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Sarcopenic obesity exacerbates gastric cancer prognosis via increased intermuscular and visceral fat accumulation

Chun-wei Li¹ , Qi Li² , Yu Liu² , Yu Zhang³ , Zhong-kui Wang² , Yu Xing² , Yi-shan Niu² ,
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Abstract

Background Ectopic fat distribution reflects patient's metabolic profile, shaping the tumor microenvironment, which may be a key prognostic indicator. Our study pursues to explore the independent and combined effects of muscle atrophy and abnormal fat distribution on survival in gastric cancer patients.

Method This retrospective cohort study analyzed body composition in 283 gastric cancer patients from Center Hospital, Tianjin University (June 2016–May 2025) using pretreatment CT at L₃, assessing muscle mass, intermuscular, and visceral fat. Ectopic fat phenotypes included visceral obesity (increased visceral adipose tissue, VAT) and myoste- atosis (reduced skeletal muscle density, SMD). Associations between body composition parameters/phenotypes and progression-free survival (PFS), overall survival (OS), and cachexia-related survival (CRS) were evaluated using Kaplan–Meier analysis with log-rank tests and Cox proportional hazards regression.

Results Of the 283 patients, 32 patients (11.3%) were BMI-define obese, 139 patients (49.1%) showed visceral obesity, and 176 patients (62.2%) presented with myoste- atosis. Sarcopenia was present in 234 patients (82.7%), and 151 patients (53.4%) presented with a combination of sarcopenia and myoste- atosis. During a median follow-up of 41 months (2–108 months), 53 patients developed metastasis, 6 relapse, and 142 died. Skeletal muscle mass (Nor- mal Attenuation Muscle Area, NAMA, HR = 0.989, 95% CI 0.980–0.998, $P = 0.022$, for PFS) and quality (SMD, HR = 0.975, 95% CI 0.955–0.995, $P = 0.013$, for PFS) serve as protective prognostic factors after multiple covariate adjustments. Multivariate analyses identified all adiposity-related parameters, including Low Attenuation Muscle Area (LAMA, HR = 1.015, 95% CI 1.003–1.026, $P = 0.012$, for PFS), intermuscular adipose tissue (IMAT, HR = 1.018, 95% CI 1.002–1.034, $P = 0.027$, for PFS), and VFI (HR = 1.008, 95% CI 1.001–1.015, $P = 0.042$) as negative indicators for survival. Sensitivity analyses confirmed these associations. Besides, IMAT, LAMA, and VFI significantly influence prognosis in advanced patients (TNM stage III–IV). Kaplan–Meier survival analysis revealed sarcopenic visceral obesity markedly reduces survival; when combined with myoste- atosis (SMVO), this combined phenotype further exacerbated CRS (5-year CRS: 74.7% in SMVO, $P = 0.019$) beyond the effects of individual phenotypes.

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Conclusion Sarcopenic obesity (myosteatorosis/visceral obesity) can identify poorer prognosis in gastric cancer patients, especially male patients. It is crucial for obese gastric cancer patients to evaluate their body composition, specifically focusing on fat distribution.

Trial registration: Registered in August 2016, NCT02873676 at www.clinicaltrials.gov.

Keywords Gastric cancer, Sarcopenic obesity, Survival, Ectopic fat accumulation, Intermuscular adipose tissue

Introduction

Gastric cancer (GC) stands as a formidable public health menace, ranking fifth among the most prevalent malignant tumors and occupying the fourth position in terms of cancer-related fatalities globally [1]. Despite advancements in the treatment modalities for gastrointestinal neoplasms, leading to improved survival, a substantial number still face unfavorable prognoses [2]. Thus, there is an urgent imperative to identify novel prognosis indicators for accurate prognosis prediction in gastrointestinal neoplasms. Obesity is a key etiological factor linked to poor cancer prognosis, with evidence showing that muscle atrophy and ectopic fat deposition promote gastrointestinal tumor progression [3, 4]. Body composition can reflect body shape, metabolic profile, and physiologic reserve, impacting perioperative inflammatory response and nutritional metabolism, thereby serving as a key prognostic indicator [5].

Ectopic fat deposition, a hallmark of insulin-resistant (IR) obesity, acts as a modifier of the tumor microenvironment and a potential driver of carcinogenesis and metastasis [6]. Dysfunctional visceral adipose tissue (VAT) in obesity underpins IR and chronic inflammation, potentially facilitating tumor initiation and progression via pro-inflammatory and pro-angiogenic cytokine secretion [7, 8]. With respect to muscle fat infiltration, or myosteatorosis, it is characterized by a decline in skeletal muscle quality due to ectopic lipid infiltration surpassing metabolic capacity of muscle and adipose tissue, often co-occurring with atrophy, disrupting metabolic homeostasis, and promoting IR [9, 10]. Myosteatorosis is associated with elevated systemic inflammatory responses that promote tumorigenesis, sustaining a pro-inflammatory microenvironment, which negatively impacts overall survival (OS) in patients with gastrointestinal malignancies; prognosis is further modulated by the degree of adipose infiltration within skeletal muscle tissue [11–14]. Muscle mass is an objective biomarker of nutritional and metabolic status with prognostic significance in oncology [15]. Sarcopenic atrophy interacts with systemic inflammation, immune dysregulation, and nutritional deficiencies, potentially promoting tumorigenesis and metastasis [16]. Conversely, inflammation and metabolic disturbances associated with GC may exacerbate sarcopenia progression [17]. When myosteatorosis co-occurs with sarcopenia,

forming the sarcopenic obesity phenotype, this combined condition elevates metastatic potential, is associated with poorly differentiated neoplasms [18, 19], frequently precedes cancer cachexia, and ultimately impacts post-operative oncologic outcomes [20]. Therefore, body composition assessment provides offers prognostic insights for gastrointestinal cancers by reflecting metabolic changes from chronic inflammation, guiding interventions to improve patient survival [21, 22].

Detecting muscle atrophy in obese individuals with GC remains challenging as low BMI does not reliably differentiate fat distribution, as intermuscular adipose tissue (IMAT), VAT, and muscle quality/density (SMD) [4]. To address these complexities, numerous AI-based algorithms have been developed to automate CT body segmentation and quantify muscle and fat distribution, including subcutaneous fat tissue (SAT), VAT, and IMAT [6]. This insight should be of great value for physicians who seek to counsel patients who do not have obvious obesity or clinically abnormal metabolic markers. Thus, this retrospective cohort study aimed to (1) evaluate the independent impact of ectopic fat distribution parameters-derived from CT images (SMD, IMAT, and VAT) on survival in GC patients, and (2) explore the effect of ectopic fat distribution and muscle atrophy phenotype (myosteatorosis, visceral obesity, and sarcopenia) on the survival in GC patients.

Methods

Study population

This is a multi-center, retrospective observational study [23] organized by Peking Union Medical College Hospital (PUMCH) multi-center Prospective Longitudinal Sarcopenia study (PPLSS), approved by Ethic Committee (No. HS889, registered in August 2016, NCT02873676). Participants with GC were selected, with written permission, at the General Surgery Unit of Central Hospital, Tianjin University between June 2016 and May 2025 from the Central Hospital, Tianjin University Retrospective Longitudinal Obesity-related Metabolic Tumor Study (TRLOMTS, No. IRB2021-037-02), part of the PPLSS, which aims to assess changes in body composition and clinical outcomes in patients with obesity-related metabolic tumor.

In this retrospective cohort study, we identified 597 patients with pathology-confirmed GC at CHTU's general surgery unit. Eligible individuals aged ≥ 18 histologically proven gastric adenocarcinoma before treatment, availability of digitally-stored CT imaging taken within 30-day before treatment and detailed clinical information. Criteria for exclusion included the following: (1) any evidence of combination with other primary malignancies, (2) absence of 30-day before treatment non-enhanced abdominal CT scan and suboptimal CT image quality due to anatomical structures not extend to the L₃ middle layer, (3) lack of key clinical, demographic, and anthropometric data, and (4) patients who refused follow-up. After excluding those lacking preoperative imaging, incomplete clinical data, and unrelated diagnoses, the final cohort comprised 283 patients (Figure S1).

Computed tomography image analysis for body composition phenotypes

Unenhanced abdominal CT images (DICOM format) at L₃ level [24] from hospital's Picture Archiving and Communication System were analyzed by three independent evaluators using Slice-O-Matic Version 6.0 (Serial Number: 306F4FF2, Tomovision, Montreal, Quebec, Canada) for assessing muscle cross-sectional area, radiodensity, and adiposity. Two blinded evaluators performed measurements, with a radiologist manual segmentation if necessary. Inter-rater reliability, assessed by intra-class correlation coefficient (ICC), indicated by normal attenuation muscle area (NAMA, 0.984), IMAT (0.954), SAT (0.998), and VAT (0.999).

The L₃ CT region encompasses psoas, erector spinae, quadratus lumborum, transversus abdominis, external and internal obliques, and rectus abdominis [25], and identified as SKM (NAMA, and low attenuation muscle area, LAMA) and fat metrics (IMAT, VAT and SAT) [26]. Parameters, measured in cm² and normalized for height in m², are reported as skeletal muscle index (SMI), subcutaneous adipose index (SAI), and visceral fat index (VFI) in cm²/m² [27]. Tissue areas were identified by anatomic features and quantified using Hounsfield unit (HU) range of -29 to 29 for LAMA, 30 to 150 for NAMA, -150 to -50 for VAT, and -190 to -30 for IMAT and SAT [28]. Sarcopenia was defined by sex-specific SMI cutoffs, 52.4 cm²/m² (men) and 38.5 cm²/m² (women) [29], while SO required VAT ≥ 100 cm² alongside sarcopenia [30]. Myosteatosis was defined as SMD < 33HU (men) and < 28HU (women) [31]. Visceral obesity (VO) varied by age and gender: for 17–39, males > 120.5cm², females > 62.6cm²; for 40–59, males > 134.4cm², females > 85.9cm²; and for > 60, males > 131.7cm², females > 115.6cm² [32]. This study defined ectopic combined body composition phenotypes: sarcopenic visceral

obesity (SVO), sarcopenia & myosteatosis (SM), and sarcopenia, myosteatosis & VO (SMVO).

Assessment of covariates

Medical records provided data from diagnosis to last follow-up or death, including demographics, tumor features, comorbidities, biochemical tests, and survival outcomes. Pretreatment variables encompassed age, sex, comorbidities, smoking, alcohol use, and biochemical results. Surrogate markers like systemic inflammation index (SII, platelet*neutrophil-to-lymphocyte count ratio) [33] and neutrophil-to-lymphocyte ratio (NLR) were derived from blood biochemistry data [34]. Tumor characteristics included diameter, differentiation, TNM stage, and pathological classification. All tumors were histologically confirmed and staged per the AJCC 8th edition TNM classification. [35]. Treatment factors encompass operation (radical or palliative), chemotherapy, and targeted therapy. Standard radical gastrectomy involves D2 lymphadenectomy and resection of N1 and N2 lymph nodes, as per the Japanese Classification of Gastric Carcinoma [36]. The study primary endpoints were progression-free survival (PFS), OS, and cachexia-related survival (CRS). The follow-up endpoints were determined via telephone, with the final consultation in June 2025. PFS was calculated from diagnosis to relapse, distant metastasis, or death; OS from diagnosis to death or last contact; and CRS from diagnosis to cachexia-related death or last contact. Relapse was confirmed by pathological, radiological, or endoscopic evidence at previous or adjacent sites; distant metastasis by similar evidence at remote organs. Death dates were obtained from death certificates or family reports. Surviving patients were censored at the last follow-up date.

Statistical analysis

Statistical analyses were conducted using R 4.3.1. Continuous data are reported as mean ($\pm$ SD), or median (IQR), while categorical data are reported as counts and percentages. Group comparisons applied the Mann–Whitney U-test for continuous variables and the Chi-squared or Fisher's exact test for categorical variables.

The univariate Cox proportional hazards regression model (Model-1) was utilized to evaluate the relationship between all body composition parameters/phenotypes and PFS, OS, and CRS. Subsequently, Multivariate Cox models adjusted for confounders: Model-2 included age, sex, TNM stage, and treatment; Model-3 added BMI, comorbidities, smoking, alcohol, and biochemical factors. Kaplan–Meier and log-rank tests identified prognostic phenotypes affecting PFS, OS, and CRS in GC patients with sarcopenia, myosteatosis, VO, and combined phenotypes. Prior to multivariate modeling,

we quantified the correlation structure among BMI and all parameters (IMAT, VAI, SMI, etc.) using the variance inflation factor (VIF). All VIF values were far below the threshold of 5, confirming that no significant multicollinearity existed between the three variables. Statistical significance was defined at $P < 0.05$ with a 95% confidence interval (CI).

Four sensitivity analyses were performed: (1) evaluating the association between body composition parameters/phenotype and survival separately between sexes cohorts to account for sexual dimorphism in adipose distribution; (2) stratifying patients by TNM stage to assess tumor progression effects on prognosis; (3) applying Cox regression and Kaplan–Meier analyses to patients with follow-up exceeding 41 months due to high censored data beyond 24 months; and (4) analyzing the impact of surgical management by conducting sensitivity analysis on patients receiving conservative treatment.

Results

Baseline characteristics

Patients with GC were predominantly male (79.2%), with a median age of 66.0 years (range, 62.0–73.0y), and more frequently presented with advanced TNM stage (III/IV, Table S1). Based on the TNM stage, stage IV patients exhibited inflammatory, metabolic, and nutritional disturbances, with elevated NLR (5.20, $P = 0.009$), SII (1326.95, $P = 0.005$), fasting blood glucose levels (6.72 mmol/L), and decreased albumin (36.61 g/L, $P = 0.035$) and hemoglobin concentrations (109.03 g/L, $P = 0.014$). Tumor markers were higher in stage IV: carcinoembryonic antigen levels (81.74 ng/mL, $P < 0.001$), carbohydrate antigen 19–9 (219.03 U/mL, $P < 0.001$), and carbohydrate antigen 72–4 (42.33 U/mL, $P < 0.001$), along with shorter PFS (10.67 ± 14.44 months, $P < 0.001$) and OS (11.02 ± 14.42 months, $P < 0.001$).

Of the 283 patients, 11.3% patients were obese by BMI, while 62.2% patients exhibited ectopic muscular fat accumulation, indicative of myosteatosis (Table 1). Additionally, 49.1% patients showed central fat distribution (VO). These findings suggest that BMI alone is insufficient for accurately defining obesity in the oncologic context. Concerning muscle quality, sarcopenia was present in 82.7% of patients, SVO in 43.8%, and SM in 53.4%. Figure 1 depicts the heterogeneity of ectopic fat deposition in GC patients, marked by increased intramuscular fat infiltration alongside significant muscle atrophy, correlates positively with tumor progression (Fig. 1a–d), with progressive declines in BMI ($P = 0.003$), obesity prevalence ($P < 0.001$), TAMA (128.29cm^2 , $P = 0.002$), SMI ($40.42\text{cm}^2/\text{m}^2$, $P = 0.004$), and NAMA (68.51cm^2 , $P = 0.025$, Table 1) levels, indicating a higher prevalence of sarcopenia (95.0%, $P < 0.001$) in stage IV. Regarding

fat distribution, stage IV patients exhibit the lowest SMD levels (26.07HU), reflecting increased myosteatosis (70.0%) and SM (70.0%, $P = 0.004$), and the lowest VFI ($41.85\text{cm}^2/\text{m}^2$, $P = 0.027$) levels, although the prevalence of VO exceeds 40% in stages III and IV ($P = 0.035$). However, LAMA remains relatively elevated in stage IV (45.99cm^2), approaching statistical significance ($P = 0.083$). These findings highlight the critical role of fat distribution patterns in tumor progression.

The role of specific body composition parameters in adverse clinical outcomes among patients with GC

Median follow-up was 41 months (range, 2–108 months) until June 30, 2025. Relapse occurred in 2.1% of patients, distant metastasis in 18.7% of patients, and mortality in 50.2% of patients (27 cachexia-related deaths). TNM stage I–II OS at 3, 12, 36, and 60 months was 95.4%, 88.0%, 73.2%, and 68.4% and PFS was 94.4%, 87.0%, 73.8%, and 68.8%, respectively. TNM stage III–IV OS at 3, 12, 36, and 60 months was 88.0%, 51.1%, 32.0%, and 19.0% and PFS was 85.1%, 45.3%, 26.0%, and 17.0%, respectively.

Considering the bidirectional relationship between survival, muscle atrophy, and ectopic fat distribution, we employed Cox proportional hazards modeling to identify prognostic biomarkers in GC patients. Univariate analysis identified NAMA (hazard ratio [HR] = 0.986, $P < 0.001$) and SMD (HR = 0.965, $P < 0.001$) serve as protective factors for PFS, whereas LAMA was associated with decreased PFS (HR = 1.012, $P = 0.014$, Fig. 2a). Similar trends were observed for OS and CRS (Fig. 2b, c). Multivariate analysis indicated muscle mass and quality exert protective effects on PFS (NAMA, HR = 0.989, 95% CI 0.980–0.998, $P = 0.022$; SMD, HR = 0.975, 95% CI 0.955–0.995, $P = 0.013$, Table S2) in Model-2. Conversely, ectopic fat parameters, including LAMA (HR = 1.015, 95% CI 1.003–1.026, $P = 0.012$) and IMAT (HR = 1.018, 95% CI 1.002–1.034, $P = 0.027$), were identified as adverse prognostic indicators for PFS. These associations persisted in OS and CRS (Table S2). The Model-3 revealed similar trends for muscle and fat-derived parameters with respect to survival after adjustment for BMI, surgical approach, pathological classification, etc. Additionally, VFI was associated with PFS (HR = 1.008, 95% CI 1.001–1.015, $P = 0.042$) and OS decline (HR = 1.010, 95% CI 1.002–1.017, $P = 0.015$, Table S2). These findings suggest ectopic fat accumulation, particularly intermuscular, intramuscular, and visceral fat, is correlated with poorer survival in GC patients, especially CRS.

To assess the robustness of our findings, sensitivity analyses considering four key variables demonstrated significant correlations between fat distribution and survival. Stratified by sex, basic character reveals that

Table 1 Body composition features of participants

	Total participants (n = 283)	TNM stage I (n = 60)	TNM stage II (n = 48)	TNM stage III (n = 115)	TNM stage IV (n = 60)	P*
Height, cm	168.79 ± 6.47	168.08 ± 7.30	169.06 ± 6.83	169.47 ± 6.29	167.97 ± 5.55	0.528
Weight, kg	66.53 ± 12.14	69.57 ± 13.79	69.97 ± 13.13	64.82 ± 11.48	64.00 ± 9.55	0.022
BMI ^a , kg/m ²	23.32 ± 3.83	24.56 ± 4.21	24.45 ± 4.21	22.54 ± 3.60	22.66 ± 2.97	0.003
Overweight, n (%)	71 (25.09%)	31 (52.5%)	20 (42.6%)	36 (32.1%)	16 (26.7%)	0.140
Obesity, n (%)	32 (11.31%)	14 (23.7%)	9 (19.1%)	8 (7.1%)	1 (1.7%)	<0.001
Overweight/Obesity, n (%)	103 (36.40%)	17 (28.8%)	11 (23.4%)	28 (25.0%)	15 (25.0%)	0.925
SKM, cm ²	123.27 ± 26.37	130.39 ± 31.14	127.70 ± 26.95	122.29 ± 24.33	114.50 ± 21.99	0.011
SMI, cm ² /m ²	43.05 ± 7.91	48.18 ± 9.36	44.45 ± 8.07	42.40 ± 7.11	40.42 ± 6.68	0.004
NAMA, cm ²	78.20 ± 27.77	81.86 ± 33.09	83.87 ± 31.12	78.99 ± 23.95	68.51 ± 23.96	0.025
NAMA, HU	45.26 ± 3.51	45.25 ± 3.96	45.40 ± 3.28	45.83 ± 3.32	44.04 ± 3.33	0.012
LAMA, cm ²	45.07 ± 15.94	48.53 ± 16.39	43.81 ± 15.51	43.30 ± 16.10	45.99 ± 15.28	0.083
LAMA, HU	5.71 ± 1.63	5.74 ± 1.46	5.76 ± 2.03	5.67 ± 1.58	5.74 ± 1.54	0.823
SMD, HU	28.16 ± 9.61	28.51 ± 9.64	29.87 ± 9.08	28.37 ± 10.07	26.07 ± 8.92	0.140
TAMA, cm ²	137.47 ± 28.12	146.63 ± 32.19	142.68 ± 27.27	135.30 ± 27.15	128.29 ± 22.91	0.002
NAMA/TAMA	0.56 ± 0.15	0.55 ± 0.16	0.58 ± 0.16	0.58 ± 0.14	0.53 ± 0.15	0.109
IMAT, cm ²	14.20 ± 9.40	16.24 ± 8.36	15.00 ± 13.71	13.02 ± 8.64	13.79 ± 7.10	0.028
IMAT, HU	-60.97 ± 5.55	-62.12 ± 5.69	-61.35 ± 5.23	-60.17 ± 5.55	-61.03 ± 5.52	0.095
SAT, cm ²	111.23 ± 60.89	128.59 ± 64.15	127.47 ± 72.13	95.78 ± 50.00	110.49 ± 60.37	0.002
SAT, HU	-90.57 ± 11.80	-93.73 ± 11.53	-91.95 ± 11.11	-88.70 ± 12.27	-89.91 ± 11.13	0.013
	Total participants (n = 283)	TNM stage I (n = 60)	TNM stage II (n = 48)	TNM stage III (n = 115)	TNM stage IV (n = 60)	P
SAI ^b , cm ² /m ²	39.55 ± 22.95	46.10 ± 24.03	45.18 ± 27.07	33.70 ± 18.65	39.72 ± 23.42	0.002
VAT, cm ²	134.04 ± 86.93	155.95 ± 89.90	145.29 ± 80.83	126.44 ± 91.37	117.68 ± 75.66	0.031
VAT, HU	-89.82 ± 9.38	-93.18 ± 8.72	-91.33 ± 9.47	-88.63 ± 10.02	-87.56 ± 7.59	<0.001
VFI, cm ² /m ²	46.97 ± 30.10	55.21 ± 31.55	50.44 ± 27.28	43.90 ± 31.26	41.85 ± 27.03	0.027
Sarcopenia, n (%)	234 (82.7%)	38 (63.3%)	37 (77.1%)	102 (88.7%)	57 (95.0%)	<0.001
MA, n (%)	176 (62.2%)	37 (61.7%)	23 (47.9%)	74 (64.3%)	42 (70.0%)	0.114
VO, n (%)	139 (49.1%)	36 (60.0%)	29 (60.4%)	49 (42.6%)	25 (41.7%)	0.035
SVO, n (%)	124 (43.8%)	21 (35.0%)	24 (50.0%)	51 (44.3%)	28 (46.7%)	0.415
SM, n (%)	151 (53.4%)	24 (40.0%)	20 (41.7%)	65 (56.5%)	42 (70.0%)	0.004

*Mann-Whitney test was used for continuous variables and Fisher's exact test was used for categorical variables

^a BMI/ body mass index, SKM Total skeletal muscle area, SMI Skeletal Muscle Index, NAMA Normal Attenuation Muscle Area, LAMA Low Attenuation Muscle Area, SMD Skeletal Muscle Density, TAMA Total Attenuation Muscle Area, IMAT Intermuscular adipose tissue, SAT Subcutaneous Adipose Tissue;

^b SAI Subcutaneous Adipose Index, VAT Visceral adipose tissue, VFI Visceral fat index, MA Myosteatosis, VO Visceral Obesity, SVO Sarcopenic visceral obesity, SM Patients with both Sarcopenia and Myosteatosis

female patients tend to exhibit a relatively higher proportion of SAT, whereas males are more predisposed to visceral compartment (Table S3). Univariate Cox regression revealed NAMA and SMD exerted protective effects on PFS, OS, and CRS. Conversely, nearly all ectopic fat-derived metrics, except for VFI, were identified as adverse prognostic factors for PFS, OS, and CRS in male patients (Fig. 2a–c). Multivariate Cox models confirmed these associations in Model-2 (Table S4). The Model-3 yielded similar trends among male patients after adjustment for BMI, surgical approach, pathological

classification, etc., with VFI consistently associated with poorer survival metrics. In female patients, only SAI demonstrated a protective effect (HR=0.849, $P=0.040$) on CRS within multivariate model (Fig. 2, Table S5). Regarding TNM stage, univariate analyses indicated different fat parameters variably influenced survival across stages. In early-stage, SMD conferred protective effects on PFS (Figure S2a, b) and OS (Figure S2c, d). As tumor progression advanced, NAMA began to show protective associations with PFS (Fig. 3a), while ectopic fat metrics, SMD (Fig. 3b), LAMA (Fig. 3c), and IMAT (Fig. 3d)

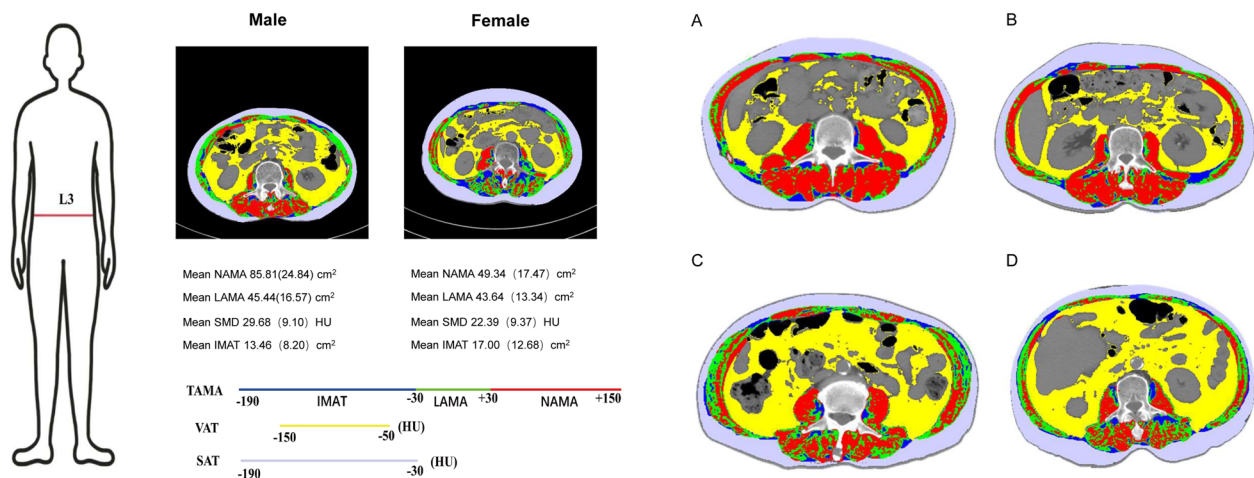


Fig. 1 CT measurement images (at L₃ level) of body composition in patients with gastric cancer. **a** TNM stage I male GC patient: BMI 20.04 kg/m², aged 43y, NAMA: 87.61cm², LAMA: 26.17cm², IMAT: 11.23cm², SMD: 35.62HU, VAT: 47.91cm²; **b** TNM stage II male GC patient: BMI 23.67 kg/m², aged 65y, NAMA: 103.9cm², LAMA: 34.19cm², IMAT: 15.45cm², SMD: 34.59HU, VAT: 85.27cm²; **c** TNM stage III male GC patient: BMI 24.61 kg/m², aged 71y, NAMA: 76.69cm², LAMA: 58.81cm², IMAT: 15.03cm², SMD: 25.44HU, VAT: 153.90cm²; **d** TNM stage IV male GC patient: BMI 22.66 kg/m², aged 76y, NAMA: 52.91cm², LAMA: 51.07cm², IMAT: 19.41cm², SMD: 24.05HU, VAT: 186.4cm²; *MA* Myosteatosis, *SMA* Skeletal Muscle Area, *VAT* Visceral Adipose Tissue, *SAT* Subcutaneous Adipose Tissue, *SMD* Skeletal Muscle Density, *NAMA* Normal Attenuation Muscle Area, *LAMA* Low Attenuation Muscle Area, *IMAT* Intermuscular Adipose Tissue. The figure was generated with Slice-O-Matic Version 6.0 software. The figure illustrated the mean levels of NAMA, LAMA, IMAT, VAT, and SAT among male and female GC patients in the left

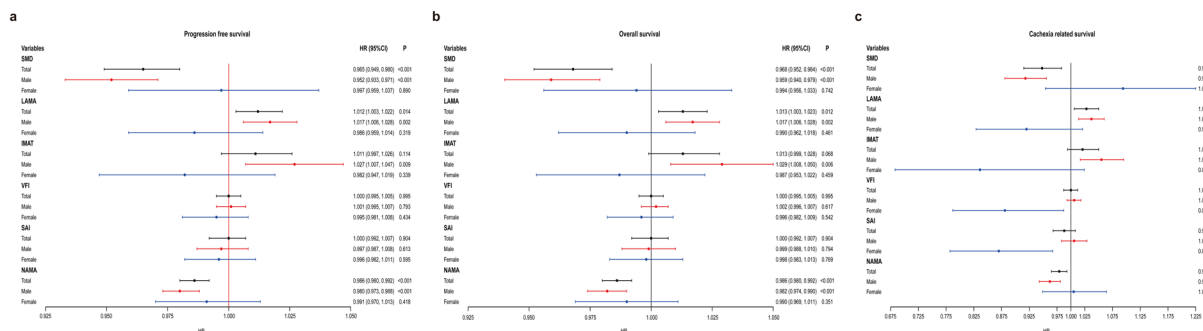


Fig. 2 The forest plot of associations between body composition parameters and survival outcome stratified by sex. **a** The hazard ratio of different body composition parameters and progression-free survival in total, male, and female patients with gastric cancer. **b** The hazard ratio of different body composition parameters and overall survival in total, male, and female patients with gastric cancer. **c** The hazard ratio of different body composition parameters and cancer-related survival in total, male, and female patients with gastric cancer. *SMD* Skeletal Muscle Density, *LAMA* Low Attenuation Muscle Area, *IMAT* Intermuscular Adipose Tissue, *VFI* Visceral Fat Index, *SAI* Subcutaneous Adipose Index, *NAMA* Normal Attenuation Muscle Area, *SMI* Skeletal Muscle Index

emerged as adverse prognostic indicators for PFS. Similar correlations were observed for OS (Fig. 3e–h) and CRS (Table S6). In advanced-stage, IMAT remained an independent predictor of poorer PFS (Figure S3a, b), OS (Figure S3c, d), and CRS, with VFI also linked to poor survival (Table S6). Multivariate models reaffirmed these associations in Model-2 (Table S7). In stage IV, SMD (HR=0.921, $P=0.039$) and LAMA (HR=1.067, $P=0.032$) contributed to CRS. The Model-3 yielded similar trends as Model-2 controlling for surgical approach, hypertension, albumin, neutrophil and lymphocyte

count etc., with nearly all fat-derived parameters consistently associated with poorer survivals, especially CRS (Table S7). This progression pattern suggests a trajectory involving initial deterioration of muscle quality, followed by muscle atrophy and ectopic fat infiltration within muscle, including inter- and intramuscular fat compartments. With the median follow-up exceeding 41 months, consistent trends persisted in male patients across models. Multivariate analyses, adjusting for age, sex, BMI, surgical approach, TNM stage, preoperative and postoperative treatments, smoking, diabetes mellitus, platelet

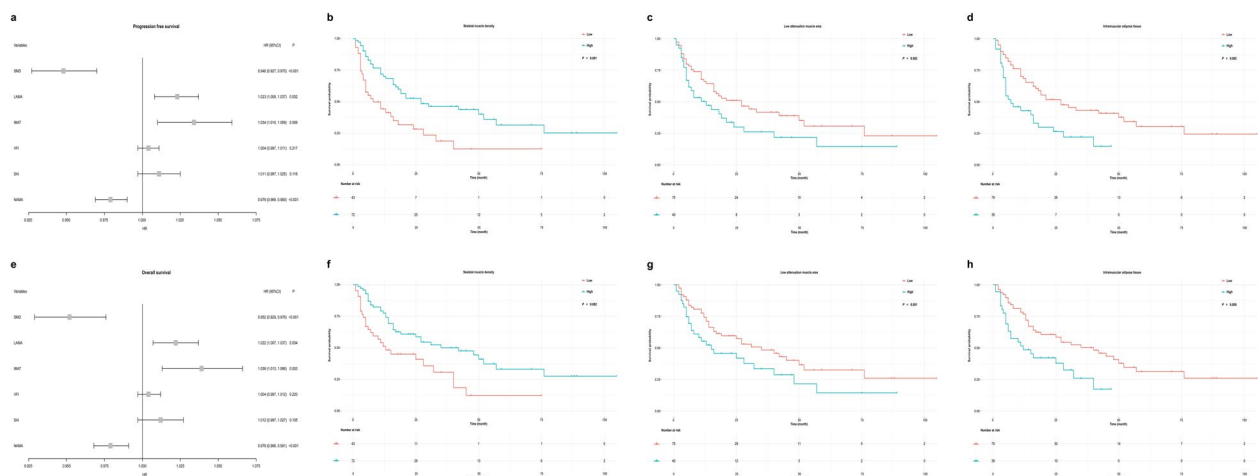


Fig. 3 Prognostic impact of ectopic fat accumulation parameters on progression-free and overall survival in TNM-III patients. **a** The forest plot of associations between body composition parameters and progression-free survival in TNM stage III GC patients; The Kaplan–Meier analysis compared progression-free survival based on SMD (**b**), LAMA (**c**), and IMAT (**d**) in TNM stage III GC patients; **e** The forest plot of associations between body composition parameters and overall survival in TNM stage III GC patients; The Kaplan–Meier analysis compared overall survival based on SMD (**f**), LAMA (**g**), and IMAT (**h**) in TNM stage III GC patients; SMD Skeletal Muscle Density, LAMA Low Attenuation Muscle Area, IMAT Intermuscular Adipose Tissue, VFI Visceral Fat Index, SAI Subcutaneous Adipose Index, NAMA Normal Attenuation Muscle Area, SMI Skeletal Muscle Index

count, albumin, and lymphocyte count, confirmed these associations (Table S8). In patients undergoing non-radical surgery, univariate analysis identified NAMA and SMD as protective factors for PFS and OS, whereas LAMA worsens PFS, OS, and CRS (Table S9). Multivariate models further established LAMA as an independent adverse prognostic factor, with VFI also exerting detrimental effects on this survival (Table S9). Concerning CRS, aside from fat-derived parameters, muscle mass (NAMA, HR=0.942, 95% CI 0.912–0.973, $P<0.001$) and quality (SMD, HR=0.879, 95% CI 0.817–0.946, $P=0.001$) served as significant protective prognostic biomarkers in GC patients. Overall, ectopic fat-related metrics appear to be critical prognostic indicators in GC.

The association between specific body composition phenotype and adverse clinical outcomes in patients with GC

Seven distinct phenotypic subgroups based on body composition were characterized: control (non-sarcopenia-VO-myosteatorsis), sarcopenia, VO, SVO, SM, and SMVO. Kaplan–Meier survival analysis demonstrated myosteatorsis (Fig. 4a–c), SM (Fig. 4d–f), and SMVO phenotype (Fig. 4g–i) significantly worsened survival in GC patients. Furthermore, the SMVO phenotype further worsened PFS (5-year PFS: 27.7% in M, 23.6% in SM, 18.6% in SMVO, versus 40.8% in non-S-O-M, $P=0.002$, Fig. 5a), OS (5-year OS: 28.4% in M, 25.3% in SM, 17.6% in SMVO, versus 42.8% in non-S-O-M, $P=0.004$, Fig. 5b), and CRS (5-year CRS: 78.8% in M, 81.1% in SM, 74.7%

in SMVO, versus 85.9% in non-S-O-M, $P=0.019$, Fig. 5c) than other subgroups. Notably, sarcopenia alone did not significantly impact survivals in GC patients (table S10); however, when combined with myosteatorsis and/or VO, this composite phenotype progressively worsens survival (Fig. 6a–c). These figures indicate ectopic fat distribution phenotypes adversely influence prognosis in GC.

Sensitivity analysis of ectopic adiposity phenotypes in GC patients revealed myosteatorsis-related traits (myosteatorsis, SM, SMVO) are key poorer survival predictors. In males, univariate analysis showed VO adversely affects PFS (VO: HR=1.588, 95% CI 1.088–2.318, $P=0.016$; SVO: HR=1.500, 95% CI 1.026–2.191, $P=0.036$), OS (VO: HR=1.755, 95% CI 1.189–2.591, $P=0.005$; SVO: HR=1.647, 95% CI 1.115–2.433, $P=0.012$), and CRS (VO: HR=2.562, 95% CI 1.090–6.022, $P=0.030$; SMVO: HR=2.752, 95% CI 1.191–6.357, $P=0.018$) in Model-2. In Model-3, further adjustment for BMI, NAFLD, hypertension, etc., revealed, except for sarcopenia, nearly all VO- and myosteatorsis-related phenotypes exacerbated survival (Table S11). Adjusted models confirmed VO and SVO exacerbate survival decline, with SVO significantly reducing OS and SMVO negatively impacting CRS. According to TNM stage, in early stage, ectopic body composition phenotypes did not influence survival. As tumor progression advanced, myosteatorsis, VO, SVO, and SMVO significantly decreased OS and PFS (Table S12). In stage IV, VO remained an independent prognostic phenotype for OS. Multivariate models affirmed VO as a significant predictor for

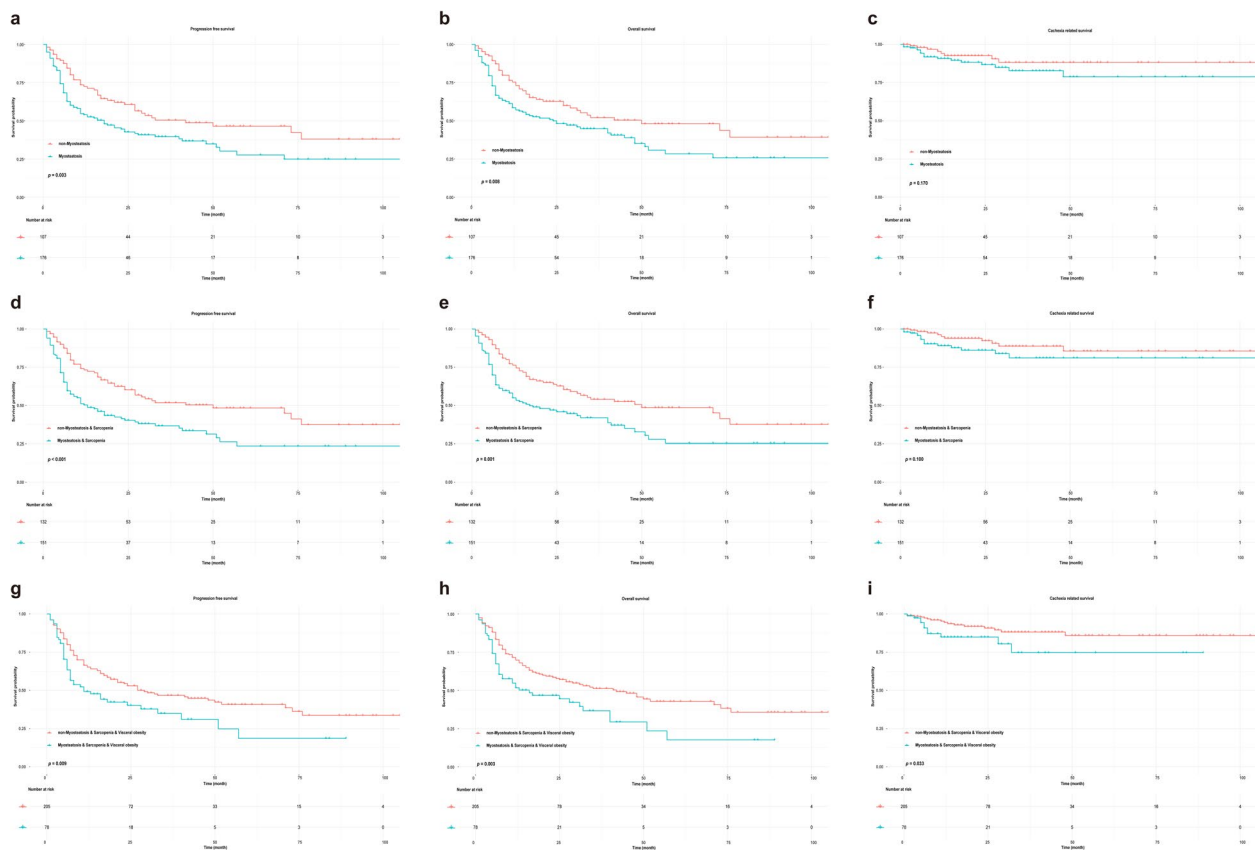


Fig. 4 Kaplan–Meier analysis of the relationship between different body composition phenotypes and survival outcomes. The Kaplan–Meier analysis of myosteatoses and survival outcomes, including progression-free survival (a), overall survival (b), and cachexia-related survival (c); The Kaplan–Meier analysis of SM and survival outcomes, including progression-free survival (d), overall survival (e), and cachexia-related survival (f); The Kaplan–Meier analysis of SMVO and survival outcomes, including progression-free survival (g), overall survival (h), and cachexia-related survival (i). The figures were generated with R software (Version 4.3.1). S Sarcopenia, SM Patients with both sarcopenia and myosteatoses, SMVO Patients with sarcopenia, myosteatoses, and visceral obesity

PFS and OS in Model-2 (Table S12). Additionally, SVO and SMVO contributed to worsen OS and CRS. Further adjustments for histopathological classification, alcohol consumption, NAFLD, etc., in Model-3 indicated VO-derived phenotypes were associated with decreased survival (Table S12). Collectively, VO-related metrics appear to be critical prognostic indicators in GC. With the median follow-up exceeding 41 months, nearly all phenotypes, except sarcopenia, worsened PFS and OS. When combined with sarcopenia, myosteatoses and VO phenotypes further amplified adverse survival (myosteatoses: HR=1.886, 95% CI 1.241–2.866, $P=0.003$; SM: HR=1.973, 95% CI 1.315–2.962, $P=0.001$; SMVO: HR=2.106, 95% CI 1.378–3.219, $P=0.001$, Table S13). In Model-2, VO-related phenotypes (VO and SVO) continued to exhibit harmful effects on PFS and OS. Further adjustment for BMI, hypertension, pathological classification, etc., in Model-3 confirmed Model-2 associations. Regarding CRS, SMVO consistently

worsen survival across all models. In non-radical surgery patients, myosteatoses and SM were primary adverse phenotypes, with SM independently predicting shorter OS (Table S14). Multivariate models reinforced SM as an independent adverse prognostic phenotype, with SVO and SMVO also exerting detrimental effects on CRS (Table S14). Overall, sarcopenia alone does not impact survival, but its combination with abnormal fat phenotypes significantly deteriorate prognosis.

Discussion

Our study reveals gastric carcinoma patients exhibit atypical body composition, notably hidden obesity (SO) from ectopic fat (LAMA, IMAT, VFI), linked to poor prognosis. Conventional metrics, like BMI and body fat%, are inadequate for detecting IMAT or intramyocellular lipids (IMCL, LAMA) in GC patients, as the “Low/Normal-Weight” Obesity phenotype often presents with a lean or normal external morphology. Our data

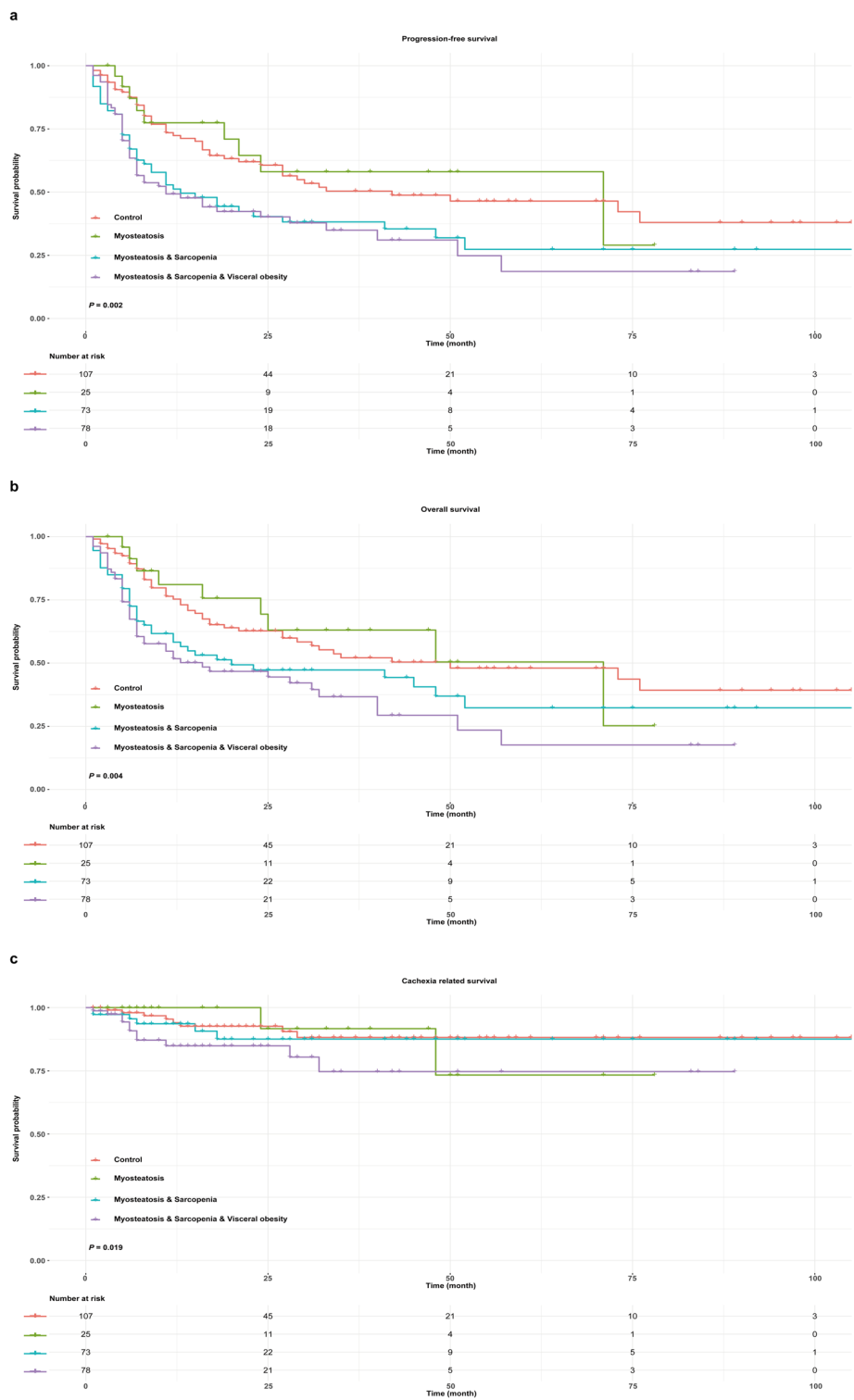


Fig. 5 Kaplan–Meier analysis of the relationship between myosteatorsis-derived phenotypes and survival outcomes. **a** The Kaplan–Meier analysis compared progression-free survival based on myosteatorsis, sarcopenia & myosteatorsis, and sarcopenia & myosteatorsis & visceral obesity body composition phenotypes; **b** The Kaplan–Meier analysis compared overall survival based on myosteatorsis, sarcopenia & myosteatorsis, and sarcopenia & myosteatorsis & visceral obesity body composition phenotypes; **c** The Kaplan–Meier analysis compared cachexia-related survival based on myosteatorsis, sarcopenia & myosteatorsis, and sarcopenia & myosteatorsis & visceral obesity body composition phenotypes. The figures were generated with R software (Version 4.3.1)

suggest muscle mass (NAMA) and quality (SMD) serve as protective prognostic factors after multiple covariate adjustments. Multivariate analyses identified all adiposity-related parameters, including LAMA, IMAT, and VFI as negative indicators for survival. Sensitivity analyses confirmed these associations, with elevated IMAT, LAMA, and VFI linked to decreased survival, whereas higher SMD exhibited protective effects. Intermuscular (IMAT), intramuscular (LAMA), and visceral fat (VFI) significantly influence prognosis in advanced GC (TNM III–IV), with ectopic fat persisting even in cachexia. Our findings also indicate SVO markedly reduces PFS, OS, and CRS; when combined with myosteatorsis (SMVO), this combined phenotype further exacerbated CRS beyond the effects of individual phenotypes. Sarcopenia impacts survival only when coupled with abnormal adipose deposition phenotypes.

A key strength of this study is that it is the first to explicitly demonstrate that BMI has become an unreliable metric for classifying obesity in GC context. Contrary to the common perception that cancer patients suffer from poor nutrition or cachexia, obesity is prevalent among this population [37]. The most popular clinical indicator to judge obesity is BMI; however, BMI exhibited poor sensitivity for identifying obesity [38]. In terms of cancer risk, Renahan, et al. (2008) has suggested anthropometric measures rather than BMI, such as waist-to-hip ratio or waist circumference, are better measures for adiposity, especially central adiposity [39]. Central adiposity, independent of BMI, may be particularly relevant to cancer development as VAT may be more metabolically active than subcutaneous adipose tissue [40]. Importantly, BMI or anthropometric measures does not reflect the physical function accurately, because of the ratio of fat/muscle mass may vary under the same BMI. Identifying low muscle mass in obese cancer patients is difficult, as BMI's limited ability to differentiate fat distribution, as intermuscular adipose tissue (IMAT), is critical [41, 42]. The low/normal-weight obesity-related malignancies, GC, often present an outwardly "normal" appearance due to hidden adipose deposits, like intra- and intermuscular adipose tissue, which obscure the consequences of muscle wasting [43]. Our research indicates that the incidence

of sarcopenia among GC patients exceeds 80%, which was consistent with Australia research [44], primarily due to skeletal muscle being the principal target tissue for tumor-induced catabolic processes [45]. However, our data also found that it is not just BMI, all muscle-related parameters, including NAMA, have decreased, while fat-related parameters, including LAMA, IMAT, SAT, and SMD, have shown aggregation in stage IV patients. Skeletal muscle functions as a "metabolic organ" regulating immune responses, nutrient metabolism, and treatment tolerance, while excess ectopic fat drives chronic inflammation and metabolic perturbation that promotes tumor angiogenesis and invasion [43]. Understanding variations in body composition under the same BMI may provide new insights on the obesity paradox and deliver important clinical and public health messages about healthy body composition beyond BMI [46]. Therefore, BMI is inadequate for obesity classification in GC patients due to its inability to distinguish between muscle and fat mass, account for fat distribution, and avoid confounding from cancer-related weight changes. Body composition analysis provides a more precise assessment of pathophysiologically relevant phenotypes and offers stronger prognostic insights.

Ectopic adipose accumulation enhances GC progression, necessitating lipolytic mobilization from SAT to meet energy demands, while residual visceral and intramuscular lipids contribute to abnormal fat redistribution [47]. Our data indicate that subcutaneous adiposity confers a protective effect on cachexia-related mortality and PFS in female and early-stage gastric carcinoma patients, respectively. Females tend to exhibit a relatively higher proportion of SAT, particularly in the gluteofemoral region, whereas males are more predisposed to VAT, which delineates the sex-based disparities in oncogenic vulnerability between sexes [48]. In men, none of BMI, waist circumference, and WHR were related to the incidence of esophageal and gastric cancer, while, in women, all BMI, waist circumference, and WHR were associated with significant reductions in the risk instead of increasing the risk for esophageal squamous cell carcinoma [48]. Thus, this biological rationale for sex generalizability indicated the core finding of our study that ectopic fat

(See figure on next page.)

Fig. 6 Kaplan–Meier analysis of the relationship between seven body composition phenotypes and survival outcomes. **a** The Kaplan–Meier analysis compared progression-free survival based on control, myosteatorsis, sarcopenia, visceral obesity, sarcopenia & myosteatorsis, sarcopenic visceral obesity, and sarcopenia & myosteatorsis & visceral obesity body composition phenotypes; **b** The Kaplan–Meier analysis compared overall survival based on control, myosteatorsis, sarcopenia, visceral obesity, sarcopenia & myosteatorsis, sarcopenic visceral obesity, and sarcopenia & myosteatorsis & visceral obesity body composition phenotypes; **c** The Kaplan–Meier analysis compared cachexia-related survival based on control, myosteatorsis, sarcopenia, visceral obesity, sarcopenia & myosteatorsis, sarcopenic visceral obesity, and sarcopenia & myosteatorsis & visceral obesity body composition phenotypes. The figures were generated with R software (Version 4.3.1)

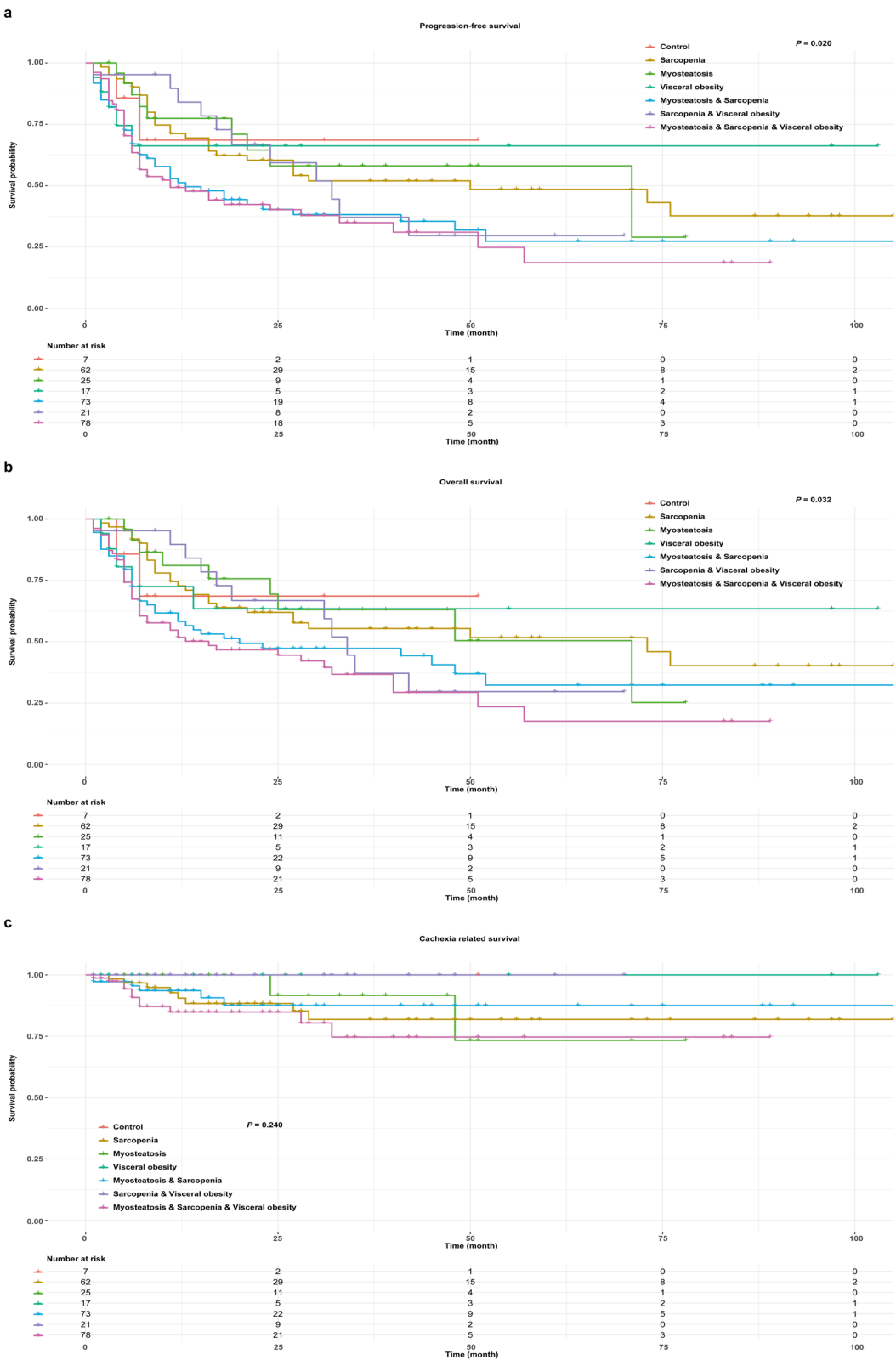


Fig. 6 (See legend on previous page.)

accumulation parameters, like VFI, consistently associated with poorer survival metrics in male patients. Over time, these distinct adipose distribution patterns can induce variations in metabolic pathways, inflammatory cytokine profiles, and insulin sensitivity between sexes, thereby influencing the differential risk profiles and clinical phenotypes of metabolic disorders like type 2 diabetes mellitus and cancer-associated metabolic syndromes [11]. Notably, when excess lipids from SAT are redistributed to skeletal muscle or visceral tissue, a deleterious cycle (known as the “Metabaging Cycle” [11]) is initiated locally at the deposition site, characterized by chronic inflammation, IR, disrupted fatty acid oxidation, increased ROS, and mitochondrial dysfunction. This local myosteatosis and IR can trigger systemic feedback, elevating lipolysis and free fatty acids, exacerbating hyperlipidemia, lipotoxicity, and inflammaging, which impair lipid metabolism and insulin signaling, leading to muscle atrophy and further adipose accumulation [49]. Prior studies have identified ectopic lipid deposition in muscle as a hallmark of metabolic disorders like diabetes mellitus [50]. Our findings extend this knowledge by demonstrating patients with advanced GC exhibit elevated fasting blood glucose and higher prevalence of diabetes mellitus. Myosteatosis is an independent tumor-related factor, linked to reduced overall and disease-free survival, and impairs immune function, facilitating tumor immune evasion and therapy resistance [44, 51, 52]. VAT acts as an endocrine organ influencing systemic immunity and metabolism [53]; excess VAT induces chronic inflammation and IR. Previous research has established links between VO and increased breast and esophageal adenocarcinoma risk [54]. Higher visceral-to-subcutaneous fat ratios are associated with accelerated tumor progression and decreased survival, suggesting visceral fat exacerbates treatment-related inflammation and worsens clinical outcomes [55]. Our findings underscore the complex relationship between VO and survival, indicating the increased mortality associated with obesity is predominantly driven by visceral fat accumulation. Consequently, subcutaneous fat depletion emerges as a primary determinant of mortality, whereas adipose redistribution correlates with tumor progression, independent of overall BMI. Sexual dimorphism on adipose tissue distribution must be taken into account when formulating intervention strategies for GC patients.

Ectopic adipose accumulation phenotypes, myosteatosis, and VO can coexist with sarcopenia, collectively termed SO, serving as independent prognostic indicators across various cancers regardless of BMI [44]. Our data demonstrate sarcopenia often occurs concurrently with myosteatosis and/or visceral obesity (SMVO), with gastrointestinal cancer patients exhibiting higher adverse

survival risk, possibly reflecting tumor-related ectopic fat deposition timing. Supporting this, Stephens et al. [56] observed increased intramyocellular lipid content (LAMA) with decreasing BMI and weight loss intensified in upper gastrointestinal cancer patients, potentially reflecting malnutrition or advanced cancer cachexia. Variations in anthropometric parameters and body composition suggest mechanisms underlying IMAT/LAMA accumulation and reduced muscle attenuation (SMD) may serve as markers of metabolic risk factors [57], which likely coexists with obesity-associated meta-inflammation, known to impair immune and inflammatory pathways [58]. Although severe cachexia is less common in the current era of rising obesity prevalence, the role of pro-inflammatory cytokines in promoting IMAT expansion during tumor progression warrants further consideration [47]. Sarcopenia alone has limited systemic impact on prognosis; muscle atrophy reduces myokine secretion, impairing the anti-inflammatory buffer and shifting the systemic milieu toward a mild, chronic inflammatory state characterized by elevated levels of TNF- α and TWEAK [11]. While sarcopenia and fat accumulation independently contribute to inflammation, their coexistence establishes a pro-inflammatory feedback loop [11] that intensifies tumor-promoting microenvironments, forming the fundamental biological basis for worsened prognosis. Rollins KE et al. [59] also found no survival difference between sarcopenic and non-sarcopenic patients ($P=0.779$), but overweight/obese sarcopenic patients had lower survival ($P=0.013$). Furthermore, univariate Cox regression identified myosteatosis, rather than sarcopenia, as an independent predictor of decreased survival, with myosteatosis associated with elevated systemic inflammation, anemia, and renal impairment, whereas sarcopenia was not. The systemic inflammatory response, as indicated by various inflammation-based prognostic scores, has been validated as a significant predictor of poor OS and DFS [60]. Sarcopenia and fat accumulation together exacerbate metabolic dysfunction: (1) Visceral fat-derived FFAs compete with tumor cells for glucose, but tumor cells preferentially use FFAs via β -oxidation (a more efficient energy source for proliferation), effectively “hijacking” fat-derived energy to accelerate growth [11]; (2) Myosteatosis impairs muscle insulin sensitivity, reducing glucose uptake by muscle cells and further diverting glucose to tumors [11]. Additionally, excess fat mass increases hepatic gluconeogenesis, maintaining high blood glucose levels that support tumor metabolism. While these mechanisms may appear straightforward, understanding the manifestation of myosteatosis is complex, given the heterogeneity in BMI, body composition, baseline physical fitness, tumor progression, and inflammatory status

within this population. In essence, sarcopenia alone does not significantly impact survival because the body retains partial capacity to compensate (via fat energy mobilization, residual anti-inflammatory signaling). However, when combined with fat accumulation, three synergistic mechanisms, exacerbated pro-inflammatory and metabolic disruption loops, create an irreversible “pathophysiological cascade” that drives worse prognosis. We propose a pathophysiological model posits sarcopenia results from chronic inflammation and tumor progression, while ectopic fat may initiate obesity-related oncogenesis, inducing inflammation and IR, creating a tumor-permissive microenvironment that worsens with disease progression, leading to muscle wasting. These findings underscore the significance of studying muscle and adipose phenotypes, SO, as key prognostic factors, where their coexistence can synergistically deteriorate outcomes.

Despite the significant findings, certain limitations must be acknowledged. Firstly, like all observational studies, it may face unmeasured confounding variables. Although we employed a surgical approach as the temporal benchmark for intervention, incorporating preoperative, intraoperative, and postoperative treatments metrics as covariates in the model, and performing sensitivity analyses across treatment modalities, there remains a potential confounding effect of treatment modality on the study. Future research will focus on a single primary treatment modality, extract computed tomography data at various treatment time points, and perform a focused analysis of the correlation between body composition parameters and tumor prognosis. We recognize that retrospective observational studies are inherently susceptible to selection bias and incomplete data collection. To address this, we established strict inclusion criteria conducted multiple sensitivity analyses and adjusted for relevant confounders in multivariate regression models to control for potential biases. Since our patient population was derived from a single tertiary care center, selection bias related to hospital choice, namely, hospital selection bias, may influence generalizability. Future multi-center studies will be conducted to validate these associations across diverse populations. Missing data primarily affected two domains: body composition metrics, due to sub-optimal or absent CT imaging, and follow-up information, such as survival status and cause of death, due to loss to follow-up. We employed censoring techniques and sensitivity analyses on cases with follow-up durations exceeding 41 months to mitigate attrition bias. Secondly, we defined sarcopenia, VO, and myosteatosis using cut-point values validated in previous report, which underscores the lack of standardized criteria

and definitive cutoffs from Chinese tumor patients’ stratification by sex. Third, this study constitutes a single-center retrospective analysis with relatively modest sample size. The robustness of our findings is constrained by the limited dataset, particularly given the stratification of patients into multiple subgroups based on varying phenotype combinations and sex. Owing to the retrospective study design, our screening revealed a higher prevalence of dual-tumor coexistence among female gastric carcinoma patients. Consequently, only 59 female patients meeting the inclusion and exclusion criteria were incorporated into this research, which may be also attributed to the influence of sex on the incidence of gastrointestinal neoplasms. Future studies with larger samples, stricter criteria, and standardized thresholds are needed to clarify the link between adipose tissue distribution and GC progression.

In summary, CT-derived ectopic fat accumulation parameters/phenotypes demonstrate superior prognostic value than BMI measurements, providing more precise identification of survival outcomes risk stratification for GC patients, especially for male patients, which directed developing targeted intervention strategies for GC patients. Understanding the different contributions of lean body mass and fat mass to BMI may provide new insights on the obesity paradox and deliver important clinical and public health messages about healthy body composition beyond BMI. Therefore, maintaining muscle mass and appropriate body composition is a significant step toward improving survival in GC patients. In the future, the accuracy of the prediction may be improved by using multidimensional integrated analyses based on CT radiomics, body composition, and markers of inflammation.

Abbreviations

CI	Confidence interval
GC	Gastric cancer
HR	Hazard ratio
SKM	Skeletal muscle mass
SMA	Skeletal muscle area
SMI	Skeletal muscle index
VAT	Visceral adipose tissue
VFI	Visceral fat index
SAT	Subcutaneous adipose tissue
SAI	Subcutaneous adipose index
SMD	Skeletal muscle density
NAMA	Normal attenuation muscle area
LAMA	Low attenuation muscle area
IMAT	Intermuscular adipose tissue
VO	Visceral obesity
SVO	Sarcopenic visceral obesity
SM	Sarcopenia and myosteatosis
SMVO	Sarcopenia, myosteatosis, and VO (SMVO)
SII	Systemic inflammation index
NLR	Neutrophil-to-lymphocyte ratio
PFS	Progression-free survival
OS	Overall survival

CRS Cachexia-related survival
 TNM Tumor node metastasis
 IR Insulin resistance
 ROS Reactive oxygen species

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s40001-025-03251-6>.

Supplementary material 1. Supplemental fig 1 The flowchart of participants.

Supplementary material 2. Supplemental fig 2 Prognostic impact of skeletal muscle density on progression-free survival and overall survival in TNM stage I GC patients. (a) The forest plot of associations between body composition parameters and progression-free survival in TNM stage I GC patients; (b) The Kaplan–Meier analysis compared progression-free survival based on SMD in TNM stage I GC patients; (c) The forest plot of associations between body composition parameters and overall survival in TNM stage I GC patients; (d) The Kaplan–Meier analysis compared overall survival based on SMD in TNM stage I GC patients. SMD: Skeletal Muscle Density, LAMA: Low Attenuation Muscle Area, IMAT: Intermuscular Adipose Tissue, VFI: Visceral Fat Index, SAI: Subcutaneous Adipose Index, NAMA: Normal Attenuation Muscle Area, SMI: Skeletal Muscle Index.

Supplementary material 3. Supplemental fig 3 Prognostic impact of intermuscular adipose tissue on progression-free survival and overall survival in TNM stage IV GC patients. (a) The forest plot of associations between body composition parameters and progression-free survival in TNM stage IV GC patients; (b) The Kaplan–Meier analysis compared progression-free survival based on IMAT in TNM stage IV GC patients; (c) The forest plot of associations between body composition parameters and overall survival in TNM stage IV GC patients; (d) The Kaplan–Meier analysis compared overall survival based on IMAT in TNM stage IV GC patients. SMD: Skeletal Muscle Density, LAMA: Low Attenuation Muscle Area, IMAT: Intermuscular Adipose Tissue, VFI: Visceral Fat Index, SAI: Subcutaneous Adipose Index, NAMA: Normal Attenuation Muscle Area, SMI: Skeletal Muscle Index.

Supplementary material 4. Supplemental table 1. Basic characteristics of participants.

Supplementary material 5. Supplemental table 2. Multivariate analysis between body composition parameters and survival outcome in GC patients.

Supplementary material 6. Supplemental table 3. Body composition features of participants between sex.

Supplementary material 7. Supplemental table 4. Multivariate analysis between body composition parameters and survival outcome in male GC patients.

Supplementary material 8. Supplemental table 5. Multivariate analysis between body composition parameters and survival outcome in female GC patients.

Supplementary material 9. Supplemental table 6. Univariate analysis between body composition parameters and survival outcome in GC patients based on the TNM stage.

Supplementary material 10. Supplemental table 7. Multivariate analysis between body composition parameters and survival outcome in GC patients after adjusting for covariates based on the TNM stage.

Supplementary material 11. Supplemental table 8. The association between body composition parameters and survival outcome in GC patients based on the median follow-up.

Supplementary material 12. Supplemental table 9. The association between body composition parameters and survival outcome in GC patients within the patients with conservative treatment.

Supplementary material 13. Supplemental table 10. The association between body composition phenotype and survival outcome in GC patients.

Supplementary material 14. Supplemental table 11. The association between body composition phenotype and survival outcome in male GC patients.

Supplementary material 15. Supplemental table 12. The association between body composition phenotype and survival outcome in GC patients based on the TNM stage.

Supplementary material 16. Supplemental table 13. The association between body composition phenotype and survival outcome in GC patients based on the median follow-up.

Supplementary material 17. Supplemental table 14. The association between body composition phenotype and survival outcome in GC patients within the patients with conservative treatment.

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Author contributions

KY, QL and C-WL: Conceptualization; C-WL: Writing -original draft preparation, review and editing; YL, ZKW, YX, YSN, and YZ: Material preparation, data collection and analysis; C-WL and YL reviewed the data; YZ performed the data analyses; KY and YP: Supervision. All authors read and approved the final manuscript.

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Data availability

Data are not publicly available due to their containing information that could compromise the privacy of research participants. Summary data can be made available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was rigorously reviewed and approved by the Human Ethics Committee of the Peking Union Medical College Hospital (No. HS889). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee. Specifically, this observational study was registered in August 2016 (NCT02873676) at www.clinicaltrials.gov. The TPLCMS protocol was approved by the Human Ethics Committee of the CHTU (No. IRB2021-037-02). All participants provided written informed consent for data collection and storage. Participants freely completed the questions after signing an informed consent form, ensuring their right to withdraw at any time. All data collected from participants was treated with complete privacy and anonymity. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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