

## Original Article

# The impact of nutritional risk and sarcopenia on postoperative complications and survival outcomes in elderly patients undergoing colorectal cancer surgery: a retrospective cohort study

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**Abstract:** Objective: To investigate individual and combined effects of preoperative nutritional risk and sarcopenia on postoperative complications and survival in elderly colorectal cancer (CRC) patients. Methods: Data from 260 elderly patients (>60 years) undergoing radical CRC surgery (2022-2024) were retrospectively analyzed. Nutritional risk was assessed by NRS-2002 (score  $\geq 3$ ). Sarcopenia was diagnosed by AWGS 2019 criteria (handgrip strength + CT muscle index). Patients were grouped into No-risk, Nutritional risk only, Sarcopenia only, and Combined. Outcomes: Overall (Clavien-Dindo  $\geq$ II) and severe ( $\geq$ IIIa) complications, and overall survival. Multivariate Cox regression was used. Results: Mean age  $68.08 \pm 5.32$  years. Nutritional risk prevalence 44.6% (116/260), sarcopenia 28.5% (74/260), coexistence 16.2% (42/260). The Combined group had highest overall complication rate (64.3% vs. 15.2% in No-risk,  $P < 0.001$ ) and severe complication rate (23.8% vs. 7.1%,  $P = 0.007$ ). Median follow-up 18 months; Combined group lowest 18-month survival (69.0% vs. 96.4%,  $P < 0.001$ ). Multivariate Cox regression (adjusting for age, sex, BMI) showed Nutritional risk only (HR = 3.954, 95% CI: 1.369-11.420,  $P = 0.011$ ) and Sarcopenia only (HR = 4.095, 95% CI: 1.181-14.195,  $P = 0.026$ ) were poor prognostic indicators. Coexistence was the strongest predictor (HR = 10.173, 95% CI: 3.699-27.977,  $P < 0.001$ ). Conclusion: Preoperative coexistence of nutritional risk and sarcopenia significantly increases complications and reduces survival in elderly CRC patients, with risks far exceeding single factors. Routine dual assessment and intensive prehabilitation should be implemented.

**Keywords:** Colorectal cancer, elderly, nutritional risk, sarcopenia, postoperative complications, survival analysis

## Introduction

Colorectal cancer (CRC) is a common malignancy worldwide, with its incidence and mortality rates remaining stubbornly high in most countries. According to the 2022 Global Cancer Statistics, CRC ranks third in incidence and second in cancer-related mortality globally [1, 2]. In China, the disease burden of CRC is becoming increasingly heavy - driven by the intensifying aging population, the westernization of dietary patterns, and the widespread implementation of screening programs - making it a major public health issue [3-5]. For early- and mid-stage CRC, radical surgical resection combined with necessary adjuvant therapies remains the primary approach offering a potential cure [6, 7].

However, surgical management poses significant challenges for elderly patients. Older adults often present with multiple comorbidities, reduced physiological reserves, and are prone to pre-frailty or frailty states. This leads to diminished tolerance to surgical trauma, an increased risk of postoperative complications, prolonged recovery processes, and potentially compromised long-term oncological outcomes [8]. Therefore, identifying modifiable preoperative high-risk factors and implementing targeted assessments and prehabilitation strategies are crucial for improving perioperative safety and long-term outcomes in elderly patients with CRC.

Among the numerous preoperative risk factors, nutritional status and body composition are

recognized as two core, modifiable dimensions. Malnutrition is prevalent among hospitalized elderly patients but is often overlooked. It is not merely weight loss or inadequate intake but rather a metabolic disorder involving multiple organ systems [9]. Systematic assessment using the Nutritional Risk Screening 2002 (NRS-2002) tool effectively identifies patients at nutritional risk who may benefit from nutritional support [10, 11]. Numerous studies have confirmed that preoperative nutritional risk is a significant predictor of postoperative outcomes, including infectious complications, non-infectious complications, length of hospital stay, and short-term mortality [12-14].

Closely related to malnutrition but possessing an independent pathophysiological basis is sarcopenia. Sarcopenia is defined as a syndrome characterized by the progressive and generalized loss of skeletal muscle mass, strength, and function associated with aging [3, 15]. In cancer patients, the prevalence of sarcopenia is significantly elevated due to systemic inflammation, metabolic alterations caused by the tumor itself, and treatment-related side effects. It can thus be viewed as a “cancer-related syndrome” [16, 17]. In recent years, imaging assessments (such as CT-measured skeletal muscle index) have made the objective diagnosis of sarcopenia possible. Research indicates that preoperative sarcopenia is an independent predictor of postoperative complications (such as anastomotic leakage and pulmonary infections), chemotherapy tolerance, and overall survival in colorectal cancer [18, 19].

Although nutritional risk and sarcopenia are often discussed separately in clinical practice, they are tightly intertwined etiologically, creating a vicious cycle. Inadequate nutrient intake or impaired utilization directly leads to a lack of substrates for muscle protein synthesis; conversely, as a major metabolic and endocrine organ, the depletion of muscle tissue exacerbates systemic inflammation and insulin resistance, further deteriorating nutritional status [20]. This coexisting state, sometimes conceptualized as “malnutrition-related sarcopenia”, theoretically exerts synergistic negative effects on patients, posing a more severe challenge than either factor alone [21]. However, existing studies have predominantly focused on single factors or merely considered sarcopenia as an aspect of nutritional assessment. Comprehensive evidence regarding the specific high-

risk phenotype characterized by the concomitant presence of overt nutritional risk (based on standardized tools) and definitive sarcopenia (based on consensus criteria), and its impact on the postoperative complication spectrum (particularly severe complications graded by Clavien-Dindo) and long-term survival in elderly colorectal cancer patients, remains insufficient [4]. Whether this coexistence constitutes an independent and paramount risk marker - and whether its risk magnitude significantly exceeds that of patients with only one risk factor - requires further elucidation through prospective study designs or large-scale retrospective analyses.

Based on the aforementioned background, this study aims to conduct a rigorous single-center retrospective cohort analysis to achieve the following objectives: First, to determine the prevalence and overlap of NRS-2002-based nutritional risk and AWGS 2019 criteria-based sarcopenia in a cohort of elderly colorectal cancer patients undergoing radical surgery. Second, through multivariable analysis, to specifically explore the independent impact of the coexistence of preoperative nutritional risk and sarcopenia on the risk of overall and severe postoperative complications (Clavien-Dindo  $\geq$  grade III) within 30 days. Finally, to evaluate the independent prognostic value of this coexisting state on long-term overall survival. We anticipate that the findings will provide a basis for establishing a more refined preoperative risk assessment model for elderly surgical patients with colorectal cancer and underscore the importance of combined screening and comprehensive intervention targeting the “nutrition-muscle” axis.

### Materials and methods

#### *Study design*

This study is a single-center, observational, retrospective cohort study. It aims to evaluate the independent impact of the coexistence of preoperative nutritional risk and sarcopenia on postoperative complications and long-term survival outcomes in elderly patients with colorectal cancer by analyzing completed clinical data. The study design strictly adheres to the guidelines for retrospective cohort studies outlined in the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.

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## *Study population*

The study population consisted of patients with primary colorectal cancer who underwent consecutive elective radical surgery in the Department of Colorectal Surgery at Jinhua Hospital, Zhejiang University School of Medicine between July 1, 2022, and July 1, 2024. A total of 315 patients were initially screened during the study period, of which 260 patients meeting all inclusion criteria were ultimately included in the analysis.

## *Inclusion and exclusion criteria*

Eligible patients were required to meet all of the following criteria: (1) Histopathologically confirmed primary colorectal adenocarcinoma; (2) Underwent standard radical resection (laparoscopic or open); (3) Completed comprehensive nutritional risk screening (NRS-2002) and sarcopenia assessment (handgrip strength, calf circumference, and imaging) within one week prior to surgery; (4) Possessed complete perioperative clinical data and traceable follow-up information.

Patients meeting any of the following criteria were excluded: (1) Underwent emergency surgery, palliative resection, or endoscopic mucosal resection; (2) Had other active malignancies except non-melanoma skin cancer; (3) Had severe preoperative organ dysfunction; (4) Had severely incomplete clinical or follow-up data. Following this screening process, a total of 260 patients were included in the final analysis.

## *Ethical review*

The study protocol was approved by the Ethics Committee of Jinhua Hospital, Zhejiang University School of Medicine. Since this study was a retrospective analysis that did not involve new patient interventions or specimen collection, and only utilized existing anonymized medical records, the requirement for individual patient informed consent was waived by the Ethics Committee. However, strict de-identification of all patient data was mandated to protect patient privacy.

## *Data collection and processing*

Data collection was performed independently by two clinical researchers using a pre-designed, standardized electronic data collection

form. All data were retrospectively extracted from the following hospital information systems:

Hospital Information System (HIS): Demographic information, operative records, pathology reports, and complication records.

Laboratory Information System (LIS): Preoperative laboratory indicators (e.g., serum albumin) within one week prior to surgery.

Picture Archiving and Communication System (PACS): Preoperative abdominal CT images for muscle mass assessment.

Electronic medical record system: Follow-up clinic records, readmission records, and vital status.

After data collection, a third senior researcher conducted cross-verification and logic checks. Discrepant entries were resolved by reviewing the original medical records to ensure data accuracy.

## *Definition and measurement of study variables*

*Exposure variables (basis for grouping):* Patients were categorized into four groups based on the following criteria:

**Nutritional risk:** Assessed using the Nutritional Risk Screening 2002 (NRS-2002), which comprises three dimensions: severity of disease, impairment of nutritional status, and age. A total score  $\geq 3$  was defined as being at nutritional risk.

**Sarcopenia:** Diagnosed according to the 2019 consensus criteria of the Asian Working Group for Sarcopenia (AWGS). The specific operational definitions were as follows:

**Low muscle strength:** Handgrip strength (HGS) was measured using a Jamar hydraulic dynamometer on the dominant hand. Patients were seated with the elbow flexed at 90° and the forearm in a neutral position. Three consecutive measurements were taken, and the maximum value was recorded. The diagnostic cut-offs were <28 kg for men and <18 kg for women.

**Low muscle quantity:** Skeletal muscle cross-sectional area was measured on preoperative plain abdominal CT images at the level of the

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third lumbar vertebra ( $L_3$ ). Using Slice-O-Matic software (Tomovision, Canada), the cross-sectional areas of the psoas, erector spinae, transversus abdominis, internal and external obliques, and rectus abdominis muscles were manually delineated. The Skeletal Muscle Index (SMI) was then calculated. The diagnostic cut-offs were  $<7.0 \text{ cm}^2/\text{m}^2$  for men and  $<5.4 \text{ cm}^2/\text{m}^2$  for women.

A diagnosis of sarcopenia required the presence of both low muscle strength and low muscle quantity.

*Final grouping:* Group A (No-risk group): NRS-2002  $<3$  and did not meet the criteria for sarcopenia.

Group B (Nutritional risk only group): NRS-2002  $\geq 3$  but did not meet the criteria for sarcopenia.

Group C (Sarcopenia only group): NRS-2002  $<3$  but met the criteria for sarcopenia.

Group D (Combined group): NRS-2002  $\geq 3$  and met the criteria for sarcopenia.

*Outcome variables:* Postoperative complications: All complications occurring within 30 days postoperatively were recorded and classified according to the international, standardized Clavien-Dindo classification system.

Overall complications: Defined as any complication graded  $\geq \text{II}$  on the Clavien-Dindo scale.

Severe complications: Defined as complications graded  $\geq \text{IIIa}$ , which require surgical, endoscopic, or radiological intervention, are life-threatening, or result in organ dysfunction/failure.

Survival outcomes: Overall Survival (OS): Defined as the time from the date of surgery to the date of death from any cause. For patients still alive at the cutoff date (December 31, 2025), survival time was censored at the date of last follow-up.

Vital status: Confirmed through regular outpatient reviews, telephone follow-ups, and queries of the regional death registry system. All patients received at least 6 months of follow-up, with a median follow-up time of 18 months.

*Covariates (confounding factors):* The following potential confounders were collected for adjustment in the multivariable analysis model:

Demographic factors: Age (years), sex.

Anthropometric factors: Body Mass Index (BMI,  $\text{kg}/\text{m}^2$ ).

Tumor-related factors: Tumor TNM stage (AJCC 8th edition).

Surgery-related factors: Surgical approach (laparoscopic vs. open), operative duration (minutes).

### *Sample size consideration*

This was an exploratory retrospective cohort study and did not perform a priori sample size calculation. The sample size was determined by the total number of eligible patients during the study period, resulting in 260 patients included for analysis. A post-hoc power analysis indicated that, at a significance level of  $\alpha = 0.05$ , the statistical power of this study to detect the primary outcome (differences in complication rates between groups) exceeded 80%.

### *Statistical analysis*

All statistical analyses were performed using Python 3.9 and its scientific computing ecosystem (including Pandas, NumPy, SciPy, lifelines, and statsmodels libraries). Statistical significance was set at a two-sided  $P$  value  $<0.05$ .

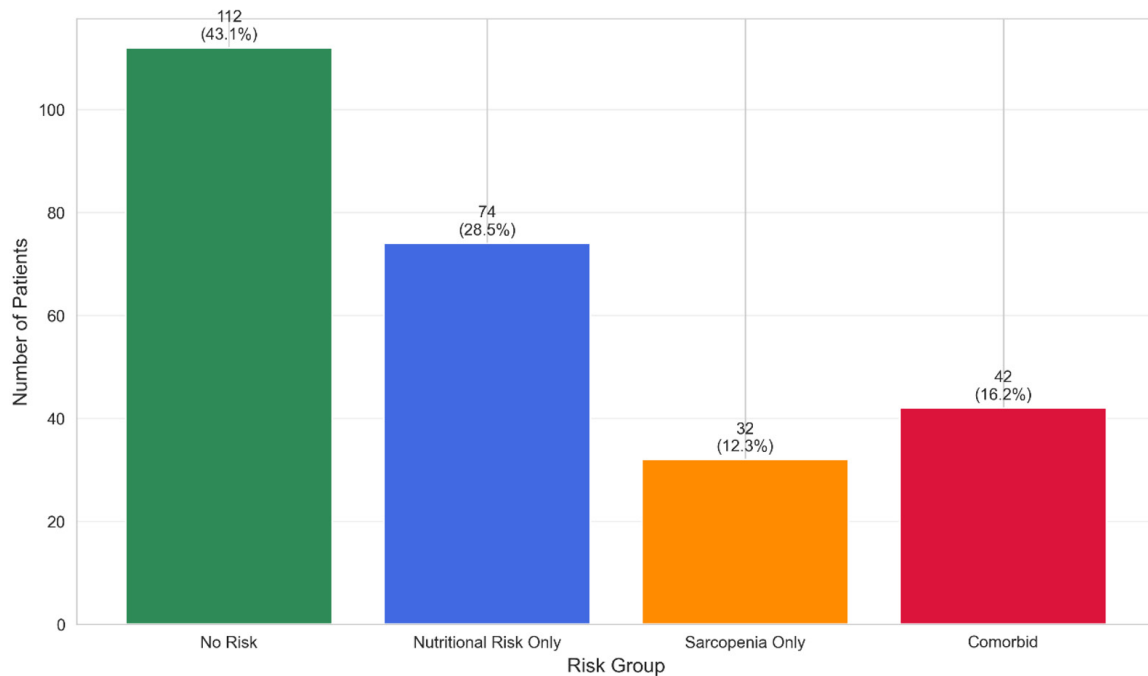
Descriptive statistics: Normally distributed continuous variables were presented as mean  $\pm$  standard deviation. Inter-group comparisons were performed using one-way ANOVA; if homogeneity of variance was not met, Welch's ANOVA was used. Post-hoc pairwise comparisons were conducted using the Tukey HSD test.

Non-normally distributed continuous variables were presented as median (interquartile range). Inter-group comparisons were performed using the Kruskal-Wallis H test, with post-hoc pairwise comparisons using Dunn's test.

Categorical variables were presented as frequency (percentage). Inter-group comparisons were performed using the Chi-square test. When the expected frequency in any cell was  $<5$ , Fisher's exact test was used.

Survival analysis: Survival functions for each group were estimated using the Kaplan-Meier method, and inter-group differences were compared using the Log-rank test.

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**Figure 1.** Patient distribution by risk group.

Multivariable Cox proportional hazards regression models were used to analyze the independent impact of different risk statuses on overall survival. Group A (no-risk) was used as the reference. Risk grouping was included as a categorical variable, adjusting for pre-specified confounders (age, sex, BMI, tumor stage, surgical approach). The proportional hazards assumption was tested by examining Schoenfeld residuals, and the assumption was satisfied. Results were presented as Hazard Ratios (HR) with 95% Confidence Intervals (CI).

**Sensitivity analysis:** To test the robustness of the primary results, two sensitivity analyses were performed: (1) Relaxing the sarcopenia diagnostic criteria to require only one of either low muscle strength or low muscle quantity, followed by re-grouping and survival analysis; (2) Excluding patients who died within 30 days postoperatively ( $n = 3$ ), followed by re-running the Cox regression. The main conclusions did not change substantially in either sensitivity analysis.

**Missing data handling:** The missing rate for key variables (grouping and outcome variables) was  $<1\%$ . For minor covariates (e.g., operative duration, missing,  $n = 3$ ), multiple imputation was performed, generating 5 complete data-

ets for analysis, with results pooled according to Rubin's rules.

### Results

#### *Patient baseline characteristics and grouping*

A total of 260 elderly patients (age  $>60$  years) undergoing colorectal cancer surgery were included in this study. According to their nutritional risk and sarcopenia status, patients were divided into four groups: No-risk group, Nutritional Risk Only group, Sarcopenia Only group, and Comorbid group. The distribution of patients across the groups is shown in **Figure 1**, with the No-risk group having the largest number of patients (112 cases, 43.1%) and the Comorbid group having 42 patients (16.2%).

The baseline demographic and clinical characteristics of each group are detailed in **Table 1**. There were no statistically significant differences among the four groups regarding continuous variables such as age, body mass index (BMI), serum albumin, handgrip strength, and calf circumference (all  $P > 0.05$ ). However, significant inter-group differences were observed regarding postoperative complications: the Comorbid group had the highest overall complication rate (64.3%), whereas the No-risk group had the

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**Table 1.** Baseline characteristics

Variable	No Risk	Nutritional Risk Only	Sarcopenia Only	Comorbid	Overall	H/F/ $\chi^2$	P-value
Age	68.02 ± 5.27	67.50 ± 5.22	68.25 ± 4.67	69.14 ± 6.05	68.08 ± 5.32	1.849	0.604
BMI	23.02 ± 3.01	22.41 ± 3.27	23.29 ± 3.36	22.67 ± 2.95	22.82 ± 3.12	0.869	0.458
Albumin_gL	38.71 ± 4.91	38.06 ± 5.37	37.94 ± 4.99	38.85 ± 5.06	38.45 ± 5.06	0.446	0.721
Grip_Strength_kg	24.77 ± 6.16	24.48 ± 6.70	25.15 ± 5.90	24.87 ± 5.24	24.75 ± 6.12	0.099	0.961
Calf_Circumference_cm	33.81 ± 3.24	33.83 ± 3.24	34.81 ± 3.62	33.91 ± 3.05	33.96 ± 3.26	0.843	0.471
Gender							
Male	52/112 (46.4%)	29/74 (39.2%)	10/32 (31.2%)	17/42 (40.5%)	108/260 (41.5%)	2.685	0.443
Female	60/112 (53.6%)	45/74 (60.8%)	22/32 (68.8%)	25/42 (59.5%)	152/260 (58.5%)		
Postoperative complication							
No	95/112 (84.8%)	38/74 (51.4%)	21/32 (65.6%)	15/42 (35.7%)	169/260 (65.0%)	41.241	<0.001
Yes	17/112 (15.2%)	36/74 (48.6%)	11/32 (34.4%)	27/42 (64.3%)	91/260 (35.0%)		
Severe complication (≥III)							
No	104/112 (92.9%)	70/74 (94.6%)	29/32 (90.6%)	32/42 (76.2%)	235/260 (90.4%)	12.036	0.007
Yes	8/112 (7.1%)	4/74 (5.4%)	3/32 (9.4%)	10/42 (23.8%)	25/260 (9.6%)		
TNM Stage							
I	31/112 (27.7%)	23/74 (31.1%)	2/32 (6.2%)	1/42 (2.4%)	57/260 (21.9%)	20.420	0.002
II	37/112 (33.0%)	23/74 (31.1%)	13/32 (40.6%)	21/42 (50.0%)	94/260 (36.2%)		
III	44/112 (39.3%)	28/74 (37.8%)	17/32 (53.1%)	20/42 (47.6%)	109/260 (41.9%)		
Surgical approach							
Laparoscopic	79/112 (70.5%)	50/74 (67.6%)	23/32 (71.9%)	23/42 (54.8%)	175/260 (67.3%)	3.840	0.279
Open	33/112 (29.5%)	24/74 (32.4%)	9/32 (28.1%)	19/42 (45.2%)	85/260 (32.7%)		

Abbreviation: NRS-2002, Nutritional Risk Screening 2002; AWGS, Asian Working Group for Sarcopenia; BMI, body mass index; SD, standard deviation; TNM, tumor-node-metastasis; AJCC, American Joint Committee on Cancer; ANOVA, analysis of variance; H, Kruskal-Wallis H statistic;  $\chi^2$ , chi-square.

**Table 2.** Prevalence of risk factors

Group	N	Percentage	Nutritional Risk	Sarcopenia	Comorbid
No Risk	112	43.1%	0.0%	0.0%	0.0%
Nutritional Risk Only	74	28.5%	100.0%	0.0%	0.0%
Sarcopenia Only	32	12.3%	0.0%	100.0%	0.0%
Comorbid	42	16.2%	100.0%	100.0%	100.0%
Overall	260	100.0%	44.6%	28.5%	16.2%

Abbreviation: NRS-2002, Nutritional Risk Screening 2002; AWGS, Asian Working Group for Sarcopenia.

lowest (15.2%) ( $P < 0.001$ ). Furthermore, the Comorbid group exhibited a significantly higher rate of severe complications (Clavien-Dindo grade  $\geq$ IIIa) compared to the other groups (23.8% vs. 7.1% in the No-risk group,  $P = 0.007$ ).

### Prevalence of nutritional risk and sarcopenia

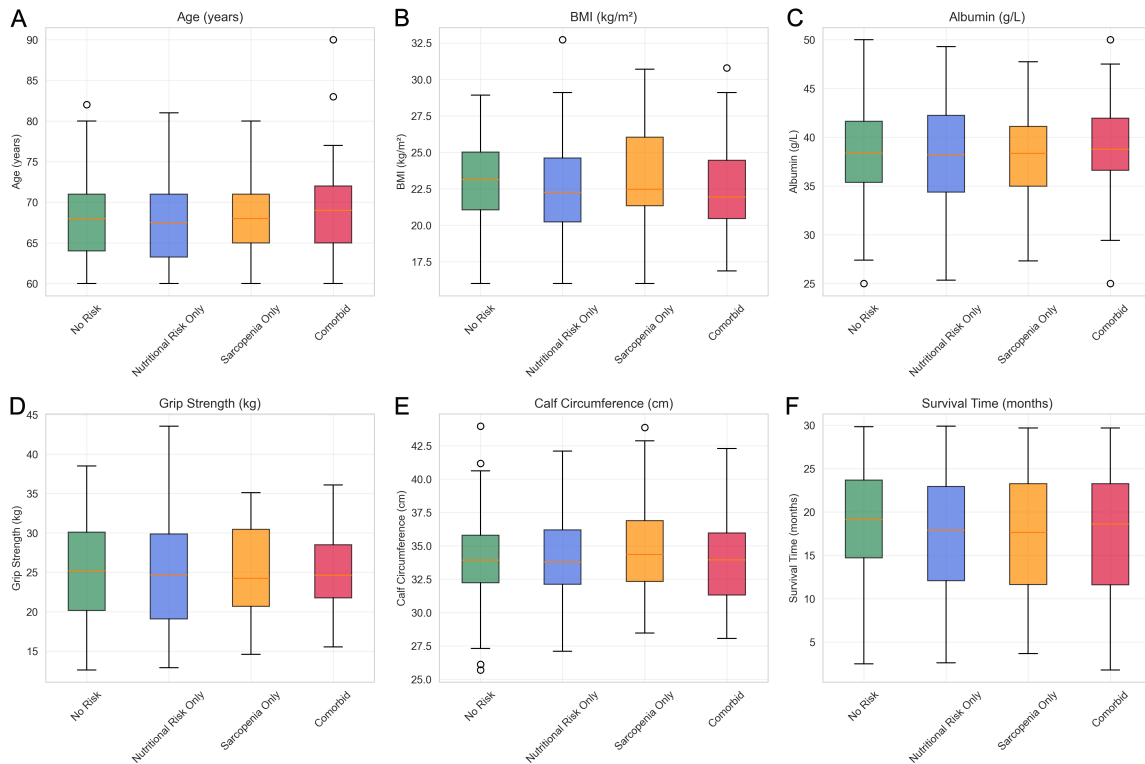
The overall prevalence of nutritional risk (NRS-2002  $\geq 3$ ) was 44.6% (116/260), and the overall prevalence of sarcopenia (based on the AWGS 2019 criteria) was 28.5% (74/260). The coexistence of both conditions (i.e., the Comorbid group) was observed in 16.2% (42/260) of patients. The distribution of risk factors across subgroups is presented in **Table 2**. Box plots visually demonstrate the distribution of key clinical indicators (such as age, BMI, hand-

grip strength, and survival time) across the four groups (**Figure 2**).

### Postoperative complication rates

A comparison of postoperative complication rates among the groups is detailed in **Table 3**. The results indicate that complication risk increases with the accumulation of risk factors: the overall complication rate was only 15.2% in the No-risk group but reached 64.3% in the Comorbid group. Regarding severe complications, the Comorbid group had a significantly higher incidence (23.8%) than the other three groups, suggesting that the coexistence of nutritional risk and sarcopenia greatly increases the risk of severe adverse events postoperatively (**Figure 3**).

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**Figure 2.** Baseline characteristics (Boxplot Data). Abbreviation: CRC, colorectal cancer; BMI, body mass index; SD, standard deviation; IQR, interquartile range.

**Table 3.** Complication rates

Group	N	Overall Complications	Severe Complications (Clavien-Dindo $\geq$ III)
No Risk	112	17.0/112 (15.2%)	8.0/112 (7.1%)
Nutritional Risk Only	74	36.0/74 (48.6%)	4.0/74 (5.4%)
Sarcopenia Only	32	11.0/32 (34.4%)	3.0/32 (9.4%)
Comorbid	42	27.0/42 (64.3%)	10.0/42 (23.8%)
Overall	260	91.0/260 (35.0%)	25.0/260 (9.6%)

Abbreviation: Clavien-Dindo, Clavien-Dindo classification.

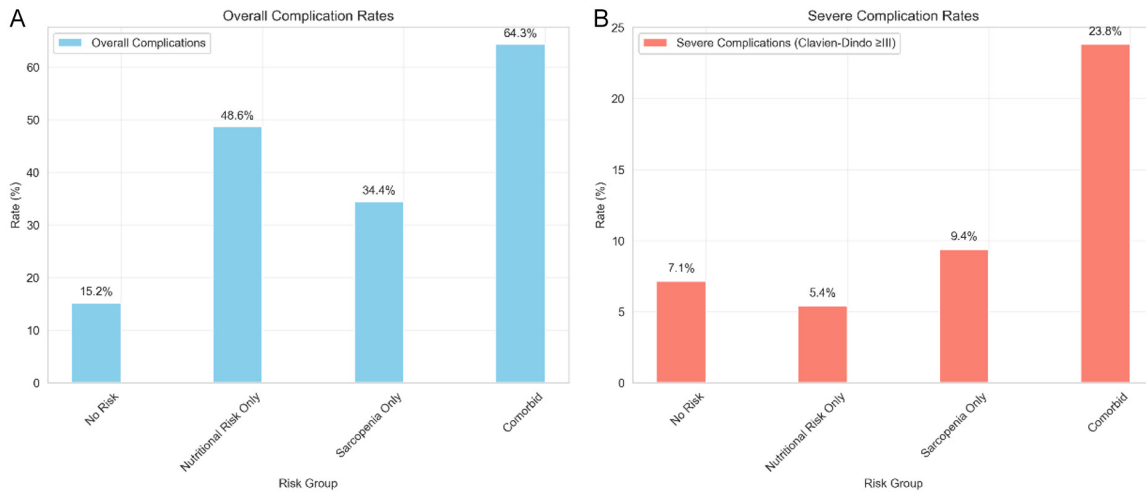
### Survival outcome analysis

After a median follow-up of 18 months, significant differences in survival outcomes were observed among the groups (**Table 4**). The No-risk group had the highest 18-month survival rate (96.4%), whereas the Comorbid group had the lowest (69.0%). The median survival times were 15.2 months for the No-risk group, 8.4 months for the Nutritional Risk Only group, 11.2 months for the Sarcopenia Only group, and 11.0 months for the Comorbid group. These inter-group differences in survival were further confirmed by Kaplan-Meier survival curves (**Figure 4**), where the survival curve for

the Comorbid group consistently remained below those of the other groups.

To clarify the independent impact of different risk statuses on survival outcomes, multivariable Cox proportional hazards regression analysis was performed (**Table 5**). After adjusting for age, sex, and BMI, both Nutritional Risk Only (HR = 3.954, 95% CI: 1.369-11.420, P = 0.011) and Sarcopenia Only (HR = 4.095, 95% CI: 1.181-14.195, P = 0.026) were identified as poor prognostic indicators compared to the No-risk group. Notably, the combination of both conditions carried the highest risk and was the strongest independent predictor of mortality (HR = 10.173, 95% CI: 3.699-27.977, P < 0.001).

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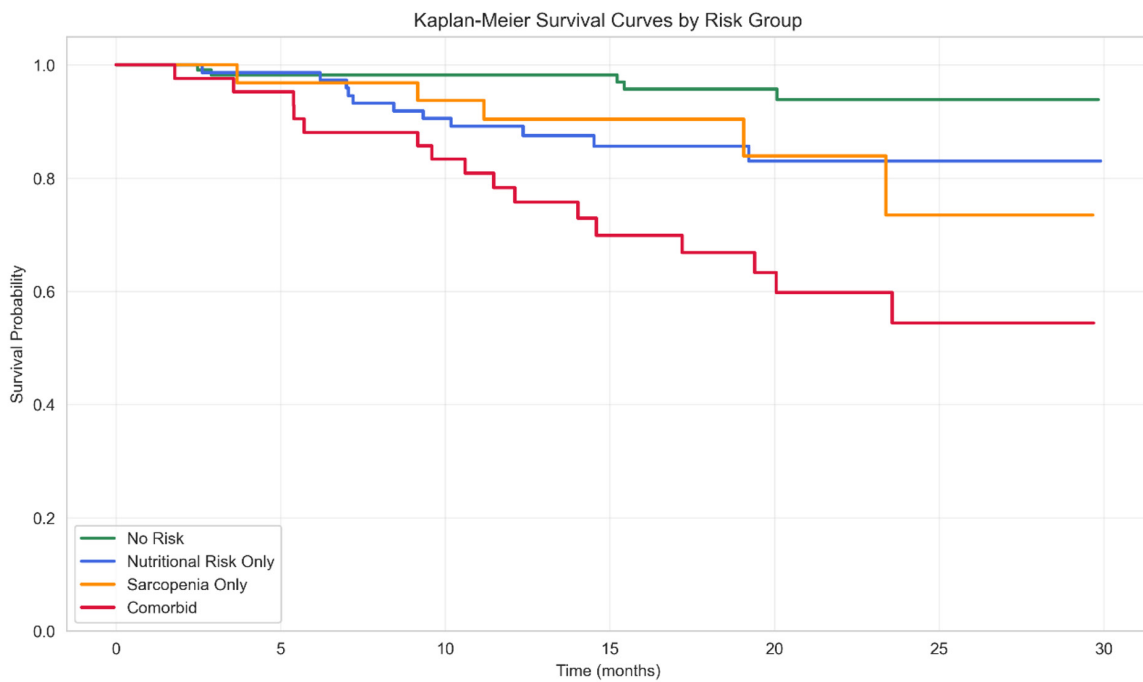


**Figure 3.** Complication rates. Abbreviation: Clavien-Dindo, Clavien-Dindo classification (for postoperative complications).

**Table 4.** Survival analysis

Group	N	18-month Survival Rate	Median Survival (months)
No Risk	112	96.4%	15.2
Nutritional Risk Only	74	86.5%	8.4
Sarcopenia Only	32	90.6%	11.2
Comorbid	42	69.0%	11.0

Abbreviation: OS, overall survival; mo, months.



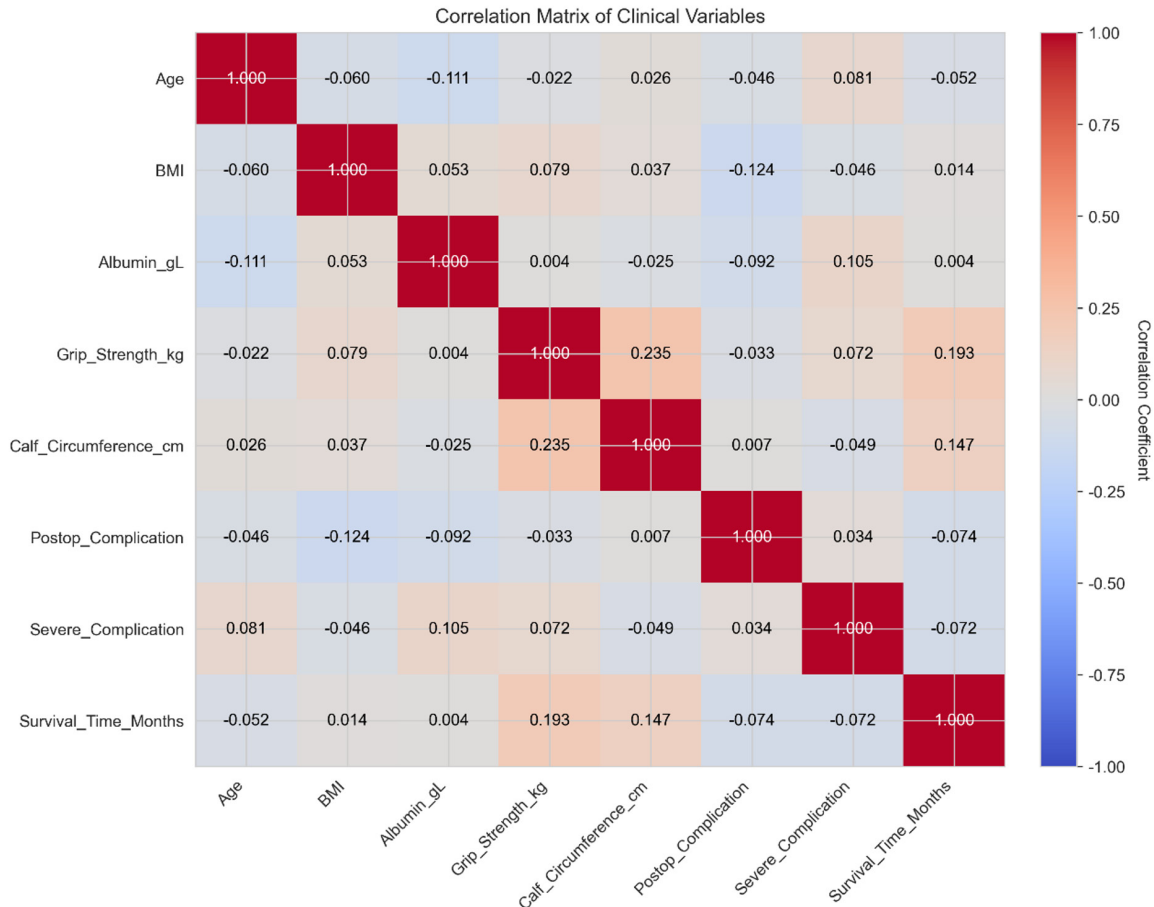
**Figure 4.** Kaplan-Meier survival analysis. Abbreviation: KM, Kaplan-Meier; CI, confidence interval; HR, hazard ratio.

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**Table 5.** Cox regression analysis

Variable	HR	95% CI	z	Wald $\chi^2$	P-value
Age	1.023	0.965-1.084	0.771	0.595	0.441
Gender	0.561	0.293-1.075	-1.743	3.036	0.081
BMI	1.046	0.944-1.160	0.858	0.736	0.391
Group_Nutritional_Risk_Only	3.954	1.369-11.420	2.540	6.452	0.011
Group_Sarcopenia_Only	4.095	1.181-14.195	2.222	4.939	0.026
Group_Comorbid	10.173	3.699-27.977	4.494	20.200	<0.001

Abbreviation: HR, hazard ratio; CI, confidence interval; Wald  $\chi^2$ , Wald chi-square; BMI, body mass index.



**Figure 5.** Correlation matrix data. Abbreviation: BMI, body mass index; r, Pearson correlation coefficient.

### Correlation of key clinical variables

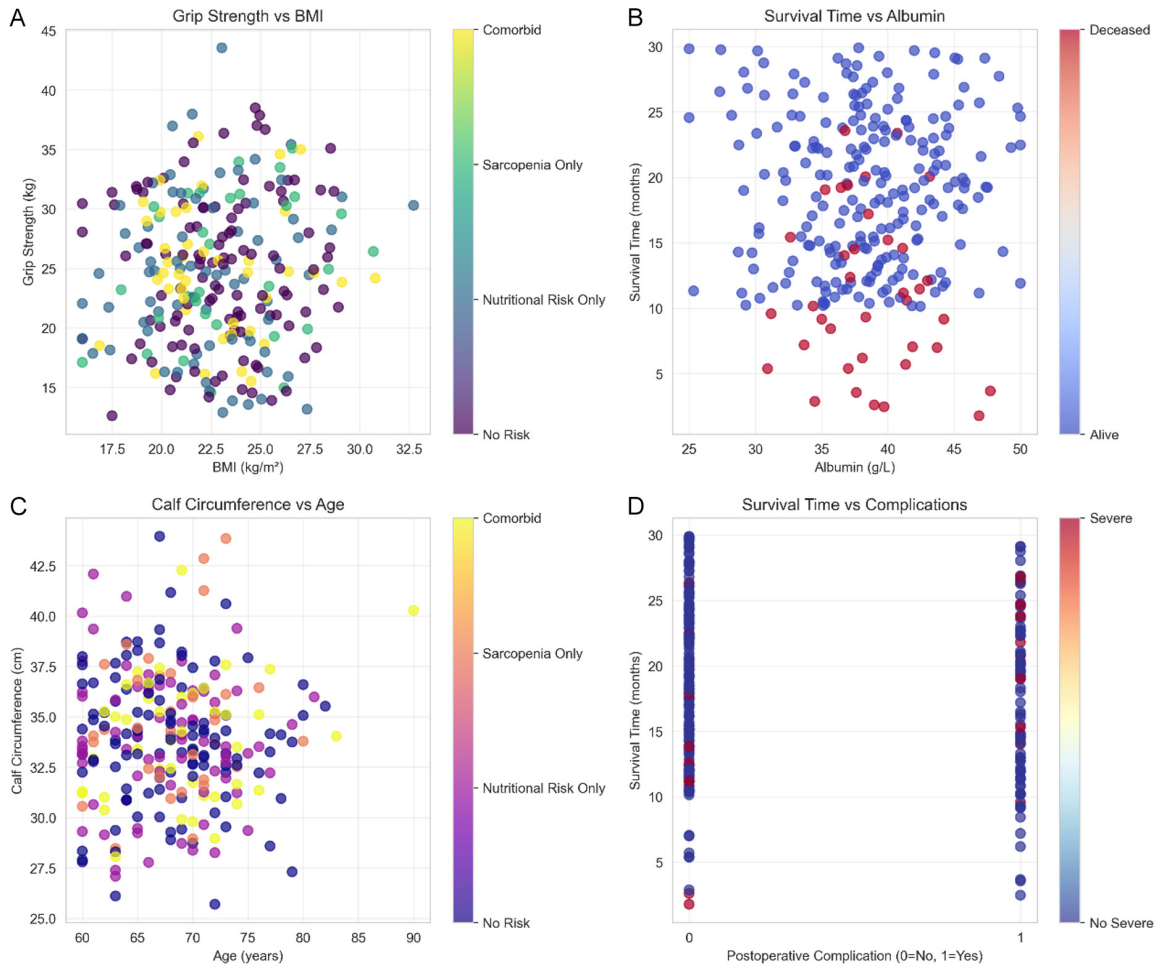
**Figure 5** shows the heatmap illustrating the correlations among key clinical variables. The analysis revealed a positive correlation between handgrip strength and calf circumference ( $r = 0.235$ ). Both handgrip strength ( $r = 0.193$ ) and calf circumference ( $r = 0.147$ ) were positively correlated with survival time. Furthermore, postoperative complications were negatively correlated with survival time ( $r = -0.074$ ).

These relationships are visualized more intuitively in the scatter plots (**Figure 6**). For instance, handgrip strength showed a weak positive correlation with BMI, whereas the direct correlation between albumin levels and survival time was weak.

### Discussion

This study systematically evaluated the impact of preoperative nutritional risk and sarcopenia

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**Figure 6.** Scatter plot key statistics. Abbreviation: BMI, body mass index;  $r$ , correlation coefficient;  $R^2$ , R-squared.

on the prognosis of elderly patients undergoing colorectal cancer surgery through a retrospective cohort analysis. The main findings are as follows: (1) In this cohort, our observed prevalence of combined nutritional risk and sarcopenia (16.2%) is comparable to but slightly lower than reports from other Asian populations. For instance, a study by Chen et al. [22] reported a coexistence rate of 19.5% using similar NRS-2002 and AWGS criteria in elderly CRC patients. In contrast, a Japanese multicenter study found a lower rate (11.8%), possibly due to inclusion of patients with better baseline nutritional status. These discrepancies may be attributed to differences in regional dietary patterns, body composition (e.g., lower muscle mass in some Asian subgroups), and variations in tumor stage distribution. Our intermediate prevalence likely reflects the specific characteristics of our hospital's catchment area in Zhejiang province,

which includes both urban and rural elderly populations. This contextualization suggests that while the coexistence is a significant issue across Asian elderly CRC patients, local factors should be considered when generalizing our findings. (2) Compared to patients with a single risk or no risk, patients in the Comorbid group had a significantly higher risk of overall and severe postoperative complications (Clavien-Dindo  $\geq$  grade III). (3) Regarding survival outcomes, the Comorbid group had the lowest 18-month survival rate, and multivariable analysis confirmed that the coexistence of nutritional risk and sarcopenia was the strongest independent predictor of reduced overall survival (HR = 10.17), with a risk magnitude far exceeding that of single factors. These results suggest that in elderly patients with colorectal cancer, the concomitant presence of preoperative nutritional risk and sarcopenia constitutes a dis-

tinct high-risk phenotype that poses a serious threat to both perioperative safety and long-term survival.

The synergistic effect observed in our Comorbid group may be particularly pronounced in colorectal cancer due to tumor-specific pathophysiology. CRC tumors are known to secrete pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- $\alpha$ ), which not only drive cancer progression but also directly induce skeletal muscle catabolism via the ubiquitin-proteasome pathway. This tumor-induced systemic inflammation, combined with age-related anabolic resistance, creates a 'perfect storm' for muscle wasting. Furthermore, the gut microbiome - increasingly recognized as a key modulator of both systemic inflammation and nutrient absorption - is often dysregulated in CRC patients. Preoperative bowel preparation and surgery itself can further disrupt this microbial ecosystem, potentially exacerbating postoperative catabolism. Thus, the coexistence of nutritional risk and sarcopenia in CRC patients may reflect an advanced state of cancer-related metabolic dysregulation, making them exceptionally vulnerable to surgical stress.

One of the most significant findings of this study is the synergistic effect of accumulating risk factors. Compared to the No-risk group, the presence of either nutritional risk only or sarcopenia only increased the mortality risk by approximately 3- to 4-fold, whereas the coexistence of both conditions led to a more than 10-fold surge in risk. This effect is not merely additive but is more likely synergistic or multiplicative [5, 23, 24]. The underlying mechanisms are complex and may involve multi-organ systems: Nutritional deficiency weakens the substrate base for anabolism and immune defense, while the loss of muscle mass not only depletes a vital protein reservoir but also exacerbates systemic chronic inflammation through dysregulated myokine secretion and mitochondrial dysfunction. Together, these factors lead to a sharp decline in the patient's resistance to stressors such as surgical trauma and infection, impair tissue repair capacity, and may foster a microenvironment conducive to tumor progression [22, 25]. The significantly higher rate of severe complications (particularly those requiring interventional management) observed in the Comorbid group is a direct clinical mani-

festation of this comprehensive depletion of physiological reserve. This observation is consistent with previous studies in gastrointestinal tumors indicating that the combination of muscle loss and malnutrition is a stronger predictor of severe postoperative complications than either factor alone [26, 27].

Viewing our results in the context of the existing literature, our findings further refine and support the importance of the "nutrition-muscle" axis. Multiple studies have independently confirmed that preoperative malnutrition [28, 29] or sarcopenia [30] are predictors of poor outcomes following colorectal cancer surgery. However, studies that, like ours, employ standardized tools (NRS-2002) and the latest consensus criteria (AWGS 2019) for strict definition, and directly compare the four risk states (no risk, nutritional risk only, sarcopenia only, and both combined), are relatively limited. Our data clearly indicate that if clinical risk assessment focuses on only one dimension, the extreme vulnerability of patients possessing both risks may be underestimated. This underscores the necessity of comprehensive preoperative assessment; specifically, routine nutritional screening should be integrated with sarcopenia assessment (at least including handgrip strength and/or a simple measure of muscle mass) to identify these "extremely high-risk" patients who require the most intensive interventions.

From a clinical practice perspective, our findings have clear translational implications. First, they strongly support the integration of "combined nutritional risk and sarcopenia screening" into the routine preoperative assessment pathway for elderly patients with colorectal cancer. For patients identified as having both conditions (Comorbid group), initiating an intensive, multimodal prehabilitation program should be considered. This approach should extend beyond traditional nutritional supplementation to incorporate individualized nutritional support (particularly adequate high-quality protein), exercise therapy centered on resistance training, and potentially pharmacological or nutritional strategies to modulate inflammation (e.g., Omega-3 fatty acids), aiming to improve physiological reserve within the limited timeframe prior to surgery [31, 32]. Second, surgical teams must be prepared for the higher risk of complications in these patients and

should adopt a more vigilant and proactive approach regarding postoperative monitoring, supportive care, and subsequent decisions regarding adjuvant therapy.

This study has several limitations. First, as a retrospective study, its conclusions are susceptible to confounding factors and selection bias. Although we adjusted for known important covariates through multivariable analysis, unmeasured confounders (such as socioeconomic status, severity of specific comorbidities, and tumor molecular characteristics) may still exist. Second, the single-center design and limited sample size - particularly the relatively small number of patients in the Sarcopenia Only and Comorbid groups - may affect the statistical power of subgroup analyses and the generalizability of the results, necessitating validation in larger, multicenter cohorts. Third, although sarcopenia diagnosis combined handgrip strength and CT-measured muscle mass, it did not include a physical performance assessment (e.g., gait speed), which may have led to the under-identification of some sarcopenic patients. Finally, the follow-up period was relatively short, and the long-term survival impact requires further observation. Consequently, the prevalence of sarcopenia (28.5%) might be underestimated, and our findings should be interpreted with caution when comparing to studies that fully operationalized the AWGS criteria. Future studies incorporating physical performance measures are needed to validate our results.

Looking ahead, prospective interventional studies are needed to verify whether comprehensive prehabilitation programs targeting patients with concomitant nutritional risk and sarcopenia can effectively reduce complications and improve survival. Simultaneously, exploring specific biomarkers (e.g., inflammatory cytokines, myokine profiles) and metabolic characteristics unique to this patient population will enhance our understanding of the underlying pathophysiological mechanisms and provide direction for the development of targeted therapeutic strategies.

### Conclusion

In conclusion, this study demonstrates that the coexistence of preoperative nutritional risk and sarcopenia is a prevalent and significant issue

in elderly patients undergoing surgery for colorectal cancer. This comorbid state is strongly associated with the highest incidence of postoperative complications and the poorest overall survival, serving as the strongest independent risk indicator, irrespective of traditional factors such as age and gender. Our findings underscore the imperative of implementing routine dual assessment of nutritional status and muscle health in the preoperative evaluation of elderly colorectal cancer patients. Furthermore, they highlight the necessity of delivering intensive, multimodal prehabilitation programs - centered on optimized nutrition and exercise therapy - to these high-risk individuals in order to improve surgical outcomes.

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### Disclosure of conflict of interest

None.

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