# World Journal of Gastroenterology

World J Gastroenterol 2023 April 21; 29(15): 2222-2358





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The WJG is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports, Index Medicus, MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJG as 5.374; IF without journal self cites: 5.187; 5-year IF: 5.715; Journal Citation Indicator: 0.84; Ranking: 31 among 93 journals in gastroenterology and hepatology; and Quartile category: Q2. The WJG's CiteScore for 2021 is 8.1 and Scopus CiteScore rank 2021: Gastroenterology is 18/149.

#### **RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Yi-Xuan Cai; Production Department Director: Xiang Li; Editorial Office Director: Jia-Ru Fan.

#### NAME OF JOURNAL

World Journal of Gastroenterology

#### ISSN

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

#### LAUNCH DATE

October 1, 1995

#### **FREQUENCY**

Weekly

#### **EDITORS-IN-CHIEF**

Andrzei S Tarnawski

#### **EDITORIAL BOARD MEMBERS**

http://www.wignet.com/1007-9327/editorialboard.htm

#### **PUBLICATION DATE**

April 21, 2023

#### COPYRIGHT

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https://www.wjgnet.com/bpg/gerinfo/242

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#### **ONLINE SUBMISSION**

https://www.f6publishing.com

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DOI: 10.3748/wjg.v29.i15.2310

World J Gastroenterol 2023 April 21; 29(15): 2310-2321

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

# **Case Control Study**

# Can visceral fat parameters based on computed tomography be used to predict occult peritoneal metastasis in gastric cancer?

Li-Ming Li, Lei-Yu Feng, Chen-Chen Liu, Wen-Peng Huang, Yang Yu, Peng-Yun Cheng, Jian-Bo Gao

Specialty type: Gastroenterology and hepatology

#### Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

# Peer-review report's scientific quality classification

Grade A (Excellent): 0 Grade B (Very good): B, B Grade C (Good): C Grade D (Fair): D Grade E (Poor): 0

P-Reviewer: Hori T, Japan; Koganti SB, United States; Sun D, China; Tanabe H, Japan

Received: November 4, 2022 Peer-review started: November 4,

First decision: January 3, 2023 Revised: January 21, 2023 Accepted: March 20, 2023 Article in press: March 20, 2023 Published online: April 21, 2023



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#### Abstract

#### **BACKGROUND**

The preoperative prediction of peritoneal metastasis (PM) in gastric cancer would prevent unnecessary surgery and promptly indicate an appropriate treatment plan.

#### **AIM**

To explore the predictive value of visceral fat (VF) parameters obtained from preoperative computed tomography (CT) images for occult PM and to develop an individualized model for predicting occult PM in patients with gastric carcinoma (GC).

# **METHODS**

A total of 128 confirmed GC cases (84 male and 44 female patients) that underwent CT scans were analyzed and categorized into PM-positive (n = 43) and PM-negative (n = 85) groups. The clinical characteristics and VF parameters of two regions of interest (ROIs) were collected. Univariate and stratified analyses

based on VF volume were performed to screen for predictive characteristics for occult PM. Prediction models with and without VF parameters were established by multivariable logistic regression analysis.

#### **RESULTS**

The mean attenuations of  $VF_{ROI\,2}$  and  $VF_{ROI\,2}$  varied significantly between the PM-positive and PM-negative groups (P=0.044 and 0.001, respectively). The areas under the receiver operating characteristic curves (AUCs) of  $VF_{ROI\,2}$  and  $VF_{ROI\,2}$  were 0.599 and 0.657, respectively. The mean attenuation of  $VF_{ROI\,2}$  was included in the final prediction combined model, but not an independent risk factor of PM (P=0.068). No significant difference was observed between the models with and without mean attenuation of VF (AUC: 0.749 vs 0.730, P=0.339).

#### CONCLUSION

The mean attenuation of VF is a potential auxiliary parameter for predicting occult PM in patients with GC.

**Key Words:** Gastric carcinoma; Peritoneal metastasis; Visceral fat; Tomography; X-ray computed; Prediction; Individualized model

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**Core Tip:** The preoperative prediction of peritoneal metastasis (PM) in gastric cancer would prevent unnecessary surgery and promptly indicate an appropriate treatment plan. We therefore aimed to explore the predictive value of visceral fat (VF) parameters obtained from preoperative computed tomography images for occult PM and to develop an individualized model for predicting occult PM in patients with gastric carcinoma (GC). Consequently, mean attenuation of VF is a potential auxiliary parameter to predict occult PM in patients with GC.

**Citation:** Li LM, Feng LY, Liu CC, Huang WP, Yu Y, Cheng PY, Gao JB. Can visceral fat parameters based on computed tomography be used to predict occult peritoneal metastasis in gastric cancer? *World J Gastroenterol* 2023; 29(15): 2310-2321

**URL:** https://www.wjgnet.com/1007-9327/full/v29/i15/2310.htm

**DOI:** https://dx.doi.org/10.3748/wjg.v29.i15.2310

#### INTRODUCTION

Peritoneal metastasis (PM) is the major cause of postoperative distant metastasis and occurs in more than 10% of patients with newly diagnosed gastric cancer[1]. Gastric carcinoma (GC) is the third leading cause of cancer-related deaths worldwide. In gastric cancer with PM, the survival time is only a few months[2]. Many recent studies[3] have shown that the combination of complete cell reduction and intraperitoneal thermal perfusion chemotherapy can significantly prolong the median survival time in gastric cancer with PM. Thus, the preoperative prediction of PM in gastric cancer would prevent unnecessary surgery and promptly indicate an appropriate treatment plan. For example, laparoscopic exploration may be the preferred choice. Additionally, intraperitoneal hyperthermic chemotherapy may be prepared, and open exploration may be the final choice for a patient with occult PM.

Traditional preoperative imaging methods, such as computed tomography (CT) and magnetic resonance imaging, demonstrate high specificity and low sensitivity in the detection of PM[4]. Therefore, occult PM has attracted extensive attention; it refers to metastasis not indicated on preoperative CT imaging but detected during surgery and pathologic examination[5]. In the last few years, many studies have demonstrated the great potential of radiomics in the prediction of occult PM in gastric cancer[6]. However, most studies have used manual delineation of regions of interest (ROIs) in PM, which reduces repeatability and increases subjective dependence. Therefore, the urgent exploration for new parameters for predicting occult PM is warranted.

Tumor infiltration of the peritoneum alters the characteristics of the surrounding visceral fat (VF) on CT, and these changes have been investigated in previous radiomics studies[7]. In addition, the feature referred to as "smudge-like ground-glass opacity" in the abdominal cavity, which presents an increased CT attenuation of VF, is a common but easily overlooked sign of early-stage omental metastasis[8]. In addition, the adipose microenvironment has a subtle relationship with tumor progression[9].

We therefore aimed to explore the predictive value of VF parameters based on preoperative CT imaging for occult PM in GC and to develop an individualized model for predicting occult PM preoperatively.

#### MATERIALS AND METHODS

#### **Patients**

This retrospective study was approved by the local institutional review board, and the requirement for informed consent was waived.

Patients at our hospital who met the inclusion/exclusion criteria were consecutively enrolled between July 2012 and July 2021. The inclusion criteria were as follows: (1) Diagnosis of gastric cancer by endoscopy and biopsy, with complete biopsy information; (2) Diagnosis of cT3 and cT4 gastric cancer by CT without obvious PM characteristics; and (3) PM status confirmed by exploratory surgery and pathological biopsy. The exclusion criteria were follows: (1) A history of abdominal tumors, cirrhosis, or other inflammatory diseases; (2) A history of abdominal surgery; (3) An interval between CT and surgical exploration longer than 2 wk; and (4) The presence of artifacts that affect the evaluation of VF

Clinical patient data (e.g., sex and age), blood test information [e.g., carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199), and carbohydrate antigen 125 (CA125)], and biopsy information (e.g., pathological type and differentiation) were collected for further analysis.

#### CT examination

CT examinations were performed using SOMATOM Definition Flash CT or SOMATOM Force (Siemens, Germany). All patients fasted for 6 h, and drank 800-1000 mL water 5-15 min before CT examination. Following an unenhanced scan, dual-phase enhanced CT images were obtained at 30- and 70-s delays. Approximately 1.3 mL/kg iodinated contrast agent (Ultravist 370, Bayer Schering Pharma) was injected intravenously at a rate of 3.0 mL/s. The parameters of the unenhanced scan were as follows: 120 kV tube voltage, 250-350 mAs, and 5 mm slice thickness and slice interval. The parameters of the enhanced scan were as follows: 120 kV tube voltage, automatic tube current modulation techniques, and 5- or 1.25mm slice thickness and slice interval.

#### Fat assessment

The volume and mean CT attenuation of VF and subcutaneous fat (SF) were measured using unenhanced scan CT images on a workstation (MM Research Frontier SyngoVia, VB2.0, Siemens Healthineers, Forchheim, Germany). VF was defined as fat within the abdominal cavity, whereas SF was defined as fat below the skin. ROIs were manually drawn by tracing the medial edge of the abdominal muscle using a semiautomated technique, starting from the maximal axial section of the tumor and extending 15 mm (ROI 1) and 25 mm (ROI 2) downward. The contour of each layer can be adjusted manually as necessary. A primary radiologist (with 6 years of experience) was responsible for outlining, while another senior radiologist (with 25 years of experience) was responsible for supervising each operation (Figure 1). Twenty cases were randomly chosen for outlining by another radiologist (with 3 years of experience) to verify the consistency.

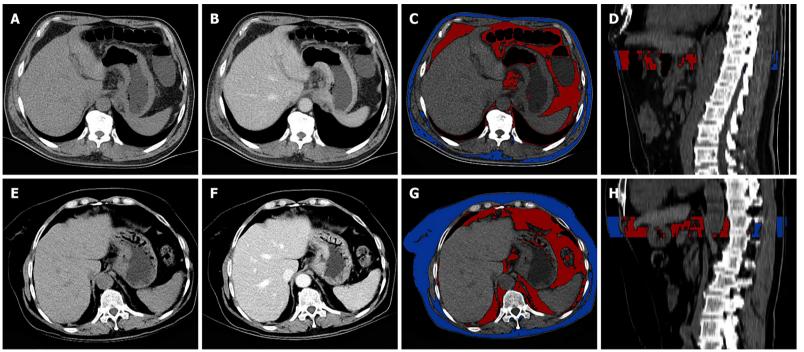
CT attenuation between -150 and -50 Hounsfield units (HU) was performed to evaluate voxels containing adipose tissue [10]. Adipose tissue volume was measured in cubic centimeters (cm³), while mean CT attenuation was measured in HU. The mean CT attenuation and volume of VF were obtained directly on the workstation simultaneously with a table including the CT attenuation of each voxel. The 10th, 30th, 50th, 70th, 90th, 25th, and 75th percentiles of CT attenuation were obtained during postprocessing and calculation.

#### Analysis of CT images

Two radiologists blinded to the pathologic data analyzed the CT characteristics. When disagreements occurred, a senior radiologist made the final decision. The cT and cN stages were analyzed according to the 8th American Joint Committee staging classification[11,12]. Mild ascites refers to ascites that could not be clearly determined to be caused by metastasis[5]. The GC thickness was measured at the maximal axial section[13].

# Statistical analysis

Statistical analyses were conducted using SPSS software (version 22.0) and MedCalc software (version 15.2). Interobserver reliability was assessed using the intraclass correlation coefficient (ICC), where ICC ≥ 0.80 is excellent, 0.61-0.80 is good, and < 0.60 is the difference. The discrimination capability of various VF characteristics was evaluated using the receiver operating characteristic (ROC) curve and compared using Delong's test. The relationship between volume and mean attenuation was evaluated using Pearson correlation analysis. Stratified analysis based on VF volume was performed. The differences in



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Figure 1 Determination of visceral fat parameters. A-D: Detection of visceral fat (VF) parameters in a 54-year-old male patient with gastric cancer with peritoneal metastasis (PM); A and B: Axial unenhanced and venous computed tomography (CT) images showing wall thickening in the cardia and the lesser and greater curvatures of the stomach; C: Regions of interest (ROI) were drawn using a semiautomated technique. The red area represents VF, while the blue area represents subcutaneous fat (SF); D: Sagittal image showing a three-dimensional (3D) ROI, delineated starting from the maximal axial section of the tumor and extending 25 mm; E-H: Determination of VF parameters in a 66-year-old female patient with gastric cancer without PM; E and F: Axial unenhanced and venous CT images showing irregular wall thickening and a mass in the cardia of the stomach; G and H: A 3D ROI drawn with a 25-mm height using a semiautomated technique. The red area represents VF, while the blue area represents SF.

continuous variables were compared using the two-tailed t test, Mann-Whitney U test, Kruskal-Wallis H test, and one-way ANOVA. The differences in categorical variables were compared using the  $\chi^2$  test. Significant variables were analyzed using multifactorial logistic regression analysis (backward: Conditional). P < 0.05 was considered to suggest a statistically significant difference.

# **RESULTS**

#### Patient characteristics

A total of 43 PM-positive patients were included in the study, and 85 PM-negative patients treated

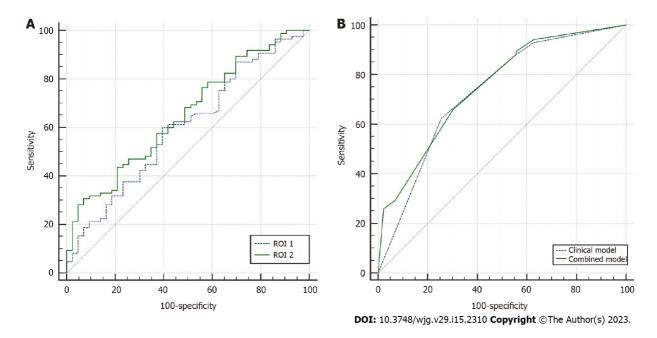


Figure 2 Predictive performance of computed tomography attenuations for visceral fat in two regions of interest and two models for predicting peritoneal metastasis in gastric cancer. A: Receiving operator characteristic (ROC) curves of the visceral fat (VF) computed tomography (CT) attenuations on ROIs 1 and 2. The VF CT attenuations on ROI 2 [area under the curve (AUC): 0.657, sensitivity 93.0%, specificity 30.6%] showed a better predictive performance than those on ROI 1 (AUC: 0.599, sensitivity 60.0%, specificity 60.0%); B: ROC curves of the clinical and combined models. The two models showed comparable predictive performance for peritoneal metastasis in gastric cancer (AUC: 0.730 vs 0.749, P = 0.399)

between January 2021 and July 2021 were included as control subjects. Significant differences in age, CA125, tumor location, thickness, mild ascites, and cT (P < 0.05 for all) were found between the PMpositive and PM-negative groups (Table 1). No significant differences were found for sex, pathological type, differentiation, CEA, CA199, or cN stage (P > 0.05 for all).

#### VF characteristics

Significant differences in the mean attenuations of  $VF_{ROI1}$  and  $VF_{ROI2}$  (P = 0.044 and 0.001, respectively) were found between the PM-positive and PM-negative groups (Table 2). No significant differences were found for the mean attenuations of SF<sub>ROI 1</sub> and SF<sub>ROI 2</sub>, the volumes of VF<sub>ROI 1</sub>, VF<sub>ROI 2</sub>, SF<sub>ROI 1</sub>, and SF<sub>ROI 2</sub>, or the volume ratio VF/SF (P > 0.05 for all).

The areas under the receiver operating characteristic curves (AUCs) of VF<sub>ROI1</sub> and VF<sub>ROI2</sub> for predicting PM in GC were 0.599 [95% confidence interval (CI): 0.509-0.685] and 0.657 (95%CI: 0.568-0.738), respectively (Figure 2A). The comparison of the ROC curves of the VF characteristics suggested that  $VF_{RO12}$  significantly outperformed  $VF_{RO11}(P = 0.002)$ . Most of the interobserver agreements between the two operators were excellent (Table 2).

Significant differences in the  $30^{th}$ ,  $50^{th}$ ,  $70^{th}$ ,  $25^{th}$ , and  $75^{th}$  percentiles of CT attenuation of  $VF_{ROI\,2}$  were found between the PM-positive and PM-negative groups (Supplementary Table 1). The AUCs of the 10th, 30th, 50th, 70th, 90th, 25th, and 75th percentiles of CT attenuation for predicting PM in GC were 0.612, 0.642, 0.641, 0.619, 0.608, 0.629, and 0.619, respectively. The comparison of ROC curves suggested no significant difference between the  $30^{th}$  percentile and the mean CT attenuation of  $VF_{ROI2}(P = 0.664)$ (Supplementary Figure 1).

# Relationship between VF and clinical characteristics

Significant differences in the mean attenuation of  $VF_{ROI\,2}$  were observed between the different cN and cT stage classifications (P = 0.030 and 0.003, respectively). The mean attenuation of VF<sub>ROL2</sub> in patients with elevated CA125, elevated CA199, and mild ascites was significantly higher than that in normal conditions (P = 0.002, 0.039, and 0.001, respectively) (Table 3).

# Stratified analysis

The mean attenuation was negatively correlated with the volume of  $VF_{ROI2}$  (Pearson correlation coefficient = -0.688; P = 0.001) (Supplementary Figure 2). Patients were divided into two groups according to the median volume of VF  $_{ROI\,2}$  (median = 141.58 cm<sup>3</sup>). Stratified analysis suggested that the mean attenuation of VF ROI2 was more effective in predicting occult PM in the high-volume group than in the low-volume group (Table 4, Figure 3).

Table 1 Comparison of clinical and computed tomography characteristics between two groups, n (%)

Variable		PM (-) (n = 85)	PM (+) (n = 43)	P value
Sex	Male	60 (70.6)	24 (55.8)	0.096
	Female	25 (29.4)	19 (44.2)	
Age (yr) (mean ± SD)		56.44±12.63	61.25±11.11	0.029 <sup>1</sup>
Pathological type	Adenocarcinoma	83 (97.6)	38 (88.4)	0.077
	Non-adenocarcinoma	2 (2.4)	5 (11.6)	
Differentiation	Poorly differentiated	50 (58.8)	30 (69.8)	0.227
	Moderately and well differentiated	35 (41.2)	13 (30.2)	
CEA	Normal	74 (87.1)	37 (86.0)	0.873
	Elevated	11 (12.9)	6 (14.0)	
CA199	Normal	74 (87.1)	32 (74.4)	0.073
	Elevated	11 (12.9)	11 (25.6)	
CA125	Normal	83 (97.6)	37 (86.0)	0.030 <sup>1</sup>
	Elevated	2 (2.4)	6 (14.0)	
Location	Cardia	44 (51.8)	7 (16.3)	0.001 <sup>1</sup>
	Body	12 (14.1)	14 (32.6)	
	Antrum	20 (23.5)	13 (30.2)	
	≥ 2 parts	9 (10.6)	9 (20.9)	
Mild ascites	(-)	75 (88.2)	24 (55.8)	0.001 <sup>1</sup>
	(+)	10 (11.8)	29 (44.2)	
cN stage	N0	26 (30.6)	11 (25.6)	0.150
	N1-2	41 (48.2)	16 (37.2)	
	N3-4	18 (21.2)	16 (37.2)	
cT stage	≤T3	57 (67.1)	14 (32.6)	0.001 <sup>1</sup>
	≥ T4	28 (32.9)	29 (67.4)	
Thickness (mm), median (IQR)		15.11 (13.02, 18.85)	13.43 (11.28, 17.83)	0.023 <sup>1</sup>

 $<sup>^{1}</sup>P < 0.05$ 

PM: Peritoneal metastasis; CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA125: Carbohydrate antigen 199; IQR: Interquartile range.

# Risk factors for occult PM

Multiple logistic regression analysis based on clinical characteristics showed that mild ascites and cT stage ( $\geq$  T4) were independent risk factors for occult PM (P = 0.003 and 0.010, respectively) (Table 5). The Hosmer-Lemeshow test revealed that the model had a good fit (P = 0.977). Furthermore, the clinical model showed a moderate prediction performance (AUC = 0.730, 95%CI: 0.644-0.804).

Multiple logistic regression analyses of both clinical characteristics and VF parameters showed that the mean attenuation of  $VF_{ROI2}$ , mild ascites, and cT stage ( $\geq T_4$ ) were included in the final prediction combined model, but the mean attenuation of  $VF_{ROI2}$  was not an independent risk factor for PM (P =0.068) (Table 5). The Hosmer-Lemeshow test indicated that the model had a good fit (P = 0.523). The combined model showed a moderate prediction performance (AUC = 0.749, 95%CI: 0.665-0.821). No significant difference was found between the prediction performance of the two models (P = 0.339) (Figure 2B).

# DISCUSSION

We explored the value of VF parameters in predicting occult PM in GC and subsequently developed a preoperative prediction model based on clinical features and VF parameters. A significant difference in the mean attenuation of VF was found between the PM-positive and PM-negative groups. The mean

Table 2 Comparison of visceral fat characteristics between the two lesions				
Variable	PM (+) (n = 43)	PM (-) (n = 85)	P value	ICC
VF <sub>ROI 1</sub>				
Volume (cc)	84.45 (36.70, 161.04)	87.92 (49.89, 160.75)	0.412	0.913
Mean attenuation (HU)	-82.07 ± 6.06	-85.33 ± 5.89	0.044 <sup>1</sup>	0.810
SD attenuation (HU)	18.82 (17.78, 21.25)	19.51 (18.63, 21.11)	0.133	0.926
SF <sub>ROI 1</sub>				
Volume (cc)	108.79 (55.10, 170.90)	115.96 (62.70, 178.72)	0.760	0.979
Mean attenuation (HU)	-85.33 ± 5.89	-86.05 ± 8.23	0.934	0.955
SD attenuation (HU)	17.94 (16.60, 19.37)	18.58 (17.27, 20.16)	0.180	0.981
VF <sub>ROI 2</sub>				
Volume (cc)	132.63 (58.85, 273.65)	145.48 (82.58, 277.42)	0.302	0.932
Mean attenuation (HU)	-82.19 ± 5.35	-85.70 ± 5.65	0.001 <sup>1</sup>	0.974
SD attenuation (HU)	19.86 (17.58, 20.46)	19.13 (18.47, 20.66)	0.317	0.950
SF <sub>ROI 2</sub>				
Volume (cc)	163.24 (82.57, 261.17)	175.86 (97.86, 267.52)	0.76	0.991
Mean attenuation (HU)	-86.28 ± 8.61	-86.41 ± 8.08	0.938	0.980
SD attenuation (HU)	17.80 (16.42, 19.33)	18.45 (17.29, 19.91)	0.124	0.993
Volume ratio				
VF/SF <sub>ROI 1</sub>	0.92 (0.44, 1.50)	1.00 (0.61, 1.65)	0.317	0.804
VF/SF <sub>ROI 2</sub>	0.98 (0.47, 1.41)	1.00 (0.63, 1.68)	0.279	0.884

 $<sup>^{1}</sup>P < 0.05$ .

PM: Peritoneal metastasis; ICC: Intraclass correlation coefficient; VF: Visceral fat; SF: Subcutaneous fat; SD: Standard deviation; ROI: Region of interest; HU: Hounsfield units; ROIs 1 and 2: Regions of interest starting at the largest axial level of the tumor and extending down 15 mm and 25 mm, respectively.

> attenuation of VF was included in the final prediction combined model but was not an independent predictor of occult PM in GC.

> Previous studies on VF have mostly focused on the effect of volume or area on postoperative prognosis, and few studies have investigated the CT attenuation of VF[14,15]. CT attenuation of pericoronary adipose tissue has been shown to be strongly correlated with cardiovascular disease [16]. Xiang et al[9] investigated the relationship between adipocytes and gastric cancer cells and found that adipocytes may promote cancer cell invasion through a specific signaling pathway. CT attenuation is an index reflecting changes in the VF microenvironment, and its increase may be closely related to tumor progression[17]. Given all of that, we believe that certain changes occur in VF with PM. The indicators used to quantify such changes in our study included the mean attenuation, volume, and volume ratio. Previous studies [5,18] have suggested that the radiomics features of the adjacent peritoneum are helpful in predicting PM in GC. Therefore, two nearby ROIs that delineated from the maximal axial section of the tumor were adopted in our study, and these ROIs were considered to be the most likely sites of metastasis.

> The regression analysis indicated that the mean attenuation of  $VF_{ROI2}$  was not an independent risk factor for PM, and it had a lower predictive ability than ascites and cT stage. The changes in the adipose microenvironment and the increase in the mean attenuation of VF may be mainly concentrated around the tumor, and the ROI of VF on the whole axial level may dilute this change and reduce the predictive sensitivity. However, the results confirmed that the mean attenuation of VF was significantly different between the PM-positive and PM-negative groups in both ROI 1 and ROI 2. The 30th, 50th, 70th, 25th, and 75th percentiles of attenuation of VF<sub>ROI2</sub> were also significantly different between the two groups. Moreover, the mean attenuation of VF was related to clinical features representing tumor invasiveness. Therefore, we have reasons to believe that the mean attenuation of VF is a potential auxiliary parameter for predicting occult PM in patients with GC, especially for those with only nonenhanced CT images or upper abdominal CT images.

> The mean attenuation was negatively correlated with the volume of VF; however, noticeably, no significant difference in the VF volume was found between the PM-positive and PM-negative groups. Considering the relationship between the mean attenuation and volume of VF, volume-stratified

Table 3 Comparison of attenuations of visceral fat between different clinical characteristic classifications

$-84.90 \pm 6.19$ $-83.83 \pm 4.88$ $-84.48 \pm 5.11$ $-84.46 \pm 5.14$ $-84.64 \pm 5.81$ $-82.49 \pm 4.99$	0.306 0.937 0.339
-84.48 ± 5.11 -84.46 ± 5.14 -84.64 ± 5.81	
-84.46 ± 5.14 -84.64 ± 5.81	
-84.64 ± 5.81	0.339
	0.339
-82.49 ± 4.99	
-84.18 ± 5.91	0.377
-85.11 ± 5.56	
-84.64 ± 5.92	0.583
$-83.81 \pm 4.86$	
$-85.04 \pm 6.04$	0.002 <sup>1</sup>
-82.07 ± 3.40	
$-84.80 \pm 5.81$	0.039 <sup>1</sup>
-80.46 ± 3.41	
-84.93 ± 5.86	0.049 <sup>1</sup>
-82.05 ± 4.67	
-85.41 ± 5.79	0.001 <sup>1</sup>
-81.52 ± 4.69	
-85.48 (-89.85, -82.95)	0.030 <sup>1</sup>
-83.08 (-86.68, -79.43)	
-84.54 (-87.51, -80.60)	
$-85.88 \pm 5.83$	0.003 <sup>1</sup>
-82.84 ± 5.29	
$-84.82 \pm 6.36$	0.517
-84.15 ± 4.98	
	$-85.11 \pm 5.56$ $-84.64 \pm 5.92$ $-83.81 \pm 4.86$ $-85.04 \pm 6.04$ $-82.07 \pm 3.40$ $-84.80 \pm 5.81$ $-80.46 \pm 3.41$ $-84.93 \pm 5.86$ $-82.05 \pm 4.67$ $-85.41 \pm 5.79$ $-81.52 \pm 4.69$ $-85.48 (-89.85, -82.95)$ $-83.08 (-86.68, -79.43)$ $-84.54 (-87.51, -80.60)$ $-85.88 \pm 5.83$ $-82.84 \pm 5.29$ $-84.82 \pm 6.36$

 $<sup>^{1}</sup>P < 0.05$ .

CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA125: Carbohydrate antigen 199; VF: Visceral fat; ROI 2: Regions of interest starting at the largest axial level of the tumor and extending down 25 mm.

Table 4 Stratified analysis of volume				
	PM (-)	PM (+)	P value	AUC (95%CI)
Volume > median				
No	45	19		
Mean attenuation (HU)	-89.08 ± 5.31	-85.44 ± 3.93	0.009 <sup>1</sup>	0.726 (0.59-0.854)
Volume ≤ median				
No	40	24		
Mean attenuation (HU)	-81.92 ± 3.01	-79.61 ± 4.94	0.046 <sup>1</sup>	0.639 (0.490-0.787)

PM: Peritoneal metastasis; No: Number; AUC: Area under the curve; HU: Hounsfield units.

Table 5 Variables and coefficients of multiple regression logistic analysis				
Variable	OR	95%CI	P value	
Based on all characteristics				
Mild ascites (+ vs -)	3.552	(1.375-9.175)	0.009 <sup>1</sup>	
Mean attenuations of $VF_{ROI2}$	3.437	(0.914-12.914)	0.068	
cT stage (≥ T4 vs ≤ T3)	2.631	(1.126-6.144)	0.025 <sup>1</sup>	
Intercept	0.009		0.001 <sup>1</sup>	
Based on clinical characteristics				
Mild ascites (+ vs -)	4.188	(1.636-10.722)	0.003 <sup>1</sup>	
cT stage (≥ T4 <i>vs</i> ≤ T3)	2.992	(1.301-6.881)	0.010 <sup>1</sup>	
Intercept	0.068		0.001 <sup>1</sup>	

 $<sup>^{1}</sup>P < 0.05$ 

VF: Visceral fat; ROI: Region of interest; OR: Odds ratio; CI: Confidence interval.

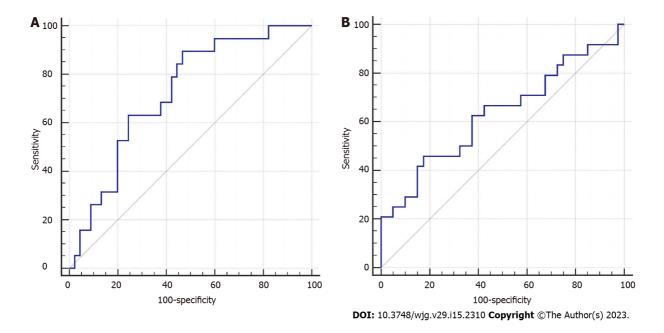


Figure 3 Performance of computed tomography attenuations for visceral fat in predicting peritoneal metastasis in gastric cancer. A: Highvolume group; B: Low-volume group.

analysis was applied to minimize the deviations in volume variation. The mean attenuation of  $VF_{ROI2}$ showed a higher predictive potential in the high-volume group than in the low-volume group. This result suggests that patients with high-volume VF may have more hypoxic or disordered adipocytes that secrete proinflammatory cytokines and angiogenic factors and promote tumor metastasis than patients with low-volume VF[19]. The attenuation of VF was significantly correlated with cT stage, cN stage, CA125, and CA199, indicating that increased VF attenuation is highly correlated with tumor progression.

Mild ascites and cT stage are independent predictive factors for occult PM. Liu et al[7] reported that cT stage was significantly correlated with occult PM, which reflects tumor aggressiveness. Mild ascites was also incorporated into a clinical model for predicting occult PM in a multicenter study[5]. Significant differences were observed in the mean attenuations of VF between the different ascites statuses and cT stages.

Compared with previous radiomics studies, the extraction of VF parameters in our study was based on unenhanced CT images through semiautomated sketching technology, which would reduce the selection differences between operators. The consistency between the operators of VF parameters was excellent. The ROIs in the peritoneum used in most previous studies on occult PM were manually sketched[5,18]. Thus, evaluating the consistency among different operators in defining the location and area of ROIs selected was difficult. In addition, three-dimensional ROIs were defined in our study,

which remain applicable in patients with lesser VF.

This study has certain limitations. First, the VF parameters were measured using data obtained from a single center with a small sample size, and multicenter studies with a large sample size are thus needed to validate the results. Second, the parameters used to quantify VF changes were obtained only from unenhanced CT images, which warrants the need to consider more parameters from multiphase enhanced images.

# CONCLUSION

In conclusion, our study demonstrates the great potential of VF parameters in predicting occult PM in GC and presents a noninvasive preoperative model that combines the mean attenuation of VF and clinical factors for predicting occult PM in GC.

# ARTICLE HIGHLIGHTS

#### Research background

The preoperative prediction of peritoneal metastasis (PM) in gastric cancer (GC) would prevent unnecessary surgery and promptly indicate an appropriate treatment plan.

#### Research motivation

Tumor infiltration of the peritoneum alters the characteristics of the surrounding VF on computed tomography (CT), and these changes have been investigated in previous studies.

## Research objectives

We therefore aimed to explore the predictive value of VF parameters obtained from preoperative CT images for occult PM and to develop an individualized model for predicting occult PM in patients with GC.

#### Research methods

A total of 128 confirmed GC cases that underwent CT scans were analyzed and categorized into PMpositive and PM-negative groups. The clinical characteristics and VF parameters of two regions of interest (ROIs) were collected. Univariate and stratified analyses based on VF volume were performed to screen for predictive characteristics for occult PM. Prediction models with and without VF parameters were established by multivariable logistic regression analysis.

# Research results

The mean attenuations of VF<sub>ROI1</sub> and VF<sub>ROI2</sub> varied significantly between the PM-positive and PMnegative groups (P = 0.044 and 0.001, respectively). The mean attenuation of VF<sub>ROI2</sub> was included in the final prediction combined model, but not an independent risk factor of PM (P = 0.068). No significant difference was observed between the models with and without mean attenuation of VF (area under the curve:  $0.749 \ vs \ 0.730, P = 0.339$ ).

#### Research conclusions

The mean attenuation of VF is a potential auxiliary parameter for predicting occult PM in patients with GC.

#### Research perspectives

Our study demonstrates the great potential of VF parameters in predicting occult PM in GC and presents a noninvasive preoperative model that combines the mean attenuation of VF and clinical factors for predicting occult PM in GC.

#### **FOOTNOTES**

Author contributions: Li LM, Huang WP, and Gao JB designed the research study; Huang WP, Li LM, and Gao JB performed the research; Yu Y and Cheng PY contributed analytic tools; Li LM, Feng LY, and Liu CC analyzed the data and wrote the manuscript; all authors have read and approved the final manuscript.

Supported by Henan Province 2023 Scientific Research Projects Focused on Higher Education Project, China, No. 23A320059.

Institutional review board statement: The study was reviewed and approved by the First Affiliated Hospital of Zhengzhou University Institutional Review Board (Approval No. 2021-KY-1070-002).

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: Dataset available from the corresponding author at jianbogaochina@163.com.

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S-Editor: Liu GL L-Editor: Wang TQ P-Editor: Liu GL

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