

Preoperative visceral fat index predicts the survival outcomes of patients with gastric cancer after surgery

LUGEN ZUO^{1*}, JIANXIU LIN^{2*}, SITANG GE¹, RONG WU³, BAOXINZI LIU⁴, YING CHENG⁴ and YUN TIAN⁴

¹Department of Gastrointestinal Surgery, The First Affiliated Hospital of Bengbu Medical College, Bengbu, Anhui 233004;

²First Clinical Medical College, Nanjing University of Chinese Medicine, Nanjing, Jiangsu 210023;

³Department of General Surgery, Zhongda Hospital, Southeast University, Nanjing, Jiangsu 210000;

⁴Department of Oncology, Affiliated Hospital of Nanjing University of Chinese Medicine and Jiangsu Province Hospital of Chinese Medicine, Nanjing, Jiangsu 210029, P.R. China

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Abstract. Visceral adipose tissue and skeletal muscle mass are associated with carcinogenesis and clinical outcomes in patients with cancer. The aim of the present study was to determine the influence of body composition parameters on postoperative survival in patients with gastric cancer. Demographic data and systemic inflammatory response data were obtained from patients with gastric cancer undergoing radical gastrectomy. The patient's skeletal muscle and visceral fat were assessed using computed tomography, and the corresponding skeletal muscle index (SMI) and visceral fat index (VFI) were calculated. Univariate and multivariate analyses were then performed. Of the 342 patients from whom information was collected, 125 of these patients eventually succumbed to the disease. A total of 271 (79.24%) of the patients were male and 71 (20.76%) were female. Regarding the entire cohort, the mean age was 64 years [interquartile range (IQR), 56-74 years], while the mean body mass index collected was 21.53 (IQR, 19.27-24.22). The median SMI and VFI of the patients were 47.73 (IQR, 41.67-55.51) and 41.28 (IQR, 36.62-45.36), respectively. It was concluded that a low SMI and VFI were associated with worse survival outcomes.

However, the neutrophil-to-lymphocyte ratio and perioperative blood transfusion were not significantly associated with overall survival (OS). Among the indicators assessed, a low VFI was an independent risk factor associated with the worst OS time (hazard ratio 1.59; confidence interval, 1.03-2.45; $P=0.038$). Finally, a prognostic nomogram was constructed which included the VFI to assist clinicians in making more informed decisions. In conclusion, after data collection and analysis, it was found that there was a significant correlation between a low VFI and a shorter OS time in patients with gastric cancer following gastrectomy, suggesting that VFI may be a promising therapeutic target for postoperative interventions to improve patient survival further.

Introduction

Gastric carcinoma is the fifth most common type of primary carcinoma and is the third most common cause of cancer-associated death. Surgery is the primary mode of treatment currently available for the management of gastric carcinoma (1,2). At present, there is a significant amount of interest in the factors influencing the prognosis of stomach cancer, allowing for a more precise risk assessment of preoperative patients. The four primary known potential risk factors for gastric cancer are preoperative carcinoembryonic antigen (CEA) and cancer antigen 19-9 (CA19-9) levels, preoperative systemic inflammation (3) and perioperative blood transfusion (4). These factors have been shown to be significantly correlated with prognosis in patients with stomach malignancies. Apart from these four acknowledged factors, the health condition of individuals with stomach cancer is a crucial factor that influences their prognosis (5). The relationship between a patient's body composition and their clinical prognosis for cancer has garnered increasing interest in recent years. It is becoming more widely acknowledged that skeletal muscle mass, a type of bodily component that can be assessed by computed tomography (CT) scan, affects the prognosis of patients who have undergone stomach cancer surgery (6-8). A decreased skeletal muscle mass has been found to be an independent risk factor for long-term survival in patients

Correspondence to: Dr Yun Tian, Department of Oncology, Affiliated Hospital of Nanjing University of Chinese Medicine and Jiangsu Province Hospital of Chinese Medicine, 155 Hanzhong Road, Qinhuai, Nanjing, Jiangsu 210029, P.R. China
E-mail: fsyy00671@njucm.edu.cn

*Contributed equally

Abbreviations: BMI, body mass index; CI, confidence interval; CT, computed tomography; HR, hazard ratio; HU, Hounsfield unit; IQR, interquartile range; NLR, neutrophil-to-lymphocyte ratio; SMI, skeletal muscle index; SMA, skeletal muscle area; VFA, visceral fat area; VFI, visceral fat index

Key words: gastric cancer, prognosis, skeletal muscle, visceral fat, computed tomography

with gastric cancer in prior clinical research (9), yet there has been disagreement on this finding due to variations in the diagnostic criteria between cohorts (10,11).

The body mass index (BMI), sometimes referred to as the weight index, provides insight into an individual's nutritional state, amount of body fat and stage of human development (12). However, as individuals have different fat distributions, BMI does not always accurately represent the buildup of adipose tissue. Visceral adipose tissue is a preferable option over BMI since it can more precisely indicate the existence of fat cell dysfunction (13,14). Previous studies have shown that metabolic diseases can have an impact on changes in visceral adipose tissue gain or loss (15), and these changes further suggest abnormalities in the intra-abdominal environment (16). As our knowledge of visceral adipose tissue has expanded, excess adiposity, a physical characteristic linked to malignant prognosis, has emerged as a topic of intense interest (17,18). Adipose tissue accumulation worsens prognosis in a number of cancer types and raises the probability of additional cancer progression; this is partly due to the interaction between adipocytes and cancer cells (19). High intraperitoneal fat thickness has been linked to a reduced OS rate in patients with locally advanced gastric cancer, according to clinical trials (20). However, these results will need to be further confirmed in further studies, as there are few investigations on whether pre-operative intraperitoneal fat impacts the long-term survival of patients with stomach cancer following surgical operations (21-23).

East Asia has a significantly higher incidence of stomach cancer than the rest of the world (24). The majority of individuals in East Asia are from China. However, there is very little research on the impact of preoperative body composition on the postoperative long-term survival of Chinese patients with gastric cancer, as the majority of studies on visceral fat and skeletal muscle focus on patients' postoperative condition (25,26). In the present study, the visceral fat area and skeletal muscle mass were measured using preoperative CT scans. Next, the collected data were used to evaluate the predictive power of body composition characteristics on overall survival (OS) time. To the best of our knowledge, this is the first study assessing how preoperative body composition affects postoperative patient survival following gastric surgery in a Chinese cohort.

Patients and methods

Patients. The present study was a retrospective cohort study including all patients with gastric cancer (stage I-III) who underwent gastrectomy between January 2007 and December 2009 in the First Affiliated Hospital of Bengbu Medical College (Bengbu, China). The criteria for patient inclusion in the study were the following: i) Histologically confirmed gastric adenocarcinoma and planned to receive elective curative surgery for gastrointestinal cancer; ii) age >18 years; iii) non-obese patients, defined as body mass index <30 kg/m²; and iv) within 1 month prior to gastric cancer surgery, the patient had abdominal CT image data. Patients were excluded from the study cohort when CT image quality was sufficient for an analysis to confirm that the patient had metastatic cancer that could not be cured by surgical treatment and when the

patient had undergone a part gastrectomy for an incomplete cure of stomach cancer. These reasons could also lead to the exclusion of patients from the cohort if contact was lost with them for some reason that prevented follow-up, or if a patient had multiple malignancies at the same time. This study used patient data from a digestive tumor clinical database that was established with approval from the First Affiliated Hospital of Bengbu Medical College (Bengbu, China; approval no. 2020KY022). The Clinical Medical Research Ethics Committee of The First Affiliated Hospital of Bengbu Medical College waived the requirement for informed consent for the collection of retrospective data.

Data collection. Anthropometric data (height and weight closest to CT time), tumor features, operative information, postoperative treatment and comorbidity data were collected for patients in the cohort from the institution's electronic medical records. Patients were staged with gastric carcinoma according to the relevant provisions in the American Joint Committee on Cancer staging manual (eighth edition) (27). In addition, to make the study more comprehensive and credible, demographic information (including age and sex), laboratory data and other relevant data for subsequent examination were included for analysis. In addition, the systemic inflammation status of the patients was quantified using the preoperative neutrophil-to-lymphocyte ratio (NLR).

Body composition assessment. For the body composition assessments, a patient was required to lie down in the supine position and then their skeletal muscle area (SMA) and visceral fat area (VFA) were measured using CT. At the time of measurement, the Hounsfield unit (HU) thresholds ranged from -29 to 150 HU for skeletal muscle and 50 to 150 HU for visceral adipose tissue (9,28). The tool used to calculate the total cross-sectional SMA and VFA for the 3rd lumbar vertebra was ImageJ (National Institutes of Health) (Fig. 1A). For these data measurements, two experienced researchers were selected. The Skeletal Muscle Index (SMI) was measured by dividing the patient's skeletal muscle measurement by the square of their height (m²), whereas the Visceral Fat Index (VFI) was obtained by dividing the patient's area of visceral fat (cm²) by the square of their height (m²). As previous studies based on CT imaging have not given a valid definition of low adiposity or low bone mass in patients with cancer (29-31), the study cohort was divided into high and low SMI and VFI groups based on the median value of the data of the present cohort.

Outcomes. In this study, all individuals diagnosed with gastric carcinoma were examined at standard outpatient clinics or subsequently monitored. The outcome of this study was the overall patient survival rate, which was the number of days the patient being studied had survived from the initial date of diagnosis. A sequence of study-related observations was performed on the individual under study until their death, regardless of the cause, or until the final follow-up visit. If the patient was still alive at the final follow-up visit, they were removed from the study cohort on the date of their last contact.

Statistical analysis. In the exploratory analysis, more structured descriptive statistics were performed on the

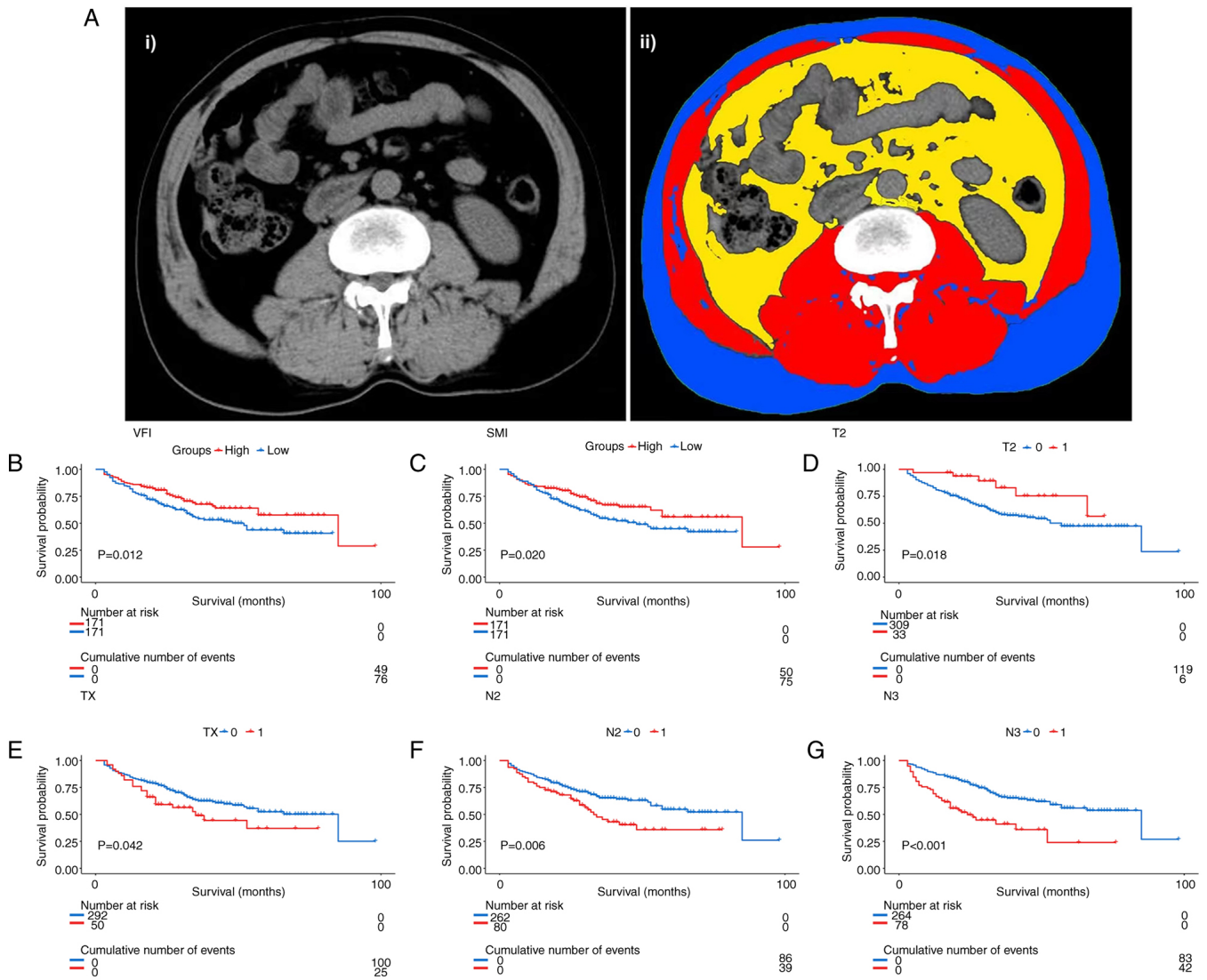


Figure 1. (A) CT images for visceral fat assessment and CT images for skeletal muscle mass assessment in patients with stomach cancer. CT images were taken at the 3rd lumbar vertebra. i) Original CT scan image. ii) CT images after labeling. The yellow color indicates visceral fat, the blue color indicates subcutaneous fat and the red color indicates skeletal muscle mass. (B) Kaplan-Meier analysis of the cumulative OS in patients with a low or high VFI. (C) Kaplan-Meier curves of OS in patients with a low or high SMI. Kaplan-Meier curves of the OS in patients with (D) T1 to T0, (E) T4 to T0, (F) N2 to N0 and (G) N3 to N0 stage cancer. OS, overall survival; CT, computed tomography; VFI, visceral fat index; SMI, skeletal muscle index.

data collected, including the means, standard deviations and percentages, which is presented in a tabular form. Kaplan-Meier curves were also used to further determine the role of each factor in survival outcomes. To compare differences between survival curves, a Log-rank test was used. A Cox proportional hazard model was used for the univariate and multivariate survival analysis on the collected data. For stratification of the SMI and VFI for Kaplan-Meier survival analysis, the median value was used to separate the patients into low and high VFI and SMI groups. For the calculation of overall patient mortality, all patients included in the study who survived gastric cancer from the time of surgery to the end of follow-up and the total number of people who died midway or were lost to follow-up for various reasons were used. Data were analyzed using SPSS version 23.0 (IBM Corp.), and all calculated P-values were two-tailed. P<0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics. Out of the total data gathered between 2007 and 2009, 342 patients fulfilled the inclusion criteria, with 271 (79.24%) of them being male. The median age of all participants in the study was 64 years, with the range of 56-74. Following the standard staging of the 342 patients, it was determined that 16 patients (4.68%) were diagnosed with stage I gastric carcinoma, 147 patients (42.98%) with stage II gastric carcinoma and 179 patients (52.34%) with stage III gastric carcinoma. Out of all the patients who were included, a total of 233 individuals (68.13%) underwent a subtotal gastrectomy, while an additional 109 patients (31.87%) underwent a total gastrectomy. Upon careful examination of the follow-up records of all participants, it was determined that 125 individuals had died by the conclusion of the study period. The median duration of follow-up for all patients included in the present study was 29.54 months, ranging between 3 and

Table I. Clinicopathological characteristics of the recruited cohort.

Clinicopathological factor	Value
Median age (range), years	64 (56-71)
Sex, n (%)	
Male	271 (79.24)
Female	71 (20.76)
Preoperative hemoglobin, g/l ^a	121.19±23.87
Preoperative albumin, g/l ^a	38.91±6.31
Preoperative neutrophil-lymphocyte ratio ^b	2.03 (1.51-3.08)
Preoperative carcinoembryonic antigen ^b	2.80 (1.60-4.95)
Preoperative CA19-9 ^b	9.60 (4.44-28.63)
Stage, n (%)	
I	16 (4.68)
II	147 (42.98)
III	179 (52.34)
Body mass index, mg/m ^{2b}	21.53 (19.27-24.22)
SMI, cm ² /m ^{2b}	47.73 (41.67-55.51)
VFI, cm ² /m ^{2b}	41.28 (36.62-45.36)
Gastrectomy type, n (%)	
Partial excision	233 (68.13)
Total excision	109 (31.87)

^aMean ± SD. ^bMedian (interquartile range).

98 months. Table I provides an overview of the baseline characteristics of the included patients.

Body composition measurement. Two investigators examined CT images from the 342 participants. The median BMI of the cohort was 21.53 (IQR, 19.27-24.22), whereas the calculated median SMI and VFI were 47.73 (IQR, 41.67-55.51) and 41.28 (IQR, 36.62-45.36), respectively (data not shown).

Association between body composition and OS. The correlation between various body composition parameters, such as SMI and VFI, and the subsequent data on OS were assessed. The Kaplan-Meier curve revealed that patients with a low VFI exhibited a lower OS time than patients with high VFI (P=0.012; Fig. 1B). The Kaplan-Meier curves also revealed a significant postoperative disparity in OS between individuals with low SMI and those with high SMI (P=0.02; Fig. 1C).

Risk factors associated with a worse prognosis. Next, other potential risk factors associated with a worse prognosis in individuals with gastric carcinoma after surgery were evaluated. Univariate Cox survival analysis was performed for all clinical factors. Subgroups were set up for TNM clinical staging (6th edition of the AJCC Cancer Staging Manual), and the results are shown in Table II, where T2, TX, N2 and N3 were independent factors affecting prognosis. Kaplan-Meier curves were plotted based on the clinical stages that independently

influenced prognosis. T2 (P=0.018; Fig. 1D) was a protective factor, and TX (P=0.042; Fig. 1E), N2 (P=0.007; Fig. 1F) and N3 (P<0.0001 Fig. 1G) were risk factors for a worse prognosis.

Other clinical factors, including age, sex, NLR, perioperative blood transfusion, preoperative CEA levels, triglycerides, low-density lipoprotein, high-density lipoprotein, plasma glucose and preoperative BMI, amongst other factors, were not significantly associated with OS in the present cohort. However, preoperative CA19-9 levels were an independent factor affecting prognosis (P=0.001).

Predictors of adverse outcomes. To obtain more accurate results on independent risk factors affecting the long-term survival of patients, multivariate Cox analyses were performed for factors with P-values <0.1. CA19-9, NLR, SMI, VFI and stages T2, TX, N2 and N3 cancer were included in the Cox regression analysis. As shown in Table II, among the validated risk factors, CA19-9 [hazard ratio (HR), 1.001; 95% confidence interval (CI), 1.000-1.002; P<0.0001] and high VFI level (HR, 0.620; 95% CI, 0.428-0.898; P=0.011) were associated with a long OS time, while N2 (HR, 2.660; 95% CI: 1.719-4.118; P<0.0001) and N3 (HR 3.313; 95% CI: 2.127-5.159; P<0.0001) were associated with a short OS time. NLR or SMI were not independent factors influencing OS. Some of the serological indicators associated with VFI were then analyzed to verify whether there were any differences in these serological indicators in patients in the high and low VFI groups. Among the serological indicators included (including triglycerides, LDL, HDL and plasma glucose), only the expression level of triglycerides was significantly different in the two groups of patients (P<0.05).

Construction of a prognostic nomogram including VFI. Next, a prognostic nomogram (Fig. 2A) was constructed using the variables that were significant in the results of the multivariate Cox survival analysis. To verify that the constructed nomogram model had good clinical value, ROC curves were plotted (Fig. 2B) as well as 1-, 3- and 5-year calibration curves (Fig. 2C-E). The area under the ROC curve was 0.718, 0.691 and 0.731 for 1, 3 and 5 years, respectively. The results showed that the nomogram had good clinical consistency and may thus be used for subsequent survival prediction in patients after gastric cancer surgery.

Discussion

The present study examined the value of CT-measured visceral adiposity and skeletal muscle mass in predicting post-operative patient prognosis in patients with gastric cancer who underwent gastrectomy. The results indicated an association between a low VFI and a poor prognosis, further suggesting a potential role for visceral fat status in identifying patients with gastric cancer who have an unfavorable clinical outcome following gastrectomy.

Recent studies have found that visceral fat can induce carcinogenesis via several pathways, including inflammation associated with adipocytokines, reducing reactive oxygen levels and inducing insulin resistance (15,16,32). Adipocytes exert local and/or systemic effects through the secretion of a wide range of signaling molecules, such as leptin, adiponectin

Table II. Multivariate Cox regression analysis.

Factor	Univariate Cox analysis		Multivariate Cox analysis	
	P-value	HR (95% CI)	P-value	HR (95% CI)
Age	0.403	1.008 (0.99-1.025)		
Sex	0.277	0.791 (0.519-1.206)		
White blood cell count	0.705	0.989 (0.934-1.047)		
Neutrophil count	0.652	0.986 (0.928-1.048)		
Lymphocyte count	0.803	1.030 (0.816-1.301)		
Neutrophil-to-lymphocyte count	0.069	1.389 (0.975-1.980)		
Hemoglobin	0.604	0.998 (0.991-1.005)		
Albumin	0.229	0.981 (0.952-1.012)		
Skeletal muscle index	0.040 ^a	0.687 (0.480-0.983)	0.349	0.806 (0.513-1.266)
Visceral fat index	0.046 ^a	0.989 (0.979-1.000)	0.011	0.620 (0.428-0.898)
Triglyceride	0.517	1.105 (0.817-1.469)		
Low-density lipoprotein	0.948	0.991 (0.759-1.294)		
High-density lipoprotein	0.122	1.468 (0.903-2.389)		
Plasma glucose	0.504	1.038 (0.931-1.157)		
Carcinoembryonic antigen	0.388	0.997 (0.990-1.004)		
CA19-9	0.002 ^b	1.001 (1.000-1.001)	<0.00001	1.001 (1.000-1.002)
Body mass index	0.311	0.977 (0.933-1.022)		
Surgical procedure	0.443	1.159 (0.795-1.689)		
T2 vs. T1	0.023 ^a	0.387 (0.170-0.879)	0.186	0.566 (0.244-1.315)
T3 vs. T1	0.454	0.864 (0.590-1.26)		
T4 vs. T1	0.159	1.290 (0.905-1.84)		
TX vs. T1	0.045 ^a	1.567 (1.011-2.431)	0.374	1.230 (0.779-1.941)
N1 vs. N0	0.036	0.592 (0.363-0.966)		
N2 vs. N0	0.008 ^b	1.677 (1.147-2.451)	<0.00001	2.660 (1.719-4.118)
N3 vs. N0	<0.0001 ^c	2.631 (1.803-3.840)	<0.00001	3.313 (2.127-5.159)
M1 vs. M0	0.132	1.879 (0.827-4.270)		

^aP<0.05, ^bP<0.01, ^cP<0.0001. HR, hazard ratio; CI, confidence interval.

and resistin, and may have an impact on tumor growth (19). It has been suggested that these adipocytokines secreted by visceral fat can attract aggregations of macrophages and T cells, which in turn produce cytokines that promote carcinogenesis, such as tumor necrosis factor- α and interleukin-6 (33,34). Conversely, visceral fat lessens adiponectin discharge, and clinical trials have shown that adiponectin exhibits anticancer activity (35,36). Additionally, cancer-associated adipocytes affect tumor biology via multiple mechanisms, including certain indirect mechanisms such as promoting angiogenesis and promoting inflammation via the secretion of inflammatory cytokines (37,38); cancer-associated adipocytes also provide direct metabolic benefits to cancer cells (39,40). Therefore, theoretically, there may be a correlation between visceral adipose tissue accumulation and a worse prognosis in patients with gastric cancer. In fact, dysregulated deposition of excess fat is associated with a worse prognosis in lethal cancer types (41-43). More importantly, trials have highlighted high intraperitoneal fat thickness as an independent correlate of shorter OS time in patients with advanced gastric cancer (20). A decrease in adipose tissue, and skeletal muscle amyotrophy

are common in the development and treatment of people who suffer from cancer. In clinical practice, tissue atrophy is a multifactorial disease, and almost all common methods used to reverse this syndrome by targeting specific circulatory factors have failed (44,45). Likewise, due to the urgent need to treat the disease, a large quantity of research is focused on muscle atrophy in patients with malignancies and its impact on survival rates (46). The notion that a low VFI may reflect cancer prognosis is supported by a previous study, which established that low visceral fat content in patients with upper gastrointestinal cancer was associated with a worse prognosis (22). The data from the present study also confirmed the notion that a low VFI was associated with a worse prognosis in patients with gastric cancer. In addition, VFI has been demonstrated to have a protective effect on cancer prognosis in other types of cancer, such as colorectal cancer (47). The present study provides evidence that VFI measured by CT preoperatively may be a useful measure of prognostic prediction in patients with gastric cancer undergoing radical gastrectomy.

Skeletal muscle, of all the body's protein pools, is the largest (48). Naturally, measuring the volume of whole-body

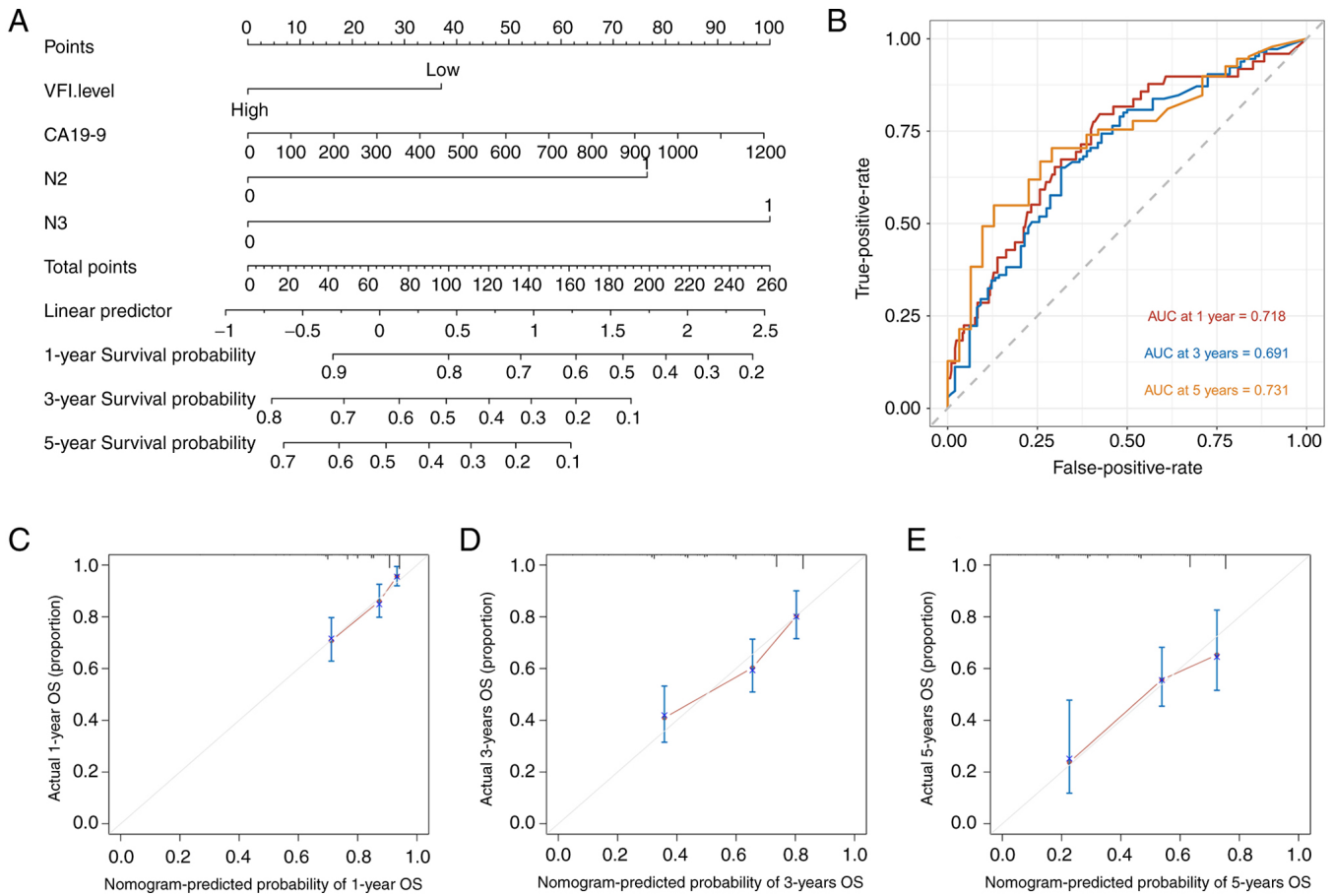


Figure 2. (A) Predictive nomogram models, including CA19-9, VFI level, N2 and N3. (B) Receiver operating characteristic curve for 1-, 3- and 5-year survival. (C-E): Validation of the 1-, 3- and 5-year calibration curves of the predictive model with the clinical reality. AUC, area under the curve; OS, overall survival.

skeletal muscle is an important parameter for assessing whole-body protein nutrition; however, this is independent of serum albumin levels (49). Nevertheless, in individuals who undergo surgery for gastric or colorectal cancer, skeletal muscle volume, relative to other influencing factors (such as weight or BMI), is a more accurate predictor of patient survival. Preoperative skeletal muscle volume is an important factor that can notably influence the prognosis of patients with gastric or colorectal carcinoma (50). Sarcopenia, a pathological syndrome of the skeletal muscle, is characterized by low muscle mass and reduced muscle function (strength or performance). In patients with a good status of nutrition, regarding the development of complications following gastrectomy, sarcopenia is an independent risk factor that has a notable impact on prognosis (51). Similarly, there is experimental evidence that low muscle mass is related to a worse prognosis following colon or gastric surgery (8,52). In one study, muscle volume was found to be significantly better than BMI for predicting survival in patients undergoing radical gastric cancer surgery under uniform diagnostic criteria (53). A systematic review and meta-analysis showed that low muscle mass was indicative of a worse prognosis in numerous clinical conditions (54). Notably, one study noted that preoperative lean body mass was not a significant risk factor for the death rate (10). Although the predictive effect of low SMI was not significant in the multivariate Cox regression analysis in the present study, in the univariate analysis, the

results supported the conclusion that a low SMI was associated with a poorer prognosis. However, in the present cohort, there was no distinct evidence that SMI was an independent factor for a worse prognosis in patients with gastric cancer in the presence of other factors such as cancer stage and VFI.

In the present study, other potential risk factors including preoperative systemic inflammation and perioperative blood transfusion were evaluated. Systemic inflammation has been reported to be reflected by certain hematological inflammatory biomarkers, for example, NLR, lymphocyte-monocyte ratio and platelet-lymphocyte ratio. Conversely, systemic or local inflammation in association with the degree of cancer progression and relevant prognosis can also be reflected by the aforementioned biomarkers (55,56). It has been shown that systemic inflammation has an undesirable influence on cancer prognosis (3,57,58). Whether perioperative blood transfusion affects recurrence, survival and prognosis in patients who have had surgery for gastric carcinoma remains contested (59-61). By contrast, perioperative allogeneic blood transfusions have been shown to be associated with no further recurrence and reduced overall patient survival after gastrectomy for gastric cancer, but not with clinicopathological factors (4). However, the results of the present study do not demonstrate an association between preoperative systemic inflammation and overall survival after gastrectomy. It was not possible to determine the influence of perioperative blood transfusion on postoperative survival.

In addition, visceral fat and skeletal muscle play an important role in human homeostasis, thus the present study analyzed certain neuroendocrine-related indices that affect homeostasis (triglycerides, low-density lipoprotein, high-density lipoprotein and plasma glucose), but unfortunately, thyroid stimulating hormone could not be included in the analysis, as it is not a common screening index in patients with gastric cancer. The results showed that only triglyceride levels were significantly different between the two groups when patients were divided into high and low groups based on the median VFI, which is in line with a previous study that concluded that visceral fat and triglycerides are significantly correlated (13,62). Based on an opinion piece by Slominski *et al* (63), neuroendocrine factors have a significant impact on body homeostasis, of which visceral fat is included, so a focus should be placed on TSH and other neuroendocrine indices in patients with gastric cancer for predicting patient prognosis.

There are several limitations to the present study. First, the results of this study, which will be limited by its retrospective nature, may not avoid the adverse effects of selection bias and inevitably lack some relevant information, such as complete information on chemotherapy, progression-free survival and pro-inflammatory phenotype-related factors (TNF- α and IL-6), which is why these factors were excluded from any analyses performed. Second, there may be other confounding factors in the study that could not be controlled for, such as the socioeconomic status and dietary habits of the patients in the cohort, which may have some influence on body composition following gastrectomy. Third, the patients' muscular function was not validated, for example, handgrip strength and walking speed, both of which are important factors reflecting muscular function. Finally, this was a study based on a population in a rural area, with no relevant data from other areas/institutes to verify whether it applies to an urban population. Although it was not possible to determine whether these patients were affected by factors such as postoperative socioeconomic status and diet or postoperative muscle and fat changes, as the study was retrospective, the data derived from the present cohort suggest that a high preoperative VFI may be a predictor of long-term survival.

In conclusion, patient pre-surgical VFI, which is a CT-based measure for the analysis of body composition, was positively associated with OS in patients with gastric carcinoma. More importantly, the present study can be applied to preoperative patient VFI assessment in the future, and the results can be used as a tool for risk stratification to assist in clinical decision-making for patients with gastric cancer. VFI may be recommended as a means to predict the perioperative risk for gastric cancer patients, with more attention required for low VFI patients prior to surgery, as these patients may benefit from nutritional support.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

YT, LZ and JL contributed to study conception and design, the acquisition, analysis, and interpretation of the data, and drafting of the manuscript. JL contributed to revising the manuscript. SG, RW, BL and YC contributed to study conception and design, interpretation of data, and critical revision of the manuscript for important intellectual content and the final article corrections. All authors have read and approved the final manuscript. YT, LZ and JL confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study used patient data from a digestive tumor clinical database that was established with approval from the First Affiliated Hospital of Bengbu Medical College (Bengbu, China; approval no. 2020KY022). The Ethics Committee of The First Affiliated Hospital of Bengbu Medical College (Bengbu, China) waived the requirement for informed consent for the collection of retrospective data.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA and Jemal A: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 68: 394-424, 2018.
2. Lepage C, Sant M, Verdecchia A, Forman D, Esteve J and Faivre J; EURO CARE working group: Operative mortality after gastric cancer resection and long-term survival differences across Europe. *Br J Surg* 97: 235-239, 2010.
3. Lin JX, Lin JP, Xie JW, Wang JB, Lu J, Chen QY, Cao LL, Lin M, Tu R, Zheng CH, *et al*: Prognostic value and association of sarcopenia and systemic inflammation for patients with gastric cancer following radical gastrectomy. *Oncologist* 24: e1091-e1101, 2019.
4. Squires MH III, Kooby DA, Poultides GA, Weber SM, Bloomston M, Fields RC, Pawlik TM, Votanopoulos KI, Schmidt CR, Ejaz A, *et al*: Effect of perioperative transfusion on recurrence and survival after gastric cancer resection: A 7-institution analysis of 765 patients from the US gastric cancer collaborative. *J Am Coll Surg* 221: 767-777, 2015.
5. Piazuelo MB and Correa P: Gastric cancer: Overview. *Colomb Med (Cali)* 44: 192-201, 2013.
6. Sakurai K, Kubo N, Tamura T, Toyokawa T, Amano R, Tanaka H, Muguruma K, Yashiro M, Maeda K, Hirakawa K and Ohira M: Adverse effects of low preoperative skeletal muscle mass in patients undergoing gastrectomy for gastric cancer. *Ann Surg Oncol* 24: 2712-2719, 2017.
7. Kudou K, Saeki H, Nakashima Y, Edahiro K, Korehisa S, Taniguchi D, Tsutsumi R, Nishimura S, Nakaji Y, Akiyama S, *et al*: Prognostic significance of sarcopenia in patients with esophagogastric junction cancer or upper gastric cancer. *Ann Surg Oncol* 24: 1804-1810, 2017.

8. Yamamoto K, Hirao M, Nishikawa K, Omori T, Yanagimoto Y, Shinno N, Sugimura K, Miyata H, Wada H, Takahashi H, *et al*: Sarcopenia is associated with impaired overall survival after gastrectomy for elderly gastric cancer. *Anticancer Res* 39: 4297-4303, 2019.
9. Nishigori T, Tsunoda S, Obama K, Hisamori S, Hashimoto K, Itatani Y, Okada K and Sakai Y: Optimal cutoff values of skeletal muscle index to define sarcopenia for prediction of survival in patients with advanced gastric cancer. *Ann Surg Oncol* 25: 3596-3603, 2018.
10. Sato T, Aoyama T, Hayashi T, Segami K, Kawabe T, Fujikawa H, Yamada T, Yamamoto N, Oshima T, Rino Y, *et al*: Impact of preoperative hand grip strength on morbidity following gastric cancer surgery. *Gastric Cancer* 19: 1008-1015, 2016.
11. Tegels JJ, van Vugt JL, Reisinger KW, Hulsewe KW, Hoofwijk AG, Derikx JP and Stoot JH: Sarcopenia is highly prevalent in patients undergoing surgery for gastric cancer but not associated with worse outcomes. *J Surg Oncol* 112: 403-407, 2015.
12. Renehan AG, Tyson M, Egger M, Heller RF and Zwahlen M: Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. *Lancet* 371: 569-578, 2008.
13. Tchernof A and Després JP: Pathophysiology of human visceral obesity: An update. *Physiol Rev* 93: 359-404, 2013.
14. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M and Galluzzo A; AlkaMeSy Study Group: Visceral adiposity index: A reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care* 33: 920-922, 2010.
15. Després JP and Lemieux I: Abdominal obesity and metabolic syndrome. *Nature* 444: 881-887, 2006.
16. Pou KM, Massaro JM, Hoffmann U, Vasan RS, Maurovich-Horvat P, Larson MG, Keaney JF Jr, Meigs JB, Lipinska I, Kathiresan S, *et al*: Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress: The framingham heart study. *Circulation* 116: 1234-1241, 2007.
17. Alemán JO, Eusebi LH, Ricciardiello L, Patidar K, Sanyal AJ and Holt PR: Mechanisms of obesity-induced gastrointestinal neoplasia. *Gastroenterology* 146: 357-373, 2014.
18. Demark-Wahnefried W, Platz EA, Ligibel JA, Blair CK, Courneya KS, Meyerhardt JA, Ganz PA, Rock CL, Schmitz KH, Wadden T, *et al*: The role of obesity in cancer survival and recurrence. *Cancer Epidemiol Biomarkers Prev* 21: 1244-1259, 2012.
19. Cozzo AJ, Fuller AM and Makowski L: Contribution of adipose tissue to development of cancer. *Compr Physiol* 8: 237-282, 2017.
20. Li XT, Tang L, Chen Y, Li YL, Zhang XP and Sun YS: Visceral and subcutaneous fat as new independent predictive factors of survival in locally advanced gastric carcinoma patients treated with neo-adjuvant chemotherapy. *J Cancer Res Clin Oncol* 141: 1237-1247, 2015.
21. Wang SL, Ma LL, Chen XY, Zhou DL, Li B, Huang DD, Yu Z, Shen X and Zhuang CL: Impact of visceral fat on surgical complications and long-term survival of patients with gastric cancer after radical gastrectomy. *Eur J Clin Nutr* 72: 436-445, 2018.
22. Harada K, Baba Y, Ishimoto T, Kosumi K, Tokunaga R, Izumi D, Ida S, Imamura Y, Iwagami S, Miyamoto Y, *et al*: Low visceral fat content is associated with poor prognosis in a database of 507 upper gastrointestinal cancers. *Ann Surg Oncol* 22: 3946-3953, 2015.
23. Li L, Li W, Xu D, He H, Yang W, Guo H, Liu X, Ji W, Song C, Xu H, *et al*: Association between visceral fat area and cancer prognosis: A population-based multicenter prospective study. *Am J Clin Nutr* 118: 507-517, 2023.
24. López MJ, Carbajal J, Alfaro AL, Saravia LG, Zanabria D, Araujo JM, Quispe L, Zevallos A, Buleje JL, Cho CE, *et al*: Characteristics of gastric cancer around the world. *Crit Rev Oncol Hematol* 181: 103841, 2023.
25. Lin YC, Lin G and Yeh TS: Visceral-to-subcutaneous fat ratio independently predicts the prognosis of locally advanced gastric cancer---- highlighting the role of adiponectin receptors and PPAR α , β/δ , γ . *Eur J Surg Oncol* 47: 3064-3073, 2021.
26. Tanaka K, Miyashiro I, Yano M, Kishi K, Motoori M, Shingai T, Noura S, Ohue M, Ohigashi H and Ishikawa O: Visceral fat changes after distal gastrectomy according to type of reconstruction procedure for gastric cancer. *World J Surg Oncol* 11: 146, 2013.
27. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR and Winchester DP: The eighth edition AJCC cancer staging manual: Continuing to build a bridge from a population-based to a more 'personalized' approach to cancer staging. *CA Cancer J Clin* 67: 93-99, 2017.
28. Malietzis G, Currie AC, Athanasios T, Johns N, Anyamene N, Glynne-Jones R, Kennedy RH, Fearon KC and Jenkins JT: Influence of body composition profile on outcomes following colorectal cancer surgery. *Br J Surg* 103: 572-580, 2016.
29. Rowan CR, McManus J, Boland K and O'Toole A: Visceral adiposity and inflammatory bowel disease. *Int J Colorectal Dis* 36: 2305-2319, 2021.
30. Li S, Liao Z, He K, Shen Y, Hu S and Li Z: Association of sex-specific abdominal adipose tissue with WHO/ISUP grade in clear cell renal cell carcinoma. *Insights Imaging* 14: 194, 2023.
31. Choe EK, Lee Y, Kang HY, Choi SH and Kim JS: Association between CT-measured abdominal skeletal muscle mass and pulmonary function. *J Clin Med* 8: 667, 2019.
32. Vongsuvan R, George J, Qiao L and van der Poorten D: Visceral adiposity in gastrointestinal and hepatic carcinogenesis. *Cancer Lett* 330: 1-10, 2013.
33. Michaud A, Drolet R, Noël S, Paris G and Tchernof A: Visceral fat accumulation is an indicator of adipose tissue macrophage infiltration in women. *Metabolism* 61: 689-698, 2012.
34. Wellen KE and Hotamisligil GS: Obesity-induced inflammatory changes in adipose tissue. *J Clin Invest* 112: 1785-1788, 2003.
35. Bråkenhielm E, Veitonmäki N, Cao R, Kihara S, Matsuzawa Y, Zhitovovskiy B, Funahashi T and Cao Y: Adiponectin-induced antiangiogenesis and antitumor activity involve caspase-mediated endothelial cell apoptosis. *Proc Natl Acad Sci USA* 101: 2476-2481, 2004.
36. Roberts DL, Dive C and Renehan AG: Biological mechanisms linking obesity and cancer risk: New perspectives. *Annu Rev Med* 61: 301-316, 2010.
37. Wagner M and Dudley AC: A three-party alliance in solid tumors: Adipocytes, macrophages and vascular endothelial cells. *Adipocyte* 2: 67-73, 2013.
38. Nieman KM, Romero IL, Van Houten B and Lengyel E: Adipose tissue and adipocytes support tumorigenesis and metastasis. *Biochim Biophys Acta* 1831: 1533-1541, 2013.
39. Meyer KA, Neeley CK, Baker NA, Washabaugh AR, Flesher CG, Nelson BS, Frankel TL, Lumeng CN, Lyssiotis CA, Wynn ML, *et al*: Adipocytes promote pancreatic cancer cell proliferation via glutamine transfer. *Biochem Biophys Res* 7: 144-149, 2016.
40. Martinez-Outschoorn UE, Sotgia F and Lisanti MP: Power surge: Supporting cells 'fuel' cancer cell mitochondria. *Cell Metab* 15: 4-5, 2012.
41. Brown JC, Caan BJ, Prado CM, Cespedes Feliciano EM, Xiao J, Kroenke CH and Meyerhardt JA: The association of abdominal adiposity with mortality in patients with stage I-III colorectal cancer. *J Natl Cancer Inst* 112: 377-383, 2020.
42. Montano-Loza AJ, Mazurak VC, Ebadi M, Meza-Junco J, Sawyer MB, Baracos VE and Kneteman N: Visceral adiposity increases risk for hepatocellular carcinoma in male patients with cirrhosis and recurrence after liver transplant. *Hepatology* 67: 914-923, 2018.
43. Moon HG, Ju YT, Jeong CY, Jung EJ, Lee YJ, Hong SC, Ha WS, Park ST and Choi SK: Visceral obesity may affect oncologic outcome in patients with colorectal cancer. *Ann Surg Oncol* 15: 1918-1922, 2008.
44. Fearon K, Arends J and Baracos V: Understanding the mechanisms and treatment options in cancer cachexia. *Nat Rev Clin Oncol* 10: 90-99, 2013.
45. Penna F, Minero VG, Costamagna D, Bonelli G, Baccino FM and Costelli P: Anti-cytokine strategies for the treatment of cancer-related anorexia and cachexia. *Expert Opin Biol Ther* 10: 1241-1250, 2010.
46. Prado CMM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L and Baracos VE: Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: A population-based study. *Lancet Oncol* 9: 629-635, 2008.
47. Charette N, Vandeputte C, Ameye L, Bogaert CV, Krygier J, Guiot T, Deleporte A, Delaunoy T, Geboes K, Van Laethem JL, *et al*: Prognostic value of adipose tissue and muscle mass in advanced colorectal cancer: A post hoc analysis of two non-randomized phase II trials. *BMC Cancer* 19: 134, 2019.
48. Frontera WR and Ochala J: Skeletal muscle: A brief review of structure and function. *Calcif Tissue Int* 96: 183-195, 2015.

49. Sánchez-Torralvo FJ, Ruiz-García I, Contreras-Bolívar V, González-Almendros I, Ruiz-Vico M, Abuín-Fernández J, Barrios M, Alba E and Oliveira G: CT-determined sarcopenia in GLIM-defined malnutrition and prediction of 6-month mortality in cancer inpatients. *Nutrients* 13: 2647, 2021.
50. Endo T, Momoki C, Yamaoka M, Hachino S, Iwatani S, Kiyota S, Tanaka H and Habu D: Validation of skeletal muscle volume as a nutritional assessment in patients with gastric or colorectal cancer before radical surgery. *J Clin Med Res* 9: 844-859, 2017.
51. Ma BW, Chen XY, Fan SD, Zhang FM, Huang DD, Li B, Shen X, Zhuang CL and Yu Z: Impact of sarcopenia on clinical outcomes after radical gastrectomy for patients without nutritional risk. *Nutrition* 61: 61-66, 2019.
52. Huang DD, Wang SL, Zhuang CL, Zheng BS, Lu JX, Chen FF, Zhou CJ, Shen X and Yu Z: Sarcopenia, as defined by low muscle mass, strength and physical performance, predicts complications after surgery for colorectal cancer. *Colorectal Dis* 17: O256-O264, 2015.
53. Zhuang CL, Shen X, Zou HB, Dong QT, Cai HY, Chen XL, Yu Z and Wang SL: EWGSOP2 versus EWGSOP1 for sarcopenia to predict prognosis in patients with gastric cancer after radical gastrectomy: Analysis from a large-scale prospective study. *Clin Nutr* 39: 2301-2310, 2020.
54. Rinninella E, Cintoni M, Raoul P, Pozzo C, Strippoli A, Bria E, Tortora G, Gasbarrini A and Mele MC: Muscle mass, assessed at diagnosis by L3-CT scan as a prognostic marker of clinical outcomes in patients with gastric cancer: A systematic review and meta-analysis. *Clin Nutr* 39: 2045-2054, 2020.
55. Aurello P, Tierno SM, Berardi G, Tomassini F, Magistri P, D'Angelo F and Ramacciato G: Value of preoperative inflammation-based prognostic scores in predicting overall survival and disease-free survival in patients with gastric cancer. *Ann Surg Oncol* 21: 1998-2004, 2014.
56. Diakos CI, Charles KA, McMillan DC and Clarke SJ: Cancer-related inflammation and treatment effectiveness. *Lancet Oncol* 15: e493-e503, 2014.
57. Okugawa Y, Toiyama Y, Yamamoto A, Shigemori T, Ide S, Kitajima T, Fujikawa H, Yasuda H, Hiro J, Yoshiyama S, *et al*: Lymphocyte-C-reactive protein ratio as promising new marker for predicting surgical and oncological outcomes in colorectal cancer. *Ann Surg* 272: 342-351, 2020.
58. Feliciano EMC, Kroenke CH, Meyerhardt JA, Prado CM, Bradshaw PT, Kwan ML, Xiao J, Alexeeff S, Corley D, Weltzien E, *et al*: Association of systemic inflammation and sarcopenia with survival in nonmetastatic colorectal cancer: Results from the C SCANS study. *JAMA Oncol* 3: e172319, 2017.
59. Pergialiotis V, Thomakos N, Frountzas M, Haidopoulos D, Loutradis D and Rodolakis A: Perioperative blood transfusion and ovarian cancer survival rates: A meta-analysis based on univariate, multivariate and propensity score matched data. *Eur J Obstet Gynecol Reprod Biol* 252: 137-143, 2020.
60. Latif MJ, Tan KS, Molena D, Huang J, Bott MJ, Park BJ, Adusumilli PS, Rusch VW, Bains MS, Downey RJ, *et al*: Perioperative blood transfusion has a dose-dependent relationship with disease recurrence and survival in patients with non-small cell lung cancer. *J Thorac Cardiovasc Surg* 157: 2469-2477, 2019.
61. McSorley ST, Tham A, Dolan RD, Steele CW, Ramsingh J, Roxburgh C, Horgan PG and McMillan DC: Perioperative blood transfusion is associated with postoperative systemic inflammatory response and poorer outcomes following surgery for colorectal cancer. *Ann Surg Oncol* 27: 833-843, 2020.
62. Maersk M, Belza A, Stødkilde-Jørgensen H, Ringgaard S, Chabanova E, Thomsen H, Pedersen SB, Astrup A and Richelsen B: Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: A 6-mo randomized intervention study. *Am J Clin Nutr* 95: 283-289, 2012.
63. Slominski RM, Raman C, Chen JY and Slominski AT: How cancer hijacks the body's homeostasis through the neuroendocrine system. *Trends Neurosci* 46: 263-275, 2023.



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