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Analysis of the value of test bolus and bolus tracking in diagnosing gastric cancer

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► ***Original article***

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ABSTRACT

Background: To explore the clinical value of Test Bolus (TB) scanning technology and Bolus Tracking (BT) technology in the preoperative TNM staging of gastric cancer (GC) patients and the enhanced display of perigastric arteries. ***Materials and Methods:*** A retrospective analysis was conducted on the clinical information of 107 gastric cancer patients with complete imaging and pathological diagnostic data (TB group: 30 cases, BT group: 77 cases). Chi-square tests and t-tests were used to compare baseline information between the TB and BT groups. The consistency between the diagnostic results of the TB and BT groups and pathological examination results was analyzed using Kappa tests. ***Results:*** There were no statistically significant differences between the TB and BT groups in terms of gender (P=0.499), age (P=0.419), family history of tumors (P=0.979), smoking history (P=0.269), and pain symptoms (P=0.464), while there was a statistically significant difference in alcohol consumption history (P=0.016). The imaging differences between the BT and TB groups were not statistically significant (P>0.05). Except for T staging (P=0.029), there were no statistically significant pathological differences between the BT and TB groups (P>0.05). The consistency of the TB group with pathological results was superior to that of the BT group (Kappa-T: 0.468 vs. 0.439; Kappa-N: 0.301 vs. 0.247; Kappa-M: 0.651 vs. 0.551). ***Conclusion:*** TB scanning technology can improve the staging accuracy of GC, achieving better diagnostic performance, but it cannot enhance the display of perigastric arteries.

INTRODUCTION

Gastric cancer (GC) is one of the most common malignant tumors of the digestive system worldwide and the second leading cause of cancer-related deaths globally [1, 2]. According to global cancer statistics in 2020, the incidence rate of GC in men and women worldwide is 5.6%, accounting for 7.7% of total cancer-related deaths [3, 4]. In China, new cases of GC each year account for approximately 42.6% of the global total. However, the detection rate of early GC in China is relatively low, with most patients being diagnosed at an advanced stage [5, 6]. Advanced GC often invades nearby organs or metastasizes to distant sites, causing patients to miss the optimal time for surgical treatment, resulting in a poor overall prognosis [7, 8]. Currently, surgical treatment is the primary approach for GC. When the cancer invades the left gastric artery, splenic artery, and celiac artery, the tumor is considered unresectable [9]. Radical gastrectomy requires the removal of affected organs and tissues while preserving major perigastric arteries and performing lymph node dissection, which is often challenging and risky due to the variations and lesions of perigastric vessels [10]. Accurate preoperative clinical staging and clear display of perigastric arterial branches are crucial for selecting the appropriate treatment plan.

Common methods for determining GC staging include multi-detector computed tomography (MDCT), magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), abdominal ultrasound, and positron emission tomography-computed Tomography (PET-CT) [11]. Multi-slice spiral CT (MSCT) is valuable for preoperative staging and differentiation of gastric cancer due to its rapidity and non-invasiveness, although there is currently no standardized CT scanning protocol [12]. Common MSCT scanning protocols for gastric cancer include Test Bolus (TB) and Bolus Tracking (BT) [13]. BT involves dynamic monitoring of the selected layer, acquiring images after reaching a suitable threshold and an appropriate delay, thereby obtaining optimal scan images. There is no unified standard for gastric

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arterial enhancement thresholds or monitoring points when using BT technology. Furthermore, due to individual circulatory differences, fixed-phase scanning may not accurately display each patient's perigastric vascular information. TB technology involves dynamic monitoring of the selected fixed layer after injecting a small amount of contrast agent, analyzing the obtained data to determine the peak time of the target vessel within the layer. TB can accurately capture the peak time of the contrast agent in the detected artery, thereby improving arterial imaging quality through personalized scanning [15]. To date, there are few reports comparing the application of TB and BT technologies in preoperative examination of gastric cancer. In this study, we innovatively made a direct comparison between TB scanning technique and BT technique, aiming to evaluate the clinical application value of the two techniques in preoperative TNM staging and perigastric arterial vascular enhancement display in gastric cancer patients. By analyzing in detail, the concordance between the imaging and pathological results between the two groups, this study reveals the potential advantages of TB scanning technique in improving the accuracy of TNM staging of gastric cancer, while clarifying its limitations in perigastric arterial vascular display. This result provides new insights for clinical selection of the most suitable imaging technique, which has important clinical reference value.

MATERIALS AND METHODS

Study subjects

A retrospective analysis was conducted on the data of 107 GC patients confirmed by gastroscopy biopsy at Qingdao Central Hospital from January 2023 to January 2024. Inclusion criteria: (i) exclusion of distant metastasis to other organs preoperatively; (ii) no prior treatment before surgery; (iii) patients consented to and could tolerate radical gastrectomy; (iv) underwent radical gastrectomy within two weeks after MSCT examination with pathological results obtained; (v) no major bleeding, gastric perforation, or obstruction within two weeks before MSCT examination; (vi) MSCT examination and previous gastroscopy biopsy were more than three days apart. Exclusion criteria: (i) allergy or contraindication to anisodamine (654-2) and/or iodine contrast agents; (ii) images with large artifacts affecting cTNM staging judgment; (iii) poor gastric cavity filling affecting cTNM staging judgment. This study was approved by the Medical Ethics Committee of Qingdao Central Medical Group (No. KY202411502).

Instruments and MSCT parameters

A 64-slice spiral CT scanner (Optima CT660, USA) was used, with data processed on a GE AW 4.6 workstation (AW 4.6, USA). Both Test Bolus and Bolus Tracking groups used a tube voltage of 120kVp and Auto mA (Min: 100 mA; Max: 400 mA; Noise Index: 7.00). Slice thickness was 0.625 mm, rotation speed was 78.75 mm/s, and pitch was 0.984:1. The BT group received an intravenous injection of iopromide (Ultravist 370, Germany) (370 mgI/ml) at a dose of 1.5 ml/kg body weight and a flow rate of 3 ml/s, with scanning times at 40 s and 70 s after injection. The TB group first injected 16 ml of iopromide (Ultravist 370, Germany) (370 mgI/ml), selecting the abdominal aorta branch at the celiac trunk layer as the ROI layer to obtain a time-density curve of aortic enhancement and determine the peak time. Subsequently, iopromide (Ultravist 370, Germany) (370 mgI/ml) was injected at a dose of 1.5 ml/kg body weight and a flow rate of 3 ml/s, using the peak time of the aorta as the delay time for arterial phase scanning, followed by portal venous phase scanning after a 20-second delay.

Image analysis

Tumor staging

Two experienced radiologists analyzed the images using a double-blind method, reaching a consensus in case of disagreement. The T staging criteria are shown in table 1 [16]. Lymph nodes were considered metastatic if the short diameter exceeded 6 mm for perigastric nodes or 8 mm for extragastric nodes. M staging: M0: no distant metastasis; M1: distant organ metastasis.

Table 1. MDCT Criteria for Gastric Cancer Staging [16].

Stage (Invasion Depth)	MDCT Criteria
T1 (mucosa)	Abnormal enhancement and/or thickening of the mucosal layer with an intact low-density layer; visible interruption of the low-density layer (less than 50%).
T2 (muscularis propria)	Destruction and interruption of the low-density layer (more than 50%) with an intact, slightly higher density outer gastric wall.
T3 (subserosa)	Difficulty distinguishing the enhanced lesion from the outer layer of the gastric wall; a smooth outer gastric wall or only a small amount of flocculent shadow in the perigastric fat space.
T4 (serosa and other structures)	Irregular or nodular changes in the outer gastric wall and/or blurred peritoneal fat space; disappearance of fat space between the lesion and adjacent structures or direct invasion into adjacent structures.

MDCT: multi-detector computed tomography

We selected T1-4 images of arterial enhancement phase of BT patients for demonstration (figure 1A-H). At the same time we selected reconstructed images of TB patients for presentation (figure 2A-H).

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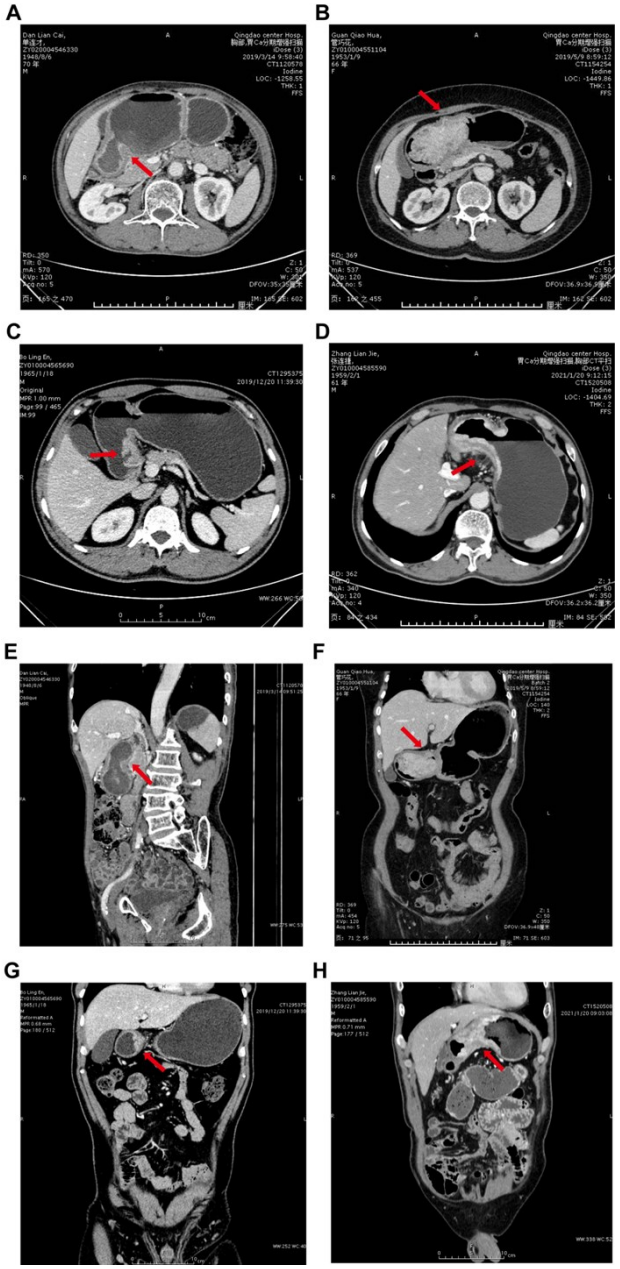

Figure 1. Transverse and reconstructed images in the venous phase of BT-GC (A-D, transverse images at T1-4; E-H, reconstructed images at T1-4).

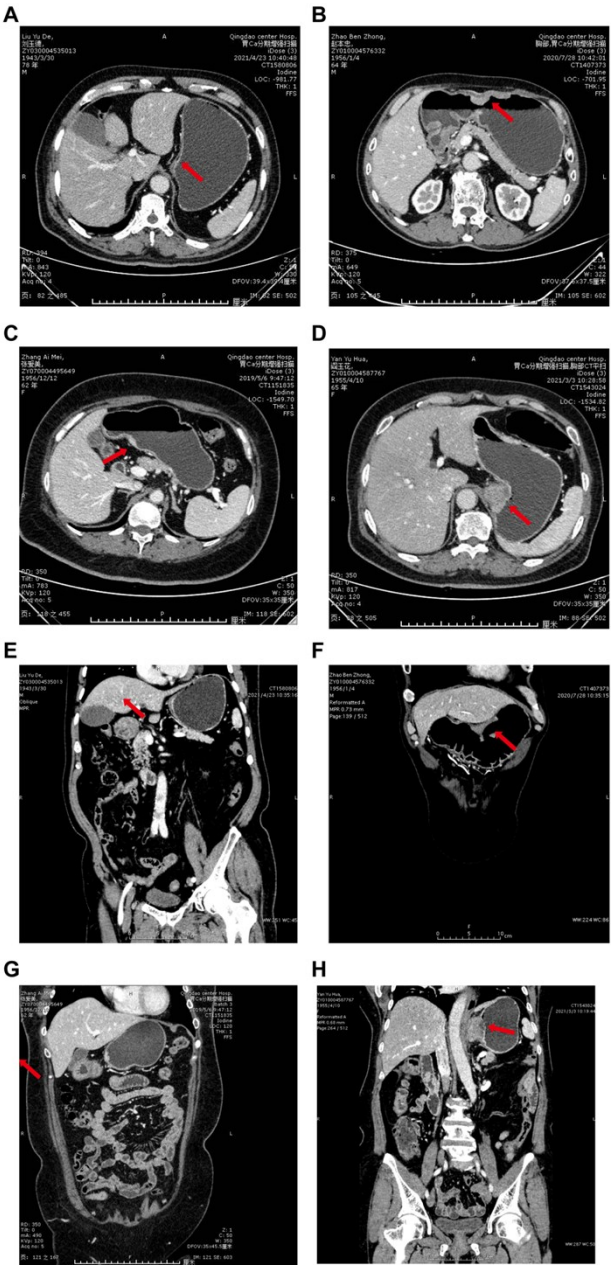

Figure 2. Transverse and reconstructed images in the venous phase of TB-GC (A-D, transverse images at T1-4; E-H, reconstructed images at T1-4).

Image processing

Two radiologists with 3-5 years of experience in abdominal imaging independently assessed the quality of the CTA images for both groups using a double-blind method. In cases of disagreement, a consensus was reached through discussion. The grading criteria were as follows: 1 point: Poor image quality (arterial vessel edges are rough, main trunks and branches are unclear, making diagnosis impossible). 2 points: Fair image quality (arterial vessel distribution is visible, but branches and distal parts are poorly defined, making diagnosis difficult). 3 points: Acceptable image quality (arterial enhancement is adequate, and main trunks are visible, but precise diagnosis is not possible). 4 points: Good image quality (main arterial trunks are clearly visible, but distal parts are blurry, allowing for diagnosis). 5 points: Excellent image quality (arteries are clearly visible, with sharp edges, and branches and distal parts are well-defined, allowing for accurate diagnosis).

Pathological examination

The postoperative specimens from GC patients were fixed in formalin, embedded in paraffin, and sectioned into 4 μm thick slices. All sections were subjected to hematoxylin and eosin (HE) staining. GC diagnosis was performed according to the pathological staging criteria of the American Joint Committee on Cancer (AJCC) [17].

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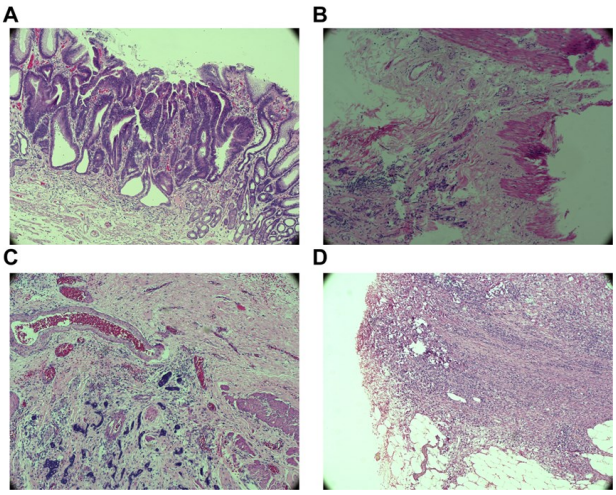

Figure 3. Pathological features of gastric cancer (**A**, pathological example of gastric cancer at T1; **B**, pathological example of gastric cancer at T2; **C**, pathological example of gastric cancer at T3; **D**, pathological example of gastric cancer at T4; 10X).

Statistical analysis

Data analysis was performed using SPSS 16.0 software (SPSS Standard version 16.0, USA), with measurement data expressed as mean ± standard deviation. Chi-square tests were used to compare T, N, and M stages between the two groups. The Mann-Whitney U non-parametric rank-sum test was used to compare subjective image quality scores. Consistency tests were analyzed using the Kappa coefficient, where Kappa ≥ 0.75 indicated good consistency, and Kappa 0.4–0.74 indicated moderate consistency. A P-value≤0.05 was considered statistically significant.

RESULTS

Basic information of patients

Table 2 shows the comparison between the two groups of patients in the BT group (n=77) and the TB group (n=30) in terms of baseline characteristics such as age, gender, and past medical history. Data were expressed as mean±standard deviation (continuous variables) or frequency (percentage) (categorical variables), and differences between groups were analyzed by *t-test* or chi-square test. There were no statistically significant differences between the two groups in terms of gender (P=0.499), age (P=0.419), family history of cancer (P=0.979), smoking history (P=0.269), and pain symptoms (P=0.464). However, there was a statistically significant difference in alcohol consumption history (P=0.016) between the BT and TB groups.

Imaging results

Gastric filling status was assessed in 105 patients. Table 3 compares the differences in the different vessel display grades in gastric imaging between the patients in the BT group (n=77) and the TB group (n=30), as well as the imaging differences in TNM staging. Left gastric artery (LGA), right gastro-esophageal artery (RGEA), and splenic artery (SA) denote the three main gastric vessel display grades assessed on imaging, respectively. The imaging grades were scored according to the clarity and visibility of the vessels and were classified as grades 1 -5. T-stage suggests the depth of invasion of the primary site of the tumor, N-stage suggests the involvement of regional lymph nodes, and M-stage suggests distant metastasis. There were no statistically significant differences in the display grades of LGA (P=0.534), RGEA (P=0.053), and SA (P=0.063) between the BT and TB groups. Additionally, there were no statistically significant differences in imaging T (P=0.819), N (P=0.096), and M stages (P=0.872) between the BT and TB groups (table 3). The mean arterial phase peak time in the TB group was 20.31 seconds.

Table 2. Baseline information of BT and TB groups.

Variables	Total (n=107)	BT(n=77)	TB(n=30)	Statistic	P
Gender, n (%)				χ^2=0.46	0.499
Female	30(28.04)	23(29.87)	7(23.33)		
Male	77(71.96)	54(70.13)	23(76.67)		
Age, Mean ± SD	62.20± 8.44	62.61± 8.21	61.13± 9.06	t=0.81	0.419
Family History of Cancer, n (%)				χ^2=0.00	0.979
No	89(83.18)	64(83.12)	25(83.33)		
Yes	18(16.82)	13(16.88)	5(16.67)		
Smoking History, n (%)				χ^2=1.22	0.269
No	101 (94.39)	71(92.21)	30(100.00)		
Yes	6(5.61)	6(7.79)	0(0.00)		
Alcohol Consumption History, n (%)				χ^2=5.79	0.016
No	91(85.05)	61(79.22)	30(100.00)		
Yes	16(14.95)	16(20.78)	0(0.00)		
Pain, n (%)				χ^2=0.54	0.464
No	56(52.34)	42(54.55)	14(46.67)		
Yes	51(47.66)	35(45.45)	16(53.33)		

SD, standard deviation; TB, Test Bolus; BT, Bolus Tracking

Pathological results

All patients were evaluated pathologically. Table 4 compares the differences between patients in the BT and TB groups in terms of tumor site (gastric sinus, gastric body, gastric fundus), gastric ulcer status and pathological stage (T, N and M stages). Differences between groups were analyzed by the chi-square test, which showed that the difference in T stage was statistically significant (P=0.029), while the differences in tumor site (gastric sinus: P=0.939, gastric body: P=0.889, gastric fundus: P=0.865), gastric ulcer condition (P=0.291), and pathological stage (N: P=0.330, M: P=1.000) were not statistically significant.

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Table 3. General information of researchers.

Variables	Total (n=107)	BT (n=77)	TB (n=30)	P
LGA Display Grade, n(%)				0.534
2	2(1.90)	1(1.32)	1(3.45)	
3	13(12.38)	8 (10.53)	5(17.24)	
4	26(24.76)	20(26.32)	6 (20.69)	
5	64(60.95)	47(61.84)	17(58.62)	
RGEA Display Grade, n (%)				0.053
3	4(3.81)	2(2.63)	2(6.90)	
4	21(20.00)	19 (25.00)	2 (6.90)	
5	80(76.19)	55(72.37)	25(86.21)	
SA Display Grade, n (%)				0.063
3	1(0.95)	0(0.00)	1(3.45)	
4	3(2.86)	1(1.32)	2(6.90)	
5	101(96.19)	75(98.68)	26(89.66)	
Imaging Stage T, n (%)				0.819
1	12(12.21)	8(10.39)	4(13.34)	
2	14 (13.08)	9		
3	25(23.36)	19(24.68)	6(20.00)	
4	56(52.34)	41(38.32)	15(50.00)	
Imaging Stage N, n (%)		9(11.69)	5(16.67)	0.096
0	32(29.91)	24(31.17)	8(26.67)	
1	43(40.19)	31(40.26)	12(40.00)	
2	23 (21.50)	16 (20.78)	7(23.33)	
3	9(8.40)	6(7.79)	3(10.00)	
Imaging Stage M, n (%)				0.872
0	98(91.50)	71(92.21)	27(90.00)	
1	6(5.61)	4(5.19)	2(6.67)	
x	3(2.80)	2(2.60)	1(3.33)	

t: t-test, χ^2: Chi-square test, -: Fisher exact. SD, standard deviation; LGA, left gastric artery; REGA, right gastric artery; SA, splenic artery, SD, standard deviation; TB, Test Bolus; BT, Bolus Tracking.

Table 4. Pathological findings in BT and TB groups.

Variables	Total (n=107)	BT (n=77)	TB (n=30)	P	Variables
Tumour site - gastric antrum, n(%)				χ^2=0.01	0.939
No	47 (43.93)	34 (44.16)	13 (43.33)		
Yes	60 (56.07)	43 (55.84)	17 (56.67)		
Tumor site-gastric body, n (%)				χ^2=0.02	0.889
No	83 (77.57)	60 (77.92)	23 (76.67)		
Yes	24 (22.43)	17 (22.08)	7 (23.33)		
Tumor site-gastric whetstone, n (%)				χ^2=0.03	0.865
No	101(94.39)	72 (93.51)	29 (96.67)		
Yes	6 (5.61)	5 (6.49)	1 (3.33)		
Ulcer, n(%)				χ^2=1.11	0.291
No	38 (35.51)	25 (32.47)	13 (43.33)		
Yes	69 (64.49)	52 (67.53)	17 (56.67)		
Pathological stage T, n (%)				-	**0.029**
1	17 (15.89)	12 (11.20)	5 (4.67)		
2	20 (18.69)	13 (16.88)	7 (23.33)		
3	23 (21.50)	18 (23.38)	5 (16.67)		
4	47 (43.93)	34 (31.78)	13(11.21)		
Pathological stage N, n (%)				-	0.330
0	45 (42.06)	29 (37.66)	16 (53.33)		
1	19 (17.76)	16 (20.78)	3 (10.00)		
2	19 (17.76)	15 (19.48)	4 (13.33)		
3	24(22.43)	17 (15.89)	7 (23.33)		
Pathological stage M, n (%)				-	1.000
x	2 (1.87)	2 (2.60)	0 (0.00)		
0	101(94.39)	72 (93.51)	29 (96.67)		
1	4 (3.74)	3 (3.90)	1 (3.33)		

t-test, χ^2: Chi-square test, -: Fisher exact. SD, standard deviation; TB, Test Bolus; BT, Bolus Tracking.

Comparison of pathological results and imaging results

Kappa test results showed that the consistency between T-stage (kappa: 0.439,95% CI: 0.289 - 0.589, P=0.000) and M-stage (kappa: 0.551,95% CI: 0.098 - 1.003, P=0.000) and pathological results of patients with gastric cancer diagnosed by BT was higher than that of N-stage (kappa: 0.247 ,95%CI: 0.107 - 0.386, P=0.000).The concordance between T-stage (kappa: 0.468,95%CI: 0.243 ~ 0.693, P=0.000) and M-stage

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(kappa: 0.651,95%CI: 0.020 -1.281, P=0.000) and pathological results of patients with TB diagnosed gastric cancer were higher than N staging (kappa: 0.301,95% CI: 0.108 - 0.495, P=0.001) (table 5).

Table 5. Kappa coefficient results.

Name	Kappa	Name	z	p	Standard error	95% CI
BT-T & Pathological Staging T	0.439	0.070	6.267	0.000 **	0.076	0.289 ~ 0.589
N	0.247	0.064	3.864	0.000 **	0.071	0.107 ~ 0.386
M	0.551	0.115	4.791	0.000 **	0.231	0.098 ~ 1.003
TB-T & Pathological Staging T	0.468	0.110	4.265	0.000 **	0.115	0.243 ~ 0.693
N	0.301	0.089	3.370	0.001 **	0.099	0.108 ~ 0.495
M	0.651	0.174	3.739	0.000 **	0.322	0.020 ~ 1.281

* p<0.05 ** p<0.01. TB, test bolus; BT, bolus tracking, CI.

DISCUSSION

Invasion of surrounding blood vessels by GC is one of the reasons for incomplete local resection. Accurate preoperative assessment of vascular conditions is crucial for improving the positive predictive value of resectability and selecting appropriate treatment strategies [18]. The results of this study indicate that the accuracy of preoperative diagnosis of GC using TB technique is higher than that using BT, regardless of the staging method used (table 5).

There are a limited number of studies directly comparing the diagnostic accuracy of TB and BT techniques in patients with GC. Previous studies have shown that TB and BT techniques are commonly used scan delay techniques in clinical practice. TB is considered the most effective method for optimizing peripheral arterial contrast enhancement [19, 20]. Some other scholars have also affirmed the superiority of homogeneous enhancement in BT [21], but others have argued that the utilization of APPROPRIATE TIMING during the use of TB can counteract this superiority [22]. Our results showed no statistically significant difference between the display grades of LGA, RGEA, and SA in TB and BT, which may be a reflection of our rational use of appropriate timing. BT, as a simple and effective method, initiates the scan after a certain delay once the region of interest (ROI) reaches a threshold (100-150 HU) [23, 24]. A significant advantage of the BT method is the reduced contrast agent usage. However, BT cannot provide individual circulatory information of patients, and due to the time needed for CT machine image reconstruction and movement of the scanning bed, there is an inherent delay when initiating the scan [25, 26]. Most studies focus on using the delayed phase and/or equilibrium phase for preoperative staging, where late scanning times result in suboptimal visualization of perigastric arteries [27]. TB technique, on the other hand, can capture the peak enhancement time of the specified vessels, personalize the scan delay, and initiate scanning at the peak enhancement, thus eliminating the influence of individual differences and optimizing vessel quality [28]. We did not deliberately delay the sweep to obtain staging information while BT was in progress, so our perigastric arteries were well visualized.

There are many studies using TB technology for preoperative staging diagnosis of GC, but no consistent results have been obtained. Shi *et al*. performed fixed delay time scans on 54 GC patients and scanned 56 GC patients after peak aortic enhancement, finding no significant difference in the diagnostic accuracy of TNM staging between the two methods [29], which is inconsistent with our findings. However, Shi *et al*. also found no significant difference in the enhancement effect of perigastric vessels between the two methods, which aligns with our results. In this study, the consistency of diagnosing N stage with pathological results was lower than that for T and M stages, regardless of whether TB or BT was used, a finding also reported by Jiang *et al*. [30]. Yu *et al*. [31] considered that T stage has important clinical reference significance for determining whether patients can undergo endoscopic treatment. They conducted CT scans, oral contrast-enhanced ultrasound imaging, and pathological examinations on 40 GC patients, finding that the combination of enhanced CT scanning and oral contrast-enhanced ultrasound imaging is a simple clinical application for assessing T stage. However, Yu *et al.*'s results showed that the consistency Kappa value between enhanced CT scan diagnosis and pathological results for T stage was 0.404, which is similar to our findings. Han *et al.* [32] investigated the optimal time interval for BT and found that monitoring the time interval 2S 10 seconds after injection of contrast agent had the best clinical extension efficacy [32]. We will enhance the exploration in this direction in our next study.

There are certain limitations in this study. First, the study subjects were all GC patients confirmed by preoperative gastroscopic pathology and all underwent surgical treatment, which may lead to bias. Second, although the TB scanning technique can obtain individual circulatory information of patients, it increases the contrast agent dosage compared to the BT scanning protocol.

CONCLUSION

The TB scanning technique can improve the staging accuracy of GC, achieving better diagnostic efficiency, but it cannot enhance the visualization of perigastric arteries.

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***Conflict of interest*:** The authors declare that there are no commercial or financial relationships that could be interpreted as potential conflicts of interest in the conduct of this study.

Ethical Considerations: This study posed a low risk to the study population and no formal ethical approval was given, but the entire study process followed ethical principles and the data were anonymized.

***Author Contributions*:** M-m.Y., led the overall study design and implementation, ensuring the accuracy and completeness of the data, and drafted the manuscript. H.S., was responsible for organizing and analyzing part of the data, assisted with statistical processing, and contributed to the revision and supplementation of the initial draft. X.J., provided significant input and suggestions during the study design phase and participated in the analysis and interpretation of some of the data. X.Y., supervised all stages of the study, including study design, data analysis, and manuscript revisions, ensuring the scientific rigor and integrity of the research, and conducted multiple revisions leading to the final version of the manuscript. All authors have read and approved the final manuscript and are accountable for all aspects of the work.

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