The 'double-track sign': A novel CT finding suggestive of the diagnosis of T1a gastric cancer

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Abstract. Effective identification of T1a stage cancer is crucial for planning endoscopic resection for early gastric cancers. The present study aimed to determine the diagnostic value of the double-track sign in patients with T1a gastric cancer using computed tomography (CT) imaging. A total of 152 patients diagnosed with pathologically proven T1a gastric cancer at The First Affiliated Hospital of Zhengzhou University (Zhengzhou, China) between July 2011 and August 2021 were retrospectively reviewed. The control group consisted of 2,926 patients with gastritis. Clinical data, including patient characteristics and preoperative CT imaging findings with gastric morphological features, were reviewed and analyzed. Out of 51 patients with T1a gastric cancer finally included, 31 (60.8%) exhibited local double-track enhancement changes of the stomach, referred to as the 'double-track sign', on CT images. In addition, four patients (7.8%) had well-enhanced mucosal thickening of the gastric wall. Of the 2,926 control subjects, none had any double-track sign and six patients (0.2%) had local gastric wall thickening with abnormally strengthened enhancement. In conclusion, a double-track sign on CT images is beneficial in the diagnostic differentiation of T1a gastric cancer.

Introduction

According to the GLOBOCAN 2020 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer, there were 19.3 million new cancer cases and ~10.0 million cancer-associated deaths worldwide in 2020 (1). In addition, the incidence of new cases of cancer in 2020 was 10.1 million in males and 9.2 million in females, and that of cancer-associated death was 5.5 million in males and 4.4 million in females (1). Therefore, one in two patients with cancer globally will die of cancer. In particular, gastric cancer is the third leading cause of cancer-related death, accounting for >1 million patients newly diagnosed with gastric cancer worldwide each year (2). The 5-year survival rate for patients with gastric cancer is <40%; gastric cancer has long been regarded as an aggressive malignancy (3). Furthermore, according to Ye *et al* (4), unresectable cases of gastric cancer account for 10% of the total number of cases in China. The median survival time is 5-12 months and the 5-year survival rate is ~9.4%.

Due to its poor prognosis and the advanced stage at which most cases are diagnosed, gastric cancer is a disease in which mortality accounts for ~70% of its incidence (1). Survival rates for gastric cancer have increased due to improved treatment strategies during the past decade; gastric cancer is by no means incurable. Early gastric cancer is difficult to diagnose immediately due to latent and nonspecific clinical symptoms. In general, numerous examinations, such as endoscopic examination, computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), positron emission tomography, explorative laparoscopy and cytological examination are required to make a definitive diagnosis. Various examinations are useful for the early detection and diagnostic differentiation of gastric cancer and may improve patient prognosis. Indeed, detection of gastric cancer at the early stage substantially improves the 5-year disease-specific survival rate to 99.3% for mucosal cancer and 97.2% for submucosal cancer, suggesting that detection of early gastric cancer may result in a good prognosis (5); however, valid screening procedures for early gastric cancer are lacking, even in high-incidence areas (Asia, Russia and South America).

The poor prognosis of gastric cancer is due to the non-specific symptoms and lack of reliable early-stage biomarkers. The most effective solution to improve the prognosis of gastric cancer is early detection and diagnosis; the prognosis of early gastric cancer is significantly more favorable than that of gastric cancer discovered in the late stages. In addition, the requirement for additional examinations for the definitive diagnosis of early gastric cancer may become a barrier to early detection. Endoscopic mucosal resection is a surgical method that may completely resect early gastric cancer that is limited to the mucosa (6). Therefore, effective identification of T1a stage cancer is crucial in the planning

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of endoscopic resection of early gastric cancer. Thus, there is an urgent requirement for new diagnostic imaging strategies to detect early gastric cancer. In the present study, the CT diagnosis of T1a gastric cancers potentially caused by gastric morphological abnormalities (double-track sign) was retrospectively investigated.

Materials and methods

Study design and patient population. The present retrospective study was approved by the institutional review board of the First Affiliated Hospital of Zhengzhou University (Zhengzhou, China). The requirement for written informed consent was waived. The T1a stage was determined according to the American Joint Committee on Cancer (AJCC, 8th edition) (7): Tumor invasion of the lamina propria or muscularis mucosae is considered T1a (7). A total of 152 patients diagnosed with pathologically proven T1a gastric cancer at the First Affiliated Hospital of Zhengzhou University (Zhengzhou, China) between July 2011 and August 2021 were retrospectively reviewed. Surgical (n=20) or endoscopic mucosal resection (n=132) was performed within one week of CT image acquisition. The inclusion criteria were as follows: i) Diagnosis of early gastric cancer (T1a) based on postoperative pathology, ii) surgical or endoscopic mucosal dissection, and iii) T1a gastric cancer as the only primary tumor. A total of 50 patients were excluded because they underwent CT at another hospital. Another 29 patients were excluded because of improper gastric distension, which resulted in images being inadequate for evaluation. A further 22 patients were excluded because their CT images could not be retrieved or presented. Ultimately, 51 patients were included in the present study. The control group consisted of 2,926 patients with gastritis who had undergone endoscopic examination at the First Affiliated Hospital of Zhengzhou University (Zhengzhou, China) between July 2011 and August 2021. Subjects were retrospectively selected according to the following inclusion criteria: i) Diagnosis of gastritis based on pathology, ii) newly diagnosed patients without any therapy, and iii) CT examination acquired within 2 weeks before endoscopic examination. A flowchart of the study is presented in Fig. 1.

CT protocol. A 600-1,000 ml oral dose of water was used to dilate the gastric cavity immediately before CT examination. CT examinations were performed using a 64 multidetector CT scanner (Discovery CT750HD; GE Healthcare). A conventional axial scan (120 kV; 350 mA; field of view, 500 mm; matrix, 512x512; section thickness, 0.75 mm) was performed before and after intravenous injection of nonionic iohexol (iopromide; 370 mg/ml; GE Medical Systems; 1.5 ml/kg and 3 ml/sec) using a dual-head pump injector (Medrad®; Bayer AG). Finally, 20 ml of saline flush was injected at a rate of 3 ml/sec. Contrast-enhanced CT scans were performed with scanning delays of 30 sec (arterial phase) and 70 sec (portal venous phase) after the start of intravenous (i.v.) injection of iopromide. The CT dose index volume for all three phases was 15 mSv.

Statistical analysis. All data were analyzed using Excel spreadsheet (version no. 2302; build 1601613020332; Microsoft Corporation). Statistical analyses were performed by SPSS software version 21.0 (IBM Corporation). The chi-square test or Mann-Whitney U-test was used for comparison between groups. $P<0.05$ was considered to indicate a statistically significant difference.

Table I. Clinicopathological features of T1a gastric cancer patients in the present study (n=51).

Feature	N
Age, years	
≤63	24
>63	27
Gender	
Male	40
Female	11
Involved segment	
Upper 1/3	23
Middle 1/3	7
Lower 1/3	21
Type of histology	
Well-differentiated	6
Moderately differentiated	39
Poorly differentiated	6

Results

Population characteristics. Detailed clinical characteristics of the included patients are presented in Table I. The patients of T1a gastric cancer consisted of 40 males and 11 females (age range, 32-86 years; mean age, 63.19 years). The control subjects consisted of 1,609 males and 1,317 females (age range, 5-90 years; mean age, 55.49 years). The proportion of males among patients with T1a gastric cancer was higher than that of the control subjects and the difference was statistically significant ($Z=12.072$, $P=0.001$). The age distribution in patients with T1a gastric cancer was different from that of the control subjects and the difference was statistically significant ($Z=4.644$, $P<0.001$).

A representative case and classification by specific abnormality of the stomach. CT images may reveal two specific morphological abnormalities of the stomach: Local double-track enhancement (double-track sign; Fig. 2) and well-enhanced mucosal thickening of the gastric wall. For example, Fig. 3 presents a typical case of a patient (male, 60 years old) with a double-track sign. The patient was diagnosed with T1a gastric cancer by pathology within one week of undergoing a CT, which revealed a double-track sign.

Based on CT findings and interpretations, patients were divided into the following three groups: Group A-double-track sign. Enhanced CT images with two or more consecutive layers indicate the double-track change; group B-well-enhanced mucosal thickening of the gastric wall on CT image; and group C-no abnormalities. Contrast-enhanced CT images did not reveal any abnormal gastric lesions.

The classification results are presented in Table II. According to the classification of CT manifestations in all

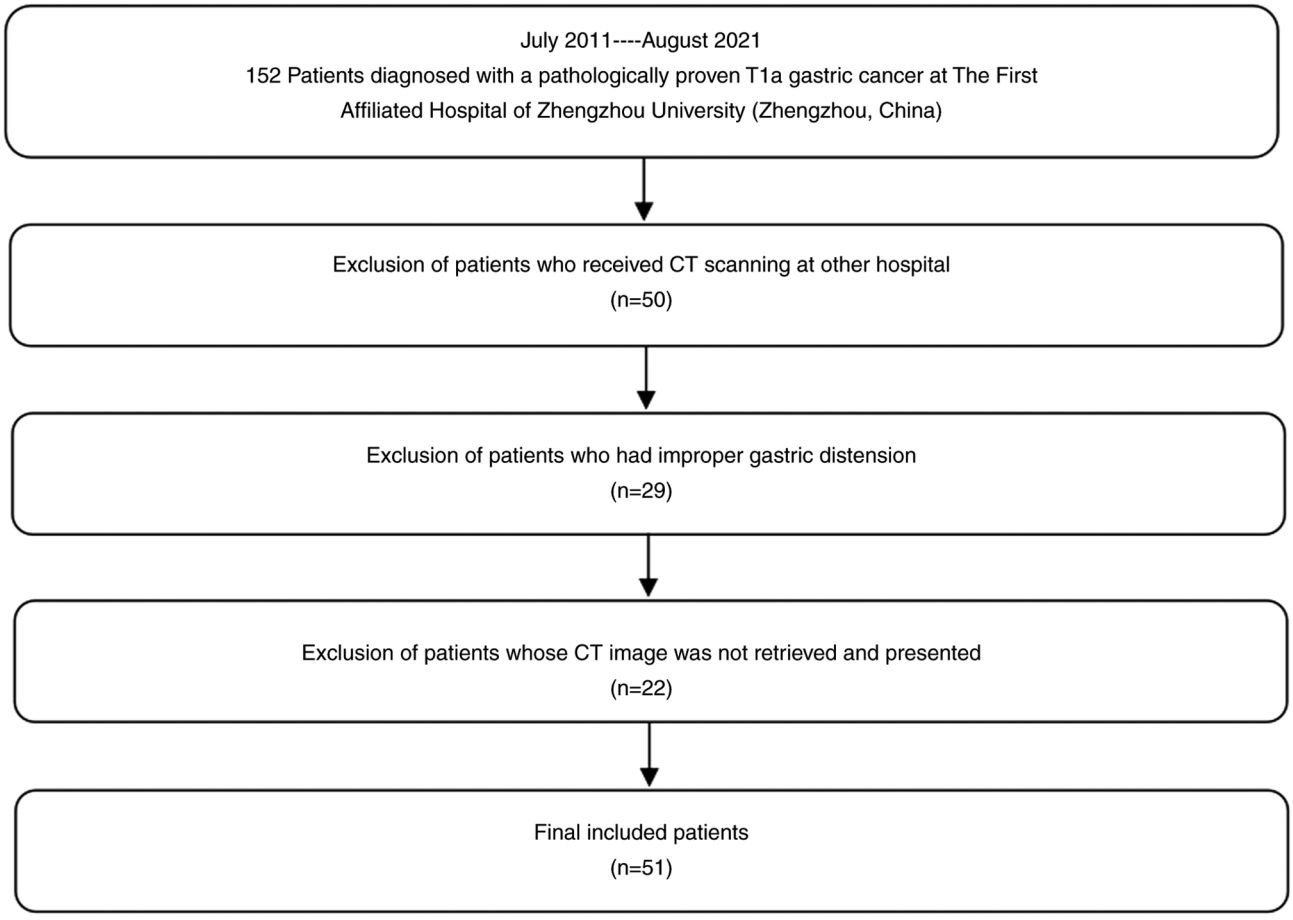

Figure 1. Flowchart of patient selection.

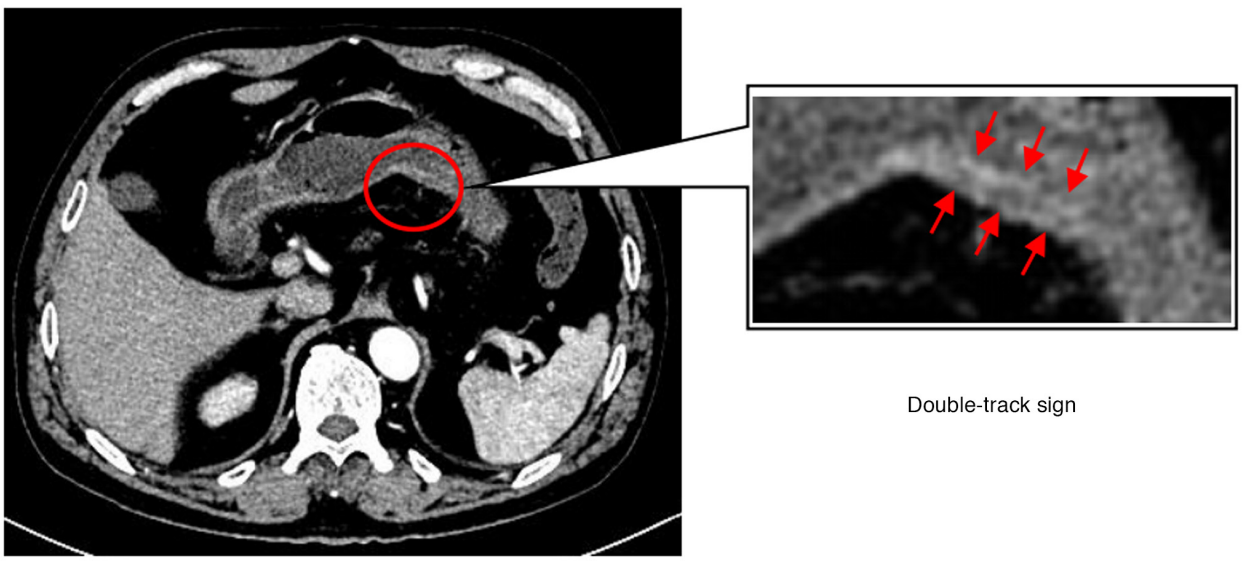

Figure 2. Illustration and definition of the double-track sign. 'Double-track sign' means that the local mucosa thickens and parallel linear enhancement changes. It looks like a 'double track' on the CT image (red circle/arrows).

patients, 31 patients were assigned to group A (60.8%), 4 to group B (7.8%; representative case; female, 51 years old; provided in Fig. 4) and 16 to Group C (31.4%). Regarding the specific locations of the manifestations in the patients, 23 cases had manifestations in the upper 1/3 of the stomach, 7 patients in the middle 1/3 and 21 patients in the lower 1/3. In addition, in Group A, the percentages of T1a gastric cancer with the double-track sign in the upper 1/3, middle 1/3 and lower 1/3 of the stomach were 51.6, 11.8 and 17.6%, respectively. In Group B, the percentages of well-enhanced mucosal

Table II. Classification of CT findings of patients in the study (n=51).

Group	CT finding	N	Location of early gastric cancer		
			Upper 1/3	Middle 1/3	Lower 1/3
A	Double-track sign	31	16	6	9
B	Well-enhanced mucosal thickening	4	0	1	3
C	No abnormality	16	7	0	9

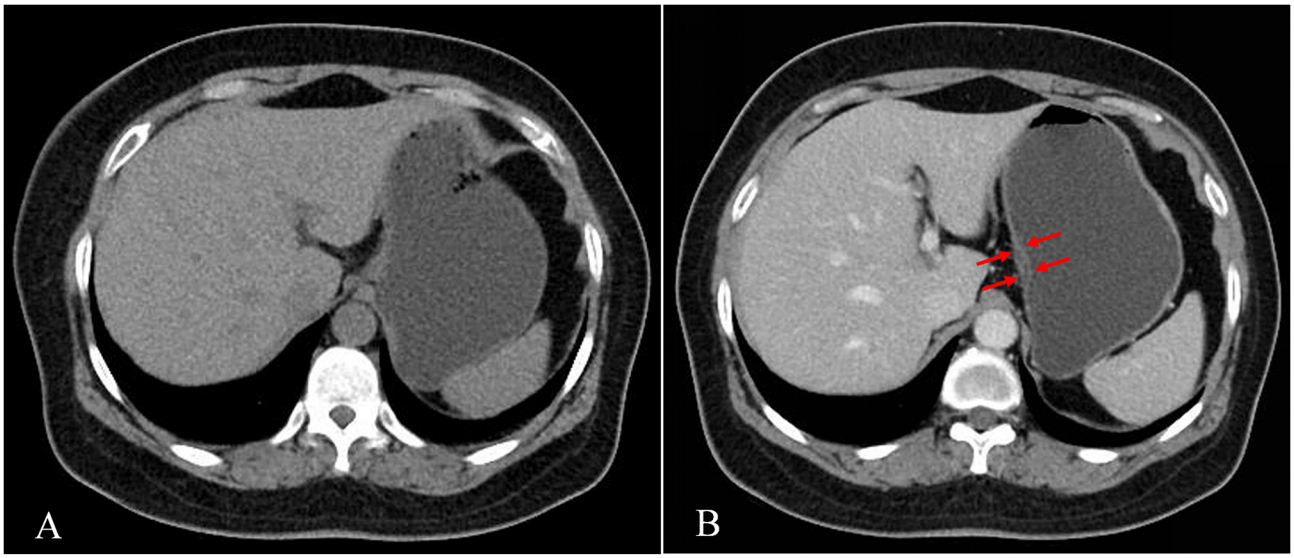

Figure 3. A typical case (male, 60 years old) with double-track sign (T1a stage, adenocarcinoma, moderately differentiated). (A) Plain CT image: No evidence of gastric abnormalities in the upper 1/3 of the stomach. (B) Enhanced CT image: The upper 1/3 of the stomach had a double-track sign (red arrows).

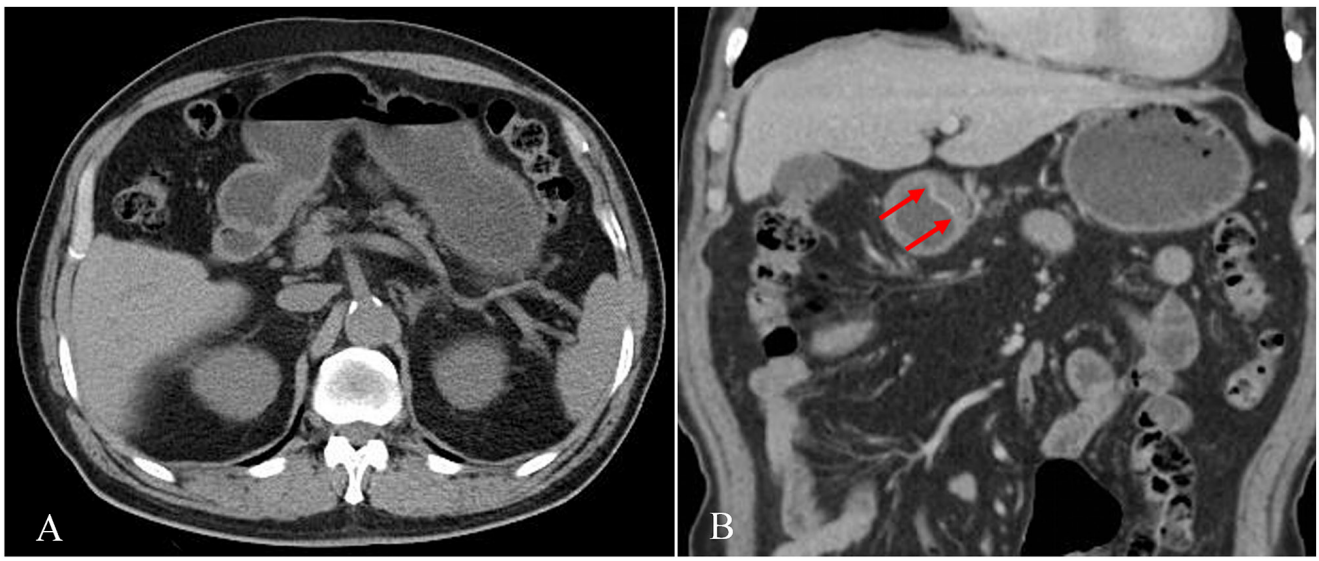

Figure 4. A typical case (female, 51 years old) with well-enhanced mucosal thickening of the gastric wall on CT (T1a stage, adenocarcinoma, moderately differentiated). (A) Plain CT image: Local gastric wall thickening in the lower 1/3 of the stomach. (B) Enhanced CT image: The lower 1/3 of the stomach exhibited well-enhanced mucosal thickening of the gastric wall (red arrows).

thickening of the gastric wall in the middle 1/3 and lower 1/3 of the stomach were 25 and 75%, respectively. Group C included seven patients with gastric cancer in the upper 1/3 of the stomach and nine patients with gastric cancer in the lower 1/3 of the stomach. All sixteen patients in Group C had no local mucosal thickening of the gastric wall or abnormal

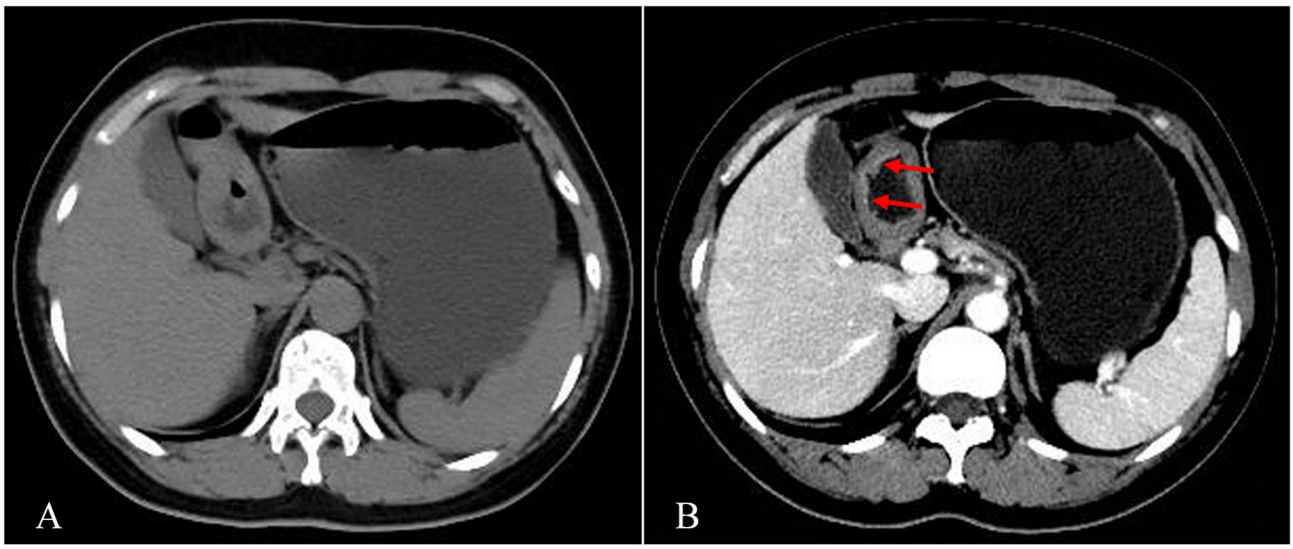

Figure 5. A typical case (female, 50 years old) with local gastric wall thickening with abnormal enhancement on CT (gastritis). (A) Plain CT image: Local gastric wall thickening in the lower 1/3 of the stomach. (B) Enhanced CT image: The lower 1/3 of the stomach had abnormal enhancement (red arrows).

enhancement changes. Of the 2,926 control subjects, none of the patients exhibited a double-track sign and six patients (0.2%) had local gastric wall thickening with abnormally strengthened enhancement (representative case; female, 50 years old; provided in Fig. 5).

Discussion

The early detection and accurate preoperative staging of T1a gastric cancer enables endoscopic resection or minimally invasive surgery in certain patients, leading to a better prognosis (8). However, detecting gastric cancer in the T1a stage may be important; one report suggested that most gastric cancers are not diagnosed until the cancer is at the progressive stage (9). In addition, <40% of patients with diagnosable early gastric cancer have typical malignant disease symptoms, indicating that early gastric cancer may be serious and difficult to diagnose (10). However, several risk factors have been noted to have a significant impact on T1a gastric cancer, such as family history, diet, alcohol consumption and smoking, as well as *Helicobacter pylori* and Epstein-Barr virus infections (11). Early gastric cancer screening has reached a consensus on the aforementioned high-risk groups; however, the need for further screening of the general population remains under discussion (5). Performing highly invasive examinations on all potential patients with T1a gastric cancer may lead to disadvantages, which would offset any advantages. The detection of appropriate tumor markers for T1a gastric cancer may be performed as a feasible scheme for general population screening (12). In particular, carbohydrate antigen (CA72-4) is superior for diagnosing early gastric cancer. A previous study indicated that when the cutoff value of CA72-4 was 18.34 IU/ml, its sensitivity and specificity were 65 and 90%, respectively (13). In addition, a novel molecular marker, dihydropyrimidinase-like 3, has been noted for its high sensitivity and specificity in diagnosing early gastric cancer (75 and 94%, respectively) (13). However, digestive system inflammation and certain drug-related diseases may lead to false-positives. The sensitivity of tumor markers is unclear. Therefore, the practice of using tumor markers for early diagnosis remains questionable. To date, various valuable tumor markers have been identified in the clinic; however, no notable tumor markers have been found that may achieve specific sensitivity and meet the screening criteria for T1a gastric cancer. Thus, discovering specific morphological changes for the diagnosis of T1a gastric cancer using non-invasive imaging modalities has become increasingly important.

Various imaging methods are typically used for diagnosing T1a gastric cancer, including endoscopic ultrasound, CT and MRI. However, only a small number of studies have investigated the diagnosis of T1a gastric cancer by detecting distinct signs on imaging. Abnormal gastric morphology is considered one of the contributing factors to poor prognosis of gastric cancer. One study addressing this issue suggested that indications for the diagnosis of early gastric cancer may be thickening and enhancement of the gastric wall (14). In addition, one report demonstrated that a tumor invading a low-density stripe layer at <50% of the thickness is a criterion used for diagnosing early gastric cancer (8). The two studies did not investigate the morphological or contour abnormalities of the stomach in detail. In the present study, CT findings indicated that morphological or enhancement abnormalities of the stomach, such as thickening and enhancement of the gastric wall, were present. This is consistent with a previous report that found a correlation between the diagnosis of T1a gastric cancer and morphological or contour abnormalities of the stomach (8). Kim *et al* (15) also reported that the hyperattenuating serosa sign may be a useful CT finding in differentiating between T4a and less-advanced gastric cancers. This further confirms the feasibility and value of gastric morphological characteristics in staging and diagnosing gastric cancer. The double-track sign is a localized morphological CT sign of T1a gastric cancer and may be caused by the direction of primary gastric cancer growth along and perpendicular to the stomach wall (16). In the

present study, it was speculated that the enhancement of the serous layer may be related to the inflammation that accompanies the tumor. In the enhanced CT images, the significantly enhanced mucosal and outer layers of the gastric wall, with the middle low-density band completely displayed, form the double-track sign of T1a gastric cancer. The underlying mechanism of the double-track sign remains elusive. However, the present study provided important insight, i.e., patients without local double-track enhancement changes of the stomach have unobvious morphological abnormalities compared to those reported in previous studies. Furthermore, these patients have minimal to no abnormalities (31.4%) or well-enhanced mucosal thickening of the gastric wall on CT images (7.8%). Although it is difficult to compare previous research results with those of the present study, the current results indicated that ~60.8% of patients with T1a gastric cancer exhibited a double-track sign, suggesting that these signs may provide a new indication for the diagnosis of T1a gastric cancer. In addition, although these CT findings may not reflect a direct relationship with the diagnosis of T1a gastric cancer, the present study demonstrated that the presence of the double-track sign is useful in diagnosing T1a gastric cancer.

The AJCC Cancer Staging Manual proposes CT criteria used for T staging of gastric cancer (8). The differentiation between T1 and T2 stage gastric cancer may be well distinguished on the enhanced CT image and it is also easy to find the abnormal enhancement of the gastric wall of T2 stage gastric cancer. Therefore, T2 stage gastric cancer was not included in the present study; T1a gastric cancer is frequently neglected in clinical practice, so it is important to propose better CT-enhanced signs for diagnosis and T1b gastric cancer may be diagnosed according to the AJCC Cancer Staging Manual. The present study is a supplement to this guideline because for T1a gastric cancer, good results may be achieved through endoscopic mucosal resection. The present results suggested that the 'double-track sign' may be used for the diagnosis of T1a gastric cancer.

In the present study, the requirement for the imaging diagnosis of T1a gastric cancer was that all patients involved had surgical pathology results. For the diagnostic differentiation of T1a gastric cancer, endoscopic examination is the first choice of screening modality. However, there are 'blind areas' in endoscopic examinations; the determination of lesion location is frequently inaccurate. In addition, patients undergoing these examinations experience obvious discomfort. The rate of missed diagnoses by endoscopic examination is ~20-30% (17). Most of these cases are of cardiac cancer. This may be related to patient compliance, gastroscopic performance and the special anatomical structure of the upper digestive tract. CT reveals the double-track sign, which is difficult to display on EUS and may be useful for accurately diagnosing T1a gastric cancer. In general, CT examinations include various imaging methods, such as plain scan, enhanced and energy CT. Several studies reported that using the gastric window in CT provides more accurate staging for early gastric cancer than that of the conventional abdominal window (8). In addition, the multiplanar reformation image provided by CT post-processing reconstruction technology is useful for accurately detecting early gastric cancer (18). However, the sensitivity of CT for early gastric cancer is relatively low. To diagnose T1a gastric cancer, more accurate diagnostic imaging is required. Although there may be challenges related to the diagnostic differentiation of T1a gastric cancer in facilities with different imaging modes, the double-track sign as detected in the present study has additional advantages as an early diagnostic indicator. Under the capturing conditions of abdominal CT, such as contrast and non-contrast CT and multidetector CT, the double-track sign may be detected in all parts of the stomach. Therefore, the double-track sign detected on any CT scan may be a meaningful diagnostic imaging finding, suggesting the presence of T1a gastric cancer.

The current study had certain limitations. First, it was a retrospective single-institution study. Furthermore, the visibility of T1a gastric cancer was not assessed based on gastric distension. In addition, quantifying the local contraction of the stomach is difficult because the double-track sign is a 'still-imaging' finding. A subsequent prospective study on the exact time of developing T1a gastric cancer in patients with the double-track sign will provide a further theoretical basis for using this sign in diagnostic differentiation. Finally, as a retrospective analysis, the present study did not compare histopathological results and CT images; these variables should be investigated in future studies.

In conclusion, the double-track sign is an important CT manifestation of stomach morphological abnormalities and may be used as a reliable indicator for diagnosing T1a gastric cancer.

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Availability of data and materials

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

Authors' contributions

PL and JG designed the study. JG critically reviewed the manuscript and revised it. PL, BZ, XR, DL and MC performed the database search and literature review. ZH and LY performed data analysis, the database search and the literature review. BZ performed the data collation/processing. PL, BZ, XR, DL and MC analysed the data. PL and JG confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of the First Hospital of Zhengzhou University (Zhengzhou, China). Any requirement of written informed consent

was waived by the Institutional Review Board due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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