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Original article

Sarcopenia as a predictor of poor surgical and oncologic outcomes after abdominal surgery for digestive tract cancer: A prospective cohort study☆

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SUMMARY

Background & aims: Sarcopenia has been widely recognized as an important predictor of poor outcomes in patients with cancer after surgery, but the controversy remains, and its impact on surgical and oncologic outcomes in patients after abdominal surgery for digestive tract cancer is poorly described. The aim of this study was to evaluate the prognostic impact of sarcopenia on surgical and oncologic outcomes in patients after abdominal surgery for digestive tract cancer.

Methods: Six thousand four hundred and forty-seven consecutive patients who underwent abdominal surgery for digestive tract cancer in our institution were prospectively included. Sarcopenia was defined as skeletal muscle index below the lowest sex-specific quartile using computed tomography scan at L3 before surgery. The surgical and oncologic outcomes were recorded, and univariate and multivariate analyses were performed.

Results: Sarcopenia was present in 1638 of 6447 patients (25.4%) with digestive tract cancer before surgery based on the diagnostic cut-off values (43.13 cm^2/m^2 for men and 37.81 cm^2/m^2 for women). The incidence of postoperative total and pulmonary complications, and 30-day readmission were significantly higher in sarcopenic group than in nonsarcopenic group (37.4% vs 12.9%, $P < 0.001$; 3.1% vs 2.1%, $P = 0.026$; 1.1% vs 0.4%, $P = 0.003$, respectively). The postoperative hospital stay was significantly longer in sarcopenic patients (9.42 ± 3.40 vs 8.51 ± 3.17 days, $P < 0.001$). There were significantly more patients receiving postoperative chemotherapy or radiotherapy in sarcopenic group than in nonsarcopenic group (73.1% vs 69.2%, $P = 0.003$; 10.6% vs 8.8%, $P = 0.038$, respectively), and patients with sarcopenia had significantly more chemotherapy modifications including delay, dose reduction, or termination (48.5% vs 44.2%, $P = 0.018$). In addition, during the follow-up period, sarcopenic patients had significantly lower rate of overall survival and disease-free survival than nonsarcopenic patients (53.9% vs 69.3%, $P = 0.002$; 36.8% vs 59.7%, $P = 0.000$, respectively). In multivariate analysis, sarcopenia was found to be a risk factor for postoperative complications [odds ratio (OR) = 5.418, 95% confidence interval (CI) = 2.986–9.828, $P < 0.001$], and was an unfavorable prognostic factor for poor overall survival [hazard ratio (HR) = 0.649, 95% CI = 0.426–0.991, $P = 0.045$] and disease-free survival (HR = 0.514, 95% CI = 0.348–0.757, $P = 0.001$).

Conclusions: Sarcopenia could be used as a strong and independent prognostic factor for poor surgical and oncologic outcomes in patients after abdominal surgery for digestive tract cancer. Identification of preoperative sarcopenia in digestive surgery for cancer and targeted approaches may improve its negative outcomes.

1. Introduction

Digestive tract cancer occurs very common and has become one of the major causes for cancer disability and death worldwide in the 21st century, seriously threatening human's life and health [1].

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Numerous studies have shown that malnutrition is one of common and major complications among patients with cancer, and has been considered as an independent risk factor of toxicity and adverse outcomes in patients with cancer, especially the digestive tract cancer [2–4]. Although great advances in nutrition support, surgical technique and enhanced recovery after surgery [5,6], patients with digestive tract cancer at risk of malnutrition often have poor surgical and oncologic outcomes including high incidence of morbidity and mortality and short survival after surgery [7–9]. Thus, identification of malnutrition is of great significance for the treatment strategy and further affects prognosis in cancer patients.

However, commonly used methods, such as anthropometric measurements (eg, body mass index (BMI) and involuntary weight loss) and biochemical markers assessment (eg, serum albumin and transthyretine), are not sensitive to identify malnutrition and not effective to predict cancer patients' prognosis, especially in the settings when patients are overweight or suffer from liver disease [10,11]. Therefore, these support a new strategy to detect malnutrition among cancer patients, in which assessment of body composition has taken a greater role and draws popular pursuits in modern oncologic surgery.

Sarcopenia is a syndrome characterized by a reduction in skeletal muscle mass and function, and has been increasingly recognized as a new significant prognostic factor to predict short- and long-term outcomes among patients undergoing surgery for cancer [12–15]. However, recent studies raised some controversial results, showing that sarcopenia was not related to postoperative complications or survival in patients with cancer after surgery [16,17]. Furthermore, most of previous studies were retrospective and only focused on the effect of sarcopenia on one cancer treatment, such as surgery, chemotherapy or radiotherapy [15,18–20], but its impact on the short- and long-term outcomes regarding the entire cancer treatment such as surgery and the followed chemoradiation is unknown.

In the present study, we therefore conducted a prospective cohort study with large-scale in the high-volume Chinese Center of Surgery for digestive tract cancer, and aimed to systematically evaluate the prognostic impact of sarcopenia by comparison of surgical outcomes, chemoradiation treatment and survival in patients after abdominal surgery for digestive tract cancer.

2. Methods

2.1. Patients

From January 2015 to December 2016, all consecutive patients preparing to receive abdominal surgery for digestive tract cancer in Zhongshan Hospital, Fudan University were prospectively collected. Among these patients, those with preoperative chemoradiation, undergoing emergency surgery, postoperative recurrence confirmed before or at surgery, or age under 18 were excluded from this analysis. The institutional review board approved this prospective study.

2.2. CT-based sarcopenia assessment

Computed tomography (CT) scans of abdomen were routinely performed within 7 days before surgery. Parameters of the CT image were contrast enhanced or unenhanced multiphase acquisitions, and 5-mm slice thickness. For the assessment of sarcopenia, two adjacent CT images at the third lumbar vertebra (L3) within the same series were selected in the noncontrast phase [21], and the ImageJ2 software (The National Institutes of Health, Washington, MD, USA) was employed to measure the total skeletal muscle area (SMA) within a range of −29 to + 150 hounsfield units (HU) for skeletal muscle on both slices as shown in Fig. 1, and SMA was averaged for each patient. Sarcopenia was defined as SMI below the lowest sex-specific quartile [22–24]. The SMI was derived as the ratio of SMA to height following previously published methods [SMA(cm^2)/height(m^2)] [13,25].

2.3. Data collection

The demographic and clinical data obtained before surgery included age, gender, height, weight, BMI calculated as weight (kg)/height (m^2), SMI, serum hemoglobin level, serum albumin level, serum creatinine level, comorbidity, cancer site, and American Society of Anesthesiologists (ASA) grade. After surgery, cancer stage was also recorded according to the eighth edition of the American Joint Committee on Cancer (AJCC) stage groupings I, II, III, and IV.

The surgical outcome data obtained included length of surgery, estimated blood loss during surgery, postoperative complications, postoperative hospital stay, in-hospital mortality, and 30-day readmission. Postoperative complications were recorded using the Dindo and Clavien classification, and pulmonary complications included atelectasis, hypoxia requiring reintubation or pneumonia defined as a sputum culture that was positive for bacteria [26]. The 30-day readmission was defined as readmission within 30 day after discharge.

The oncologic outcome data obtained after surgery included the number of patients who need chemoradiation, the incidence of chemoradiation modifications, and overall survival and disease-free survival. Chemoradiation modifications included delay, dose reduction, or termination, and were measured on a dichotomous scale (absent or present) [18]. All patients were followed up within

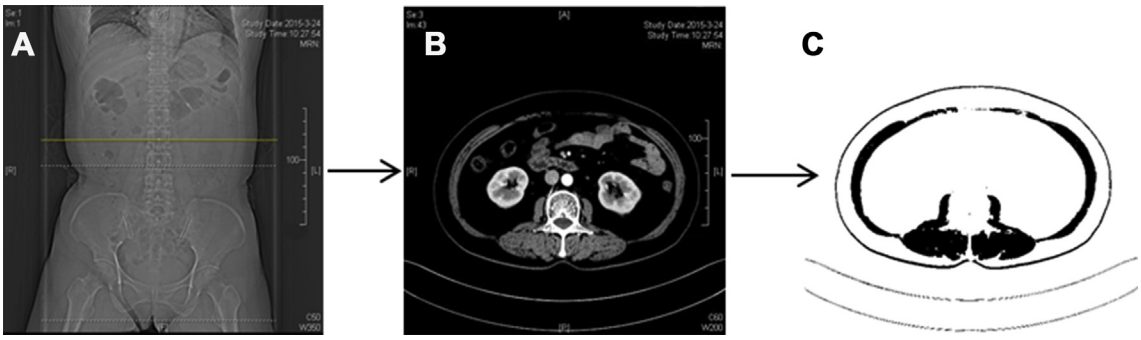

Fig. 1. Assessment of skeletal muscle mass by computed tomography. A, Two cross-sectional computed tomography images were selected to measure the areas of the skeletal muscles at the level of the third lumbar vertebra. B, After identifying individual vertebral levels, we then selected the individual imaging slice at the median aspect of the third lumbar vertebra and outlined the borders of the skeletal muscles. C, The area of the resulting regions within a range of −29 to +150 hounsfield units was then computed to calculate the total skeletal muscle area.

the first month after surgery and every 3 months thereafter. The last data of follow-up was updated in August 2018.

2.4. Statistical analysis

Statistical analyses were conducted by SPSS 23.0 software (SPSS Inc., Chicago, IL). Continuous data were compared using the independent-samples *t* test or the Mann–Whitney *U* test. For categorical data, the χ^2 test or the Fisher exact test was used. Survival curves were plotted using the Kaplan–Meier method, and any difference was analyzed by the log-rank test. To identify potential prognostic factors of surgical outcomes and survival, univariate analyses were performed first, and a multivariate analysis was further conducted using the logistic regression or Cox proportional backward stepwise procedure including all variables with P value of less than 0.05 in the univariate analysis. Data were expressed as the mean ± standard deviation (SD) unless otherwise specified. If the P value was less than 0.05, differences were considered statistically significant.

3. Results

3.1. Patient characteristics

Among 7360 consecutive patients who underwent abdominal surgery for digestive tract cancer from January 2015 to December 2016 in our institution, a total of 6447 patients met the inclusion criteria in this study cohort. The lowest sex-specific quartile of SMI at L3 in these patients was 43.13 cm^2/m^2 for men and 37.81 cm^2/m^2 for women.

The characteristics of patients included in this study are shown in Table 1. Overall, 1638 patients (25.4%) were sarcopenic and 4809 patients (74.6%) were nonsarcopenic, and sarcopenia was more prevalent in patients with gastric and pancreatic cancer and in patients with stage III and IV disease. The sarcopenic group was comparable to nonsarcopenic group with regard to patient sex, cardiovascular and respiratory comorbidity, diabetes, ASA score and serum hemoglobin and creatinine (P > 0.05). However, sarcopenia was significantly associated with an older age (62.35 ± 11.36 vs 61.58 ± 11.13 years, P = 0.016), a lower weight (62.41 ± 10.13 vs 63.22 ± 10.26 kg, P = 0.006), a lower BMI (22.43 ± 3.29 vs 23.53 ± 3.61 kg/m^2, P < 0.001), and a lower albumin (36.18 ± 4.51 vs 39.07 ± 4.88 g/L, P < 0.001). In addition, there were significant differences in cancer site (P < 0.001) and AJCC stage (P < 0.001) between sarcopenic group and nonsarcopenic group.

Table 1
Characteristics in patients with abdominal surgery for digestive tract cancer.

	Sarcopenic (n = 1638)	Nonsarcopenic (n = 4809)	P
Sex, N (%)			
Male	1109 (67.7)	3208 (66.7)	0.459
Female	529 (32.3)	1601 (33.3)	
Age, years	62.35 ± 11.36	61.58 ± 11.13	**0.016**
Weight, kg	62.41 ± 10.13	63.22 ± 10.26	**0.006**
BMI, kg/m^2	22.43 ± 3.29	23.53 ± 3.61	**< 0.001**
Serum albumin, g/L	36.18 ± 4.51	39.07 ± 4.88	**< 0.001**
Serum hemoglobin, g/L	120.97 ± 22.22	122.06 ± 23.57	0.101
Serum creatinine, μmol/L	74.89 ± 18.41	75.68 ± 18.09	0.129
Cardiovascular comorbidity, n (%)	345 (21.1)	1020 (21.2)	0.899
Respiratory comorbidity, n (%)	157 (9.6)	455 (9.5)	0.883
Diabetes, n (%)	125 (7.6)	333 (6.9)	0.358
Cancer site, n (%)			
Stomach	689 (42.1)	1291 (26.8)	**<0.001**
Colon	128 (7.8)	864 (18.0)	
Rectum	129 (7.9)	729 (15.2)	
Pancreas	196 (12.0)	177 (3.7)	
Liver	431 (26.3)	1645 (34.2)	
Gallbladder	65 (3.9)	103 (2.1)	
AJCC stage, n (%)			
I	280 (17.1)	1437 (29.9)	**<0.001**
II	345 (21.1)	1548 (32.2)	
III	797 (48.7)	1428 (29.7)	
IV	216 (13.2)	396 (8.2)	
ASA score, n (%)			
1-2	1422 (86.8)	4198 (87.3)	0.615
3-4	216 (13.2)	611 (12.7)	

Bold indicates statistically significant.
BMI: body mass index; AJCC: American Joint Committee on Cancer; ASA: American Society of Anaesthesiologists. Data are shown as the mean ± standard deviation (SD) unless otherwise specified.

3.2. Sarcopenia on surgical outcomes

There were no significant differences in the length of surgery and blood loss (P > 0.05) when the sarcopenic group was compared with nonsarcopenic group for intraoperative characteristics. For postoperative outcomes, the incidence of postoperative total and pulmonary complications, and 30-day readmission were significantly higher in sarcopenic group than in nonsarcopenic group (37.4% vs 12.9%, P < 0.001; 3.1% vs 2.1%, P = 0.026; 1.1% vs 0.4%, P = 0.003, respectively), but the in-hospital mortality was similar between two groups (P > 0.05). In addition, sarcopenia was associated with significantly longer postoperative hospital stay than nonsarcopenic patients (9.42 ± 3.40 vs 8.51 ± 3.17 days, P < 0.001) (Table 2).

The risk factors for surgical outcomes were analyzed considering various background factors, including sarcopenia. In the multivariate analysis, the presence of sarcopenia was identified to be one of the significant risk factors for postoperative complications [odds ratio (OR) = 5.418, 95% confidence interval (CI) = 2.986–9.828, P < 0.001] as shown in Table 3, but not for postoperative pulmonary complication, postoperative hospital stay and 30-day readmission (data were not shown).

3.3. Sarcopenia on chemoradiation treatment

There were significantly more patients receiving postoperative chemotherapy or radiotherapy in sarcopenic group than in nonsarcopenic group (73.1% vs 69.2%, P = 0.003; 10.6% vs 8.8%, P = 0.038, respectively), and patients with sarcopenia had significantly more chemotherapy modifications including delay, dose reduction, or termination (48.5% vs 44.2%, P = 0.018), but no difference in radiotherapy modifications was observed after abdominal surgery for digestive tract cancer (P > 0.05) when compared with nonsarcopenic patients (Table 4).

3.4. Sarcopenia on overall survival

During the follow-up period, patients with sarcopenia had significantly lower overall survival rate than those without sarcopenia (53.9% vs 69.3%, P = 0.002) as shown in Fig. 2. In addition, the univariate and multivariate analyses were employed to identify the risk factors of overall survival after abdominal surgery for digestive tract cancer, and the results were shown in Table 5. In univariate analysis, the factors identified to be statistically related to poor overall survival were age ≥65 years [hazard ratio (HR) = 0.653, 95% CI = 0.445–9.959, P = 0.030], serum albumin ≤35 g/L (HR = 0.521, 95% CI = 0.354–0.766, P = 0.001), postoperative complications (HR = 0.606, 95% CI = 0.398–0.920, P = 0.019), and sarcopenia (HR = 0.531, 95% CI = 0.354–0.797, P = 0.002). In multivariate analysis, three factors were identified to be independently related to poor overall survival: age ≥65 years (HR = 0.669, 95%

Table 2
Surgical outcomes in patients with abdominal surgery for digestive tract cancer.

	Sarcopenic (n = 1638)	Nonsarcopenic (n = 4809)	P
Length of surgery, min	149.37 ± 36.23	147.59 ± 39.17	0.106
Blood loss, mL	109.16 ± 28.59	107.89 ± 29.17	0.126
Postoperative total complications, n (%)	612 (37.4)	618 (12.9)	**<0.001**
Grade I	181 (12.9)	165 (2.8)	
Grade II	233 (16.7)	247 (4.3)	
Grade III	70 (4.9)	63 (1.1)	
Grade IV	121 (8.6)	131 (2.3)	
Grade V	7 (0.4)	12 (0.2)	
Postoperative pulmonary complication, n (%)	51 (3.1)	103 (2.1)	**0.026**
In-hospital mortality, n (%)	7 (0.4)	12 (0.2)	0.252
30-day readmission, n (%)	18 (1.1)	21 (0.4)	**0.003**
Postoperative hospital stay, days	9.42 ± 3.40	8.51 ± 3.17	**<0.001**

Bold indicates statistically significant.
Data are shown as the mean ± standard deviation (SD) unless otherwise specified.

CI = 0.453–0.990, P = 0.045), serum albumin ≤35 g/L (HR = 0.550, 95% CI = 0.370–0.818, P = 0.003), and sarcopenia (HR = 0.649, 95% CI = 0.426–0.991, P = 0.045).

3.5. Sarcopenia on disease-free survival

During the follow-up period, patients with sarcopenia had significantly lower disease-free survival rate than those without sarcopenia (36.8% vs 59.7%, P = 0.000) as shown in Fig. 3. In addition, the univariate and multivariate analyses were also employed to identify the risk factors of disease-free survival after abdominal surgery for digestive tract cancer, and the results were shown in Table 6. In univariate analysis, the factors identified to be statistically related to poor disease-free survival were postoperative complications (HR = 0.657, 95% CI = 0.453–0.953, P = 0.027), 30-day readmission (HR = 0.210, 95% CI = 0.077–0.571, P = 0.002), and sarcopenia (HR = 0.471, 95% CI = 0.332–0.669, P < 0.001). In multivariate analysis, two factors were identified to be independently related to poor disease-free survival: 30-day readmission (HR = 0.333, 95% CI = 0.119–0.931, P = 0.036) and sarcopenia (HR = 0.514, 95% CI = 0.348–0.757, P = 0.001).

4. Discussion

This prospective cohort study showed that sarcopenia had a negative impact on both surgical and oncologic outcomes in patients undergoing abdominal surgery for digestive tract cancer. These finding are not only in accordance with previous research that indicated that sarcopenia could predict morbidity, recurrence and survival after cancer surgery, but also the first report to our knowledge to reveal that sarcopenia was related to higher incidence of postoperative chemoradiation and more chemotherapy modifications including delay, dose reduction, or termination. These results have important implications for clinicians to optimally use prophylactic strategies before surgery to improve treatment outcomes in patients with sarcopenia after abdominal surgery for digestive tract cancer.

With the proportion of digestive tract cancer patients increasing rapidly worldwide [1], it is feared that the number of surgery as a cornerstone in this disease treatment may gradually increase. However, the prognostic gain of oncologic surgery must be balanced against the significant risk factors of adverse outcomes, especially the malnutrition before surgery [27,28]. Despite great advances in nutrition support, surgical technique and enhanced recovery after surgery [5,6], patients with digestive tract cancer at risk of malnutrition often have poor surgical and oncologic outcomes including high incidence of morbidity and mortality and short survival after surgery [7–9]. Thus, identification of malnutrition is of great significance for the treatment strategy and further affects prognosis in digestive tract cancer patients. Recently, sarcopenia characterized by the loss of skeletal muscle mass and strength was proposed and highlighted as a new significant prognostic factor to predict short- and long-term outcomes among numerous studies of cancer patients undergoing surgery [12–15]. However, some studies raised controversial results, showing that sarcopenia was not related to postoperative complications or survival in patients with cancer after surgery [16,17]. Furthermore, most of previous studies were retrospective and only focused on

Table 3
Univariate and multivariate analyses of prognostic factors for postoperative complications in patients with abdominal surgery for digestive tract cancer.

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P	OR (95% CI)	P
Male	0.975 (0.555–1.715)	0.931		
Age ≥ 65 years	1.854 (1.074–3.203)	0.027	1.680 (0.920–3.066)	0.091
BMI, kg/m^2				
<18.5	0.811 (0.237–2.769)	0.738		
>25	0.616 (0.324–1.171)	0.140		
Serum albumin ≤35 g/L	1.88 (1.068–3.309)	0.029	1.562 (0.833–2.930)	0.164
Cardiovascular comorbidity	0.850 (0.431–1.675)	0.639		
Respiratory comorbidity	2.631 (1.198–5.780)	0.016	3.108 (1.333–7.245)	**0.009**
Diabetes	1.858 (0.759–4.549)	0.175		
ASA score 3–4	0.766 (0.339–1.729)	0.521		
Length of surgery ≥ 145 min	1.011 (0.581–1.760)	0.969		
Blood loss ≥ 106 mL	0.794 (0.447–1.411)	0.432		
Sarcopenia	5.122 (2.861–9.171)	0.000	5.418 (2.986–9.828)	**<0.001**

Bold indicates statistically significant.
BMI: body mass index; ASA: American Society of Anaesthesiologists; OR: odds ratio; CI: confidence interval.

Table 4
Chemoradiation treatment in patients with abdominal surgery for digestive tract cancer.

	Sarcopenic (n = 1638)	Nonsarcopenic (n = 4809)	P
Chemotherapy Treatment, N (%)	1197 (73.1)	3328 (69.2)	**0.003**
Radiotherapy Treatment, N (%)	173 (10.6)	425 (8.8)	**0.038**
Chemotherapy Modifications, N (%)	795 (48.5)	2125 (44.2)	**0.018**
Delay	272 (16.6)	755 (15.7)	
Dose reduction	370 (22.6)	952 (19.8)	
Termination	153 (9.3)	418 (8.7)	
Radiotherapy Modifications, N (%)	645 (39.4)	1957 (40.7)	0.282
Delay	221 (13.5)	601 (12.5)	
Dose reduction	295 (18.0)	957 (19.9)	
Termination	129 (7.9)	399 (8.3)	

Bold indicates statistically significant.
Data are shown as the number (%).

the effect of sarcopenia on one cancer treatment, such as surgery, chemotherapy or radiotherapy [15,18–20], but its impact on the short- and long-term outcomes regarding the entire cancer treatments including surgery and the followed chemoradiation is unknown. Therefore, this study aimed to prospectively evaluate the impact of sarcopenia by comparison of short- and long-term outcomes in patients after abdominal surgery for digestive tract cancer.

To better assess sarcopenia, quantification of skeletal muscle mass by preoperative CT scan at L3 with measurement of SMI has been proposed in most of cancer studies [13,25,29–31], and the lowest sex-specific quartile has been considered increasingly as a good threshold to define sarcopenia despite numerous methods to quantify sarcopenia [22–24]. In the present study, we therefore chose these criteria, and found that 25.4% of patients with digestive tract cancer were sarcopenic before abdominal surgery. Sarcopenia was significantly associated with an older age, a lower weight, a lower BMI, and a lower albumin. In addition, different cancer site and AJCC stage were also significantly associated with sarcopenia. However, the sarcopenic group was comparable to the non-sarcopenic group regarding patient sex, cardiovascular comorbidity, respiratory comorbidity, diabetes, ASA score and serum hemoglobin and creatinine. Thus, these results revealed that the criteria used in this study is sensitive to identify sarcopenia, and measurement of skeletal muscle mass by abdominal CT scan could be used to assess all patients preoperatively because abdominal CT scan is routinely available, neither expensive nor time-consuming in digestive surgery.

With respect to surgical outcomes after surgery such as postoperative complications, mortality and readmission, it always receives a major concern for the prognostic gain after oncologic surgery. Therefore, previous studies mostly discussed the relationship between sarcopenia and surgical outcomes after surgery for cancer [15]. In this study, we also assessed the impact of sarcopenia on surgical outcomes after abdominal surgery for digestive tract cancer. The results showed that sarcopenic group had higher incidence of postoperative total and pulmonary complications and 30-day readmission, and also longer postoperative hospital stay when compared with nonsarcopenic group. In addition, further multiple regression analysis showed that sarcopenia was a risk factor of postoperative complications. Our results are similar to those of previous studies [14,25,32], and give highlight to the evidence that sarcopenia is a predictor of postoperative complications. These findings suggest that preoperative identification of sarcopenia in digestive tract cancer and giving appropriate interventions may improve surgical outcomes in patients after surgery.

As we know, not only surgery but also chemoradiation is very important to treat digestive tract cancer. Cancer patients who need

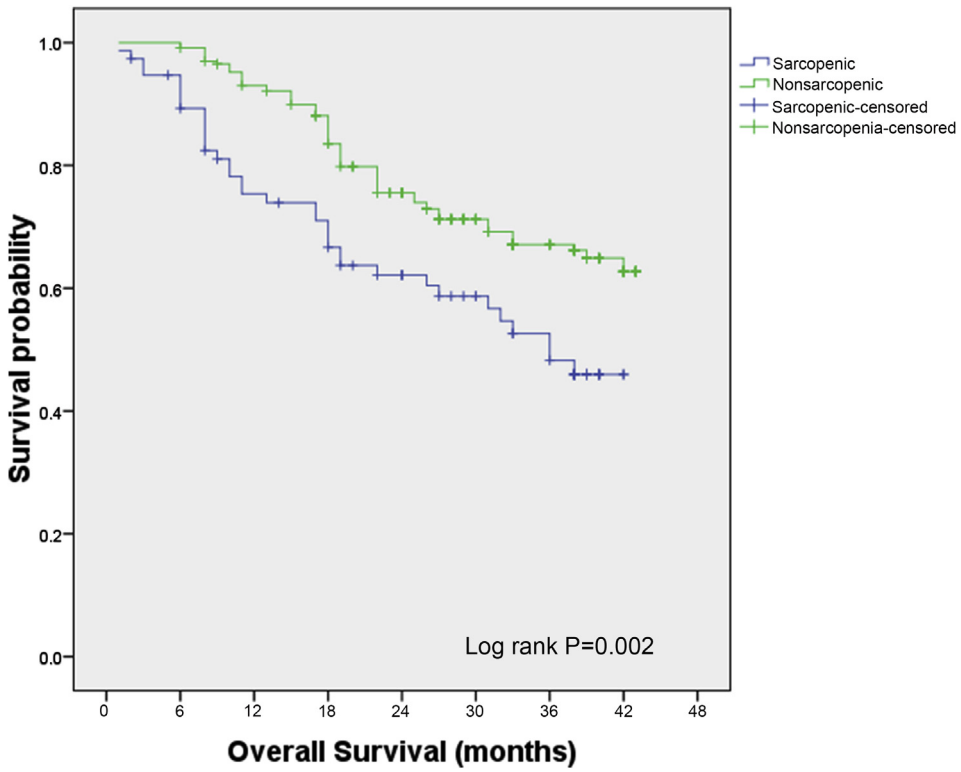

Fig. 2. Overall survival curves in patients with sarcopenia or without sarcopenia after abdominal surgery for digestive tract cancer.

Table 5
Univariate and multivariate analyses of prognostic factors for overall survival in patients with abdominal surgery for digestive tract cancer.

	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P	HR (95% CI)	P
Male	0.724 (0.476–1.101)	0.131		
Age ≥ 65 years	0.653 (0.445–0.959)	0.030	0.669 (0.453–0.990)	**0.045**
BMI, kg/m^2				
<18.5/18.5–25	1.535 (0.560–4.205)	0.405		
>25/18.5–25	1.218 (0.799–1.855)	0.359		
Serum albumin ≤ 35 g/L	0.521 (0.354–0.766)	0.001	0.550 (0.370–0.818)	**0.003**
Cardiovascular comorbidity	0.720 (0.462–0.121)	0.146		
Respiratory comorbidity	0.796 (0.426–1.487)	0.474		
Diabetes	1.144 (0.531–2.462)	0.732		
ASA score 3–4	0.956 (0.512–1.786)	0.889		
Length of surgery ≥ 145 min	1.189 (0.806–1.752)	0.383		
Blood loss ≥ 106 mL	0.834 (0.535–1.300)	0.424		
Postoperative complications	0.606 (0.398–0.920)	0.019	0.798 (0.497–1.282)	0.352
Postoperative pulmonary complication	0.912 (0.225–3.698)	0.897		
Postoperative hospital stay ≥ 9 days	1.150 (0.773–1.711)	0.489		
30-day readmission	0.552 (0.136–2.239)	0.405		
Sarcopenia	0.531 (0.354–0.797)	0.002	0.649 (0.426–0.991)	**0.045**

Bold indicates statistically significant.
BMI: body mass index; ASA: American Society of Anaesthesiologists; HR: hazard ratio; CI: confidence interval.

chemoradiation after surgery will benefit from this treatment. However, many factors especially the malnutrition could adversely affect the implementation of chemoradiation [20,33]. We highlighted that many studies did not focus on the effect of sarcopenia on postoperative chemoradiation, which underlined the limited data on this topic. Of note, this is the first report to our knowledge to prospectively estimate the relationship between sarcopenia and chemoradiation treatment in patients after abdominal surgery for digestive tract cancer. The present study revealed that there were significantly more patients receiving postoperative chemoradiation in sarcopenic group than in nonsarcopenic group, and patients with sarcopenia had significantly more chemotherapy modifications including delay, dose reduction, or termination. These results showed that sarcopenia had an adverse effect on chemoradiation after abdominal surgery for digestive tract cancer, especially on the chemotherapy. Interestingly, recent studies also reported that during chemotherapy skeletal muscle mass presented significant loss [18], and sarcopenia was related to major chemotherapy toxicities resulting in dose reduction, dose delay, or therapy termination [34,35]. Therefore, combined with these previous findings, it is suggested that identification of sarcopenia before, during and after chemotherapy is also greatly important for the targeted nutritional

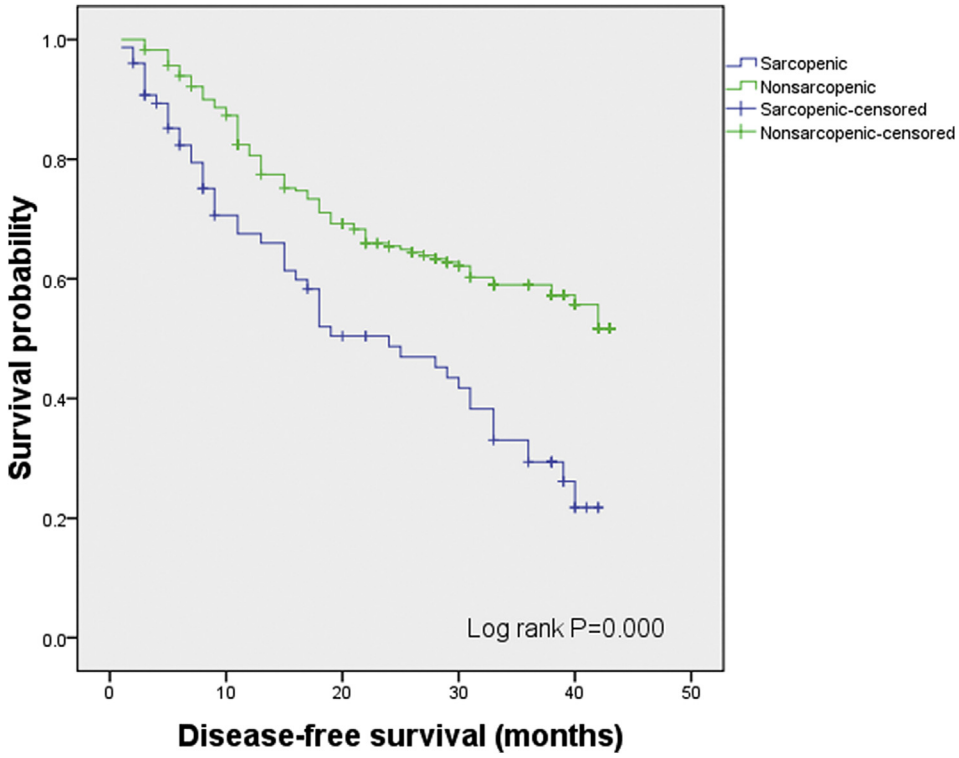

Fig. 3. Disease-free survival curves in patients with sarcopenia or without sarcopenia after abdominal surgery for digestive tract cancer.

Table 6
Univariate and multivariate analyses of prognostic factors for disease-free survival in patients with abdominal surgery for digestive tract cancer.

	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P	HR (95% CI)	P
Male	0.854 (0.595–1.199)	0.345		
Age ≥ 65 years	0.902 (0.648–1.256)	0.542		
BMI, kg/m^2				
<18.5	1.596 (0.648–3.931)	0.309		
>25	1.331 (0.925–1.916)	0.123		
Serum albumin ≤35 g/L	0.720 (0.508–1.021)	0.065		
Cardiovascular comorbidity	0.915 (0.614–1.363)	0.662		
Respiratory comorbidity	0.870 (0.501–1.511)	0.621		
Diabetes	1.140 (0.599–2.170)	0.689		
ASA score 3–4	0.964 (0.555–1.675)	0.898		
Length of surgery ≥ 145 min	1.060 (0.753–1.490)	0.739		
Blood loss ≥ 106 mL	1.243 (0.871–1.774)	0.230		
Postoperative complications	0.657 (0.453–0.953)	0.027	0.904 (0.597–1.368)	0.632
Postoperative pulmonary complication	1.328 (0.329–5.365)	0.691		
30-day readmission	0.210 (0.077–0.571)	0.002	0.333 (0.119–0.931)	**0.036**
Postoperative hospital stay ≥ 9 d	1.083 (0.765–1.531)	0.654		
Sarcopenia	0.471 (0.332–0.669)	<0.001	0.514 (0.348–0.757)	**0.001**

Bold indicates statistically significant.
BMI: body mass index; ASA: American Society of Anaesthesiologists; HR: hazard ratio; CI: confidence interval.

intervention so as to improve the outcomes of chemotherapy treatment.

In addition, our findings also highlighted the relationship between sarcopenia and survival in patients with cancer after surgery. As expected, sarcopenia was found significantly related to lower rate of overall survival and disease-free survival in patients after abdominal surgery for digestive tract cancer, and it was an unfavorable prognostic factor for poor overall survival and disease-free survival by multivariate analysis. Our results were in line with the results of previous research [22,36,37], indicating that sarcopenia is independently associated with cancer endpoints. While the underlying reason for the adverse effect of sarcopenia on survival was not explored in this study, we speculated that this poor survival may be related to the poor surgical outcomes and increased chemotherapy modifications in patients after abdominal surgery for digestive tract cancer, which were also found in the present study. Nevertheless, these findings have important implications for surgical practice to identify sarcopenia before surgery, particularly in regard to the growing application of cancer patients.

Of note, the current study has several limitations. First, as we know, CT scans of abdomen are not routinely performed for patients with esophageal cancer before surgery, and there are few patients meeting the inclusion criteria. Therefore, patients with esophageal cancer were not included in our study, otherwise, the results would be more comprehensive on the effect of sarcopenia on digestive cancer after surgery. Nevertheless, our study included most of digestive tract cancer except esophageal cancer, leading to various surgical procedures and different chemoradiation programs, and therefore the results may be influenced. Second, this is a prospective study with large-scale, but it is a single-center study, and although the differences were statistically significant, the magnitude of some of these differences such as postoperative hospital stay, pulmonary complications and readmissions were quite small and the significance was a result of the huge sample size. Further international multicenter studies are needed to confirm our findings. Third, recent studies have highlighted that not only reduced quantity of skeletal muscle, but also reduced function of skeletal muscle is a pivotal component of sarcopenia [38]. However, in the present study, we were not able to capture data on parameters of skeletal muscle function such as walking speed or grip strength due to the study's cohort observational design. Future studies in this field of research should define sarcopenia by assessment of both quantity and function of skeletal muscle, which would clearly show the impact of sarcopenia on cancer patients after surgery.

5. Conclusion

This study revealed that sarcopenia affected postoperative complications, chemotherapy treatment and survival, and could be used as a strong and independent prognostic factor for poor surgical and oncologic outcomes in patients after abdominal surgery for digestive tract cancer. Identification of sarcopenia routinely by abdominal CT imaging before digestive surgery for cancer and targeted approaches to enhance rehabilitation may improve its negative outcomes.

Statement of authorship

This study was conducted at the Department of General Surgery, Zhongshan Hospital, Fudan University, and approval from the institutional review board of Zhongshan Hospital, Fudan University was obtained.

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Conflict of interest

The authors confirm that there are no conflict of interest to declare.

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Shuze Zhang and Shanjun Tan contributed equally to this work. Guohao Wu supervised the entire project. Shuze Zhang, Shanjun Tan, Yi Jiang and Qiulei Xi collected the data. Qingyang Meng, Qiulin Zhuang, Yusong Han and Xiangyu Sui conducted the data analyses. Shanjun Tan drafted the manuscript. All the authors critically reviewed the article and approved the final manuscript.

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