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ARTICLE

Impact of visceral fat on surgical complications and long-term survival of patients with gastric cancer after radical gastrectomy

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Abstract

Background/objectives The aim of this study was to examine the impact of visceral fat on surgical complications and long-term survival for patients undergoing radical gastrectomy.

Subjects/methods From 2009 to 2013, 859 patients who underwent curative resection for gastric cancer were enrolled from a prospectively maintained database. Visceral fat area (VFA) was assessed by preoperative CT scans. Patients were divided into two groups by VFA. Perioperative variables and postoperative outcomes were compared between the high VFA group and low VFA group. Univariable and multivariable analysis were performed to investigate independent risk factors of postoperative complications and survival.

Results Some 859 patients were included in the study, 308 of whom were classified as high VFA. High VFA was correlated with advance age ($P = 0.020$), higher albumin levels ($P = 0.001$), hemoglobin levels ($P < 0.05$), ASA grade ($P = 0.043$) and Charlson Comorbidity Index ($P = 0.004$). Relative to patients with low VFA, those with high VFA had longer surgical durations ($P = 0.004$), higher rate of postoperative complications ($P = 0.004$), and longer hospital stays ($P = 0.004$). High VFA was identified as the only determinant for surgical complications by logistic regression analysis (OR, 2.236, 95% CI, 1.537–3.254; $P < 0.001$). Cox proportional hazards regression revealed no correlation between VFA and overall survival (OS) or disease-free survival (DFS).

Conclusions Increased VFA independently predicts surgical complications in patients after gastrectomy. However, VFA is not a prognostic biomarker of OS or DFS in patients with gastric cancer.

Introduction

Obesity is a growing health problem due to the improvement of life standard and changes of lifestyle [1, 2]. Substantial epidemiological evidences demonstrate that obesity is a risk factor for diabetes mellitus, cardiovascular disease, and the development of several types of cancer [3]. Body mass index (BMI) has been widely applied as an anthropometric index of obesity, because of its reliability and objectivity [3]. However, BMI cannot consistently reflect body adipose tissue accumulation since the fat distribution varies greatly between different individuals.

Recently, there is an increasing interest in the relationship between body composition and clinical outcomes [4]. Specifically, the ratio between visceral obesity and lean mass, especially skeletal muscle was strongly correlated

Su-Lin Wang and Liang-Liang Ma have contributed equally to this work.

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with physique status and mortality in patients with cancer [5]. However, the predictive value of visceral obesity has not yet been well recognized by most clinicians. Compared with BMI, visceral fat is a more accurate parameter to reflect the dysfunctional adipose tissue, and it is considered to be associated with various obesity-related comorbidities [6, 7]. Biologically, visceral fat is related to "metabolic syndrome" [8] and indicates an altered intra-abdominal environment [9]. It has been suggested that visceral fat may be more optimal than BMI for the evaluation of surgical outcomes [10].

In gastric cancer specifically, visceral fat accumulation has been examined to be associated with higher rate of postoperative complications after gastric cancer surgery, including pancreatic fistula formation [11], intra-abdominal infectious complications, and surgical site infection [12]. In addition to these surgical complications, medical complications are also common and harmful after gastrectomy. An important area of future strategy for improving surgical outcomes is stratification of postoperative complications [13]. However, impact of visceral fat on medical complications has been rarely reported. Moreover, up to date, no study has assessed the impact of visceral fat on long-term prognosis after radical resection for gastric cancer.

In this study, we measured the visceral fat area (VFA) by a preoperative CT scan, and then evaluated the predictive ability of visceral fat on clinical outcomes after gastrectomy, specifically with regard to postoperative complications and long-term prognosis.

Materials and methods

Patients

From 2009, all clinical parameters of patients undergoing gastric cancer surgery had been prospectively collected and archived in an electronic database at the Department of Surgery, the First Affiliated Hospital of Wenzhou Medical University. Consecutive patients with primary gastric cancer who received radical gastrectomy and had abdominal computed tomography (CT) image within 4 weeks before surgery were included in this study. The therapy was based on the Japanese Gastric Cancer Treatment Guideline 2010 (version 3) [14]. The study protocol was approved by institutional review board at Wenzhou Medical University.

Follow-up

All patients were evaluated in the outpatient department within the first month after surgery. After that, patients were assessed every 3 months during the first 2 year and every 6 months thereafter. Follow-up projects included a physical examination, blood tests, and necessary imaging examinations. The postoperative course, morbidity, mortality, and recurrence were collected and recorded by clinical research team in the database routinely. The last follow-up date was September 2016.

Preoperative visceral fat measurement

Visceral fat area at the plane of the third lumbar was measured from the latest preoperative CT scan. The areas covered by visceral fat were calculated within densities ranging from −150 to −50 Hounsfield units [15], which admitted visceral fat, but excludes bone, muscle, blood vessels, and other intra-abdominal organs. All slices were evaluated by an image workstation with dedicated volume assessment software (version 3.0; INFINITT Healthcare Co., Ltd). CT images were analyzed by two radiologist, who were blinded to patients' information. Visceral fat area $\geq 100\,cm^2$ in both sexes was defined as high VFA [16].

Data collection

The following parameters were prospectively collected and maintained in a gastric cancer database: (1) patient characteristics, including age, gender, BMI, hemoglobin content, plasma albumin content, ASA grade, Charlson Comorbidity Index, history of abdominal surgery, pathological type, tumor size, TNM stage; (2) operative and treatment characteristic, including operative durations, intraoperative bleeding, transfusion, postoperative chemotherapy, surgical procedures; and (3) postoperative outcomes, including postoperative complications, length of postoperative hospital stays, overall survival (OS) and disease-free survival (DFS). Postoperative complications were defined as those categorized as Grade II or above according to the Clavien–Dindo classification [17] within 30 days of surgery. In addition, postoperative complications were separated into two categories: surgical complications and medical complications. If one patient experienced more than one complication with unequal grade, the classification of surgical and medical complications was based on the highest complication. If one patient experienced more than one complication with equal grade, the classification of surgical and medical complications was based on assessment of the timing of the complications (which comes first?). Overall survival was defined as the period from the date of operation to the date of death due to any cause and was censored at the last follow-up. Disease-free survival was defined as the period from the date of operation to the date of relapse or death due to non-tumor causes and was censored at the last verifiable disease-free date.

Statistical analysis

The normal distribution data were displayed as mean and standard deviation (SD), and skewed continuous data were displayed as median and interquartile range (IQR). Categorical variables were displayed as numbers and percentages. The Student *t* test and Mann–Whitney U test were used for normally and nonnormally distributed continuous data respectively. The chi-square test was used to compare categorical variables. Cumulative overall survival and disease-free survival were assessed using Kaplan–Meier model, and log-rank test was used to evaluate differences between curves. Univariate analysis was initially performed to find potential risk factors. Any variables identified with $p < 0.10$ in univariate analysis were progressed to multivariate analysis using logistic regression or Cox proportional hazards regression. All statistical analyses were performed using SPSS version 21.0. *P*-values were considered statistically significant when < 0.05.

Result

Patients

The patients' characteristics are listed in Table 1. Because of the lack of available preoperative CT images, 212 patients were excluded. There is no significantly different of clinical features, postoperative complications, or long-term survival between the excluded patients and the patients in the analytic cohort. Ultimately, a total of 859 patients who underwent radical gastrectomy between 2009 and 2013 were involved for analysis. The median follow-up time for these patients was 60.9 months.

Patients were subsequently divided into high VFA group and low VFA group according to their preoperative CT scans. The median VAF was 143.55 cm^2 in the high VFA group and 48.19 cm^2 in the low VFA group ($P = 0.37$). Visceral fat obesity was identified in 308 patients (35.86%); it was more frequent in elderly patients (66.00 vs. 63.00, $P = 0.020$) compared with younger patients; and it was associated with higher BMI (24.19 vs. 20.52 kg/m^2, $P < 0.001$), higher albumin levels (40.90 vs. 39.60 g/L, $P = 0.001$), higher hemoglobin levels (125.00 vs. 121.00 g/L, $P < 0.001$), higher ASA grade ($P = 0.043$), and higher Charlson Comorbidity Index ($P = 0.004$). When comparing the high VFA group and low VFA group for intraoperative characteristics, we found patients with high visceral fat content were more likely to have longer operative durations (200 vs. 195 min, $P < 0.001$). There are more cases of patients who had intraoperative bleeding more than 300 ml in high VFA group (N = 115, accounted for 37.3%) than in low VFA group (N = 175, accounted for 31.8%), but this difference was not statistically significant. No significant differences were discovered in other clinical parameters between the two groups, as showed in Table 1.

Short-term outcomes

The details of short-term outcomes were list in Table 2. A total of 221 patients developed at least one complication within 30 days after surgery, for an overall morbidity of 25.7%. The rate of total postoperative complications was 34.1% ($N = 105$) for patients with high VFA and 21.1% ($N = 116$) for patients with low VFA ($P < 0.001$). Postoperative complications were then separated into two categories: surgical complications and medical complications. Our results showed that high VFA was correlated with higher risk of surgical complications ($P < 0.001$). On the contrary, no significant difference was found for medical complication rate between the two groups ($P = 0.340$). Moreover, patients with high VFA had longer duration of hospital stay compared with patients with low VFA (12.00 vs. 10.00 d, $P < 0.001$).

In the multivariate analyses of postoperative complications, age ≥ 75, high VFA, high Charlson Comorbidity Index and low albumin levels were found as independent risk factors for total postoperative complications. Age ≥ 75, high Charlson Comorbidity Index, low albumin levels and operative durations ≥ 210 min were identified as independent risk factors for medical complications, while only high VFA was identified as a risk factor for surgical complications (OR, 2.236, 95% CI, 1.537–3.254; $P < 0.001$). The factors related to surgical complications are listed in Table 3.

Long-term outcomes

In all 859 patients, the 1-, 3-, and 5-year OS rates were 85.0%, 61.9%, and 52.2% respectively; the 1-, 3-, and 5-year DFS rates were 79.4%, 60.2%, and 55.5% respectively. Figure 1 and Fig. 2 showed the Kaplan—Meier curve for OS and DFS in the two groups. The 1-, 3-, and 5-year OS rates were 86.0%, 64.9%, and 54.9% respectively, in the high VFA group, and were 84.2%, 60.1%, and 50.4%, respectively, in the low VFA group. The 1-, 3-, and 5-year DFS rates were 80.6%, 61.5%, and 56.0%, respectively, in the high VFA group, and were 78.7%, 59.3%, and 55.3%, respectively, in the low VFA group. No statistical differences in OS or DFS were detected between the two groups (log-rank, $P = 0.158$, 0.652, respectively). In the Cox proportional hazards regression analysis, age ≥ 75, BMI, type of resection, TNM stage and chemotherapy were independent predictors of OS; TNM stage, type of resection and chemotherapy were independent predictors of DFS (Table 4).

Table 1 Patient demographic and clinical characteristics

Factors	All (n=859)	High VFA group (n=308)	Low VFA group (n=551)	P
Age, median (IQR), y	64.00 (16.00)	66.00 (16.00)	63.00 (16.00)	0.020[a]
Gender				0.737
Female	187 (21.8)	69 (22.4)	118 (21.4)	
Male	672 (78.2)	239 (77.6)	433 (78.6)	
BMI, mean (SD), kg/m^2	21.83 (3.01)	24.19 (2.62)	20.52 (2.33)	<0.001[a]
Albumin, median (IQR), g/L	40.00 (6.55)	40.90 (6.5)	39.60 (6.65)	0.001[a]
Hemoglobin, median (IQR), g/L	122.00 (34.00)	125.00 (33.50)	121.00 (35.00)	<0.001[a]
VFA, median (IQR), cm^2	76.19 (86.13)	143.55 (60.39)	48.19 (48.69)	<0.001[a]
ASA grade				0.043[a]
I	64 (7.5)	18 (5.8)	46 (8.3)	
II	695 (80.9)	244 (79.2)	451 (81.9)	
III	100 (11.6)	46 (14.9)	54 (9.8)	
Charlson Comorbidity Index				0.004[a]
0	677 (78.8)	224 (72.7)	453 (82.2)	
1	132 (15.4)	59 (19.2)	73 (13.2)	
≥ 2	50 (5.8)	25 (8.1)	25 (4.5)	
Intraoperative bleeding ≥ 300 ml				0.097
No	569 (66.2)	193 (62.7)	376 (68.2)	
Yes	290 (33.8)	115 (37.3)	175 (31.8)	
Operative durations, median (IQR), min	195.00 (65.00)	200.00 (60.00)	195 (70.00)	<0.001[a]
No. of resected LN, median (IQR)	19.00 (13.00)	18.00 (11.00)	19.00 (14.00)	0.563
No. of positive LN, median (IQR)	1.00 (6.00)	1.00 (5.00)	2.00 (6.00)	0.140
Tumor size, median (IQR), cm	3.50 (3.00)	3.00 (3.00)	4.00 (2.50)	0.011[a]
TNM stage				0.202
I	239 (27.8)	90 (29.2)	149 (27.0)	
II	193 (22.5)	77 (25.0)	116 (21.1)	
III	427 (49.7)	141 (45.8)	551 (51.9)	
Combined resection				0.188
No	774 (90.1)	272 (88.3)	502 (91.1)	
Yes	85 (9.9)	36 (11.7)	49 (8.9)	
Tumor location				0.631
Upper	160 (18.6)	60 (19.5)	100 (18.1)	
Not upper	699 (81.4)	248 (80.5)	451 (81.9)	
Type of reconstruction				0.367
Roux-en-Y	314 (36.6)	109 (35.4)	205 (37.2)	
Billroth I	219 (25.5)	71 (23.1)	148 (26.9)	
Billroth II	295 (34.3)	117 (38.0)	178 (32.3)	
Others	31 (3.6)	11 (3.6)	20 (3.6)	
Extent of node dissection				0.140
D0-1	58 (6.8)	26 (8.4)	32 (5.8)	
≥D2	801 (93.2)	282 (91.6)	519 (94.2)	
Type of resection				0.671
Subtotal gastrectomy	547 (63.7)	199 (64.6)	348 (63.2)	
Total gastrectomy	312 (36.3)	109 (35.4)	203 (36.8)	

ASA American Society of Anaesthesiologists, *BMI* indicates body mass index, *NRS* Nutritional Risk Screening, *VFA* visceral fat area

The values given are number of patients unless indicated otherwise

[a] Statistically significant (P< 0.05)

Table 2 Comparisons of short-term outcomes among patients in the high VFA group and low VFA group

	All ($n = 859$)	High VFA group ($n = 308$)	Low VFA group ($n = 551$)	*P*
Total postoperative complications				
Surgical complications	132 (15.4)	69 (22.4)	63 (11.4)	<0.001*
Delayed gastric emptying	22 (2.6)	14 (4.5)	8 (1.5)	
Anastomotic bleeding	5 (0.6)	3 (1.0)	2 (0.4)	
Intra-abdominal infection	18 (2.1)	9 (2.9)	8 (1.6)	
Anastomotic leakage	25 (2.9)	16 (5.2)	9 (1.6)	
Intra-abdominal fluid collection	4 (0.5)	3 (1.0)	1 (0.2)	
Anastomotic stenosis	5 (0.6)	1 (0.3)	4 (0.7)	
Small bowel obstruction	8 (0.9)	2 (0.6)	6 (1.1)	
Intra-abdominal hemorrhage	10 (1.2)	5 (1.6)	5 (0.9)	
Wound infection	23 (2.7)	11 (3.6)	12 (2.2)	
Pancreatic fistula	6 (0.7)	4 (1.3)	2 (0.4)	
Gastrointestinal dysfunction	6 (0.7)	1 (0.3)	5 (0.9)	
Medical complications	89 (10.4)	36 (11.7)	53 (9.6)	0.340
Cerebral infarction	4 (0.5)	2 (0.6)	2 (0.4)	
Pulmonary atelectasis	4 (0.5)	1 (0.3)	3 (0.5)	
Fever	4 (0.5)	2 (0.6)	2 (0.4)	
Pneumonia	34 (4.0)	14 (4.5)	15 (2.7)	
Malnutrition	7 (0.8)	2 (0.6)	5 (0.9)	
Heart failure	4 (0.5)	2 (0.6)	2 (0.4)	
Multiple organ failure	1 (0.1)	0 (0.0)	1 (0.2)	
Respiratory failure	7 (0.8)	2 (0.6)	5 (0.9)	
Pleural effusion	9 (1.0)	6 (1.9)	8 (1.5)	
Venous thrombosis	2 (0.2)	1 (0.3)	1 (0.2)	
Anemia	13 (1.5)	4 (1.3)	9 (1.6)	
Total, *n* (%)	221 (25.7 %)	105 (34.1 %)	116 (21.1%)	<0.001*
Duration of hospital stay, median (IQR), d	11.00 (5.00)	12.00 (6.00)	10.00 (5.00)	<0.001*

Discussion

In the present study, we revealed that excess visceral fat was an independent risk factor for the development of surgical complications after gastrectomy. Higher visceral fat content was link to advanced age, more comorbidities and a higher ASA grade, suggesting that high VFA implies patients at high risk. Excessive visceral fat was also associated with prolonged length of stay. However, visceral fat was not predictive of OS or DSS.

To define obesity, several parameters have been widely used, including BMI, waist circumference [18], and waist–hip ratio [19]. However, these indicators are crude measures of body fat composition that do not reflect the intracorporeal fat distribution detailly and fail to distinguish between peripheral and abdominal adiposity. Visceral fat has emerged as a more reliable and pathogenic factor as an indicator of obesity [6]. CT assessment of intra-abdominal fat is considered as the golden standard for detecting visceral fat obesity [20]. Operable gastric cancer patients routinely undergo CT scan before surgery for tumor staging. Therefore, no extra charges and radiation is required for the assessment of visceral fat area. Asian people generally have a smaller physique and are more likely to accumulate visceral fat without developing generalized obesity compared with white people [21]. Thus, this study adopted cut-off levels of VFA recommended by the Japan Society for the Study of Obesity: the low VFA group with VFA < 100 cm^2 and the high VFA group with VFA ≥ 100 cm^2.

In recent years, it was well documented that visceral obesity was a risk factor of postoperative complications for various malignancies [22–24], and visceral obese patients had unfavorable surgical outcomes [25, 26], such as longer operative time, increased conversion rates, and prolonged hospital stay. In the field of gastric cancer, excessive visceral fat was demonstrated to be associated with

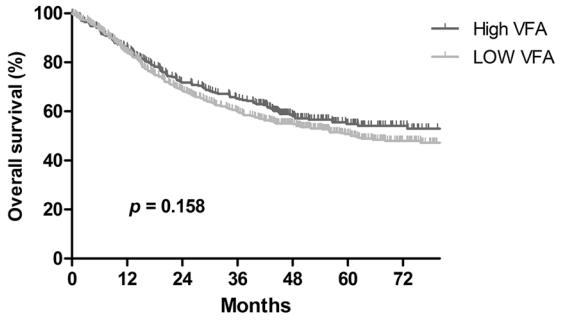
Table 3 Univariate and multivariate logistic regression analysis for surgical complications

Factors	Univariable analysis		Multivariate analysis	
	Case with complication, *n* (%)	*P*	OR (95% CI)	*P*
Age				
≥75/<75	24 (15.1)/108 (15.4)	0.916		
Gender				
Male/Female	106 (15.8)/26 (13.9)	0.531		
BMI				
≤18.5/18.5–25	17 (14.7) /84 (13.6)	0.819		
>25/18.5–25	31 (24.4) //84 (13.6)	0.002[a]		
High VFA				
Yes/No	69 (22.4)/63 (11.4)	<0.001[a]	2.236 (1.537–3.254)	<0.001[a]
Charlson Comorbidity Index				
1/0	23 (17.4)/96 (14.2)	0.476		
≥2/0	13 (26.0) /96 (14.2)	0.032[a]		
Hypoalbuminemia				
Yes/No	24 (17.9)/108 (14.9)	0.374		
ASA grade				
≥ III/II, I	21 (21.0)/111 (14.6)	0.097		
Anemia				
Yes/No	62 (14.3)/70 (16.5)	0.359		
Previous abdominal surgery				
Yes/No	18 (19.8)/114 (14.8)	0.217		
Tumor size				
>50 mm/≤50 mm	33 (15.3)/99 (15.4)	0.993		
Tumor location				
Upper/not upper	26 (16.3)/106 (15.2)	0.731		
TNM stage				
II/ I	24 (12.4) /36 (15.1)	0.200		
III/ I	72 (16.9) /36 (15.1)	0.227		
Extent of lymph node dissection				
D2/D1	126 (15.7)/6 (10.3)	0.272		
Type of resection				
Total/Subtotal	42 (13.5)/90 (16.5)	0.242		
Combined resection				
Yes/No	15 (17.6)/117 (15.1)	0.539		
Operative durations ≥210 min				
Yes/No	47 (13.4)/85 (16.8)	0.173		
Intraoperative bleeding ≥300 ml				
Yes/No	40 (13.8)/92 (16.2)	0.361		
Transfusion				
Yes/No	15 (17.2)/117 (15.2)	0.609		

Anemia hemoglobin concentration <120 g/L for men and <110 g/L for women, *Hypoalbuminemia* plasma albumin <35 g/L

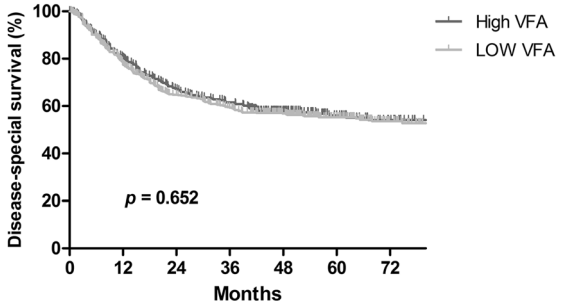
[a] Statistically significant

development of intra-abdominal infectious complications [27], pancreas-related infection [11] and surgical site infection [12], which were all closely related to the operative manipulations. Classification of surgical and medical complications, which leads to a better understanding of the pathogenesis, risks, and preventive possibilities, is a vital part of preventive strategy for surgical outcomes [13, 28]. Unfortunately, these studies did not describe the impact of



No. at risk							
The high VFA group	308	266	221	201	133	84	49
The low VFA group	551	464	379	331	238	144	80

Fig. 1 Kaplan–Meier survival curves for overall survival in patients with high VFA and in those with low VFA



No. at risk							
The high VFA group	308	240	197	177	118	75	44
The low VFA group	551	413	333	299	216	130	73

Fig. 2 Kaplan–Meier survival curves for disease-free survival in patients with high VFA and in those with low VFA

visceral fat on medical complications, and the applicability of these findings might be limited by the relatively small sample size. On the basis of a large-scale cohort, we distinguished the influence of visceral fat on the surgical and medical complications. Interestingly, high VFA was independently associated with surgical complications, but showed no correlation with medical complications, as demonstrated in the present study.

Patients with more visceral fat had an increased surgical complication rate for the following possible reasons. On the one hand, increased operative difficulty may cause more proinflammatory cytokines to be released into the systemic circulation, and these tissue damage mediators may impair motility of the intestine [29]. On the other hand, visceral fat is strongly correlated with insulin resistance and adipocytokine-related inflammation [8, 9], which may impair the normal responsion to operative stress and lead to an increased risk of surgical complications.

To our knowledge, the effects of visceral fat on survival after tumor operation remain controversial and no study reported the impact of visceral fat on long-term outcomes in gastric cancer. Balentine et al. [30] analyzed 61 patients with pancreatic cancer treated by pancreaticoduodenectomy and found that those with more intra-abdominal fat showed worse overall survival. The possible explanation is that visceral fat is linked to increased serum levels of insulin, inflammatory cytokines, angiogenic factors, and markers of oxidative stress that could promote tumor growth and expansion [9]. Among colorectal cancer patients, similar result was found in a Korean cohort of 161 patients who had undergone curative caner resection [31]. Significantly lower DFS rate was noted in patients with visceral obesity. Inconsistent with these findings, Harada et al. [32] demonstrated that low visceral fat may result in a significantly higher overall mortality rate on upper gastrointestinal cancer patients. The authors concluded that visceral obese patients have better nutritional status and a larger energy store, which they can access in time of negative energy balance. The visceral fat volume is lower in patients with advanced tumor than in patients with early-stage tumor, suggesting that visceral fat is related to tumor stage.

Our study represented the first demonstration of no association between visceral fat and survival following resection of gastric cancer. It is well recognized that the number of removed lymph nodes is an important determinant for tumor staging and long-term survival gastric cancer [33]. Excessive visceral fat impairs adequate exposure of the surgical field and makes a difficult challenge for complete lymphadenectomy around vessels. Nevertheless, in our study, there was no evidence suggest that patients with excessive visceral fat had less number of resected lymph nodes or positive lymph nodes. We believe adequate lymph node collection could be performed by a skillful and special surgeon, who had ample experience with gastric resection. Currently, visceral fat has been proved to be associated with obesity-associated metabolic disorders and high serum VEGF levels [34], which would increase the risk for developing colorectal cancer [35]. However, more research will be needed before we can fully understand the effect of visceral fat on tumor cell growth in gastric carcinoma.

There are still some limitations in the present study. First, this is an observational study from one surgical center. However, we included a large sample size and adopted a strict follow-up strategy to ensure the reliability of the result. Second, electronic records of CT images were not available for 212 patients because these patients conducted a CT scan in other institutions, which might introduce selection bias to the study. To assess for possible bias caused by these missing data, we compared the characteristics of the excluded 212 patients with the include patients. No substantial differences were observed between the two categories of patients with regard to demographic parameters, short-term outcomes, or long-term survival (Supplementary Table 1 and Supplementary Fig. 1).

Table 4 Univariable and multivariable Cox regression analyses for overall and disease-free survival

Factors	Overall survival				Disease-free survival			
	Univariable analysis		Multivariate analysis		Univariable analysis		Multivariate analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age								
≥ 75/< 75	2.041 (1.634–2.548)	<0.001[a]	1.402 (1.115–1.762)	0.004[a]	1.656 (1.296–2.116)	<0.001[a]		
Gender								
Male/Female	1.265 (0.988–1.620)	0.062			1.306 (1.005–1.698)	0.046[a]		
BMI								
≤ 18.5/18.5–25	1.489 (1.149–1.931)	0.003[a]	1.374 (1.054–1.791)	0.019[a]	1.401 (0.806–1.099)	0.019[a]		
> 25/18.5–25	0.658 (0.481–0.901)	0.009[a]	0.800 (0.581–1.100)	0.169	0.174 (0.593–1.099)	0.174		
Visceral obesity								
Yes/No	0.862 (0.701−1.060)	0.158			0.952 (0.768−1.180)	0.652		
Charlson Comorbidity Index								
1/0	1.102 (0.845−1.438)	0.472			1.048 (0.789−1.394)	0.745		
≥ 2/0	1.447 (0.989−2.117)	0.057			1.300 (0.857−1.972)	0.217		
Hypoalbuminemia								
Yes/No	1.639 (1.285−2.092)	<0.001[a]			1.622 (1.253−2.100)	<0.001[a]		
ASA grade								
≥ III/II, I	1.546 (1.178−2.030)	0.002[a]			1.290 (0.949−1.752)	0.104		
Anemia								
Yes/No	2.061 (1.683−2.523)	<0.001[a]	1.289(1.042−1.586)	0.019[a]	1.885 (1.527−2.328)	<0.001[a]		
Previous abdominal surgery								
Yes/No	0.922 (0.667−1.274)	0.622			1.075 (0.777−1.488)	0.662		
Tumor size								
> 50 mm/≤ 50 mm	2.013 (1.638−2.474)	<0.001[a]			2.072 (1.668−2.574)	<0.001[a]		
Tumor location								
Upper/not upper	1.309 (1.036−1.653)	0.024[a]			1.367 (1.070−1.746)	0.012[a]		
Histologic type								
Undifferentiated/differentiated	1.361 (0.982−1.886)	0.065			1.524 (1.093−2.124)	0.013[a]		
TNM stage								
II/I	3.168 (2.134−4.703)	<0.001[a]	3.106 (2.068–4.664)	<0.001[a]	4.492 (2.879–7.008)	<0.001[a]	4.911 (3.133–7.698)	<0.001[a]
III/I	7.418 (5.241–10.500)	<0.001[a]	7.896 (5.493–11.351)	<0.001[a]	9.682 (6.461–14.508)	<0.001[a]	11.481 (7.597–17.350)	<0.001[a]
Extent of lymph node dissection								
D2/D1	0.935 (0.645–1.357)	0.725			0.858 (0.587–1.254)	0.149		
Type of resection								
Total/Subtotal	1.857 (1.528–2.258)	<0.001[a]	1.418 (1.162–1.730)	0.001[a]	1.891 (1.538–2.324)	<0.001[a]	1.373 (1.115–1.690)	0.003[a]

Table 4 (continued)

Factors	Overall survival				Disease-free survival			
	Univariable analysis		Multivariate analysis		Univariable analysis		Multivariate analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Combined resection								
Yes/No	1.321 (0.977–1.785)	0.070			1.367 (0.998–1.874)	0.052		
Operative durations ≥210 min								
Yes/No	1.053 (0.863–1.287)	0.610			0.999 (0.809–1.233)	0.990		
Intraoperative bleeding ≥300 ml								
Yes/No	1.130 (0.922–1.384)	0.240			1.168 (0.944–1.447)	0.154		
Transfusion								
Yes/No	1.638 (1.233–2.177)	0.001[a]			1.429 (1.039–1.965)	0.028[a]		
Chemotherapy								
Yes/No	0.535 (0.439–0.653)	<0.001[a]	0.406 (0.330–0.499)	<0.001[a]	0.630 (0.512–0.774)	<0.001[a]	0.428 (0.347–0.529)	<0.001[a]

Anemia hemoglobin concentration <120 g/L for men and <110 g/L for women, *Hypoalbuminemia* plasma albumin <35 g/L

[a] Statistically significant

In conclusion, visceral fat was identified to be an independent risk factor for surgical complications but not for medical complications following gastrectomy for gastric cancer. However, excessive visceral fat did not impact the long-term survival in patients after gastrectomy. Pre-operative assessment of VFA may be an important risk-stratification tool to help the clinical decision-making precess in the treatment of patients with gastric carcinoma.

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Author contributions C-LZ and XS designed the study. L-LM and X-YC collected the data. BL, D-LZ, D-DH, and ZY did the analysis and interpretation of data. S-LW wrote the article. C-LZ revised the article and took the decision to submit the article for publication.

Compliance with ethical standards

Conflict of Interest The authors declare that they have no competing interests.

References

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. JAMA. 2014;311:806–14. https://doi.org/10.1001/jama.2014.732
2. Ji CY, Chen TJ. Working Group on Obesity in C. Empirical changes in the prevalence of overweight and obesity among Chinese students from 1985 to 2010 and corresponding preventive strategies. Biomed Environ Sci. 2013;26:1–12. https://doi.org/10.3967/0895-3988.2013.01.001
3. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008;371:569–78. https://doi.org/10.1016/S0140-6736(08)60269-X
4. Malietzis G, Currie AC, Athanasiou T, Johns N, Anyamene N, Glynne-Jones R, et al. Influence of body composition profile on outcomes following colorectal cancer surgery. Br J Surg. 2016;103:572–80. https://doi.org/10.1002/bjs.10075
5. Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol. 2008;9:629–35. https://doi.org/10.1016/S1470-2045(08)70153-0
6. Tchernof A, Despres JP. Pathophysiology of human visceral obesity: an update. Physiol Rev. 2013;93:359–404. https://doi.org/10.1152/physrev.00033.2011
7. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care. 2010;33:920–2. https://doi.org/10.2337/dc09-1825
8. Despres JP, Lemieux I. Abdominal obesity and metabolic syndrome. Nature. 2006;444:881–7. https://doi.org/10.1038/nature05488

9. Pou KM, Massaro JM, Hoffmann U, Vasan RS, Maurovich-Horvat P, Larson MG, et al. Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress: the Framingham Heart Study. Circulation. 2007;116:1234–41. https://doi.org/10.1161/CIRCULATIONAHA.107.710509
10. Kang J, Baek SE, Kim T, Hur H, Min BS, Lim JS, et al. Impact of fat obesity on laparoscopic total mesorectal excision: more reliable indicator than body mass index. Int J Colorectal Dis. 2012;27:497–505. https://doi.org/10.1007/s00384-011-1333-2
11. Tanaka K, Miyashiro I, Yano M, Kishi K, Motoori M, Seki Y, et al. Accumulation of excess visceral fat is a risk factor for pancreatic fistula formation after total gastrectomy. Ann Surg Oncol. 2009;16:1520–5. https://doi.org/10.1245/s10434-009-0391-y
12. Nishigori T, Tsunoda S, Okabe H, Tanaka E, Hisamori S, Hosogi H, et al. Impact of sarcopenic obesity on surgical site infection after laparoscopic total gastrectomy. Ann Surg Oncol. 2016;23:524–31. https://doi.org/10.1245/s10434-016-5385-y
13. Kehlet H, Jorgensen CC. Advancing surgical outcomes research and quality improvement within an enhanced recovery program framework. Ann Surg. 2016;264:237–8. https://doi.org/10.1097/SLA.0000000000001674
14. Japanese Gastric Cancer A. Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric Cancer: Off J Int Gastric Cancer Assoc Jpn Gastric Cancer Assoc. 2011;14:113–23. https://doi.org/10.1007/s10120-011-0042-4
15. Doyle SL, Bennett AM, Donohoe CL, Mongan AM, Howard JM, Lithander FE, et al. Establishing computed tomography-defined visceral fat area thresholds for use in obesity-related cancer research. Nutr Res. 2013;33:171–9. https://doi.org/10.1016/j.nutres.2012.12.007
16. Examination Committee of Criteria for 'Obesity Disease' in J. Japan Society for the Study of O. New criteria for 'obesity disease' in Japan. Circ J: Off J Jpn Circ Soc. 2002;66: 987–92.
17. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240:205–13.
18. Ford ES, Maynard LM, Li C. Trends in mean waist circumference and abdominal obesity among US adults, 1999-2012. JAMA. 2014;312:1151–3. https://doi.org/10.1001/jama.2014.8362
19. Heid IM, Jackson AU, Randall JC, Winkler TW, Qi L, Steinthorsdottir V, et al. Meta-analysis identifies 13 new loci associated with waist-hip ratio and reveals sexual dimorphism in the genetic basis of fat distribution. Nat Genet. 2010;42:949–60. https://doi.org/10.1038/ng.685
20. Seidell JC, Bakker CJ, van der Kooy K. Imaging techniques for measuring adipose-tissue distribution—a comparison between computed tomography and 1.5-T magnetic resonance. Am J Clin Nutr. 1990;51:953–7.
21. Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. Obesity Rev: Off J Int Assoc Study Obes. 2002;3:141–6.
22. Pecorelli N, Carrara G, De Cobelli F, Cristel G, Damascelli A, Balzano G, et al. Effect of sarcopenia and visceral obesity on mortality and pancreatic fistula following pancreatic cancer surgery. Br J Surg. 2016;103:434–42. https://doi.org/10.1002/bjs.10063
23. Cakir H, Heus C, Verduin WM, Lak A, Doodeman HJ, Bemelman WA, et al. Visceral obesity, body mass index and risk of complications after colon cancer resection: A retrospective cohort study. Surgery. 2015;157:909–15. https://doi.org/10.1016/j.surg.2014.12.012
24. Sandini M, Bernasconi DP, Fior D, Molinelli M, Ippolito D, Nespoli L, et al. A high visceral adipose tissue-to-skeletal muscle ratio as a determinant of major complications after pancreatoduodenectomy for cancer. Nutrition. 2016;32:1231–7. https://doi.org/10.1016/j.nut.2016.04.002
25. Tsujinaka S, Konishi F, Kawamura YJ, Saito M, Tajima N, Tanaka O, et al. Visceral obesity predicts surgical outcomes after laparoscopic colectomy for sigmoid colon cancer. Dis Colon Rectum. 2008;51:1757–65; discussion1765-1757. https://doi.org/10.1007/s10350-008-9395-0.
26. Park BK, Park JW, Ryoo SB, Jeong SY, Park KJ, Park JG. Effect of visceral obesity on surgical outcomes of patients undergoing laparoscopic colorectal surgery. World J Surg. 2015;39:2343–53. https://doi.org/10.1007/s00268-015-3085-6
27. Sugisawa N, Tokunaga M, Tanizawa Y, Bando E, Kawamura T, Terashima M. Intra-abdominal infectious complications following gastrectomy in patients with excessive visceral fat. Gastric Cancer: Off J Int Gastric Cancer Assoc Jpn Gastric Cancer Assoc. 2012;15:206–12. https://doi.org/10.1007/s10120-011-0099-0
28. Kehlet H. Enhanced Recovery After Surgery (ERAS): good for now, but what about the future? Can J Anaesthesia. 2015;62:99–104. https://doi.org/10.1007/s12630-014-0261-3
29. van Bree SH, Cailotto C, Di Giovangiulio M, Jansen E, van der Vliet J, Costes L, et al. Systemic inflammation with enhanced brain activation contributes to more severe delay in postoperative ileus. Neurogastroenterol Motility: Off J Eur Gastroint Motility Soc. 2013;25:e540–9. https://doi.org/10.1111/nmo.12157
30. Balentine CJ, Enriquez J, Fisher W, Hodges S, Bansal V, Sansgiry S, et al. Intra-abdominal fat predicts survival in pancreatic cancer. J Gastrointest Surg. 2010;14:1832–7. https://doi.org/10.1007/s11605-010-1297-5
31. Moon HG, Ju YT, Jeong CY, Jung EJ, Lee YJ, Hong SC, et al. Visceral obesity may affect oncologic outcome in patients with colorectal cancer. Ann Surg Oncol. 2008;15:1918–22. https://doi.org/10.1245/s10434-008-9891-4
32. Harada K, Baba Y, Ishimoto T, Kosumi K, Tokunaga R, Izumi D, et al. Low visceral fat content is associated with poor prognosis in a database of 507 upper gastrointestinal cancers. Ann Surg Oncol. 2015;22:3946–53. https://doi.org/10.1245/s10434-015-4432-4
33. Smith DD, Schwarz RR, Schwarz RE. Impact of total lymph node count on staging and survival after gastrectomy for gastric cancer: data from a large US-population database. J Clin Oncol: Off J Am Soc Clin Oncol. 2005;23:7114–24. https://doi.org/10.1200/JCO.2005.14.621
34. Miyazawa-Hoshimoto S, Takahashi K, Bujo H, Hashimoto N, Saito Y. Elevated serum vascular endothelial growth factor is associated with visceral fat accumulation in human obese subjects. Diabetologia. 2003;46:1483–88. https://doi.org/10.1007/s00125-003-1221-6
35. Otake S, Takeda H, Suzuki Y, Fukui T, Watanabe S, Ishihama K, et al. Association of visceral fat accumulation and plasma adiponectin with colorectal adenoma: evidence for participation of insulin resistance. Clin Cancer Res. 2005;11:3642–46. https://doi.org/10.1158/1078-0432.CCR-04-1868