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ARTICLE

Sarcopenia Predicts Postoperative Complications and Survival of Colorectal Cancer Patients Undergoing Radical Surgery

Jiwei Wang[1,2,*], Yi Chen[1], Jixin He[1], Chunmei Yin[1,2], Ming Xie[1]

[1]Department of General Surgery, Digestive Disease Hospital, Affiliated Hospital of Zunyi Medical University, Zunyi, Guizhou, China
[2]Day Chemotherapy Ward, Affiliated Hospital of Zunyi Medical University, Zunyi, Guizhou, China
*Correspondence: wjw@smail.nju.edu.cn (Jiwei Wang)

Abstract

Aims/Background Previous literature has indicated that sarcopenia is related to poor outcomes after radical resection for colorectal cancer (CRC). However, its effect on the postoperative clinical outcomes of CRC remains controversial. This study aimed to elucidate the predictive value of sarcopenia for postoperative complications and survival in CRC patients.

Methods This investigation retrospectively assessed the clinical data of 226 CRC patients who underwent radical resection at the Department of Gastrointestinal Surgery, Affiliated Hospital of Zunyi Medical University from January 2018 to December 2020. Sarcopenia was diagnosed according to the recommendations of the Asian Working Group for Sarcopenia in 2019, and patients were categorized into sarcopenia and non-sarcopenia groups. Multivariate and univariate analyses were employed to assess the risk factors for postoperative complications. The Kaplan-Meier method and survival curve were used to analyze postoperative survival time. Cox proportional hazards regression models were used to evaluate risk factors affecting the prognosis of CRC patients.

Results This investigation included 226 patients, of which 68 were diagnosed with sarcopenia. Furthermore, it was revealed that sarcopenia was linked with older age ($p < 0.001$), low body mass index ($p < 0.001$), high prevalence of diabetes ($p = 0.002$), high cystatin level ($p = 0.017$), and low 3rd lumbar spine (L3) planar skeletal muscle index ($p < 0.001$), but was not related to the tumour stage or the gender. Moreover, sarcopenia was also correlated with increased occurrence of all postoperative complications ($p = 0.050$). The results of the multivariate analysis indicated that sarcopenia was an independent risk factor for postoperative complications (odds ratio (OR): 7.154; 95% confidence interval (CI): 2.261–22.633; $p = 0.017$). The Kaplan-Meier analysis revealed that sarcopenia patients had significantly lower 5-year disease-free survival (DFS) (48.5% vs 59.5%; log-rank $p = 0.033$) and 5-year overall survival (OS) (57.4% vs 77.2%; log-rank $p < 0.001$) rates. Sarcopenia was an independent risk factor for poor DFS (hazard ratio (HR) = 1.404; $p = 0.016$) and OS (HR = 1.290; $p = 0.021$).

Conclusion In CRC patients undergoing radical surgery, sarcopenia is an independent risk factor for postoperative complications. Sarcopenia may be a predictive factor for the prognosis and survival of CRC patients undergoing radical resection.

Key words: sarcopenia; L3 skeletal muscle index; colorectal cancer; postoperative complications; survival

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Introduction

Colorectal cancer (CRC) is the 3rd most prevalent cancer and the 4th major cause of cancer mortality globally. Currently, for CRC, surgical resection is the main treatment strategy (Biller and Schrag, 2021). Despite the progress in surgical treatment and adjuvant therapy, 20% to 45% of patients who undergo radical surgery still experience recurrence or metastases, with poor prognosis and high mortality (Baratti et al, 2021). At present, the main clinical treatment for CRC is surgical resection; however, postoperative patients are prone to infection, anastomotic leakage, intestinal obstruction, and other complications, which are not conducive to prognosis and recovery (Pallan et al, 2021). A study has shown that the incidence of complications in the surgical treatment of CRC is as high as 20%–30%, among which the common postoperative complications are incision infection (14%–18%), intestinal obstruction (10%–30%), and anastomotic leakage (2.1%–9.2%) (Khot et al, 2002). Therefore, early assessment of risk factors for postoperative complications and taking measures to decrease the occurrence of surgical complications are of great significance for the comprehensive treatment of CRC (van Rooijen et al, 2019).

Sarcopenia is characterized by the loss of skeletal muscle strength and mass, as well as decreased physical activity, which results in substandard quality of life, physical disability, and even death (Chen et al, 2020). Sarcopenia is diagnosed based on three criteria: muscle strength, muscle mass, and muscle function (Cruz-Jentoft et al, 2019). Muscle mass can be measured using a variety of techniques, among which computed tomography (CT) scanning of a specific muscle's cross-sectional area is the gold standard technique for noninvasive muscle mass analysis (Jones et al, 2020). The measurement of muscle mass using CT has the characteristics of objectivity, repeatability, and accuracy. Several studies have reported a significant association between sarcopenia and substandard prognosis for patients with various malignant tumours (such as the liver (Ponziani and Gasbarrini, 2018), pancreatic (Basile et al, 2019), lung (Jogiat et al, 2023) breast (Zhang et al, 2020), ovarian (Ubachs et al, 2019), bladder (Fukushima et al, 2018), gastric (Kuwada et al, 2019) cancers, etc.), as well as the association between sarcopenia and poor prognosis (Jochum et al, 2019; Nakanishi et al, 2018).

The incidence of sarcopenia in CRC patients ranges from 12%–60% (Vergara-Fernandez et al, 2020). Several studies have elucidated factors that influence sarcopenia in the elderly population (Xiao et al, 2019) and cancer-diagnosed patients (Zhang and Zhu, 2023). However, sarcopenia's effect on postoperative complications and prolonged postoperative survival remains inconclusive. Therefore, we conducted a retrospective analysis to explore whether sarcopenia is a risk factor for postoperative complications and survival in CRC patients.

Methods

Study Design

This research was authorized by the Ethical Board of the Affiliated Hospital of Zunyi Medical University (approval number: KLLY-2021-089). The study was

conducted in compliance with the Declaration of Helsinki and all participants provided informed consent. Clinical information was collected from the CRC patients who were admitted to the Department of Gastrointestinal Surgery, Affiliated Hospital of Zunyi Medical University between January 2018 and December 2020 and underwent radical surgery. The inclusion criteria were as follows: patients who were diagnosed with CRC and underwent radical surgery (Zhang et al, 2023); abdominal CT examination performed at our hospital within 1 month before surgery; and high-quality CT images that could be used for analysis. Exclusion criteria were as follows: missing clinical or pathological data; combined with other malignant tumours; patients with preoperative long-term use of hormones and immunosuppressants.

Data Collection

Each patient's preoperative data was retrospectively collected, including sex, age, serum data, body mass index (BMI), abdominal CT, history of abdominal surgery, medical diseases (cardiovascular and cerebrovascular diseases, respiratory diseases, diabetes, etc.), and tumour location. Intraoperative data included tumour size, blood loss, surgical approach, operative time, and blood transfusion during the surgery. The postoperative data included pathological Tumour Node Metastasis (TNM) stage according to the Union for International Cancer Control (UICC) classification (8th edition), length of postoperative hospital stay, postoperative survival time, and type of postoperative complication (including intestinal obstruction, anastomotic leakage, anastomotic bleeding, infection). The postoperative complications were assessed using the Clavien-Dindo system (Manekk et al, 2022), and those classified as grade II or more were considered postoperative complications.

Measurement of Muscle Mass

To assess the skeletal muscle mass, CT scans acquired within a month before surgery were retrospectively examined. The landmark was set as the 3rd lumbar spine (L3), and the cross-sectional area of the skeletal muscle was estimated by selecting two consecutive sections, with the Hounsfield unit threshold of –29 to +150. At the L3 level, the skeletal muscles included paraspinal (tetragonal lumbar and erector spinae), psoas major, and abdominal wall muscles (internal and external oblique, transversus abdominis, and rectus abdominis). The average image size was calculated for each patient using SYNAPSE VINCENT software (version 4.4, Fujifilm Co., Tokyo, Japan). These values were standardized according to the patient's height in square meters (m^2) to acquire the L3 planar skeletal muscle index (SMI) (cm^2/m^2). The examiner who performed all the aforementioned calculations and measurements was blinded to the surgical results during the quantification (Fig. 1). All the assessments were performed independently. A diagnosis of muscle mass loss, based on an Asian population reference, was made using cut-points of SMI <36 and <29 cm^2/m^2 in males and females, respectively (Iritani et al, 2015).

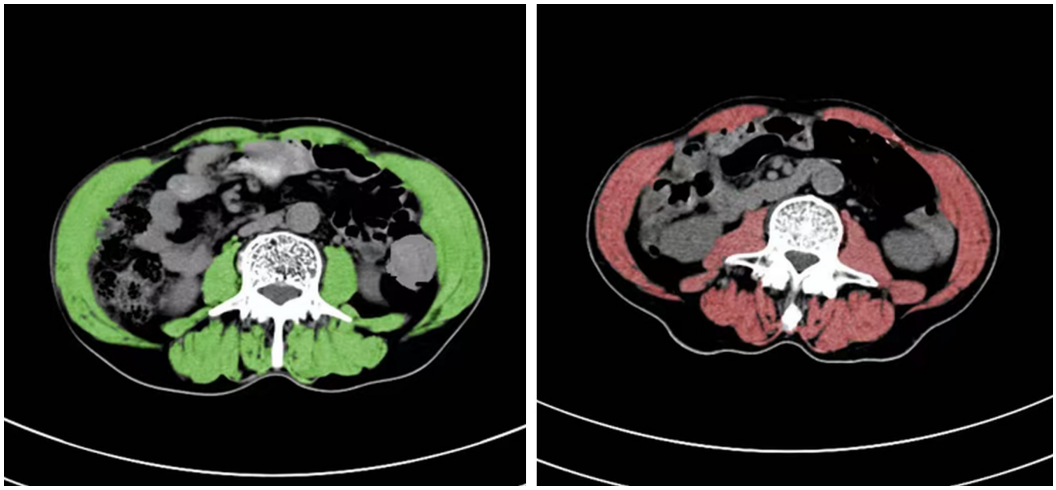

Fig. 1. Skeletal muscle area at 3rd lumbar spine (L3) level in normal (Green) and low skeletal muscle index (SMI) patients (Red) in the abdominal computed tomography (CT) images.

Physical Fitness and Muscle Strength Analyses

A grip strength meter was employed to measure muscle strength. Patients were asked to perform at least two isometric contraction tests using their dominant hand. For the subsequent analyses, the highest value of these tests was used. According to the Asian Working Group for Sarcopenia (AWGS), the recommended values of grip strength in males and females are $<$28.0 and $<$18.0 kg, respectively, which are the diagnostic cutoff values for reduced muscle strength (Chen et al, 2022). The physical fitness of the patients was evaluated by a 6-m walking test. We measured the total time taken by the patients to complete a normal-speed 6-m walk without any deceleration or acceleration, twice. The average speed was calculated for the subsequent analyses. The diagnostic cutoff value for physical decline is a walking speed of $<$1.0 m/s, as recommended by AWGS (Arai et al, 2023). Patients who lacked these essential data were excluded from the study.

Sarcopenia Evaluation

The participants in this study were diagnosed with sarcopenia according to the latest consensus guidelines of AWGS (Chen et al, 2020). This standard included three basic aspects: muscle strength, physical fitness, and muscle mass. The criteria for diagnosis of sarcopenia included weakened muscle strength (grip strength $<$28.0 and $<$18.0 kg in males and females, respectively), simultaneous decrease in muscle mass (SMI $<$36 and $<$29 cm^2/m^2 in males and females, respectively), and/or impaired physical fitness (walking speed of $<$1.0 m/s). Based on the aforementioned data, the participants were categorized into sarcopenia and non-sarcopenia cohorts.

Follow-up and Outcomes

The follow-up included regular visits and telephone conversations every 3–6 months in the 1st year, then every 6–12 months from the 2nd year until death. Disease-free survival (DFS) was defined as the period between operation and disease recurrence, death, or the last follow-up. Overall survival (OS) was defined as

the time from operation to death from any cause or to the last follow-up. The last follow-up date was December 31, 2023.

Statistical Analysis

The SPSS software (version 26.0, IBM SPSS Statistics, Chicago, IL, USA) was employed for all statistical analyses and the Shapiro-Wilk test was used to assess the normality of the data. Normally distributed data were presented as the mean ± standard deviation, while non-normal data were presented as the median or interquartile range. The relationship between sarcopenia and postoperative complications was assessed using the chi-square, Wilcoxon rank sum test, and further logistic regression analyses. In addition, the Kaplan-Meier method was used to elucidate the survival data and estimate the probability of death and survival. Cox proportional hazards regression models with forward selection were used to evaluate risk factors affecting the prognosis of CRC patients. The statistical threshold for significant differences was set as $p < 0.05$.

Results

Patient's Clinical Characteristics

Between January 2018 and December 2020, 226 patients satisfied the selection parameters (Fig. 2). Based on the sarcopenia diagnostic criteria, 68 patients had sarcopenia, accounting for 30% of the enrolled patients. Table 1 summarizes the patients' demographic and clinical characteristics. In comparison with the non-sarcopenia cohort, the average age of sarcopenia patients was older (67.2 ± 11.7 vs 55.5 ± 10.2 years; $p < 0.001$). Furthermore, sarcopenia patients had a higher incidence of diabetes (13.2% vs 1.9%; $p = 0.002$) and a higher average level of cystatin (1.06 ± 0.25 vs 0.98 ± 0.22; $p = 0.017$). The sarcopenia patients had lower BMI (17.51 ± 2.88 vs 22.33 ± 2.35; $p < 0.001$) and SMI (30.7 ± 3.25 vs 39.54 ± 5.79; $p < 0.001$) compared to the non-sarcopenia cohort. No significant differences were observed in the history of abdominal surgery, sex, creatinine, tumour location, cardiovascular, carcinoembryonic antigen (CEA), or respiratory diseases between the two groups ($p > 0.05$) (Table 1). Moreover, no significant differences were identified in the operation method, operation time, intraoperative blood transfusion, blood loss, tumour size, or tumour size between the two groups ($p > 0.05$) (Table 2). The sarcopenia group had a longer postoperative hospital stay (10.13 ± 2.55 vs 8.97 ± 2.32; $p < 0.001$) and a higher incidence of postoperative complications (30.9% vs 19.0%; $p = 0.050$). The incidence of postoperative infection in the sarcopenia patients was higher than that in the non-sarcopenia patients (23.5% vs 12.0%, $p = 0.028$); however, there was no significant difference in TNM staging ($p > 0.05$) (Table 3).

Correlation between Sarcopenia and Postoperative Complications

Due to the statistical differences in the incidence of complications between the two groups, factors potentially related to postoperative complications were further explored. Among a total of 226 patients, postoperative complications occurred in 51 patients (30 in the non-sarcopenia group, while 21 in the sarcopenia group).

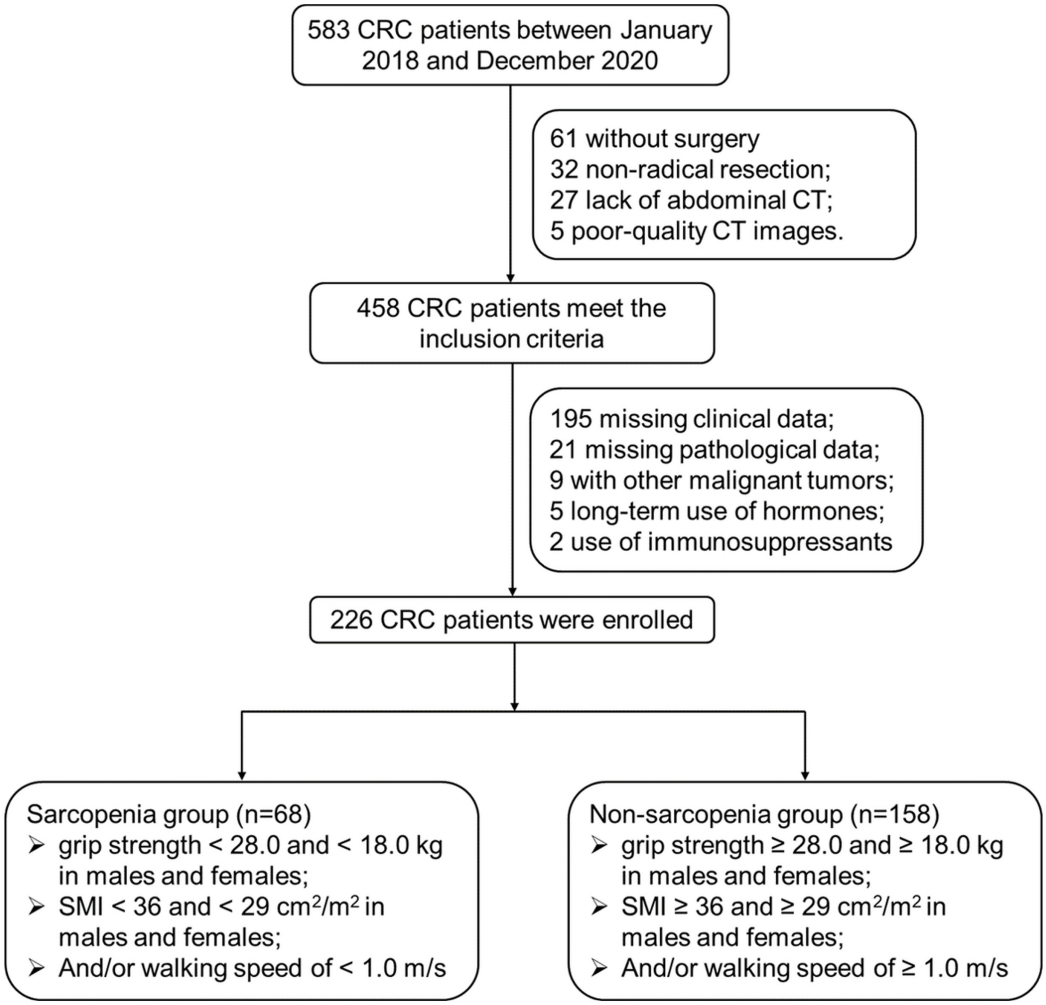

Fig. 2. Patients' selection flow chart. CRC, colorectal cancer.

In univariate analysis, we found that age ≥65 (odds ratio (OR): 2.274; 95% confidence interval (CI): 1.205–4.303; $p = 0.012$), Cystatin ≥2.5 mg/L (OR: 1.874; 95% CI: 1.210–2.561; $p = 0.046$), intraoperative blood transfusion (OR: 3.638; 95% CI: 1.877–15.097; $p = 0.041$) and sarcopenia (OR: 2.109; 95% CI: 1.220–4.137; $p = 0.032$) were potential risk factors of postoperative complications (Table 4). The results of the multivariate logistic regression revealed that sarcopenia (OR: 7.154; 95% CI: 2.261–22.633; $p = 0.017$) was an independent risk factor for postoperative complications (Table 5).

Correlation between Sarcopenia and Survival

Based on the last follow-up, among 226 patients with CRC, 99 (43.8%) experienced recurrence and 65 (28.8%) died. In the Kaplan-Meier analysis, patients in the sarcopenia group had a significantly lower 5-year DFS rate (48.5% vs 59.5%; log-rank $p = 0.033$) and a lower 5-year OS rate (57.4% vs 77.2%; log-rank $p < 0.001$), as shown in Figs. 3,4.

Next, factors associated with DFS and OS were evaluated by univariate and multivariate Cox regression analyses. Multivariate analysis revealed that sarcope-

Table 1. General clinical data of the two groups.

Variable	Sarcopenia (n = 68)	Non-sarcopenia (n = 158)	$t/Z/\chi^2$	p-value
Age (years)	67.2 ± 11.7	55.5 ± 10.2	7.56	<0.001[a]
Gender			1.518	0.218[b]
Male	38	102		
Female	30	56		
Tumour site			0.966	0.326[b]
Colon	22	62		
Rectum	46	96		
History of abdominal surgery			0.206	0.650[b]
Yes	12	32		
No	56	126		
Medical diseases (yes/no)				
Angiocarpy	11/57	20/138	0.497	0.481[b]
Diabetes	9/59	3/155	10.002	0.002[b]
COPD	6/62	9/149	0.331	0.565[b]
Creatinine (μm/L)	26.5 (11.4, 54.6)	54.4 (13.7, 145.1)	–0.838	0.402[c]
Cystatin (mg/L)	1.06 ± 0.25	0.98 ± 0.22	2.405	0.017[a]
CEA (μ/m)	17.16 (0.08, 78.42)	10.11 (0.24, 68.55)	–0.787	0.431[c]
BMI	17.51 ± 2.88	22.33 ± 2.35	–12.17	<0.001[a]
SMI	30.7 ± 3.25	39.54 ± 5.79	–14.58	<0.001[a]

Notes: [a]: sample t-test. [b]: Pearson's χ^2 test or Yates's correction for continuity. [c]: Wilcoxon rank sum test.
Abbreviations: CEA, carcinoembryonic antigen; COPD, chronic obstructive pulmonary disease; SMI, skeletal muscle index; BMI, body mass index.

nia was an independent risk factor for poor DFS [hazard ratio (HR) = 1.404; p = 0.016] and OS (HR = 1.290; p = 0.021) (Tables 6,7).

Discussion

Sarcopenia often coexists with cachexia in patients with malignant tumours or other chronic diseases. Body composition and functional status have been shown to be important prognostic factors for patients and are associated with weight and muscle mass loss (Cederholm et al, 2017). Sarcopenia is common in CRC patients and is possibly linked with enhanced postoperative complications, poor quality of life, and reduced survival (He et al, 2023). Based on the results of previous studies, the present study explored the predictive value of sarcopenia for postoperative complications and CRC patient's survival from the aspects of general clinical data, intraoperative conditions, postoperative complications, and survival of patients. The early screening of patients with risk factors can help clinicians develop individualized treatment plans in advance, thereby reducing the occurrence of perioperative complications.

Table 2. Comparison of intraoperative conditions between the two groups.

Variable	Sarcopenia (n = 68)	Non-sarcopenia (n = 158)	$t/Z/\chi^2$	*p*-value
Surgical approach			0.05	0.824[b]
Open surgery	5	13		
Laparoscope	63	145		
Operation time (min)	192.7 ± 28.5	200.4 ± 34.6	–1.614	0.108[a]
Blood transfusion			0.15	0.698[b]
Yes	6	10		
No	62	148		
Intraoperative bleeding (mL)	48.5 (19, 95)	42 (15, 82)	–0.663	0.507[c]
Tumour size (cm)	4.55 ± 1.69	4.88 ± 1.97	–1.203	0.23[a]

Notes: [a]: sample *t*-test. [b]: Pearson's χ^2 test or Yates's correction for continuity. [c]: Wilcoxon rank sum test.

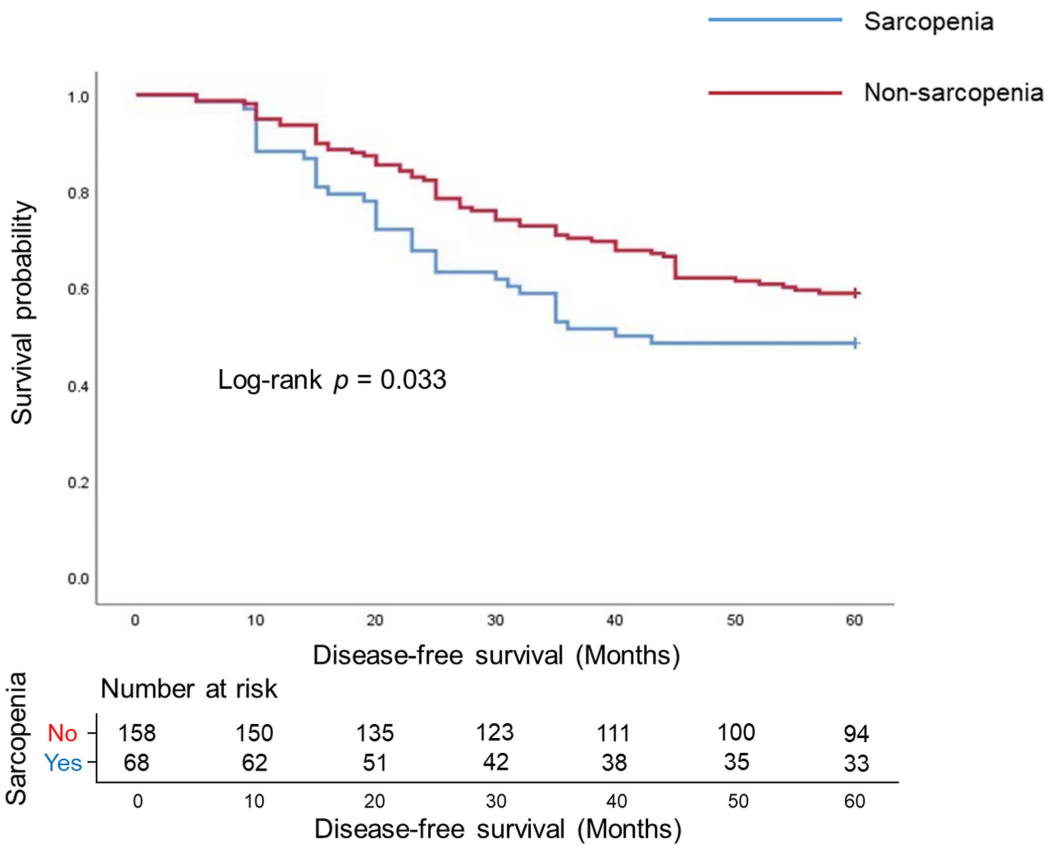

Fig. 3. Kaplan-Meier curve of disease-free survival (DFS) in patients with and without sarcopenia.

The occurrence of sarcopenia is related to factors such as decreased exercise volume, decreased protein intake and synthesis, and the depletion of some chronic diseases (Cosquéric et al, 2006). In this study, we found that the occurrence of sarcopenia was closely related to age, BMI, cystatin C, and diabetes, which is con-

Table 3. Comparison of postoperative conditions between the two groups.

Variable	Sarcopenia (n = 68)	Non-sarcopenia (n = 158)	t/χ^2	p-value
Postoperative hospital stays (day)	10.13 ± 2.55	8.97 ± 2.32	3.345	0.001[a]
TNM stage, n (%)			3.067	0.216[b]
I stage	8 (11.8)	32 (20.3)		
II stage	32 (47.1)	59 (37.3)		
III stage	28 (41.1)	67 (42.4)		
Postoperative complications, n (%)	21 (30.9)	30 (19.0)	3.849	0.050[b]
Anastomotic leak	6 (8.8)	8 (5.1)		
Anastomotic bleeding	1 (1.5)	2 (1.3)		
Pneumonia	9 (13.3)	11 (6.9)		
Abdominal infection	2 (2.9)	3 (1.9)		
Urinary tract infection	2 (2.9)	3 (1.9)		
Incision infection	1 (1.5)	2 (1.3)		
Infection complications, n (%)	16 (23.5)	19 (12.0)	4.807	0.028[b]

Notes: [a]: sample t-test. [b]: Pearson's χ^2 test.
Abbreviation: TNM, Tumour Node Metastasis.

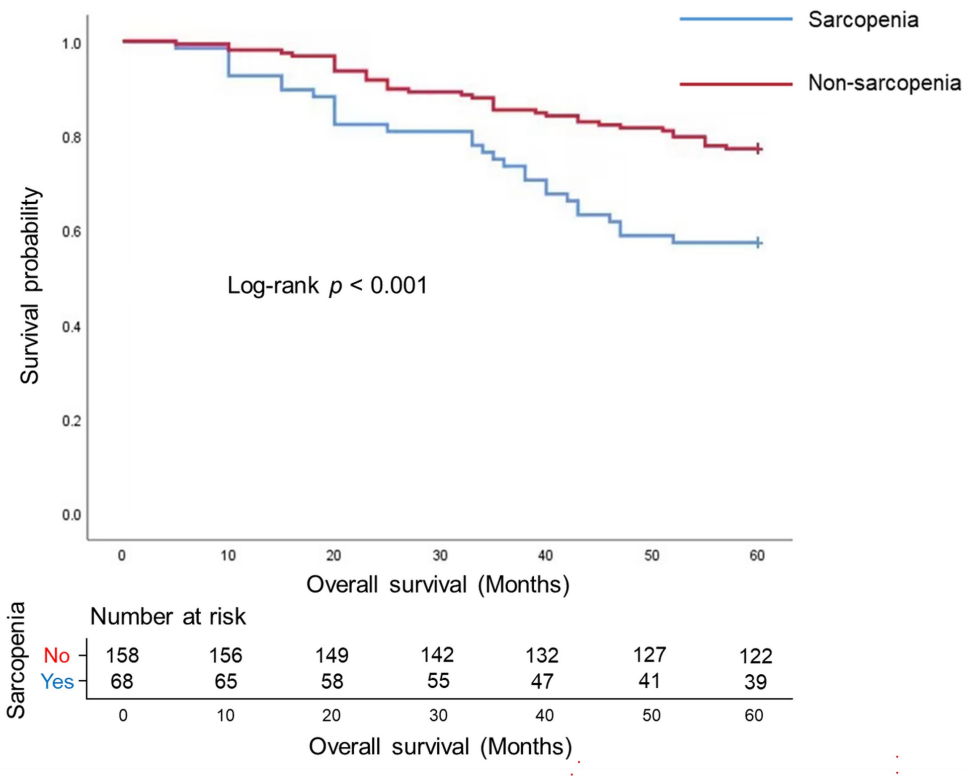

Fig. 4. Kaplan-Meier curve of overall survival (OS) in patients with and without sarcopenia.

sistent with previous studies. A recent study by Zhang and Zhu (2023) established a diagnostic nomogram to predict the sarcopenia incidence in CRC patients, which included the history of drinking and smoking, nutritional status, TNM stage, di-

Table 4. Univariate analysis of postoperative complications.

Variable	With complications (n = 51)	No complications (n = 175)	OR (95% CI)	*p*-value
Age			2.274 (1.205–4.303)	0.012
<65	26	123		
≥65	25	52		
Gender			0.685 (0.364–1.288)	0.24
Female	23	63		
Male	28	112		
Tumour site			0.901 (0.47–1.727)	0.753
Rectum	33	109		
Colon	18	66		
History of abdominal surgery			1.375 (0.648–2.917)	0.407
No	39	143		
Yes	12	32		
Cardiovascular disease			1.23 (0.514–2.943)	0.643
No	43	152		
Yes	8	23		
Diabetes			1.153 (0.3–4.427)	0.836
No	48	166		
Yes	3	9		
Respiratory disease			0.23 (0.03–1.793)	0.161
No	50	161		
Yes	1	14		
Creatinine			1.078 (0.412–2.822)	0.878
Normal	45	153		
Abnormal	6	22		
Cystatin			1.874 (1.21–2.561)	0.046
<2.5 mg/L	34	155		
≥2.5 mg/L	17	20		
CEA			0.708 (0.35–1.433)	0.337
Normal	13	57		
Abnormal	38	118		
BMI			0.672 (0.359–1.257)	0.214
≥18.5 kg/m^2	25	103		
<18.5 kg/m^2	26	72		
Surgical approach			0.667 (0.185–2.42)	0.535
Laparoscope	48	160		
Open surgery	3	15		
Time of operation			0.933 (0.496–1.758)	0.831
<3.5 h	30	100		
≥3.5 h	21	75		
Intraoperative bleeding			0.989 (0.527–1.856)	0.972
<20 mL	22	75		
≥20 mL	29	100		

Table 4. Continued.

Variable	With complications (n = 51)	No complications (n = 175)	OR (95% CI)	*p*-value
Intraoperative blood transfusion			3.638 (1.877–15.097)	0.041
No	47	171		
Yes	4	4		
TNM staging (n/%)			1.631 (0.931–2.854)	0.097
I stage	8	36		
II stage	32	120		
III stage	11	19		
Sarcopenia			2.109 (1.220–4.137)	0.032
No	30	128		
Yes	21	47		

Notes: TNM staging, pathological staging according to the Union for International Cancer Control (UICC) TNM grading (8th edition).
Abbreviations: OR, odds ratio; CI, confidence interval.

Table 5. Multivariate analysis of postoperative complications.

Variable	β	Standard error	Wald	OR (95% CI)	*p*-value
Sarcopenia	1.05	0.417	9.549	7.154 (2.261–22.633)	0.017
Cystatin	0.241	0.602	0.161	0.671 (0.290–1.553)	0.352
Intraoperative blood transfusion	0.238	0.16	2.204	3.797 (0.637–22.628)	0.143
Age	0.74	0.64	0.835	1.687 (0.653–4.361)	0.28

abetes, and physical activity. Older sarcopenia patients had a markedly reduced BMI, consistent with the results of Takeda et al (2018). A meta-analysis of 12 non-metastatic CRC studies showed that patients with sarcopenia had a lower BMI than the non-sarcopenia cohort, but patients with sarcopenic obesity may develop sarcopenia (Sun et al, 2018). Cystatin, a low-molecular-weight protein, is produced at a steady rate and is freely filtered by the glomerulus, which may be considered a novel index for glomerular filtration rate (GFR) estimation (Shlipak et al, 2022). As it is not affected by dietary factors or muscle mass, it is superior to serum creatinine as a renal function marker (Shah et al, 2023). Recent studies have shown that the sarcopenia index (SI), the ratio of serum creatinine to serum cystatin levels, is a better indicator of muscle mass (Wu et al, 2023). Thus, cystatin and creatinine may hold promise as cheaper and more accessible predictors of sarcopenia (Ge et al, 2022).

In this study, we found that sarcopenia is closely associated with increased postoperative complications in CRC. In order to clarify the effect of sarcopenia on postoperative complications, we analyzed predictors of postoperative complications and found that in CRC patients, independent risk factors for postoperative complications included sarcopenia, with a 7-fold increase in risk of postoperative complications. In the univariate analysis, intraoperative blood transfusion also pre-

Table 6. Univariate and multivariate analyses of factors influencing DFS in CRC patients.

Clinicopathological characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age (≥65 years)	1.183 (1.017–1.403)	0.032	1.077 (0.815–1.478)	0.694
Gender (Female)	0.865 (0.513–1.216)	0.839		
BMI (≥25 kg/m^2)	1.188 (0.639–1.680)	0.783		
Tumour site (rectum)	0.805 (0.677–1.091)	0.063		
History of abdominal surgery (Yes)	1.128 (0.791–1.632)	0.591		
Cardiovascular disease (Yes)	1.184 (0.706–1.719)	0.496		
Diabetes (Yes)	1.241 (0.650–1.823)	0.748		
Respiratory disease (Yes)	1.056 (0.532–1.796)	0.88		
CEA (≥5 ng/mL)	1.702 (1.416–2.050)	<0.001	1.427 (1.216–1.693)	<0.001
laparoscopic surgery	1.089 (0.630–1.521)	0.872		
Tumour stage T3–T4	1.951 (1.614–2.224)	<0.001	1.318 (1.045–1.708)	0.041
Lymph node metastasis	2.279 (1.483–3.064)	<0.001	1.955 (1.329–2.630)	<0.001
Sarcopenia (Yes)	1.614 (1.305–1.982)	<0.001	1.404 (1.127–1.620)	0.016

Abbreviation: HR, hazard ratio.

dicted the occurrence of postoperative complications. Nakanishi et al (2018) retrospectively analyzed 494 patients with CRC and found no significant association between sarcopenia and operative time, intraoperative blood loss, or blood transfusion. However, a retrospective report from a cohort of 47 patients with locally advanced CRC showed a higher incidence of blood transfusions and overall postoperative complications in patients with sarcopenia (Jochum et al, 2019). In the present study, intraoperative blood transfusion in patients with CRC was not associated with postoperative complications, but this was a controversial result and needed further study.

Our study showed that sarcopenia was an independent predictor of postoperative complications. There are several possible mechanisms of the association between sarcopenia and postoperative complications. First, the activation of inflammatory pathways due to chronic inflammation is speculated to be associated with sarcopenia. During a state of oxidative stress and chronic systemic inflammation, skeletal muscle may exhibit exacerbated atrophy through mechanisms mediated particularly by tumour necrosis factor-alpha, which may promote the occurrence of postoperative inflammatory reactions (Fujiya et al, 2024). Second, respiratory muscle strength can support coughing to effectively clear the airway, and pneumonia is more likely to occur if the muscle mass is reduced. A previous study showed that patients with sarcopenia have a higher risk of pneumonia (Wang et al, 2021). Third, the reduced amount of physical activity in sarcopenia is accompanied by a decrease in cardiac output, which leads to a reduction in organ blood flow and function (Koh et al, 2024). Strategies to combat this may include a mixture of pharmacological, nutritional, and exercise-based interventions. Evidence has shown that prehabilitation is possible in sarcopenic patients, and may increase functional capability and recovery from surgery. Further research is required to better characterize the path-

Table 7. Univariate and multivariate analyses of factors influencing OS in CRC patients.

Clinicopathological characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age (≥65 years)	1.214 (1.171–1.523)	<0.001	1.382 (1.118–1.590)	0.004
Gender (Female)	1.162 (0.635–1.801)	0.682		
BMI (≥25 kg/m^2)	2.214 (1.232–4.511)	0.01	1.284 (0.563–1.618)	0.477
Tumour site (rectum)	1.160 (1.029–1.515)	0.042	0.983 (0.834–1.158)	0.835
History of abdominal surgery (Yes)	0.911 (0.452–1.426)	0.766		
Cardiovascular disease (Yes)	1.165 (0.753–1.892)	0.496		
Diabetes (Yes)	1.208 (0.632–1.624)	0.712		
Respiratory disease (Yes)	1.088 (0.514–1.966)	0.88		
CEA (≥5 ng/mL)	1.922 (1.619–2.364)	<0.001	1.443 (1.261–1.742)	<0.001
Laparoscopic surgery	1.009 (0.535–1.944)	0.971		
Tumour stage T3–T4	1.890 (1.584–2.282)	<0.001	1.508 (1.242–1.882)	<0.001
Lymph node metastasis	2.632 (1.747–4.166)	<0.001	2.052 (1.344–4.628)	0.012
Sarcopenia (Yes)	1.472 (1.108–1.737)	0.001	1.290 (1.037–1.604)	0.021

ways of sarcopenia which cause substandard clinical outcomes in cancer patients, and more studies are needed to identify additional ways to decrease postoperative problems.

Although the mechanism by which sarcopenia affects the prognosis of cancer patients remains unclear, some studies indicated that sarcopenia may predict elevated metabolic activity in tumour biology and may be more aggressive, resulting in systemic inflammation (Miyamoto et al, 2015a; Miyamoto et al, 2015b). This can enhance the risk of cancer and reduce the effectiveness of treatment (Feliciano et al, 2017). A prospective investigation of the impact of preoperative sarcopenia and inflammatory status on prognosis included 2470 stage I–III CRC patients. At later follow-up, the team identified that sarcopenia and elevated neutrophil-lymphocyte ratio independently predicted cancer-linked mortality and OS (Feliciano et al, 2017). In the present study, it was revealed that patients with sarcopenia are more susceptible to infection, which leads to adverse consequences.

Patients with alleviated sarcopenia indicated a longer DFS and OS than persistent sarcopenia patients. Miyamoto et al (2015b) found that patients with sarcopenia who underwent radical resection of CRC had significantly higher morbidity than those without sarcopenia. Previous literature has indicated that SMI is linked with survival. Recently, a meta-analysis and systematic review of 5337 patients from 12 non-metastatic CRC studies revealed that the sarcopenia patients had a substantially reduced OS compared to the non-sarcopenia cohort (HR = 1.63; 95% CI: 1.24–2.14) (Sun et al, 2018). Another updated meta-analysis reported that CT-diagnosed sarcopenia could serve as a potential survival prognosis marker in CRC patients. The incidence of sarcopenia reduced DFS (HR = 1.42; 95% CI: 1.26–1.60) and OS (HR = 1.72; 95% CI: 1.45–2.03) (He et al, 2023). Combined with our findings, sarcopenia may be a negative indicator of postoperative and survival outcomes. Clinicians should identify sarcopenia in CRC patients who plan to undergo

curative surgery, and should suggest interventions according to specific disease and nutritional needs based on those risk factors to improve postoperative outcomes and survival.

This investigation has certain limitations. (1) It is a single retrospective cohort study and may have been affected by inherent bias, and some indicators could not be accurately collected. (2) This single-center study had a relatively limited sample size. Further multicenter prospective investigations are required in the future to address these issues. Moreover, the comorbidities and associated medications that might affect the patient's body composition were not considered. Therefore, it is recommended to take more factors into account in subsequent studies to obtain more robust results. In the future, randomized controlled trials could be conducted to assess whether improving muscle mass and muscle function can improve postoperative survival in CRC individuals.

Conclusion

In conclusion, this study demonstrates that sarcopenia is an independent risk factor for postoperative complications of CRC. Sarcopenia may also have a negative impact on the OS and DFS in CRC patients. Therefore, CRC patients should be screened for sarcopenia at their first visit to inform them of the potential negative effects, thereby providing prevention and treatment strategies for sarcopenia. Adding sarcopenia assessment to routine nutritional assessment can identify other at-risk individuals who may benefit from early nutritional interventions.

Key Points

- In CRC patients, sarcopenia is associated with older age, lower body mass index, higher prevalence of diabetes, elevated cystatin levels, and reduced skeletal muscle index.
- Sarcopenia significantly correlates with increased postoperative complications, longer hospital stays, and reduced 5-year disease-free survival and overall survival rates.
- Sarcopenia is an independent risk factor for postoperative complications and poor prognosis in CRC patients undergoing radical surgery.

Availability of Data and Materials

The analyzed data sets generated during the study are available from the corresponding author upon reasonable request.

Author Contributions

JW, YC, and MX were responsible for the study design. JW, JH, and CY contributed to the collection of data. JW and YC drafted the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read

and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This research was authorized by the Ethical Board of the Affiliated Hospital of Zunyi Medical University (approval number: KLLY-2021-089). The study was conducted in compliance with the Declaration of Helsinki and all participants provided informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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