



# Metabolic Syndrome, as Defined Based on Parameters Including Visceral Fat Area, Predicts Complications After Surgery for Rectal Cancer

Chong-Jun Zhou<sup>1</sup> · Yi-Fan Cheng<sup>2</sup> · Lin-Zhen Xie<sup>2</sup> · Wan-Le Hu<sup>1</sup> · Bo Chen<sup>3</sup> · Lei Xu<sup>3</sup> · Chong-Jie Huang<sup>1</sup> · Mao Cai<sup>1</sup> · Xian Shen<sup>1,4</sup> · Chang-Bao Liu<sup>1</sup> 

Published online: 17 October 2019  
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## Abstract

**Background/Objectives** Metabolic syndrome (MetS) has become a major public health problem. However, few studies have examined the impact of MetS on the postoperative complications of colorectal cancer and the conclusions remain controversial. The present study aimed to investigate whether MetS, as defined based on visceral fat area (VFA) instead of BMI or waist circumference, would predict complications after surgery for rectal cancer.

**Subjects/Methods** We conducted a retrospective study of patients who underwent surgery for rectal cancer at our department between January 2013 and August 2018. Univariate and multivariate analyses evaluating the risk factors for postoperative complications were performed. A receiver operating characteristic curve analysis was used to determine the gender-specific cut-off values for VFA.

**Results** A total of 381 patients were included in the study. The optimal cut-off values for VFA were 117.9 cm<sup>2</sup> for men and 76.9 cm<sup>2</sup> for women, and 153 patients were diagnosed as having MetS. The rate of postoperative complication was significantly higher in the MetS group than that in the non-MetS group (34.6% versus 15.8%,  $P < 0.001$ ). The multivariate logistic regression analysis demonstrated that MetS (OR 3.712,  $P < 0.001$ ), NRS 2002 scores  $\geq 3$  (OR 2.563,  $P = 0.001$ ), and tumor located at the lower 1/3 (OR 3.290,  $P = 0.001$ ) were independent risk factors for complications after surgery for rectal cancer.

**Conclusion** Metabolic syndrome, as defined based on parameters including visceral fat area, was an independent risk factor for complications after surgery for rectal cancer.

**Keywords** Metabolic syndrome · Visceral obesity · Rectal cancer · Postoperative complication

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Chong-Jun Zhou and Yi-Fan Cheng contributed equally to this work.

- ✉ Xian Shen  
shenxian5166@126.com
- ✉ Chang-Bao Liu  
752453166@qq.com

- <sup>1</sup> Department of Anorectal Surgery, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang, China
- <sup>2</sup> The Second Clinical Medical Institute, Wenzhou Medical University, Wenzhou, China
- <sup>3</sup> Department of Radiology, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China
- <sup>4</sup> Department of Gastrointestinal Surgery, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China

## Introduction/Purpose

Metabolic syndrome (MetS) is characterized by a cluster of metabolic disturbances which has been associated with an increased risk for coronary heart disease, stroke, type 2 diabetes, and the development of cancer [1]. Due to urbanization, aging, and lifestyle changes, the incidence of MetS is rising dramatically worldwide, and has become a major public health problem [2]. Although emerging evidences suggest MetS is associated with poor prognosis for common cancer types (such as hepatocellular [3], prostate [4], breast [5], gastric [6], and colorectal cancer [7]), a number of studies have opposite conclusions [8–12]. Apart from the differences in age, populations, races, and diseases, the various definitions of MetS could be the main cause for the controversy in previous studies [13].

Nowadays, the definition of MetS has reached a consensus, including at least three of the following criteria: abdominal obesity, elevated blood pressure, decreased high-density lipoprotein cholesterol (HDL-C), increased triglycerides (TG), and elevated fasting glucose [14]. The discrepancy mainly focuses on the assessment of abdominal obesity. In the previous studies, BMI or waist circumference (WC) with different cut-offs were used to diagnose abdominal obesity, which had been proved to be inaccurate, because BMI cannot reflect body adipose tissue distribution and WC includes metabolically inactive subcutaneous fat [15, 16]. And the visceral fat was considered to be a more accurate parameter to reflect the dysfunctional adipose tissue which was the main cause of various obesity-related comorbidities [15]. In the current study, MetS was defined based on visceral fat area (VFA) measured by CT (the gold standard [16]).

Colorectal cancer (CRC) is the third most common malignant disease and ranks as the fourth leading cause of cancer-related death [17]. In spite of the development of minimally invasive surgery and the enhanced recovery program, the complications after colorectal cancer surgery are still in a high level of 19 to 30%, especially in rectal cancer [18, 19]. Therefore, preoperative risk assessment is important for identifying patients with higher risks of developing postoperative complications. Up to date, few studies have examined the impact of MetS on the postoperative complications of colorectal cancer and the conclusions remain controversial [1, 20, 21].

Therefore, we conducted a retrospective study to investigate whether MetS, as defined based on VFA, insulin resistance, decreased HDL-C, increased TG, and hypertension, would predict complications after surgery for rectal cancer.

## Materials and Methods

### Patients

From January 2013 to August 2018, all patients who underwent surgery for rectal cancer at the Department of Surgery, The Second Affiliated Hospital of Wenzhou Medical University were included in this study. The inclusion criteria included patients who (i) were  $\geq 18$  years; (ii) had ASA grade  $\leq$  III; (iii) planned to receive elective surgery for rectal cancer with curative intent; and (iv) had preoperative abdominal multiple rows CT scans and serum lipids available for review (within 1 month before surgery). Exclusion criteria included (i) those undergoing palliative surgery or emergency surgery; (ii) those receiving neoadjuvant chemotherapy or radiotherapy; and (iii) those with a history of other malignant tumors. All operations were performed

by surgeons with extensive experience in rectal cancer resection (more than 100 cases).

### Data Collection

Referring to our prospectively maintained computer database, the following data were collected and analyzed retrospectively: (1) clinicopathological characteristics, including age, gender, body mass index (BMI), plasma albumin concentration, hemoglobin concentration, systolic blood pressure, diastolic blood pressure, fasting blood glucose, plasma triglyceride level, plasma high-density lipoprotein cholesterol level, current medication, comorbidity (assessed by Charlson comorbidity index [22], American Society of Anesthesiology (ASA) grade, Nutritional Risk Screening (NRS) 2002 scores [23], VFA, previous abdominal surgery, tumor location, tumor-node-metastasis (TNM) tumor stage, epidural analgesia, laparoscopic-assisted surgery, and surgical duration; (2) postoperative outcomes, postoperative complication (during hospital stay or within 30 days after surgery), postoperative hospital stays, and hospital costs. Complications classified as grade II or above according to the Clavien–Dindo classification [24] were analyzed in this study.

### Diagnosis of Metabolic Syndrome

According to the American Heart Association/National Heart, Lung and Blood Institute Scientific Statement (AHA/NHLBI) [25], MetS was defined by the presence of three or more of the following five components: high glucose (fasting glucose  $\geq 100$  mg/dL or diabetes diagnosis), high blood pressure (systolic  $\geq 130$  mmHg or diastolic  $\geq 85$  mmHg, or hypertension diagnosis), low HDL-C ( $< 40$  mg/dL [men];  $< 50$  mg/dL [women]), high triglycerides ( $\geq 150$  mg/dL or antilipids), and visceral fat (instead of waist circumference). The metabolic disorders were defined by the presence of two or more of four components among the AHA/NHLBI criteria (excluding visceral fat) [26].

### Assessment of Visceral Fat Area

A transverse computed tomography (CT) image of each scan at the third lumbar vertebra was used to calculate the areas of visceral fat as described previously [15]. Predefined Hounsfield unit (HU) thresholds were used for specific tissue demarcation. At the densities ranging from  $-150$  to  $-50$  HU, the adipose tissue stood out, while bone, muscle, blood vessels, and other intra-abdominal organs were excluded. One trained investigator who was blinded for all anthropometric and surgical characteristics identified and measured VFA on a dedicated processing system (version 3.0; INFINITT Healthcare Co, Ltd).

## Statistical Analyses

Continuous variables are presented as the mean and standard deviation or median and interquartile ranges (non-normally distributed data). Categorical variables are presented as numbers and percentages. Clinical variables were compared using Student's *t* test, Pearson's chi-square test or Fisher's exact test, and the Mann–Whitney U test as appropriate. A receiver operating characteristic (ROC) curve analysis was used to develop a cut-off for VFA associated with metabolic disorders. And the cut-off values for VFA that maximized the Youden index (sensitivity + specificity – 1) were defined as optimal. Variables with a significant trend in the univariate analysis, as well as variables with known prognostic value, were included in the multivariate forward logistic regression analysis. All of the tests were two-sided and considered statistically significant at  $P < 0.05$ . All data were analyzed using SPSS statistics version 22.0 (IBM, Armonk, New York, USA).

## Results

### Cut-off Values for VFA in Different Genders

From January 2013 to August 2018, a total of 381 patients met the inclusion criteria and were included in this study. There were no significant differences in age, BMI, elevated BP, elevated TG, and elevated glucose, but had significant differences in VFA ( $P < 0.001$ ) and reduced HDL-C ( $P = 0.006$ ) between the two genders. According to the AHA/NHLBI criteria (excluding abdominal obesity), 105 of men and 73 of women were diagnosed with metabolic disorders (Table 1). ROC curves of VFA were used to identify metabolic disorders in men (Fig. 1a) and in women (Fig. 1b), and the AUC were 0.818 and 0.764, respectively. The optimal cut-off values for VFA were 117.9 cm<sup>2</sup> and for men and 76.9 cm<sup>2</sup> for women.

**Table 1** Baseline characteristics for MetS in different genders

Characteristics	Men ( $n = 234$ )	Women ( $n = 147$ )	<i>P</i>
Age, mean (SD), years	64.2 ± 11.8	65.4 ± 11.4	0.349
BMI, mean (SD), kg/m <sup>2</sup>	22.8 ± 3.3	22.2 ± 3.2	0.101
Visceral fat area (SD) cm <sup>2</sup>	116.4 ± 70	92.9 ± 46.2	< 0.001*
Fasting glucose ≥ 100 mg/dL or Med	54 (23.1)	43 (29.3)	0.178
BP ≥ 130/85 mmHg or Med	107 (45.7)	68 (46.3)	0.919
TG ≥ 150 mg/dL or Med	54 (23.1)	36 (24.5)	0.752
Low HDL-C (< 40 mg/dL [men] < 50 mg/dL [women]) or Med	111 (47.4)	91 (61.9)	0.006*
Metabolic disorders <sup>a</sup>	105 (44.9)	73 (49.7)	0.362

Values in parentheses are percentages unless indicated otherwise

SD, standard deviation; BMI, body mass index; BP, blood pressure; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; Med, medication

\*Statistically significant ( $P < 0.05$ )

<sup>a</sup> Two or more of four components among AHA/NHLBI criteria excluding abdominal obesity

## Clinicopathologic Characteristics

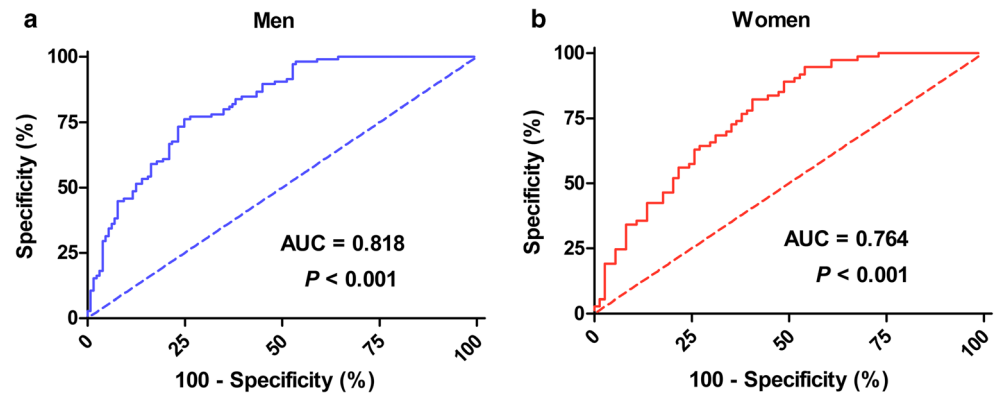
Patient clinicopathologic characteristics were summarized in Table 2. Based on the diagnostic criteria, 153 patients (40.2%) were diagnosed with MetS and the remaining 228 patients (59.8%) with non-MetS. There were no significant differences in gender, albumin, hemoglobin, previous abdominal surgery, tumor location, TNM stage, epidural analgesia, and laparoscopic-assisted surgery between MetS and non-MetS groups. Patients with MetS had an advanced age ( $P = 0.006$ ), a higher BMI ( $P < 0.001$ ), higher ASA grade ( $P = 0.002$ ), higher Charlson comorbidity index ( $P < 0.001$ ), longer surgical duration ( $P < 0.001$ ), and lower NRS 2002 scores ( $P = 0.013$ ) compared with patients without MetS.

## Short-term Surgical Outcomes

As shown in Table 3, a total of 89 (23.4%) patients suffered from postoperative complications. The postoperative complication rate was significantly higher in the MetS group than that in the non-MetS group (34.6% versus 15.8%,  $P < 0.001$ ), as well as the severe complications (7.8% versus 2.6%,  $P = 0.019$ ). Further analysis of the complications showed that MetS were correlated with higher risk of both surgical complications ( $P = 0.006$ ) and medical complications ( $P = 0.004$ ). Compared with the non-MetS group, the MetS group had higher costs ( $P = 0.004$ ), but had comparable postoperative hospital stays ( $P = 0.264$ ).

In univariate analysis (Table 4), postoperative complications were associated with NRS 2002 scores  $\geq 3$  ( $P = 0.025$ ), ASA grade III ( $P = 0.012$ ), Charlson comorbidity index  $\geq 2$  ( $P = 0.004$ ), tumor location ( $P = 0.012$ ), surgical duration  $\geq 210$  min ( $P = 0.006$ ), and MetS ( $P < 0.001$ ). No significant associations were shown between postoperative complications and other variables. The multivariate logistic regression analysis demonstrated that MetS (odds ratio 3.712, 95% CI 2.195–6.278,  $P < 0.001$ ), NRS 2002 scores  $\geq 3$  (odds ratio

**Fig. 1** ROC curves to identify metabolic disorders in both men (a) and women (b). The area under the ROC curve (AUC) values for VFA were shown



**Table 2** Patient clinical characteristics

Factors	Total (n = 381)	MetS (n = 153)	Non-MetS (n = 228)	P
Age, mean (IQR), years	65 (16)	66 (14)	64 (18)	0.006*
Gender				0.155
Female	147 (38.6)	66 (43.1)	81 (35.5)	
Male	234 (61.4)	87 (56.9)	147 (64.5)	
BMI, mean (SD), kg/m <sup>2</sup>	22.54 (3.27)	23.75 (2.97)	21.73 (3.21)	< 0.001*
Low weight (< 18.5)	40 (10.5)	5 (3.3)	35 (15.4)	
Normal (18.5–24)	217 (57.0)	80 (52.3)	137 (60.1)	
Overweight (24–28)	102 (26.8)	53 (34.6)	49 (21.5)	
Obesity (≥ 28)	22 (5.8)	15 (9.8)	7 (3.1)	
Albumin, mean (IQR), g/L	39 (4.95)	39.7 (4.45)	39.6 (5.45)	0.551
Hemoglobin, mean (IQR), g/L	131.0 (21.0)	131.0 (18.5)	130 (21.8)	0.957
ASA grade				0.002*
I	37 (9.7)	8 (5.2)	29 (12.7)	
II	286 (75.1)	112 (73.2)	174 (76.3)	
III	58 (15.2)	33 (21.6)	25 (11.0)	
NRS 2002 scores (IQR)				0.013*
< 3	283 (74.3)	124 (81.0)	159 (69.7)	
≥ 3	98 (25.7)	29 (19.0)	69 (30.3)	
Charlson comorbidity index				< 0.001*
0	267 (70.1)	79 (51.6)	188 (82.5)	
1	85 (22.3)	50 (32.7)	35 (15.4)	
≥ 2	29 (7.6)	24 (15.7)	5 (2.2)	
Previous abdominal surgery				0.367
Yes	43 (11.3)	20 (13.1)	23 (10.1)	
No	338 (88.7)	133 (86.9)	205 (89.9)	
MetS components				
VFA, mean (IQR), cm <sup>2</sup>	101.1 (81.5)	139 (73.1)	74 (69.3)	< 0.001*
Elevated BP	175 (45.9)	125 (81.7)	50 (21.9)	< 0.001*
TG, mean (SD), mg/dL	1.21 (0.77)	1.64 (0.965)	1.08 (0.475)	< 0.001*
HDL-C, mean (SD), mg/dL	1.12 (0.365)	0.96 (0.290)	1.21 (0.353)	< 0.001*
Elevated glucose	97 (25.5)	82 (53.6)	15 (6.6)	< 0.001*
Tumor location				0.122
Lower 1/3	167 (43.8)	60 (39.5)	107 (46.7)	
Middle 1/3	131 (33.4)	52 (34.0)	79 (34.9)	
Upper 1/3	83 (21.8)	41 (26.8)	42 (18.4)	
TNM stage				0.782
I/Tis	93 (24.4)	40 (26.1)	53 (23.2)	
II	122 (32.0)	49 (32.0)	73 (32.0)	
III	166 (43.6)	64 (41.8)	102 (44.7)	
Epidural analgesia				0.066
Yes	269 (70.6)	100 (65.4)	169 (74.1)	
No	112 (29.4)	53 (34.6)	59 (25.9)	
Laparoscopic-assisted surgery				0.468
Yes	49 (12.9)	22 (14.4)	27 (11.8)	
No	332 (87.1)	131 (85.6)	201 (88.2)	
Surgical duration, median (IQR) min	150 (60)	160 (67.5)	145 (58.8)	< 0.001*

Values in parentheses are percentages unless indicated otherwise

IQR, interquartile range; ASA, American Society of Anesthesiologists; NRS, nutritional risk screening; TNM, tumor-node-metastasis

\*Statistically significant ( $P < 0.05$ )

**Table 3** Postoperative outcomes

Factors	Total (n = 381)	MetS (n = 153)	Non-MetS (n = 228)	P
Total complications	89 (23.4)	53 (34.6)	36 (15.8)	< 0.001*
Severe complications <sup>a</sup>	18 (4.7)	12 (7.8)	6 (2.6)	0.019*
Detail of complications				
Surgical complications	52 (13.6)	30 (19.6)	22 (9.6)	0.006 *
Gastrointestinal dysfunction <sup>b</sup>	5 (1.3)	3 (2.0)	2 (0.9)	0.651
Wound infection	15 (0.8)	6 (3.9)	9 (3.9)	0.990
Bleeding	5 (1.3)	4 (2.6)	1 (0.4)	0.171
Intra-abdominal abscess	8 (2.1)	5 (3.3)	3 (1.3)	0.348
Anastomotic leakage	8 (1.8)	6 (3.9)	2 (0.9)	0.095
Intestinal obstruction	7 (3.3)	4 (2.6)	3 (1.3)	0.592
Urinary retention	3 (0.8)	2 (1.3)	1 (0.4)	0.727
Ureteral fistula	1 (0.3)	0 (0)	1 (0.4)	0.841
Medical complications	37 (9.7)	23 (15.0)	14 (6.1)	0.004*
Pulmonary complications	6 (1.6)	5 (3.3)	1 (0.4)	0.079
Cardiac complications	5 (1.3)	3 (2.0)	2 (0.9)	0.651
Venous thrombosis	2 (0.5)	1 (0.7)	1 (0.4)	0.661
Urinary infection	10 (2.6)	5 (3.3)	5 (2.2)	0.752
Fever	6 (1.6)	3 (2.0)	3 (1.3)	0.939
Transfusion <sup>c</sup>	7 (1.8)	6 (3.9)	1 (0.4)	0.036 *
Stroke	1 (0.3)	0 (0)	1 (0.4)	0.841
Mortality	1 (0.3)	0 (0)	1 (0.4)	0.841
Postoperative hospital stays, median (IQR), days	14 (4.0)	14.4 (6.0)	14 (4.5)	0.264
Costs (¥; median (IQR))	46,174.7 (14,090.5)	48,685.2 (16,693.1)	45,014.1 (12,465.8)	0.004*

IQR, interquartile range

\*Statistically significant ( $P < 0.05$ )

<sup>a</sup> Clavien-Dindo grade  $\geq$  III

<sup>b</sup> Including prolonged postoperative ileus and diarrhea

<sup>c</sup> Including albumin and/or erythrocyte

2.563, 95% CI 1.606–6.740,  $P = 0.001$ ), and tumor located at the lower 1/3 (odds ratio 3.290, 95% CI 1.606–6.674,  $P = 0.001$ ) were independent risk factors for complications after surgery for rectal cancer.

## Discussion

Given the high rate of colorectal cancer in China, as well as the ongoing obesity epidemic, understanding the consequences of MetS on the prognosis of CRC is becoming increasingly significant. This issue remains controversial due to different age, populations, races, and various definitions of MetS [13]. In the present study, we concluded that MetS, when defined based on VFA, was an independent risk factor for postoperative complications of rectal cancer.

According to the AHA/NHLBI diagnostic criteria [25], abdominal obesity was an important component of MetS, and which remains the bone of contention in the previous studies. Due to the convenience and low cost, waist circumference was commonly used to define abdominal obesity [14]. Some retrospective studies [7, 20] and even the guidelines from the Diabetes Society of Chinese Medical Association adapted the BMI to define abdominal obesity. Regrettably, it has been proved that VFA is superior to both WC and BMI for discriminating abdominal obesity, because visceral adipose has multiple endocrine, metabolic, and immunological functions, not

the subcutaneous adipose [27]. Because of the lack of available cut-off values for VFA, western studies used the top quartile to signify visceral adiposity [28, 29]. The most commonly used cut-offs for VFA in Asians were 132.6 cm<sup>2</sup> for men and 91.5 cm<sup>2</sup> for women, coming from a Japanese study of 1893 teachers with routine medical checkups [30]. Recently, a Korean cross-sectional study, involving 39,181 subjects who underwent health check-up tests, provided a cut-off value of 134.6 cm<sup>2</sup> for men and 91.1 cm<sup>2</sup> for women [26]. Obviously, these cut-offs coming from the healthy populations were inappropriate for cancer patients who usually accompanied with malnutrition. In the present study, we calculated a cut-off of 117.9 cm<sup>2</sup> for men and 76.9 cm<sup>2</sup> for women, which were smaller than that from the Japanese and Korean studies.

Using the new gender-specific cut-off values for VFA from our department, we showed an incidence of MetS of 40.2%. As expected, the presence of MetS indicated a significantly increased risk of postoperative complications in patients with rectal cancer. When further analyzing the complications, MetS was correlated with higher risk of both surgical complications and medical complications. The possible mechanisms by which MetS confers increased risk of postoperative complications are provided as following. First, the insulin resistance presented in MetS influences an abnormal metabolism in adipocytes (especially visceral fat adipocytes), with subsequent increased levels of pro-inflammatory and lower levels of

**Table 4** Univariate and multivariate analysis of risk factors for postoperative complications

Factors	Univariate analysis			Multivariate analysis	
	Complication (%)	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Age			0.684		
≥ 65/< 65	47 (24.2)/42 (22.5)	1.104 (0.686–1.775)			
Gender			0.679		
Male/female	53 (22.6)/36 (24.5)	1.108 (0.682–1.799)			
BMI			0.377		
< 18.5	11 (27.5)	1.450 (0.673–3.124)			
18.5–24	45 (20.7)	1			
> 24	33 (26.6)	1.386 (0.827–2.322)			
Hypoalbuminemia			0.359		
Yes/no	15 (28.3)/74 (22.6)	1.355 (0.706–2.599)			
Anemia			0.793		
Yes/no	13 (22.0)/76 (23.6)	0.915 (0.469–1.783)			
NRS 2002 scores			0.025*	2.563 (1.606–6.740)	0.001*
≥ 3/< 3	31 (31.6)/58 (20.5)	1.795 (1.073–3.002)			
ASA grade			0.012*		
III/II,I	21 (36.2)/68 (21.1)	2.128 (1.170–3.873)			
Charlson comorbidity index			0.004*		
≥ 2/< 2	13 (44.8)/76 (21.6)	2.951 (1.360–6.402)			
Metabolic syndrome				3.712 (2.195–6.278)	<0.001*
Yes/no	53 (34.6)/36 (15.8)	2.827 (1.736–4.602)	<0.001*		
High VFA/norm	58 (28.7)/31 (17.3)	1.923 (1.175–3.147)	0.009*		
Elevated BP/norm	52 (32.4)/37 (18.0)	1.931 (1.193–3.125)	0.007*		
Elevated TG/norm	26 (28.9)/63 (21.6)	1.470 (0.862–2.509)	0.156		
Reduced HDL-C/norm	59 (29.2)/30 (16.8)	2.049 (1.248–3.364)	0.004*		
Elevated glucose/norm	34 (35.1)/55 (19.4)	2.247 (1.349–3.744)	0.002*		
Previous abdominal surgery			0.454		
Yes/no	12 (27.9)/77 (22.8)	1.312 (0.643–2.677)			
Tumor location			0.012*		
Upper 1/3	13 (15.7)	1		1	
Middle 1/3	25 (19.1)	1.270 (0.609–2.649)		1.474 (0.687–3.162)	0.319
Lower 1/3	51 (30.5)	2.367 (1.203–4.661)		3.290 (1.606–6.674)	0.001*
TNM stage			0.104		
I	16 (17.2)	1			
II	26 (21.3)	1.303 (0.653–2.602)			
III	47 (28.3)	1.901 (1.007–3.589)			
Epidural analgesia			0.824		
Yes/no	62 (23.0)/27 (24.1)	0.943 (0.562–1.582)			
Laparoscopic-assisted surgery			0.601		
Yes/no	10 (20.4)/79 (23.8)	0.821 (0.392–1.720)			
Surgical duration ≥ 210 min			0.006*		
Yes/no	26 (35.6)/63 (20.5)	2.151 (1.237–3.741)			

OR, odds ratio; CI, confidence interval

\*Statistically significant ( $P < 0.05$ )

adiponectin (protective adipokine), which lead to infectious complications, such as surgical site infection and pneumonia [31]. What's more, abdominal obesity impairs surgical exposure and dissection, raising the difficulty of operation (especially in rectal cancer surgery), which would result in an increase of the surgical complications [32]. In addition, high blood pressure and dyslipidaemia were correlated with an impaired microvascular circulation, which could cause poor tissue healing and increase the risk of wound complications and anastomotic leakage [21]. Each diagnostic component has a little influence on the outcomes after surgery, and when these minor damages occur together, it leads to a substantially increased risk of postoperative complications. As a result, in the present study, the multivariate analysis showed that MetS was an independent risk factor for postoperative complications with a high odds ratio of 3.712.

As reported, the prevalence of malnutrition was identified in 40 to 60% of patients with malignant gastrointestinal cancer, and it had a significant impact on increasing the risk of postoperative complications [33]. Consistent with previous studies, we also found that malnutrition was an independent risk factor for postoperative complications in patients with rectal cancer. Overweight and obesity are now prevalent in patients with cancer and it makes it more challenging to define malnutrition based on criteria of clinically significant weight loss [34]. This may lead to a lower prevalence of malnutrition in cancer patients, especially patients with rectal cancer which has less impact on gastrointestinal function and earlier diagnosis than other gastrointestinal cancers. The prevalence of malnutrition in our study was 25.7%, which was lower than that previously reported. The remaining 283 patients without malnutrition were considered to be safe for surgery

traditionally. In fact, the patients without malnutrition suffered a high incidence of postoperative complications of 20.5%. More importantly, if malnourished patients combined with MetS, the incidence of postoperative complications would reach to 48.3%. These findings indicated that it is important to perform preoperative screening for MetS, especially for patients without malnutrition who are usually ignored because of their thin body type.

In the present study, we also identified tumor located at the lower 1/3 as an independent risk factor for postoperative complications, which was consistent with previous studies [19, 32]. The lower the tumor located, the more difficult it is to perform operative procedure within narrow pelvic exposure. Abdominal obesity would further raise the difficulty of rectal cancer surgery. Taken together, these may partly explain the negative results concluded by previous studies. Zarzavadjian et al. [20] only included colon cancer and concluded MetS does not jeopardize postoperative outcomes following laparoscopic colectomy. André Goularta et al. [35] included colorectal cancer and indicated that MetS do not have any influence in surgical outcomes of colorectal cancer surgery. Therefore, colon and rectal cancer should be investigated separately in the future studies and it seems to be more meaningful to investigate the impact of MetS on rectal cancer.

There are several limitations in our study. First, this is a single-center retrospective study; the conclusions of this study need to be validated in multicenter prospective studies in the future. Second, due to the inaccurate preoperative staging and poor compliance, a subset of patients should be able to receive neoadjuvant therapy (but not) had been enrolled in this study. However, our study remains meaningful and representative because TNM stage had no influence on the preoperative complications and the implementation of neoadjuvant therapy are still in difficulty in the clinical practice nowadays.

## Conclusions

The present study is the first study reporting the gender-specific cut-off values of VFA for cancer patients in Asian. We find that MetS, defined based on this new cut-offs of VFA, adversely impacts the postoperative complications for rectal cancer, including both surgical complications and medical complications. Moreover, MetS, malnutrition, and tumor located at the lower 1/3 were identified as independent risk factors for complications after surgery for rectal cancer. Assessing MetS before surgery could provide useful information to surgeon for a better preoperative preparation to reduce the risks of operation, especially for patients with malnutrition.

**Author Contributions** Chang-Bao Liu and Xian Shen contributed to the study design. Yi-Fan Cheng, Lin-Zhen Xie, Wan-Le Hu, Chong-Jie

Huang, Bo Chen, and Lei Xu collected the data. Chong-Jun Zhou and Yi-Fan Cheng did the analysis and interpretation of data. Chong-Jun Zhou wrote the article. Xian Shen and Mao Cai revised the article. Chang-Bao Liu took the decision to submit the article for publication.

**Funding Information** This work was supported by the foundation of Science and Technology Bureau of Wenzhou (Y20170437).

## Compliance with Ethical Standards

**Ethics and Consent Statement** This study was approved by the ethics committee of The Second Affiliated Hospital of Wenzhou Medical University. And informed consent was obtained from all individual participants included in the study.

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Statement of Human and Animal Rights** This article does not contain any experiments with human participants or animals performed by any of the authors.

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