperative complication; Survival

Introduction

In recent years, sarcopenia has been increasingly recognized as a strong predictor for morbidity and mortality after surgery [1-3]. According to the revised European consensus on definition and diagnosis of sarcopenia recommended by the European Working

Group on Sarcopenia in Older People 2 (EWGSOP2), sarcopenia is diagnosed based on the measurement of muscle strength plus muscle quality/quantity [4]. Computed tomography (CT) is considered to be a gold standard for the assessment of muscle mass and

attenuation [4]. Moreover, preoperative abdominal CT scan is necessary for patients with gastrointestinal tumors for staging of the tumor and guidance of surgery. However, muscle mass measurement before surgery is not a routine practice for radiologists in most medical centers. Therefore, sarcopenia has not been widely used in clinical practice for preoperative assessment. A recent study showed that CT measured sarcopenia may have only little additional value over Malnutrition Universal Screening Tool (MUST) for the prediction of postoperative complications after colorectal cancer surgery [5]. This finding aroused us to speculate whether measurement of sarcopenia is still necessary for preoperative risk assessment in the context of nutritional risk screening before surgery for other types of malignancy, such as gastric cancer.

Malnutrition is present in about 30% of hospitalized patients, and the prevalence is especially high in patients with gastrointestinal tumors, such as gastric cancer [6, 7]. There is convincing evidence that nutritional risk is associated with increased postoperative morbidity and mortality following elective surgery [8, 9]. In contrast to the limited application of sarcopenia assessment in clinical practice, screening of nutritional risk has been applied in many medical centers world-widely. Therefore, it is worthwhile to investigate whether sarcopenia has additional predictive value besides nutritional screening tools for prediction of surgical prognosis when the nutritional screening has already been well implemented. Besides, although there are many nutritional screening tools, such as Malnutrition Universal Screening Tool (MUST) [10], Nutrition Risk Screening 2002 (NRS-2002) [11], Malnutrition Screening Tool (MST) [12], and Short Nutritional Assessment Questionnaire (SNAQ) [13], it has as yet not been established which is the optimal nutritional assessment tool in patients scheduled to receive gastrectomy for gastric cancer.

In the present study, we aimed to investigate whether sarcopenia has additional predictive value besides 4 common nutritional screening tools (MUST, NRS-2002, MST, and SNAQ) for the prediction of postoperative complications and long-term survival after radical gastrectomy for gastric cancer.

Methods

Patients

From August 2014 to February 2018, patients who underwent radical gastrectomy for gastric cancer at the Gastrointestinal Surgery Department of the First Hospital Affiliated to Wenzhou Medical University were included in this prospective study. The inclusion criteria included patients who (1) were

aged 18 years old or more; (2) had American Society of Anesthesiologists (ASA) grade \leq III; (3) planned to receive elective gastrectomy for gastric cancer with curative intent; (4) had preoperative abdominal CT images available for review (no more than 1 month before operation); and (5) agreed to take part in this study and signed the informed consent. Exclusion criteria included patients who (1) were aged <18 years; (2) were unable to be assessed for nutritional status due to mental disorder or disturbance of consciousness; (3) were unable to be measured for muscle strength or physical performance due to physical deformity; (4) declined to take part in the study; and (5) underwent palliative operation. This project was approved by the Ethical Review Board of The First Affiliated Hospital of Wenzhou Medical University and registered in China Clinical Trial Registry (NO. ChiCTR1800019717). All patients received standard managements and treatments following the Japanese gastric cancer treatment guidelines 2010 (version 3) [14].

Data collection

The following data were collected prospectively: (1) preoperative patient and disease characteristics, including age, gender, body mass index (BMI), plasma albumin concentration, haemoglobin concentration, ASA grade, comorbidity, tumor-node-metastasis (TNM) stage of tumor, differentiation of tumor, tumor location, previous abdominal surgery; (2) operative and treatment details, including laparoscopy-assisted surgery, type of resection, extent of lymph node dissection, combined organ resection, adjuvant chemotherapy; and (3) postoperative outcomes, including postoperative complications and mortality. Only complications classified as Grade II or above according to the Clavien-Dindo classification were analyzed in this study [15], and complications classified as Grade III or above were identified as severe complications.

Diagnosis of sarcopenia

According to the revised European consensus on definition and diagnosis of sarcopenia recommended by EWGSOP2, sarcopenia was defined by low muscle strength plus low muscle quantity or quality. Severe sarcopenia was defined when the sarcopenic patients had additional low physical performance [4]. Muscle quantity was measured using cross sectional CT images at the third lumbar vertebra (L3) level on the first image with both vertebral spines visible [16]. Skeletal muscle tissues were identified by the Hounsfield units (HU) with the thresholds range of -29 to +150, using the image processing system (version 3.0.11.3 BN17 32 bit; INFINITT Healthcare

Co., Ltd). Cross-sectional area of skeletal muscle tissue was normalized by the height squared to calculate the skeletal muscle index (SMI, cm^2/m^2). Patients with L3 skeletal muscle index $<40.8 \text{ cm}^2/\text{m}^2$ for men and $<34.9 \text{ cm}^2/\text{m}^2$ for women were identified as having low muscle mass [1]. Muscle quality was measured by using mean muscle attenuation. The sex-specific cutoff values for defining low muscle attenuation were 28.6 HU for females and 38.5 HU for males according to our previous study [17]. All patients received measurements of handgrip strength and 6-m usual gait speed tests in the first hospitalized day before surgery. Muscle strength was determined by handgrip strength tests, using an electronic hand dynamometer (EH101; CAMRY, Guangdong Province, China). Patients with handgrip strength $<26 \text{ kg}$ for men and $<18 \text{ kg}$ for women were identified as having low muscle strength. Physical performance was determined by 6-m usual gait speed tests as described previously [1, 3]. Patients with 6-m usual gait speed $<0.8 \text{ m/s}$ were identified as having low physical performance.

Nutritional screening

All patients received nutritional screening using 4 common nutritional screening tools, including Malnutrition Universal Screening Tool (MUST) [10], Nutrition Risk Screening 2002 (NRS-2002) [11], Malnutrition Screening Tool (MST) [12], and Short Nutritional Assessment Questionnaire (SNAQ) [13]. The MUST scores are based on BMI, unplanned weight loss, and reduced food intake for more than 5 days due to the effect of acute diseases. Patients with an MUST score of ≥ 1 are classified as being at nutritional risk [10]. NRS-2002 identify the risk of malnutrition based on 5 variables, including general condition, BMI, weight loss, food intake over the last week, and the patients' age. Patients with an NRS 2002 score of ≥ 3 are classified as being at nutritional risk [11]. The MST tool is based on unintentional weight loss, the extent of weight loss, and reduced food intake due to decreased appetite. Patients with an MST score of ≥ 2 are classified as being at nutritional risk [12]. The SNAQ tool is based on unintentional weight loss, decreased appetite over the last month, and usage of supplemental drinks or tube feeding over the last month. Patients with an SNAQ score of ≥ 2 are classified as being at nutritional risk [13].

Follow up

All patients were routinely followed up within the first month after surgery in the outpatient. After that, patients were followed up every 3 months for 2 years and every 6 months thereafter by telephone

interviews or outpatient visits. The follow-up program was consisted of physical examination, laboratory tests, and ultrasonography and/or CT and/or endoscopy. The last follow-up date was January 2019. Overall survival (OS) was defined as the period from the time of surgery to the time of death due to any causes. Disease-free survival (DFS) was calculated from the date of surgery to the date of relapse or death due to cancer-free causes.

Statistical analysis

Normally distributed data were presented as mean and standard deviation (SD) and compared using the t-test. Nonnormally distributed data were presented as median and interquartile range (IQR) and compared using the Mann-Whitney U-test. Categorical data were compared using the chi-square test or Fisher exact test. Univariate analysis was used to identify potential risk factors for postoperative complications, overall survival and disease-free survival. Multivariate logistic regression analysis or Cox proportional-hazards analysis included variables with a P-value of <0.10 in the univariate analysis, as well as other clinical relevant variables, including age, gender, BMI or adjuvant chemotherapy. Survival curves were estimated using the Kaplan-Meier method and compared using log-rank tests. All data were analyzed using SPSS statistics version 22.0 (IBM, USA). Two-tailed P values <0.05 were considered statistically significant.

Results

From August 2014 to February 2018, 948 patients who underwent gastrectomy for gastric cancer met our inclusion criteria initially. Sixty-eight patients were excluded for reasons of underwent palliative surgery, unable to be assessed for muscle strength or physical performance, failed to be screened for nutritional status or refused to participate in the study. Finally, a total of 880 patients were included in the analyses.

Sarcopenia was identified in 167 (18.98%) of the patients, in which 53 (6.02%) patients were identified as having severe sarcopenia. Compared with nonsarcopenic patients, patients with sarcopenia had older age, higher ASA grade, higher TNM stage, lower BMI, lower L3 SMI, lower muscle attenuation, lower handgrip strength, lower gait speed, lower preoperative albumin and hemoglobin levels, and received less laparoscopy-assisted surgery (Table 1). The incidence of nutritional risk identified by the 4 nutritional screening tools in our patients were 44.66% (MUST ≥ 1), 35.23% (NRS-2002 ≥ 3), 29.89% (MST ≥ 2), and 20.34% (SNAQ ≥ 2). Sarcopenia showed a significant correlation with nutritional risk identified

by all of 4 nutritional screening tools (Table 1). However, the agreement of sarcopenia with nutritional risk is slight ($\kappa < 0.2$).

Table 1. Patient demographic and clinical characteristics

Factors	All (n=880) ^a	Nonsarcopenic (n=713) ^a	Sarcopenic (n=167) ^a	P
Age, mean (SD), years	64.47 (10.80)	62.35 (10.35)	73.54 (7.50)	<0.001*
Gender				0.645
Female	230	184	46	
Male	650	529	121	
BMI, mean (SD), kg/m²	22.63 (3.07)	22.91 (3.04)	21.48 (2.96)	<0.001*
NRS-2002 scores				<0.001*
< 3	570	496	74	
≥ 3	310	217	93	
MUST scores				<0.001*
< 1	487	419	68	
≥ 1	393	294	99	
MST scores				0.003*
< 2	617	516	101	
≥ 2	263	197	66	
SNAQ scores				0.005*
< 2	701	581	120	
≥ 2	179	132	47	
L3 SMI, mean (SD), cm²/m²	42.73 (7.74)	43.86 (7.60)	37.89 (6.41)	<0.001*
Muscle attenuation, mean (SD), HU	36.12 (7.81)	37.43 (7.39)	30.54 (7.10)	<0.001*
Handgrip strength, mean (SD), kg	28.40 (9.22)	30.84 (8.21)	18.11 (5.25)	<0.001*
Gait speed, median (IQR), m/s	1.00 (0.27)	1.03 (0.25)	0.81 (0.28)	<0.001*
Albumin, mean (SD), g/L	38.11 (4.45)	38.71 (4.16)	35.51 (4.74)	<0.001*
Hemoglobin, mean (SD), g/L	120.97 (21.61)	123.52 (21.16)	110.08 (20.15)	<0.001*
ASA grade				<0.001*
I	208	183	25	
II	522	426	96	
III	150	104	46	
Charlson comorbidity index				0.088
0	622	513	109	
1	174	139	35	
≥ 2	84	61	23	
Previous abdominal surgery				0.145
No	777	635	142	
Yes	103	78	25	
Tumor location				0.579
Not at cardia	765	622	143	
At cardia	115	91	24	
Differentiation of tumor				0.505
Well differentiated	304	250	54	
Poorly differentiated	576	463	113	
TNM stage				0.001*
I	310	272	38	
II	214	167	47	
III	356	274	82	
Extent of lymph node dissection				0.219
D1	115	98	17	
D2	765	615	150	
Type of resection				0.103
Subtotal gastrectomy	549	454	95	
Total gastrectomy	331	259	72	
Combined resection				0.069
No	810	662	148	
Yes	70	51	19	
Laparoscopy-assisted surgery				0.001*
No	644	504	140	
Yes	236	209	27	

a: Values are number of patients unless indicated otherwise;

*Statistically significant;

SD, standard deviation; BMI, body mass index; L3 SMI, third lumbar vertebra skeletal muscle index; IQR, interquartile range; ASA, American Society of Anesthesiologists; TNM, tumor-node-metastasis.

Table 2. Univariate analysis for risk factors associated with postoperative complications

	Without complications (n=649)	With complications (n=231)	P
MUST			0.022*
<1	374	113	
≥1	275	118	
NRS-2002			0.001*
<3	441	129	
≥3	208	102	
MST			0.067
<2	466	151	
≥2	183	80	
SNAQ			0.004*
<2	532	169	
≥2	117	62	
Sarcopenia			<0.001*
No	560	153	
Yes	89	78	
Gender			0.144
Female	178	52	
Male	471	179	
Age			<0.001*
<75 y	555	166	
≥75 y	94	65	
BMI			0.285
≥18.5	604	210	
<18.5	45	21	
ASA			0.001*
I, II	555	175	
III	94	56	
Charlson comorbidity index			<0.001*
0	482	140	
≥1	167	91	
Anemia			<0.001*
No	439	117	
Yes	210	114	
Hypoproteinemia			<0.001*
No	522	155	
Yes	127	76	
Previous abdominal surgery			0.155
No	579	198	
Yes	70	33	
TNM stage			0.188
I	240	70	
II	153	61	
III	256	100	
Tumor differentiation			0.974
Differentiated	224	80	
Undifferentiated	425	151	
Tumor location			0.007*
Not cardia	576	189	
Cardia	73	42	
Type of resection			0.110
Subtotal gastrectomy	415	134	
Total gastrectomy	234	97	
Laparoscopic surgery			0.010*
No	460	184	
Yes	189	47	
Combined organ resection			0.305
No	601	209	
Yes	48	22	
Extent of lymph node dissection			0.619
D1	87	28	
D2	562	203	

*Statistically significant ($P < 0.05$);

BMI, body mass index; ASA, American Society of Anesthesiologists; TNM, tumor-node-metastasis.

In the 880 included patients, 231 (26.25%) occurred postoperative complications graded II and above (Table 2). The details of postoperative

complications were listed in Table S1. Univariate analyses showed that $MUST \geq 1$, $NRS-2002 \geq 3$, $SNAQ \geq 2$, sarcopenia, age ≥ 75 years, $ASA=III$, Charlson comorbidity index ≥ 1 , anemia, hypoproteinemia, tumor located at cardia, and laparoscopic surgery were significantly associated with postoperative complications (Table 2). None of the 4 nutritional screening tools had good sensitivity for the prediction of postoperative complications, ranging from 26.84% to 51.08% (Table S2). Sarcopenia had a high specificity (86.29%) but low sensitivity (33.77%) for the prediction of postoperative complications (Table S2). To further compare the predictive values of the 4 nutritional screening tools on the postoperative complications, we performed 4 separate multivariate analyses, adjusting the effect of the 4 nutritional screening tools for the same covariates, including gender, age, BMI, Charlson comorbidity index, anemia, hypoproteinemia, tumor location, laparoscopic surgery, and sarcopenia. None of these nutritional screening tools remained independently associated with postoperative complications after adjusting for these covariates in the multivariate analyses. Sarcopenia, tumor located at cardia, and Charlson comorbidity index ≥ 1 were the independent risk factors for postoperative complications in all of the 4 multivariate analyses (Table 3).

Univariate analyses and Kaplan–Meier analyses showed that $MUST \geq 1$, $MST \geq 2$, $SNAQ \geq 2$, and $NRS-2002 \geq 3$ were all associated with worse OS (Table 4, Figure S1). However, in the multivariate analyses, only $NRS-2002 \geq 3$ remained an independent risk factor for OS. Other independent risk factors for OS were sarcopenia, higher TNM stage, undifferentiated tumor histological type, total gastrectomy in all of the 4 multivariate analyses, whereas adjuvant chemotherapy was an independent protective factor (Table 5). Univariate analyses and Kaplan–Meier analyses showed that $MUST \geq 1$, $MST \geq 2$ and $SNAQ \geq 2$ were associated with worse DFS (Table 4, Figure S1). However, none of these nutritional screening tools remained significant in the multivariate analyses for DFS. Sarcopenia, higher TNM stage, undifferentiated tumor histological type, total gastrectomy were independently associated the worse DFS in all of the 4 multivariate analyses, whereas adjuvant chemotherapy was an independent protective factor (Table 6).

Discussion

The 4 nutritional screening tools in the present study were initially developed to screen the nutritional risk. *MUST* was developed by the Malnutrition Advisory Group for application to all adult patients across all health care settings. It is

supported by many governmental and non-governmental organizations and is the commonly used globally, especially in the European countries [10]. *NRS-2002* was created on the basis of its power to predict the therapeutic effect of nutritional support [11], and was recommended by ESPEN for the screening of nutritional risk in hospitalized patients [6]. *MST* was developed based on its predictive ability of subjective global assessment (SGA) in mixed hospital patient population [12]. *SNAQ* was created based on its predictive values for nutritional status in patients in the mixed internal and surgery/oncology wards [13]. In the present study, we compared the 4 nutritional screening tools for their predictive value for postoperative outcomes after gastrectomy for gastric cancer. We found that most of these nutritional screening tools showed significant association with postoperative complications, OS, and DFS, suggesting the close relationship between nutritional status and postoperative outcomes. However, none of these tools showed a good sensitivity for the prediction of postoperative complications, ranging from 26.84% to 51.08%. Receiver operating characteristic (ROC) curves showed a low predictive power of postoperative complications for the 4 tools, ranging from 0.532 to 0.561 (Table S2). Moreover, none of these tools were independent risk factors for postoperative complications or long-term survival in the multivariate analyses, except for *NRS2002* as an independent risk factor for overall survival. This indicated that *NRS-2002* had a superior predictive value for postoperative survival over the other 3 nutritional screening tools. Based on the above findings, we suggested that nutritional screening is not enough for surgical risk assessment in patients underwent radical gastrectomy for gastric cancer.

In the multivariate analyses, sarcopenia always remained an independent risk factor for postoperative complications and long-term survival after adjusting for nutritional risk determined by each of these nutritional screening tools and the other covariates. This result strongly demonstrated the additional predictive value of sarcopenia on postoperative complications and long-term survival over all of these nutritional screening tools. One of our recent study showed that sarcopenia was an independent risk factor for postoperative complications after gastrectomy in patients without nutritional risk [18], which also demonstrated the additional predictive value of sarcopenia over the nutritional screening tools.

Few studies have compared the value of sarcopenia with nutritional screening tools for the prediction of postoperative outcomes. A recent study by Kroft et al. showed sarcopenia measured by CT

have only little additional value over the MUST for the prediction of postoperative morbidity after colorectal cancer surgery, which was in contrast with our findings [5]. The reason of the inconsistent results can be explained by the following factors. First, in the study of Kroft et al., sarcopenia was diagnosed by measuring skeletal muscle quantity/quality only. However, the functional aspects of sarcopenia, including muscle strength and physical performance, are also significant for the prediction of postoperative outcomes [1, 3]. Second, the study of Kroft et al. was based on patients underwent colorectal cancer surgery, which has certain differences with our

patient underwent gastrectomy for gastric cancer. However, the present study and the previous study by Kroft et al. are all single-center studies including patients underwent surgery for homogeneous types of malignancy. It is unknown whether the predictive value of sarcopenia besides nutritional risk is dependent on certain types of surgery or universal among general major abdominal surgeries. Therefore, we suggest that future multi-center studies including patients with various types of malignancy were needed to further demonstrate the predictive value of sarcopenia besides nutritional risk for the post-operative outcomes.

Table 3. Multivariate analysis for risk factors associated with postoperative complications

	MUST ≥ 1		NRS-2002 ≥ 3		MST ≥ 2		SNAQ ≥ 2	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Nutritional risk	1.172 (0.834-1.647)	0.361	1.198 (0.847-1.694)	0.308	1.098 (0.775-1.555)	0.600	1.417 (0.968-2.073)	0.073
Sarcopenia	2.270 (1.523-3.383)	<0.001*	2.252 (1.509-3.360)	<0.001*	2.288 (1.536-3.410)	<0.001*	2.270 (1.522-3.385)	<0.001*
Gender (male/female)	1.247 (0.856-1.818)	0.251	1.245 (0.855-1.815)	0.253	1.246 (0.853-1.820)	0.255	1.256 (0.862-1.830)	0.236
Age ≥ 75 y	1.443 (0.962-2.165)	0.076	1.412 (0.940-2.123)	0.097	1.430 (0.952-2.146)	0.085	1.455 (0.968-2.187)	0.071
BMI <18.5	0.971 (0.524-1.799)	0.926	0.987 (0.539-1.807)	0.966	1.035 (0.570-1.879)	0.910	1.016 (0.559-1.847)	0.958
Charlson comorbidity index ≥ 1	1.838 (1.319-2.562)	<0.001*	1.823 (1.308-2.542)	<0.001*	1.821 (1.306-2.540)	<0.001*	1.819 (1.304-2.537)	<0.001*
Anemia	1.407 (0.979-2.021)	0.065	1.422 (0.991-2.039)	0.056	1.426 (0.994-2.046)	0.054*	1.399 (0.974-2.008)	0.069
Hypoproteinemia	1.243 (0.827-1.869)	0.295	1.225 (0.813-1.846)	0.333	1.251 (0.833-1.881)	0.280	1.219 (0.809-1.835)	0.344
Tumor located at cardia	1.784 (1.154-2.756)	0.009*	1.759 (1.138-2.719)	0.011*	1.777 (1.150-2.746)	0.010*	1.791 (1.158-2.769)	0.009*
Laparoscopic surgery	0.785 (0.536-1.151)	0.215	0.790 (0.538-1.159)	0.277	0.780 (0.533-1.144)	0.203	0.787 (0.537-1.154)	0.220

*Statistically significant ($P < 0.05$);

OR, odds ratio; CI, confidence interval; BMI, body mass index.

Table 4. Univariate analysis for risk factors associated with overall survival and disease-free survival

	Overall survival		Disease-free survival	
	HR (95% CI)	P	HR (95% CI)	P
MUST ≥ 1	1.765 (1.333-2.336)	<0.001*	1.474 (1.097-1.982)	0.010*
NRS-2002 ≥ 3	1.884 (1.427-2.489)	<0.001*	1.269 (0.937-1.719)	0.124
MST ≥ 2	1.632 (1.226-2.173)	0.001*	1.446 (1.061-1.971)	0.020*
SNAQ ≥ 2	1.554 (1.135-2.129)	0.006*	1.892 (1.370-2.611)	<0.001*
Sarcopenia	2.540 (1.855-3.423)	<0.001*	2.295 (1.662-3.170)	<0.001*
Gender (male/female)	1.136 (0.819-1.576)	0.445	1.063 (0.756-1.496)	0.725
Age ≥ 75 y	1.744 (1.268-2.398)	0.001*	1.296 (0.898-1.870)	0.165
BMI <18.5	1.567 (0.997-2.463)	0.052	1.515 (0.930-2.467)	0.095
ASA $\geq III$	1.620 (1.176-2.232)	0.003*	1.661 (1.181-2.337)	0.004*
Charlson comorbidity index ≥ 1	1.056 (0.777-1.437)	0.726	1.240 (0.904-1.701)	0.183
Anemia	1.790 (1.355-2.363)	<0.001*	1.892 (1.408-2.543)	<0.001*
Hypoproteinemia	1.645 (1.221-2.215)	0.001	1.764 (1.290-2.413)	<0.001*
Previous abdominal surgery	0.945 (0.763-1.170)	0.602	1.207 (0.779-1.872)	0.400
TNM stage		<0.001*		
II/I	2.627 (1.494-4.620)	0.001*	5.802 (2.885-11.668)	<0.001*
III/I	8.502 (5.270-13.717)	<0.001*	14.994 (7.875-28.549)	<0.001*
Tumor differentiation Undifferentiated/Differentiated	2.404 (1.694-3.413)	<0.001*	2.813 (1.908-4.147)	<0.001*
Tumor location at cardia	1.191 (0.803-1.766)	0.384	1.145 (0.750-1.745)	0.531
Type of resection (Total gastrectomy/Subtotal gastrectomy)	2.096 (1.586-2.776)	<0.001*	2.121 (1.577-2.853)	<0.001*
Laparoscopic surgery	0.453 (0.306-0.672)	<0.001*	0.504 (0.338-0.751)	0.001*
Combined organ resection	1.904 (1.252-2.896)	0.003*	2.176 (1.415-3.348)	<0.001*
Extent of lymph node dissection (D2/D1)	1.225 (0.805-1.865)	0.343	1.273 (0.807-2.009)	0.300
Adjuvant chemotherapy	0.813 (0.616-1.073)	0.144	1.062 (0.788-1.430)	0.693
Postoperative complications		0.002*		0.257
Grade II/ No	1.592 (1.146-2.210)	0.006*	1.258 (0.872-1.816)	0.220
Grade III-V/ No	1.887 (1.166-3.054)	0.010*	1.433 (0.825-2.491)	0.202

*Statistically significant ($P < 0.05$);

HR, hazard Ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists; TNM, tumor-node-metastasis.

Table 5. Multivariate analysis for risk factors associated with overall survival

	MUST ≥1		NRS-2002 ≥3		MST ≥2		SNAQ ≥2	
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
Nutritional risk	1.192 (0.878-1.619)	0.260	1.391 (1.029-1.878)	0.032*	1.159 (0.859-1.564)	0.335	1.007 (0.852-1.189)	0.937
Sarcopenia	1.609 (1.141-2.268)	0.007*	1.562 (1.108-2.201)	0.011*	1.598 (1.134-2.252)	0.007*	1.605 (1.137-2.264)	0.007*
Gender (male/female)	1.189 (0.846-1.669)	0.319	1.178 (0.840-1.653)	0.343	1.183 (0.843-1.660)	0.330	1.165 (0.831-1.634)	0.377
Age ≥75 y	1.042 (0.716-1.515)	0.831	1.022 (0.704-1.484)	0.909	1.030 (0.708-1.498)	0.877	1.042 (0.717-1.514)	0.829
BMI <18.5	1.249 (0.765-2.039)	0.373	1.209 (0.748-1.954)	0.439	1.308 (0.812-2.106)	0.270	1.355 (0.843-2.178)	0.209
ASA ≥III	1.129 (0.804-1.586)	0.485	1.110 (0.789-1.562)	0.548	1.118 (0.796-1.570)	0.520	1.118 (0.796-1.569)	0.520
Anemia	1.071 (0.779-1.474)	0.672	1.079 (0.785-1.482)	0.640	1.073 (0.779-1.476)	0.668	1.083 (0.787-1.491)	0.624
Hypoproteinemia	0.882 (0.624-1.246)	0.475	0.847 (0.599-1.197)	0.346	0.904 (0.642-1.275)	0.566	0.904 (0.639-1.277)	0.566
Undifferentiated Histologic type	1.532 (1.058-2.218)	0.024*	1.528 (1.056-2.211)	0.025*	1.549 (1.070-2.240)	0.020*	1.544 (1.067-2.234)	0.021*
TNM stage		<0.001*		<0.001*		<0.001*		<0.001*
II/I	2.623 (1.438-4.784)	0.002*	2.619 (1.437-4.776)	0.002*	2.638 (1.446-4.812)	0.002*	2.688 (1.475-4.898)	0.001*
III/I	8.059 (4.736-13.711)	<0.001	8.265 (4.865-14.040)	<0.001*	8.131 (4.783-13.821)	<0.001*	8.306 (4.889-14.114)	<0.001*
Total gastrectomy	1.569 (1.173-2.098)	0.002*	1.566 (1.171-2.094)	0.002*	1.571 (1.175-2.101)	0.002*	1.589 (1.189-2.124)	0.002*
Laparoscopic surgery	0.888 (0.588-1.342)	0.574	0.915 (0.605-1.386)	0.676	0.878 (0.582-1.326)	0.536	0.877 (0.580-1.325)	0.533
Combined resection	1.257 (0.812-1.945)	0.305	1.252 (0.809-1.936)	0.313	1.219 (0.786-1.892)	0.377	1.249 (0.808-1.932)	0.317
Postoperative complications		0.358		0.333		0.335		0.315
Grade II/ No	1.218 (0.863-1.719)	0.262	1.221 (0.865-1.724)	0.255	1.230 (0.872-1.735)	0.239	1.231 (0.872-1.736)	0.238
Grade III-V/No	1.349 (0.805-2.259)	0.256	1.370 (0.818-2.293)	0.231	1.352 (0.808-2.263)	0.251	1.376 (0.819-2.309)	0.228
Adjuvant chemotherapy	0.444 (0.326-0.603)	<0.001*	0.436 (0.321-0.594)	<0.001*	0.440 (0.323-0.599)	<0.001*	0.444 (0.326-0.605)	<0.001*

*Statistically significant (P < 0.05);

HR, hazard Ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists; TNM, tumor-node-metastasis.

Table 6. Multivariate analysis for risk factors associated with disease-free survival

	MUST ≥1		NRS-2002 ≥3		MST ≥2		SNAQ ≥2	
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
Nutritional risk	0.936 (0.678-1.292)	0.687	0.853 (0.615-1.184)	0.342	1.009 (0.733-1.389)	0.956	0.893 (0.755-1.056)	0.186
Sarcopenia	1.611 (1.121-2.314)	0.011*	1.636 (1.136-2.356)	0.008*	1.609 (1.119-2.312)	0.010*	1.579 (1.097-2.274)	0.014*
Gender (male/female)	1.033 (0.726-1.470)	0.855	1.039 (0.732-1.475)	0.831	1.042 (0.733-1.482)	0.817	1.060 (0.746-1.506)	0.746
Age ≥75 y	0.732 (0.480-1.118)	0.149	0.738 (0.483-1.128)	0.160	0.731 (0.478-1.118)	0.149	0.725 (0.474-1.109)	0.139
BMI <18.5	1.524 (0.897-2.591)	0.119	1.561 (0.927-2.629)	0.094	1.474 (0.885-2.456)	0.136	1.454 (0.876-2.414)	0.148
ASA ≥III	1.351 (0.946-1.929)	0.098	1.353 (0.948-1.931)	0.096	1.356 (0.950-1.936)	0.094	1.356 (0.949-1.937)	0.094
Anemia	1.153 (0.823-1.614)	0.408	1.153 (0.823-1.614)	0.408	1.149 (0.821-1.609)	0.418	1.142 (0.815-1.599)	0.440
Hypoproteinemia	1.011 (0.701-1.458)	0.954	1.029 (0.711-1.488)	0.880	1.002 (0.697-1.441)	0.992	0.971 (0.674-1.400)	0.876
Undifferentiated Histologic type	1.727 (1.154-2.585)	0.008*	1.734 (1.159-2.594)	0.007*	1.720 (1.150-2.573)	0.008*	1.714 (1.146-2.563)	0.009*
TNM stage		<0.001*		<0.001*		<0.001*		<0.001*
II/I	6.180 (2.978-12.824)	<0.001*	6.199 (2.990-12.850)	<0.001*	6.122 (2.951-12.702)	<0.001*	6.063 (2.923-12.573)	<0.001*
III/I	14.374 (7.235-28.588)	<0.001*	14.271 (7.192-28.297)	<0.001*	14.215 (7.157-28.234)	<0.001*	13.915 (7.007-27.633)	<0.001*
Total gastrectomy	1.530 (1.124-2.082)	0.007*	1.528 (1.124-2.078)	0.007*	1.521 (1.118-2.070)	0.008*	1.517 (1.116-2.063)	0.008*
Laparoscopic surgery	0.958 (0.631-1.453)	0.839	0.941 (0.619-1.430)	0.775	0.961 (0.634-1.457)	0.851	0.974 (0.642-1.478)	0.902
Combined resection	1.459 (0.939-2.267)	0.093	1.458 (0.939-2.264)	0.093	1.466 (0.943-2.279)	0.089	1.489 (0.958-2.315)	0.077
Postoperative complications		0.952		0.952		0.957		0.992
Grade II/ No	0.983 (0.671-1.438)	0.928	0.984 (0.673-1.440)	0.935	0.978 (0.669-1.431)	0.910	0.977 (0.667-1.430)	0.905
Grade III-V/No	1.086 (0.605-1.950)	0.783	1.087 (0.606-1.950)	0.778	1.076 (0.598-1.935)	0.807	1.004 (0.551-1.826)	0.991
Adjuvant chemotherapy	1.727 (1.154-2.585)	0.008*	0.474 (0.342-0.658)	<0.001*	0.471 (0.340-0.654)	<0.001*	0.465 (0.335-0.645)	<0.001*

*Statistically significant (P < 0.05);

HR, hazard Ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists; TNM, tumor-node-metastasis.

Although the 4 nutritional screening tools showed a significant correlation with sarcopenia, their agreements with sarcopenia was low (kappa <0.2), because they focus on different aspects in their components of definition compared with sarcopenia. Generally, these nutritional screening tools mainly focus on the BMI, weight loss or reduced intake of food. However, none of these tools distinguish the body compositions. Different body compositions have distinct impact on the surgical outcomes. Low muscle mass has been recognized to be associated with poor clinical outcomes [19, 20]. However, visceral obesity

has been found to be a risk factor for postoperative complications [21, 22]. Sarcopenic obesity, which is characterized by low muscle mass and high BMI or high visceral fat mass, was associated with negative clinical outcomes [23, 24]. However, these patients cannot be identified by traditional nutritional screening tools. One important feature of sarcopenia is the loss of muscle mass. Therefore, measurement of sarcopenia could add significant information for risk assessment before surgery. Moreover, physical function has been increasingly recognized to be associated with adverse postoperative outcomes.

Reddy et al. reported that timed stair climbing is the single strongest predictor of perioperative complications in patients undergoing abdominal surgery, even better than the ACS NSQIP calculator [25]. Sato et al. showed that low hand grip strength was a significant risk factor for morbidity after gastric cancer surgery [26]. Physical function is another important component of sarcopenia, which can also explain the additional predictive value of sarcopenia over nutritional screening tools. In the present study, we used the revised European consensus on definition and diagnosis of sarcopenia recommended by EWGSOP2 [4]. Compared with the previous consensus of sarcopenia definition recommended by EWGSOP1 [27], the revised consensus added low muscle quality to the diagnosis of sarcopenia. Muscle quality is a relatively new term, referring to the changes in muscle architecture and composition [28]. Low muscle quality, as measured by the attenuation of the muscle has been proved to have significant influence on the prognosis after surgery [17]. This can also explain the superior predictive value of sarcopenia in our study.

In conclusion, our study demonstrated that none of the 4 nutritional screening tools have strong predictive power for postoperative complications and long-term survival in patients underwent radical gastrectomy for gastric cancer. Sarcopenia had additional predictive value for postoperative complications and long-term survival besides these nutritional screening tools. Our study demonstrated the superior predictive value of sarcopenia over nutritional screening tools for the prediction of postoperative outcomes. Therefore, measurement of sarcopenia is necessary for optimizing the preoperative risk assessment for gastric cancer surgery, even when the nutritional screening has already been well implemented.

Abbreviations

EWGSOP: European Working Group on Sarcopenia in Older People; CT: computed tomography; MUST: Malnutrition Universal Screening Tool; NRS-2002: Nutrition Risk Screening 2002; MST: Malnutrition Screening Tool; SNAQ: Short Nutritional Assessment Questionnaire; ASA: American Society of Anesthesiologists; BMI: body mass index; TNM: tumor-node-metastasis; L3: third lumbar vertebra; HU: Hounsfield units; SMI: skeletal muscle index; OS: overall survival; DFS: disease-free survival; SD: standard deviation; IQR: interquartile range; OR: odds ratio; HR: hazard Ratio; CI: confidence interval; ROC: receiver operating characteristic.

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Supplementary Material

Supplementary figures and tables.

<http://www.jcancer.org/v11p5852s1.pdf>

Authors' contribution

Qian-Tong Dong and Xiao-Lei Chen designed the study. Hui-Yang Cai, Drugyel Wangchuk, and Xi-Yi Chen collected the data. Dong-Dong Huang, Wen-Xi Dong and Jing-Yi Yan did the analysis and interpretation of data. Dong-Dong Huang wrote the article. Xiao-Lei Chen revised the article and took the decision to submit the article for publication.

Compliance with ethical standards

This study was approved by the Ethics Committee of The First Affiliated Hospital of Wenzhou Medical University.

Human rights statement and informed consent

All procedures followed were in accordance with the ethical standards of the Ethics Committee of The First Affiliated Hospital of Wenzhou Medical University and with the Helsinki Declaration of 1964 and later versions. Informed consent to be included in the study was obtained from all patients.

Competing Interests

The authors have declared that no competing interest exists.

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