Article

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The Evaluation of Gastric Cancer Lymphovascular Invasion Using CT Volume Perfusion

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Background: The best treatment option for patients with resectable gastric cancer is radical gastric cancer surgery. However, the postoperative overall survival rate is low. Lymphovascular invasion (LVI) is a risk factor for cancer recurrence and a stand-alone predictor of a poor post-operative prognosis for gastric cancer (GC) patients. Current evaluation of tumor LVI performed on histological specimens, which can only be assessed after surgery, is also limited by intra-tumoural heterogeneity via biopsy. This study explored the value of CT volume perfusion in assessing tumors' lymphovascular invasion of gastric cancer.

Methods: 59 gastric cancer patients confirmed by pathology who underwent both computed tomography (CT) volume perfusion examinations and gastrectomy surgery were prospectively included. Tumour lymphovascular invasion (LVI, positive or negative) was evaluated. The relationship between clinicopathological variables associated with LVI and CT perfusion parameters was analyzed by univariate analysis, followed by multivariate logistic regression analysis and receiver operating characteristic (ROC) analysis.

Results: The LVI-positive and LVI-negative groups differed significantly in terms of time to start (TTS), mean transit time (MTT), Tmax, and flow extraction product (FEP). Both FEP (odds ratio (OR), 1.048; 95% confidence interval (CI): 1.005–1.092) and MTT (OR, 0.549; 95% CI: 0.351–0.858) have the potential to be employed as independent predictors of LVI (both $p < 0.05$). There were different correlations between LVI, lower MTT and greater FEP. The specificity of MTT (87.88%) was higher than that of FEP (72.73%), while the sensitivity of MTT (53.85%) was lower than that of FEP (57.69%). Compared to MTT and FEP alone, the combination demonstrated a comparatively higher area under the curve (AUC) (0.797) and sensitivity (84.62%).

Conclusions: CT volume perfusion helps evaluate LVI in gastric cancer before surgery. MTT and FEP are independent predictors for LVI, and the combination variation has better diagnostic performance.

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Keywords: gastric cancer; adenocarcinoma; X-ray computed tomography; lymphovascular invasion; prognosis

Introduction

The most frequent malignant tumor of the upper gastrointestinal tract, gastric cancer (GC), ranks third globally in terms of cancer-related deaths [1]. The detection rate of early gastric cancer in China is low, and most patients are diagnosed with advanced gastric cancer. Radical gastric cancer surgery is the recommended course of action for patients with resectable stomach cancer. Since gastric cancer patients are prone to postoperative local recurrence or distant metastasis, the overall survival rate after surgery is low. The five-year overall survival rate of patients with advanced gastric cancer is lower than 30% [2]. Accurate preoperative assessment of risk factors in gastric cancer patients contributes to individualized treatment. Therefore, it is necessary to identify markers to detect those patients with a higher risk for recurrence.

Postoperative pathological Tumor Node Metastasis (TNM) staging proposed by the American Joint Committee on Cancer (AJCC) is recognized as the most reliable prognostic assessment for gastric cancer. Among these, postoperative pathologic assessment of depth of infiltration staging and lymph node metastasis staging are the main factors in assessing patient prognosis. However, TNM staging ignores tumor heterogeneity; patients with the same TNM stage have different prognoses. Tumor lymphovascular invasion (LVI), in addition to the AJCC TNM stage, is an independent risk factor for patients with gastric cancer's prognosis for survival [3,4]. LVI is an independent predictor of a poor result for GC patients after surgery and a risk factor for the cancer's recurrence [4–7]. Accurate assessment of tumor LVI can help physicians identify patients at high risk for cancer recurrence and develop a personalized treat-

ment plan for gastric cancer patients. Current evaluation of tumor LVI performed on histological specimens, which can only be assessed after surgery and is also limited by intra-tumoural heterogeneity via biopsy. It would be helpful to evaluate tumor LVI by a non-invasive means preoperatively, which will help clinicians further customize and select the best treatment options for individuals with GC. Therefore, we attempt to find an additional quantitative, non-invasive method to predict tumor LVI preoperatively from a functional perspective.

As a functional imaging technique, computed tomography (CT) perfusion is an attractive technique to assess tissue perfusion and permeability [8–10]. CT perfusion can evaluate the hemodynamic and functional changes of gastric cancer tumor tissue by measuring its blood perfusion parameters, an important reference value for clinical diagnosis and treatment. Yao *et al*. [10] have found a positive correlation between blood flow (BF) and microvessel density in gastric cancer tumor tissue. Meanwhile, tumor neovascularization is related to LVI in gastric cancer [11]. Theoretically, CT perfusion might predict the LVI of tumor tissue in gastric cancer.

Therefore, we aimed to investigate whether CT perfusion can predict LVI of tumor tissue in gastric cancer patients by measuring tumor perfusion parameters.

Materials and Methods

Patients

This research was authorized by our hospital's institutional ethics committee, and all patients provided informed written permission. From March 2022 to September 2023, 77 patients who met the following inclusion criteria were prospectively enrolled in this study: (i) primary gastric adenocarcinoma proven by endoscopic biopsy; (ii) no chemoradiotherapy performed before CT perfusion scanning and surgery; and (iii) visible GC on preoperative non-contrast CT. CT volume perfusion was performed on all 77 patients, among whom 18 were excluded for the following reasons: (i) obvious motion artifact (n = 3); (ii) pathological type was mucous adenocarcinoma (n = 3); patients did not receive gastrectomy because of distant metastasis or other reasons (n = 12). Finally, 59 patients (M/F = 35/24) were included in our study. The patient inclusion and exclusion process is shown in Fig. 1. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki.

CT Volume Perfusion Acquisition

A 2 × 192-slice dual-source CT scan (Somatom Force, Siemens Healthineers, Forcheim, Germany) was used to assess each patient. Before the CT scan, all patients had a fast of over eight hours and were given a thousand milliliters of water. 10 mg of scopolamine hydrochloride (Buscopan; Boehringer Ingelheim, Ingelheim am Rhein, Germany) was injected 10 min before the examination to inhibit gastrointestinal peristalsis. To reduce abdominal wall motion, the doctor gave the patient gentle breathing instructions and placed a compression band over their belly before the examination. To find the tumor, a standard upper abdomen non-contrast CT scan was carried out. The radiologist then performed a CT dynamic volume perfusion scan centering on the tumor's maximum level, selecting a scan range of 114 mm in the z-axis. Using a pump injector (MEDRAD Stellant, MEDRAD, Leverkusen, Germany), 50 mL of nonionic iodinated contrast agent (Iopamiro; Bracco, Shanghai, China) (370 mg of iodine per milliliter) was injected through a 19-gauge venous cannula through the anterior tibial vein at a flow rate of 5 mL/sec. CT perfusion scanning was started 8 s after contrast injection, using the CT body perfusion scanning sequence. The following parameters were used for CT volume perfusion: 80 kV, 80 mAs, gantry rotation speed (0.25 s), collimation (0.6 mm), and matrix (512 × 512), scanning distance (114 mm), scan time (1.5 s), number of scans (30), and examination time (45 s).

CT Volume Perfusion Image Analysis

CT perfusion images were processed using a commercially available software program (syngo. via VB10, Siemens Healthineers, Forcheim, Germany) by a radiologist (C. XM, with 7 years of expertise in abdominal radiology). CT perfusion image analysis was performed using the deconvolution method to generate functional maps (Fig. 2): blood flow (BF, mL/100 g/min), blood volume (BV, mL/100 g), time to start (TTS, seconds), mean transit time (MTT, seconds), time to drain (TTD, seconds), Tmax = TTS + MTT/2, flow extraction product (FEP, mL/100 g/min). The post-processing steps are as follows: (1) Motion calibration: the overall contour was automatically calibrated. (2) Input vessel selection: the abdominal aorta was selected as the input artery at the tumor level. (3) Region of interest (ROI) selection: select the largest level of the tumor, avoid blood vessels and necrotic tissues, and outline the ROI close to the gastric mucosal surface to encompass as much tumor tissue as possible, but the diameter of the ROI is less than 1/2 of the thickened gastric wall [12]. (4) Measurements were made of the following perfusion parameters: BF, BV, MTT, TTS, TTD, Tmax, and the FEP. After two weeks, CT perfusion parameter measurements of gastric cancer tumor tissue were repeated in random order by the same radiologist applying the same method.

Pathological Evaluation

According to standard pathological procedures, all gastric postoperative specimens were fixed, standardized, paraffin-embedded, sectioned, and hematoxylin-eosin (HE) stained. The pathological diagnosis was determined after a discussion between 2 experienced pathologists. Tumor emboli inside either the vascular or lymphatic channels was

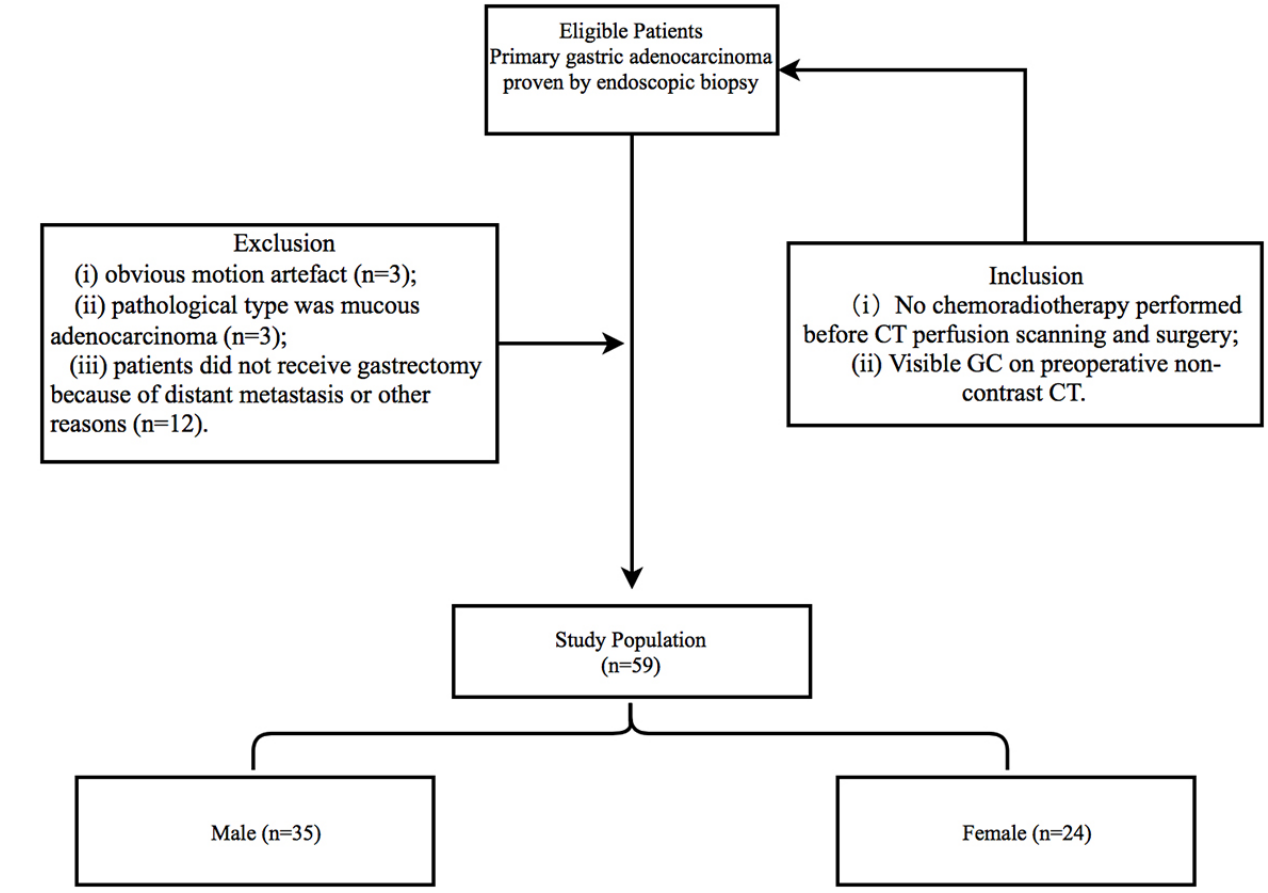

Fig. 1. Flowchart of the patient inclusion and exclusion process. GC, gastric cancer; CT, computed tomography.

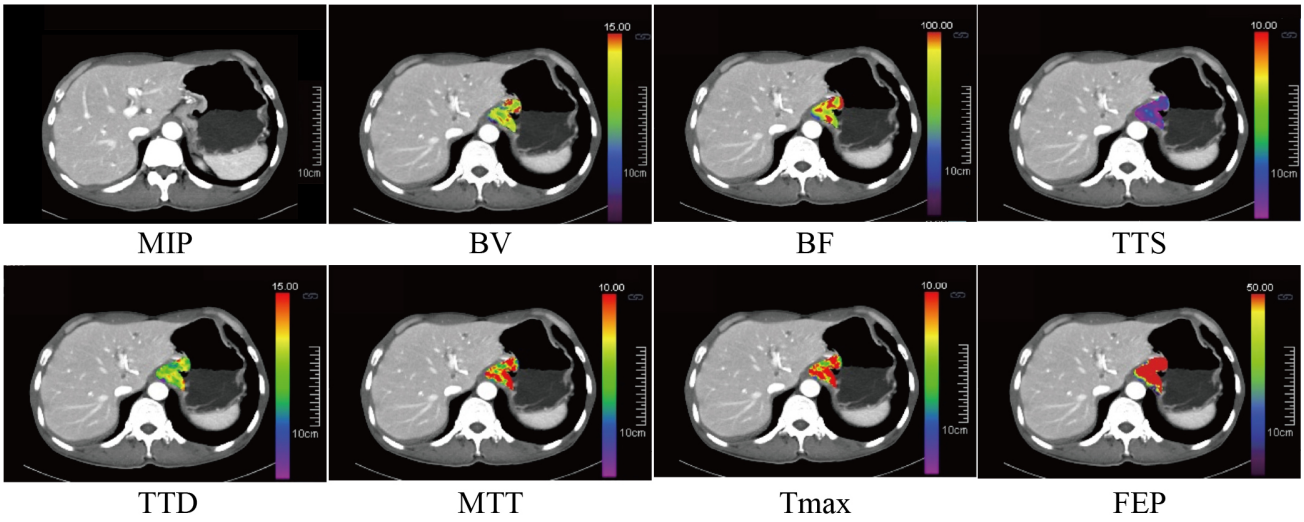

Fig. 2. CT perfusion functional maps of a 51-year-old man with poorly differentiated carcinoma in the cardia of the stomach. MIP, maximal intensity projection; BV, blood volume; BF, blood flow; TTS, time to start; TTD, time to drain; MTT, mean transit time; FEP, flow extraction product.

the definition of LVI positive (LVI-P) (Fig. 3); otherwise, it was defined as LVI negative (LVI-N) [4]. Pathological TNM staging was evaluated according to AJCC 8th edition staging. Tumour pathological differentiation was assessed according to the following criteria [13]: moderately and highly differentiated adenocarcinoma was defined as

consisting of well-differentiated gland-like structures, with tumor cells having mild anisotropy and arranged in cords and small nests; poorly differentiated adenocarcinoma cells showed marked anisotropy and diffuse distribution, with a large and darkly stained nucleus, the disappearance of the gland-like structures, and the formation of a mucus lake could be seen. According to gastric cancer's tissue structure and biological behavior, it was divided into intestinal, diffuse, and mixed types, namely the Lauren classification [14].

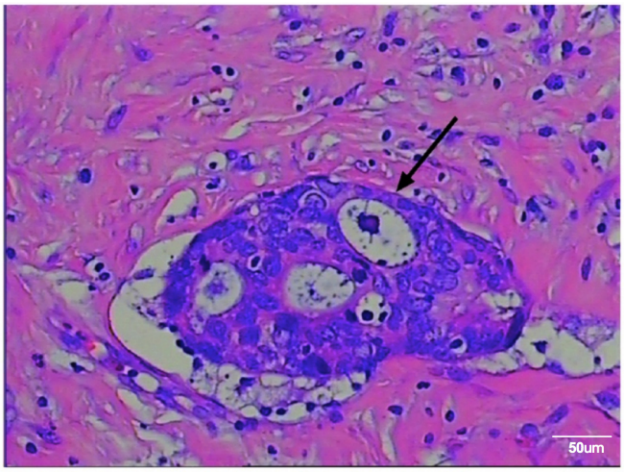

Fig. 3. Gastric cancer tissue lymphovascular invasion positive (LVI-P), tumor emboli within lymphovascular (arrow) [hematoxylin-eosin (HE), ×200].

Statistical Analysis

SPSS Statistics (version 25.0, IBM Corporation, Armonk, NY, USA) was used for statistical analyses. CT perfusion parameter values were expressed as mean ± standard deviation ($\bar{x} \pm s$). Normality was tested using the Kolmogorov-Smirnov method, and variance homogeneity was then tested with Levene's test.

To assess the systematic bias of repeated ROI measurements, a paired Student's *t*-test was used; if there was no discernible difference between the two measurements, the ROI mean values were computed for further examination. Moreover, the intra-observer reproducibility of CT perfusion parameter values was evaluated using the interclass correlation coefficient (ICC). Good agreement was defined as an ICC >0.75. Student's *t*-test or Mann-Whitney U test was used to statistically examine the difference in CT perfusion parameters between the LVI-P and LVI-N groups. A p value of less than 0.05 was deemed statistically significant. Sex, pathological differentiation, Lauren classification, Carcinoembryonic antigen (CEA) level (Carcinoembryonic antigen, CEA >5 ng/mL was considered positive, otherwise negative), and Carbohydrate antigen199 (CA199) level (Carbohydrate antigen199, CA199 >37 ng/mL was considered positive, otherwise negative) between groups were tested by chi-square test or Fisher's exact test, $p < 0.05$ was considered a statistically significant difference. Using relevant factors from univariate analysis as inputs, multivariate logistic regression analysis identified independent predictors of LVI and constructed combinations of these predictors. The receiver operating characteristic (ROC) curve was also examined to find the sensitivity, specificity, and area under the curve (AUC). Calibration curves and the Delong test were used to evaluate the diagnostic performance of the predictive model.

Results

Clinicopathologic Manifestation

Table 1 summarises the clinicopathological characteristics of the study population. All 59 cases were confirmed as gastric adenocarcinoma by postoperative histopathology, among which 36 cases were low-differentiation and 23 cases were well differentiation; 29 cases were diffuse, 13 cases were intestinal, and 17 cases were mixed in Lauren's typing; 33 cases were LVI-positive, while 26 cases were LVI-negative. CEA levels were elevated in 19 and CA199 in 10 patients, respectively.

Comparison of Clinicopathological Characteristics of the LVI-P Group and LVI-N Group

Significant differences in pathological differentiation, Lauren classification, lymph node metastasis, and CA199 value between the two groups demonstrated that low differentiation, diffuse type, and elevated CA199 value were more likely to present LVI-P. At the same time, LVI-P patients were more likely to have lymph node metastasis (Table 2).

Reproducibility of CT Perfusion Parameter Measurements

There was no difference between two repeated measurements of CT perfusion parameters (p = 0.218–0.929, Table 3). The ICC was 0.821–0.974 between two repeated measurements of perfusion CT parameters. All of them were in good agreement.

Comparison of CT Perfusion Parameters of the LVI-P Group and LVI-N Group

The BF and FEP were higher in the LVI-P than in the LVI-N group, and the BV, TTS, TTD, MTT, and Tmax were lower than in the LVI-N group (Table 4).

The univariate statistical analysis revealed a difference ($p < 0.05$) in TTS, MTT, Tmax, and FEP between the two groups. Compared to the LVI-N group, the FEP was considerably more significant, and TTS, MTT, and Tmax were much lower in the LVI-P group (Table 4).

Logistic regression assessed the TTS, MTT, Tmax, and FEP variables. The results showed that both MTT (odds

Table 1. Clinicopathological characteristics of the study population.

Parameter	
Age	
>61	33
≤61	26
Gender	
Male	35
Female	24
Differentiation	
Well-moderate	23
Poor	36
Lauren classification	
Intestinal type	13
Diffuse type	29
Mixed type	17
LVI	
Positive	33
Negative	26
T stage	
T2	4
T3	24
T4	31
Lymph node metastasis	
Yes	36
No	23
CEA	
Normal	40
Elevated	19
CA199	
Normal	49
Elevated	10

LVI, lymphovascular invasion; CEA, Carcinoembryonic antigen; CA199, Carbohydrate antigen199.

Table 2. Clinicopathological characteristics of 59 patients with comparative statistics.

Characteristics	LVI		χ^2	*p*-value
	Positive	Negative		
Age				
>61	18	15	0.058	0.809
≤61	15	11		
Gender				
Male	17	18	1.891	0.169
Female	16	8		
Differentiation				
Well-moderate	9	14	4.317	**0.038**
Poor	24	12		
Lauren classification				
Intestinal type	3	10	8.688	**0.014**
Diffuse type	17	12		
Mixed type	13	4		
T stage				
T2	2	2	0.761	0.684
T3	12	12		
T4	19	12		
Lymph node metastasis				
Yes	25	11	6.841	**0.009**
No	8	15		
CEA				
Normal	20	20	1.773	0.183
Elevated	13	6		
CA199				
Normal	24	25		**0.032**
Elevated	9	1		

χ^2, chi-square value; LVI, lymphovascular invasion; CEA, Carcinoembryonic antigen; CA199, Carbohydrate antigen199. *p* values were determined using the chi-square test or Fisher's exact test, *p* values in bold indicate a statistical significance.

ratio (OR), 0.549; 95% confidence interval (CI): 0.351–0.858) and FEP (OR, 1.048; 95% CI: 1.005–1.092) could be utilized as independent predictors of LVI (both $p < 0.05$). There were different correlations between the occurrence of LVI and lower MTT and greater FEP (Table 5).

We analyzed the sensitivity, specificity, and area under the curve (AUC) of MTT, FEP, and their combination (MTT+FEP) using the receiver operating characteristic (ROC) curve. These results are shown in Table 6. By comparing the results in Table 6, it showed that the specificity of MTT (87.88%) was higher than that of FEP (72.73%), while the sensitivity of MTT (53.85%) was lower than that of FEP (57.69%). The combination of MTT and FEP showed a relatively higher AUC (0.797) and sensitivity (84.62%) than those of MTT and FEP. The results of the Delong test showed that the difference between the MTT+FEP combination and the FEP was statistically significant ($p = 0.031$), and the differences between the MTT and the FEP, MTT+FEP, respectively, were not statistically significant ($p = 0.532$, $p = 0.136$). Fig. 4 shows the ROC curve of MTT and FEP and their combination in predicting LVI in gastric cancer.

The Hosmer-Lemeshow test showed $p > 0.05$ for MTT, FEP, and MTT+FEP, indicating no significant difference between predicted and observed probability. The calibration plot of MTT, FEP, and their combination for predicting LVI in gastric cancer is shown in Fig. 5.

CT Perfusion Radiation Dose to Patients

After the gastric cancer patients' CT perfusion scanning was completed, the computer automatically generated the scanning protocol containing the volumetric CT dose index (CTDIvol) and the dose-length product (DLP). According to the European guidelines for CT quality standards, the weighting factor k for the adult abdomen was 0.015, and the effective dose (ED) was calculated as ED = DLP × k.

Table 3. Comparison of two measurements of CT perfusion parameter values.

Variables (n = 59)	Mean ± SD	*t*	*p*-value
BF1	88.21 ± 33.74	–0.959	0.342
BF2	93.93 ± 34.79		
BV1	8.94 ± 3.96	–0.306	0.761
BV2	9.11 ± 2.67		
MTT1	6.49 ± 1.50	0.520	0.605
MTT2	6.40 ± 1.60		
TTD1	7.59 ± 1.55	–0.271	0.788
TTD2	7.67 ± 1.79		
TTS1	1.19 ± 0.72	0.159	0.874
TTS2	1.17 ± 0.85		
Tmax1	6.55 ± 1.45	–0.089	0.929
Tmax2	6.57 ± 1.55		
FEP1	59.20 ± 17.47	1.245	0.218
FEP2	55.25 ± 18.53		

SD, Standard Deviation.

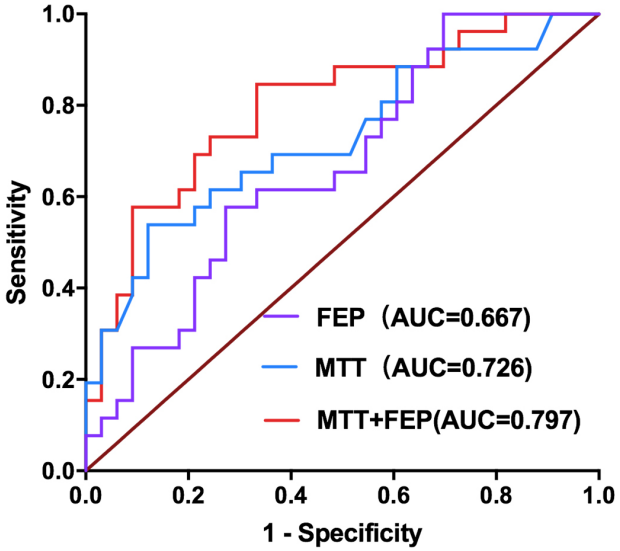

Fig. 4. Receiver operating characteristic (ROC) analysis curve in gastric cancer patients with and without LVI.

The CTDIvol of the gastric cancer patients in this study was 39.28 L, the DLP was 582.7 mGycm, and the ED was 8.73 mSv.

Discussion

We compared CT perfusion parameters in gastric cancer between the LVI-P and LVI-N groups. We found that MTT and FEP were independent predictors of LVI in gastric tumors, and their combinations had better predictive performance. Our study demonstrated that CT perfusion was a quantitative and non-invasive method that could predict LVI in gastric cancer patients.

LVI is the basis of tumor cell spread and is significantly related to gastric cancer T stage and lymph node metastasis [15]. Prior research revealed a substantial correlation between the existence of LVI in gastric cancer and the amount of CA199, Lauren classification, tumor differentiation, gastric wall invasive depth, and lymph node involvement [4]. Our results are consistent with those research published before. We found that low differentiation, diffuse type, and elevated CA199 value were more likely to present LVI-P, while LVI-P patients were more likely to have lymph node metastasis. Patients with gastric cancer who are LVI positive have poorer overall survival [7]. The 5-year survival rate of gastric cancer patients in the LVI-negative group was 55.95%; however, in the LVI-positive group, the 5-year survival rate was 13.9% [7]. The hypothesis that the existence of LVI is a risk factor for cancer recurrence in GC patients after surgery is supported by this research as well as other publications. When evaluating the prognosis and choosing the appropriate course of therapy for the patient, the LVI status should be considered.

In recent years, some researchers have applied CT-enhanced scanning to assess gastric cancer LVI preoperatively: By comparing the contrast enhancement ratio of CT scan in gastric cancer tissues between the LVI-positive group and the negative group, Yin *et al.* [16] found that there was a difference in contrast enhancement ratio between the two groups. Ma *et al.* [17] found that enhanced CT could predict the LVI of tumors in gastric cancer patients preoperatively by measuring the CT attenuation value ratio of the tumor to the spleen in the portal phase. Although conventional CT is a common preoperative examination in gastric cancer patients, its parameters are limited and cannot quantitatively assess tumor perfusion or permeability. Moreover, conventional CT could not completely avoid a site-by-site bias when placing regions of interest in all phases. CT perfusion is an attractive technique to assess permeability in gastric cancer, and its parameters are more than those of conventional CT.

Sun *et al.* [18] found that BF, BV, and permeability surface (PS) values could be used to predict tumor tissue differentiation in gastric cancer. Zhang *et al.* [19] reported that the CT perfusion parameter permeability surface (PS) was significantly correlated with lymphatic involvement and an independent predictor of prognosis in gastric cancer.

To our knowledge, no studies applying CT perfusion to explore tumor lymphovascular invasion, including gastric cancer. Our study is the first to compare CT perfusion parameters between the LVI-P and LVI-N groups. In our study, FEP was higher in the LVI-P group, and it was an independent predictor for LVI. PS or FEP indicates vessel integrity and maturity because it reflects the permeability of the contrast agent from the capillary endothelium to the interstitial space [14]. If the vascular continuity is disrupted, the permeability of the tumor tissue will increase, manifesting as elevated FEP. In the LVI-P group, tumor cells infiltrated and disrupted the lymphatic or vascular structure,

Table 4. Univariate analysis of perfusion CT parameters between the LVI-P and LVI-N groups.

Parameters	LVI-P (n = 33)	LVI-N (n = 26)	*t*/Z	*p*-value
	(Mean ± SD)/M (P25, P75)	(Mean ± SD)/M (P25, P75)		
BV (mL/100 g)	8.96 ± 2.73	9.11 ± 2.90	–0.211	0.834
BF (mL/min/100 mL)	98.26 ± 25.35	84.80 ± 26.12	1.998	0.051
TTS (s)	0.83 (0.63,1.12)	1.05 (0.76,1.78)	–2.184	**0.029**
TTD (s)	7.47 ± 1.59	7.75 ± 1.51	–0.683	0.497
MTT (s)	5.84 ± 1.34	7.13 ± 1.57	–3.387	**0.001**
Tmax (s)	6.09 ± 1.54	7.03 ± 1.28	–2.510	**0.015**
FEP (mL/100 g/min)	59.12 (48.78,78.40)	49.73 (43.01,63.10)	–2.183	**0.029**

BF, blood flow (mL/100 g/min); BV, blood volume (mL/100 g); MTT, mean transit time (seconds); TTD, time to drain (seconds); TTS, time to start (seconds); Tmax = TTS + MTT/2; FEP, flow extraction product (mL/100 g/min); SD, Standard Deviation. *p* values were determined using Student *t* test or Mann-Whitney U test. A *p*-value < 0.05 indicates a significant difference in CT perfusion parameters between the LVI-P and LVI negative (LVI-N) groups. *p* values in bold indicate statistical significance.

Table 5. Multivariate analysis of CT perfusion parameters in predicting LVI in gastric cancer.

Parameters	B	SE	Wald	*p*-value	OR	95% CI
MTT (s)	–0.600	0.228	6.923	0.009	0.549	0.351–0.858
FEP (mL/100 g/min)	0.047	0.021	4.835	0.028	1.048	1.005–1.092

MTT, mean transit time (seconds); FEP, flow extraction product (mL/100 g/min); CI, confidence interval; OR, odds ratio.

Table 6. ROC analysis and diagnostic performance of MTT, FEP, and their combination.

Variables	Cut-off	AUC (95% CI)	Sensitivity (%)	Specificity (%)
MTT (s)	7.41	0.726 (0.594–0.859)	53.85	87.88
FEP (mL/100 g/min)	50.52	0.667 (0.529–0.804)	57.69	72.73
MTT+FEP	0.60	0.797 (0.681–0.913)	84.62	66.67

MTT, mean transit time (seconds); FEP, flow extraction product (mL/100 g/min). ROC, receiver operating characteristic curve.

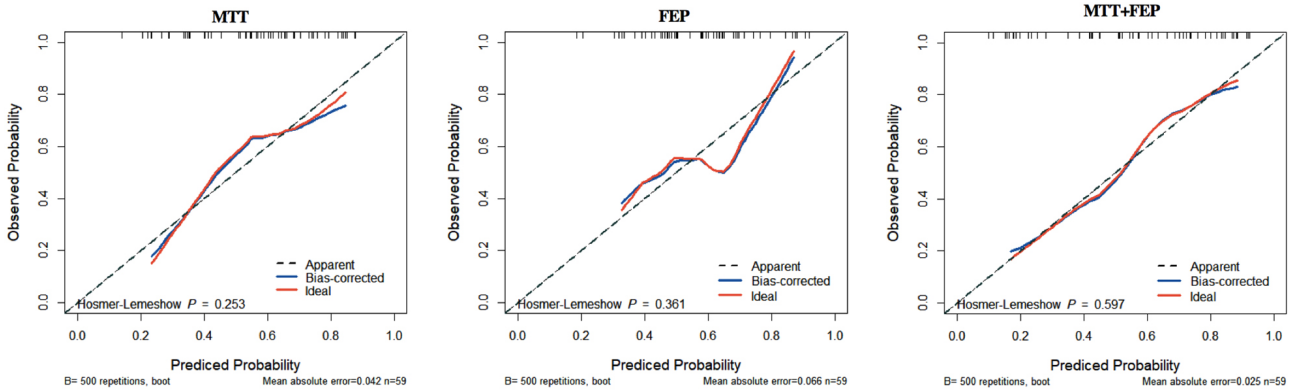

Fig. 5. Calibration plot of MTT, FEP, and their combination for the prediction of LVI in gastric cancer.

which was the reason for the elevated FEP in the LVI-P group in this study. Therefore, our results demonstrated that FEP might be a helpful independent predictor for LVI in gastric cancer.

We also found that MTT was lower in the LVI-P group and was a useful independent predictor. Lee *et al.* [20] found that MTT was significantly elevated in the poorly cohesive carcinoma (PCC) group by comparing CT perfusion parameters of gastric cancer tumor tissues in the PCC and non-PCC groups. They suggested that the elevation of MTT was due to the widening of endothelial junctions and disruption of the basement membrane in the PCC type of gastric cancer. According to the central volume principle proposed by Miles [9], MTT = BV/BF. MTT is the time of transit of

blood flowing into an artery and out from a vein, and it reflects the tissue perfusion pressure. The tumor tissue in the LVI-P group contained abundant microvessels with disordered structures presenting as arteriovenous shunts, while blood flow resistance decreased [20]. We believe this is why the lower MTT in the LVI-P group compared to the LVI-N group of gastric cancer.

In addition to CT perfusion, dynamic contrast-enhanced (DCE) MRI can also reflect the perfusion characteristics of tumor tissues. However, because the stomach is a hollow organ with physiologic peristalsis and DCE MRI examination takes a long time, DCE MRI is currently less used in gastric cancer. There are no studies applying DCE MRI for preoperative assessment of LVI in gastric cancer.

Our study has some limitations. First, fewer patients were in this study, which would have resulted in lower test efficacy. Moreover, our research is a single-center study. However, this is the first preliminary report about the usefulness of CT perfusion in predicting LVI in gastric cancer. A large number of patients from multiple institutions are strongly warranted to confirm our study results and to firmly establish the value of CT perfusion in gastric cancer patients. Second, the radiation dose of CT perfusion cannot be avoided. Our study performed CT perfusion with an 80 kVp tube voltage, and the reduced tube voltage in CT perfusion studies has the advantage of significantly reducing radiation dose levels while simultaneously increasing contrast attenuation [21]. Third, the stomach is a tubular organ with peristalsis, which may cause motion artifacts during CT perfusion examination. In our study, 10 mg of scopolamine was administered 10 min before scanning to minimize stomach peristalsis. Moreover, motion correction was performed before the CT perfusion data analysis.

Conclusions

CT perfusion is helpful in evaluating LVI in gastric cancer patients before surgery. MTT and FEP are independent predictors for LVI, and the combination variation has better diagnostic performance.

Availability of Data and Materials

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

Author Contributions

Conception and interpretation of this work: all authors; Drafting of the manuscript: YL, LH, PC; Critical revisions of the manuscript: LL, LC, XC; Approved the final version of the manuscript: all authors; Accountable for all aspects of the work: all authors.

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Research Ethics Committee of Jiangmen Central Hospital (No.2018-1). Written informed consent was obtained from each patient participating in this study before enrollment.

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Conflict of Interest

The authors declare no conflict of interest.

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