Original Article

Feasibility of differentiating T3 from T4a gastric cancer in different Lauren classification by determining serosa invasion: Diagnostic performance of high enhanced serosa sign

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Abstract

Objective: To study the value of high enhanced serosa sign on contrast-enhanced computed tomography (CT) in differentiating T3 from T4a gastric cancer in different Lauren classification.

Methods: This study included 276 consecutive patients with surgically confirmed pT3 or pT4a gastric cancers. The pre-operative CT images were reviewed by two radiologists blinded. The demonstration of the high enhanced serosa on CT between T3 and T4a was compared with chi-square test. The diagnostic performance of this sign on CT in the differentiation of T4a from T3 in different Lauren classification was calculated.

Results: The accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the judgement of serosa invasion using the high enhanced serosa sign on CT was 74.6%, 63.7%, 83.6%, 76.0% and 73.8% by one radiologist and 76.4%, 66.1%, 84.9%, 78.1% and 75.4% by the other radiologist. Compared to the intestinal-type, the sensitivity of the judgement of serosa invasion using the high enhanced serosa sign on CT in diffuse-type was significant higher (80% in both readers), while the specificity trended to be lower (65.9% and 80.5%, respectively). There is no significant difference in the accuracy of diagnosis between intestinal-type and diffuse-type of gastric cancers (the P-values of two radiologists were 0.968, 0.591, respectively). The combination of the high enhanced serosa sign with conventional CT signs is significant different in diagnosis of T3 and T4a (P<0.001). The diagnostic accuracy was increased in both radiologists after the combination. The two readers achieved substantial agreement, with Kappa coefficient of 0.63, P<0.001.

Conclusions: The high enhanced serosa sign on CT is associated with serosa involvement. The sensitivity of the judgement of serosa invasion using this sign on CT in diffuse-type was significant higher than that in intestinal-type.

Keywords: Computed tomography; gastric cancer; staging; serosa invasion; imaging

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Introduction

Gastric cancer is one of the leading causes of cancer death worldwide, which is particularly common in eastern Asia (1). Tumor invasion and lymph node metastasis are two important prognostic factors of gastric cancer. Conventional fiberoptic endoscopy and upper gastrointestinal series have been used as first line procedures for the early detection of gastric cancer. Although these methods can discriminate between early gastric cancer (EGC) and advanced gastric cancer (AGC) to some degree (2), they cannot provide sufficient information regarding the transmural invasion of tumor. Given the growing popularity of less-invasive

therapeutic options such as endoscopic mucosal resection, endoscopic submucosal dissection and laparoscopy-assisted gastric resection, accurate preoperative staging is particularly important for alternative treatment strategies and prognostic evaluations (3,4).

In the eighth TNM staging system of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC) released in 2016, the T categories for gastric cancer is the same as it was defined in the seventh TNM staging system (5,6). T1 tumor have been divided into T1a (lamina propria or muscularis mucosae) and T1b (submucosa), T2 is defined as a tumor invading the muscularis propria, T3 is defined as a tumor invading the subserosal connective tissues and T4 is defined as a tumor invading the serosa (T4a) or adjacent structures (T4b).

The assessment of serosa invasion before the surgery has a crucial significance because for locally AGC with serosal invasion, neoadjuvant chemotherapy is being used more frequently to downstage the tumor and treat micrometastases (7,8). Moreover, differentiation between T3 and T4a gastric carcinoma is very important to determine the appropriate procedure of surgery and expect the prognosis, especially for the risk of peritoneal dissemination. For T4a gastric cancer staging, the reported computed tomography (CT) accuracy varies considerably, ranging from 77.8% to 93.5% (6-8). The reported CT criteria for T4a gastric cancer are extraluminal extension of the gastric wall and haziness of the perigastric fat (8). The paragastric inflammatory strands may mimic the cancer infiltration out of the serosa and lead to the overstaging of T3 tumors during the preoperative staging of gastric cancers. A previous study founded that the high density outer layer of the gastric wall might be associated with cancer involvement of the serosa, and refered to this sign as hyperattenuating serosa sign, which was assumed to indicate a poor prognosis (9).

Lauren classification is also reported to be a factor associated with the prognosis, which is one of the most commonly used pathological classification systems of gastric adenocarcinoma (10,11). This system classifies gastric adenocarcinoma into the intestinal, diffuse, or mixed types on the basis of histology. Each type has a distinct pathology, epidemiology, and prognosis (10-14). The intestinal-type is known to have a higher survival rate than the diffuse-type (11). Gastric cancers may thus show diverse enhancement patterns on contrast-enhanced CT.

The purpose of our study was to further evaluate the clinical value of the high enhanced serosa sign on CT in determining the serosa invasion in patients with different Lauren types of gastric cancers.

Materials and methods

This retrospective study was approved by the Institutional Review Board of Peking University Cancer Hospital, and the requirement of informed consent was waived.

Patients

Between January 2012 and December 2015, 570 consecutive patients who underwent both preoperative contrast enhanced CT scan and gastrectomy in Peking University Cancer Hospital were retrospectively enrolled in this study according to the following inclusion criteria. Patients were enrolled who: 1) had not undergone neoadjuvant chemotherapy; 2) had not undergone previous gastrectomy or endoscopic surgery; and 3) had undergone gastrectomy within 2 weeks after preoperative CT. Two hundred and ninety-four patients were excluded because 1) pathologically proven pT1 or pT2 gastric cancers (n=285); or 2) CT images with poor distention (n=5) or artifacts (n=4). Finally, 276 patients (159 males, mean age 58.3±9.4 years and 117 females, mean age 61.7±11.8 years) were included in this study (*Figure 1*).

CT protocol

Multi-detector row was performed using a 64-detector row CT scanner (LightSpeed 64; GE Healthcare, Milwaukee, Wisconsin, USA). Each patient had been fasting for more than 6 h prior to the CT examination. To reduce gastric motility and enable gastric distention, the patients were given an intramuscular injection of 10 mg anisodamine 10–15 min before the examination and received 8 g gas-producing crystals orally with 10 mL of water orally shortly before CT scanning. Upper abdominal unenhanced CT scans from the diaphragmatic domes to 2 cm below the lower margin of the air-distended gastric body were acquired. Subsequently, a total of 100 mL of non-ionic contrast medium (Ultravist; Schering, Berlin, Germany) was administered intravenously through an 18-gauge angiographic catheter inserted into an antecubital vein at 3 mL/s by using an automatic injector. Contrast-enhanced CT scans were performed in the arterial phase (start delay, 30 s), in the portal venous phase (70 s). Unenhanced scan was also required for all patients. The CT parameters used were as follows: collimation of 0.625 mm, gantry rotation

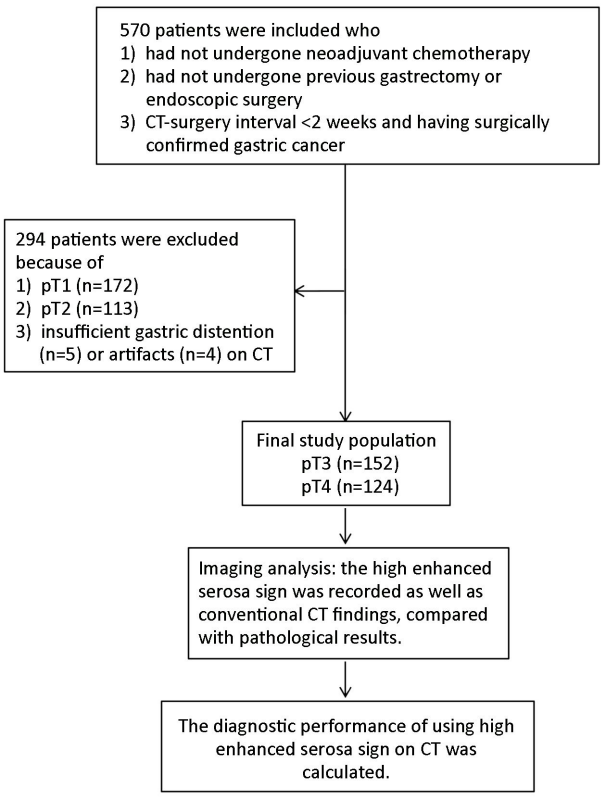

Figure 1 Flow chart of study profile based on inclusion criteria.

time of 0.5 second, tube voltage of 120–140 kVp, tube current-time product of 300–350 mAs, and table feed per rotation of 15 mm. Using these raw data sets, both the arterial and portal venous phase axial CT images were reconstructed with a 5 mm section thickness and a 5 mm reconstruction interval for clinical interpretation. To further analyze the status of serosa invasion, multiplanar reconstruction (MPR) images were done with section thickness of 0.625 mm.

Image analysis

Two abdominal radiologists (with 5 and 15 years of experience, respectively, in abdominal CT, as well as 4 and 8 years of experience in three-dimensional MPR approaches and interpretation performed the image analysis. They were blinded to clinical and pathological data and independently evaluated CT images at the workstation before surgery by using transverse CT (5 mm) and MPR images (0.625 mm or greater) with soft-tissue window settings. Differences in assessment were evaluated by kappa coefficient analysis.

We defined the serosa involvement criteria based on the paper written by Kim *et al* (9). In that paper, the association between the high density outer layer of the gastric wall and the involvement of the serosa was hypothesized and defined as hyperattenuating serosa sign. The high enhanced serosa sign on CT was defined as a focal or diffuse thickened hyperattenuating outer layer of the gastric wall. We concluded the standards of the evaluation of the high enhanced serosa as follows: 1) It was calculated when it was seen in either the arterial or portal phase; 2) The gastric layers could be stratified by the attenuation value. As in *Figure 2*, the high enhanced serosa located in the outer layer of the gastric wall (white arrow) can be differentiated clearly from the inner hypoattenuating layer; and 3) The high enhanced serosa was evaluated in the largest tumor section on transverse or coronal or sagittal images using MPR.

The high enhanced serosa sign was the only criteria we use to evaluate the serosa involvement. Moreover, for all cancerous lesions, the following conventional CT features were recorded as well: the extraluminal extension, the blurring and obliteration of the fat plane. The extraluminal extension was defined as the irregular outer layer of the gastric wall. The blurring and obliteration of the fat plane was defined as linear or reticular structures in the fatty layer surrounding the cancerous lesion.

The efficacy of the discrimination of T3 from T4a in different Lauren types of gastric cancers by the high enhanced serosa sign on CT and the conventional CT features was calculated. The diagnostic accuracy was

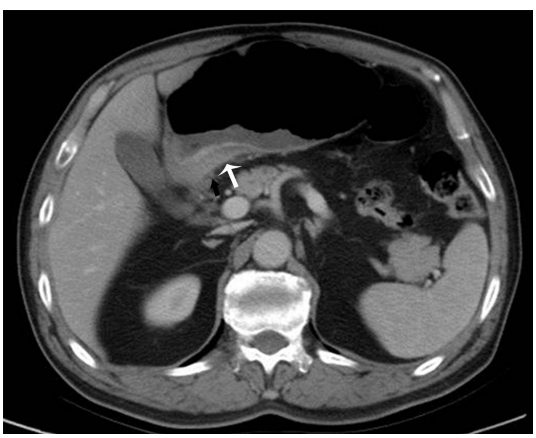

Figure 2 Mixed-type of gastric cancer (pT4a) in a 62-year-old man. Axial contrast-enhanced CT shows abnormal enhancement accompanied by wall thickening at lesser curvature of stomach body. A high enhanced serosa (white arrow) is seen, as well as the nodular or irregular outer layer of gastric wall and a blurring perigastric fat surrounding the gastric lesion (black arrow).

calculated by using surgical and histopathologic results as reference standards.

Pathological evaluation

The pathological features of gastric cancers were officially reported by a specialist with 10 years of experience in gastrointestinal pathology of Department of Pathology, Peking University Cancer Hospital. T-stage was determined using the pathological findings of surgical specimens as reference standards according to the eighth edition of the AJCC and the UICC TNM classification (5).

Intestinal or differentiated types include papillary and tubular adenocarcinomas. In intestinal tumors, tumor cells exhibit adhesion, and are arranged in tubular or glandular formations and are often associated with intestinal metaplasia (10,14). This type of gastric cancer is associated with lymphatic or vascular invasion, and the lesions are scattered in distant positions (15). By contrast, in diffuse gastric cancer, tumor cells lack adhesion and infiltrate the stroma as single cells or small subgroups, leading to a population of noncohesive, scattered tumor cells (11,12). Intracellular mucus may push the nucleus of the cell aside to form signet-ring cell carcinoma. Mixed-type shows a mixture of glandular and signet ring/poorly cohesive cellular histological components (16).

The locations of tumors were recorded as fundus, body and antrum. When the tumor occupied more than two areas, the larger region affected by the tumor was selected.

Statistical analysis

The demonstration of the high enhanced serosa seen on CT between T3 and T4a was compared with chi-square test, as well as the conventional CT findings. For each of the three Lauren types of gastric cancer, accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for the diagnosis of serosa invasion (pT4a stage) using the demonstration of the high enhanced serosa on CT. The difference in the judgement of serosa invasion between intestinal-type and diffuse-type was also tested with chi-square test. Multiple comparison was corrected by the Bonferroni method.

The agreement of judging hyperattenuating serosa sign between two raters was assessed using Kappa coefficient, 0–0.20, 0.21–0.40, 0.41–0.60, 0.61–0.80 and 0.81–1 indicated very poor, poor, moderate, substantial and excellent agreement, respectively.

All statistical analyses were performed using the IBM SPSS Statistics (Version 22.0; IBM Corp., New York, USA). $P<0.05$ was considered statistically significant.

Results

Pathological findings

In the 276 patients with AGC, T stages of gastric cancer of T3 and T4a were respectively found in 152 and 124 patients. The locations of gastric cancer included the fundus (n=96), body (n=93) and antrum (n=87). The histological types of gastric cancer included 89 intestinal-type, 86 diffuse-type and 101 mixed-type lesions.

Diagnosis performance using the high enhanced serosa sign

The two abdominal radiologists achieved substantial agreement, with Kappa coefficient of 0.63, $P<0.001$. The emergence rate of high enhanced serosa was significantly higher in T4a gastric cancer than in T3 gastric cancer in both two readers ($P<0.001$). The diagnosis performance of two radiologists using the high enhanced serosa sign on CT in determining the serosa invasion of patients of gastric cancers are shown in *Table 1*.

The judgement of serosa invasion with the highest sensitivity was in the diffuse-type (80.0%). The results indicated that, compared to the diffuse-type, the sensitivity of the judgement of serosa invasion using the high enhanced serosa seen on CT in intestinal-type was significant lower (the P-values of two radiologists were

Table 1 Diagnostic performance of the high enhanced serosa sign (N=276)

Variables	T3 (n=152)	T4a (n=124)	Accuracy (%, 95% CI)	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	PPV (%, 95% CI)	NPV (%, 95% CI)	P
Radiologist 1	25	79	74.6 (69.0–79.6)	63.7 (54.5–72.0)	83.6 (76.5–88.9)	76.0 (66.4–83.6)	73.8 (66.5–80.1)	<0.001
Radiologist 2	23	82	76.4 (70.9–81.2)	66.1 (57.0–74.2)	84.9 (78.0–90.0)	78.1 (68.8–85.3)	75.4 (68.2–81.6)	<0.001

95% CI, 95% confidence interval; PPV, positive predictive value; NPV, negative predictive value.

0.001, 0.012, respectively), while the specificity of diagnosis was higher (the P-values of two radiologists were 0.020, 0.611, respectively). There is no significant difference in the accuracy of diagnosis between intestinal-type and diffuse-type of gastric cancers (the P-values of two radiologists were 0.968, 0.591, respectively). The specificity between the mixed-type and diffuse-type was significant different in one radiologist (the P-value was 0.003), while there was no significant difference between the mixed-type and intestinal-type. The accuracy, sensitivity, specificity, PPV and NPV of the high enhanced serosa sign on CT in determining the serosa invasion of patients with different Lauren types are shown in *Table 2*.

All CT findings were seen more often in T4a than in T3 gastric cancers, these conventional CT findings were not significantly different between T3 and T4a gastric cancer. The diagnostic performance of the conventional CT findings between patients with T3 and T4a gastric cancer are shown in *Table 3*. However, the combination of the high enhanced serosa sign with conventional CT signs shows significant difference between T3 and T4a gastric cancers. The diagnostic accuracy was increased in both radiologists after the combination.

Discussion

Our study demonstrated that the high enhanced serosa sign on CT is associated with gastric cancer involvement of the serosa, probably owing to these causes. Gastric cancers are affected by diverse pathological factors such as cell differentiation, the amount of tissue stroma, the infiltration pattern, and the presence or absence of ulceration (15). Gastric cancers may thus show diverse findings on contrast-enhanced multidetector CT (MDCT).

Our study also demonstrated that the sensitivity of the judgement of serosa invasion using the high enhanced serosa sign on CT in diffuse-type was significant higher than that in intestinal-type, some published studies of Lauren's classification could explain this result (13-21). Pathologically, intestinal and diffuse gastric cancers differ in cellular cohesion, which is low in the diffuse-type (21). In diffuse gastric cancer, clusters of tumor cells infiltrate the gastric layers. Therefore, desmoplastic reaction and inflammatory peritumoral reaction are limited to the gastric wall, and a smooth and regular appearance of the outer surface is often seen (*Figure 3*). In intestinal gastric cancer, cells are more closely linked and organized in solid or glandular structures that replace the gastric layers completely. In these cases, desmoplastic and inflammatory reaction and necrosis produce a distortion of the outer gastric wall, which appears with reticular or linear soft-tissue density on CT images (*Figure 4A*), mimicking tumor invasion of the perigastric fat (21). The enhanced serosa was seen in intestinal gastric cancer (*Figure 5*), which

Table 2 Accuracy, sensitivity, specificity, PPV and NPV of using the high enhanced serosa seen on CT in determining the serosa invasion of patients with different Lauren types (N=276)

Variables	T3 (n=152)	T4a (n=124)	Accuracy (%, 95% CI)	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	PPV (%, 95% CI)	NPV (%, 95% CI)
Radiologist 1							
Intestinal-type	6/53	15/36	69.7 (58.9–78.7)	41.7 (26.0–59.1)	88.7 (76.3–95.3)	71.4 (47.7–87.8)	69.1 (56.6–79.5)
Diffuse-type	14/41	36/45	73.3 (62.4–82.0)	80.0 (65.0–89.9)	65.9 (49.3–79.4)	72.0 (57.3–83.3)	75.0 (57.5–87.3)
Mixed-type	5/58	28/43	80.2 (70.8–87.2)	65.1 (49.0–78.6)	91.4 (80.3–94.3)	84.8 (67.3–94.3)	77.9 (65.9–86.7)
Radiologist 2							
Intestinal-type	6/53	18/36	73.0 (62.4–81.6)	50.0 (33.2–66.8)	88.7 (76.3–95.3)	75.0 (53.0–89.4)	72.3 (59.6–82.4)
Diffuse-type	8/41	36/45	80.2 (67.0–87.7)	80.0 (65.0–90.0)	80.5 (64.6–90.6)	81.8 (66.8–91.3)	78.6 (62.8–89.2)
Mixed-type	9/58	28/43	76.2 (66.5–83.9)	65.1 (49.0–78.6)	84.5 (72.1–92.2)	75.7 (58.5–87.6)	76.6 (64.0–85.9)

PPV, positive predictive value; NPV, negative predictive value; CT, computed tomography; 95% CI, 95% confidence interval; P value for accuracy, sensitivity, specificity between intestinal and diffuse type is 0.968, 0.001, 0.020 and 0.591, 0.012, 0.611 in two radiologists, respectively; between intestinal and mixed type is 0.270, 0.100, 0.745 and 0.942, 0.421, 0.887 in two radiologists, respectively; between diffuse and mixed type is 0.596, 0.312, 0.003 and 0.882, 0.312, 0.938 in two radiologists, respectively.

Table 3 Diagnostic performance of conventional CT findings between patients with T3 and T4a gastric cancer (N=276)

Variables	T3 (n=152)	T4a (n=124)	Accuracy (%, 95% CI)	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	PPV (%, 95% CI)	NPV (%, 95% CI)	P
Extraluminal extension								
Radiologist 1	118 (77.6%)	103 (83.1%)	49.6 (43.6–55.7)	83.1 (75.3–89.2)	22.4 (16.0–29.8)	46.6 (39.9–53.4)	61.8 (47.7–74.6)	0.261
Radiologist 2	114 (75.0%)	98 (79.0%)	49.3 (43.2–55.3)	79.0 (70.8–85.8)	25.0 (61.4–81.7)	46.2 (39.4–53.2)	59.4 (46.4–71.5)	0.430
Combination with serosa sign								
Radiologist 1	22 (14.5%)	74 (59.7%)	73.9 (68.3–79.0)	59.7 (50.5–68.4)	85.5 (78.9–90.7)	77.1 (67.4–85.1)	72.2 (65.1–75.6)	<0.001
Radiologist 2	25 (16.4%)	68 (54.8%)	70.7 (64.9–76.0)	54.8 (45.7–63.8)	83.6 (76.7–89.1)	73.1 (62.9–81.8)	69.4 (62.2–72.0)	<0.001
Blurring and obliteration of the fat plane								
Radiologist 1	50 (32.9%)	88 (71.0%)	68.8 (63.0–74.3)	71.0 (62.1–78.7)	67.1 (59.0–74.5)	63.8 (55.2–71.8)	73.9 (65.8–81.0)	<0.001
Radiologist 2	73 (48.0%)	72 (58.1%)	54.7 (48.6–60.7)	58.1 (48.9–66.9)	52.0 (43.7–60.1)	49.7 (41.9–58.7)	60.3 (51.4–68.7)	0.097
Combination with serosa sign								
Radiologist 1	13 (8.6%)	49 (39.5%)	68.1 (62.3–73.6)	39.5 (62.3–73.6)	91.4 (85.8–95.4)	79.0 (66.8–88.3)	65.0 (58.2–71.3)	<0.001
Radiologist 2	21 (13.8%)	57 (46.0%)	68.1 (62.3–73.6)	46.0 (37.0–55.1)	86.2 (79.7–91.2)	73.1 (61.8–82.5)	66.2 (59.1–72.7)	<0.001

CT, computed tomography; 95% CI, 95% confidence interval; PPV, positive predictive value; NPV, negative predictive value.

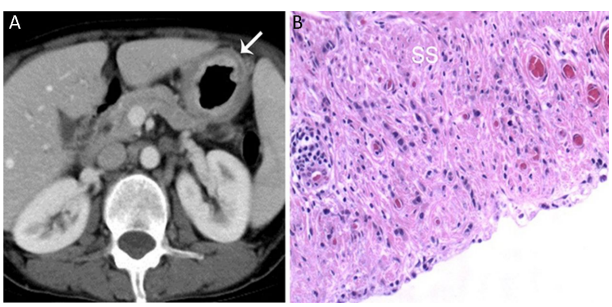

Figure 3 Diffuse-type of gastric cancer (pT4a) in a 48-year-old woman. (A) Axial contrast-enhanced CT shows a high enhanced serosa (arrow), but perigastric fat surrounding the gastric lesion appears to be clear and surface of the gastric wall appears to be smooth; (B) Photomicrograph of corresponding pathologic specimen shows serosal invasion by cancer cells. SS, subserosa.

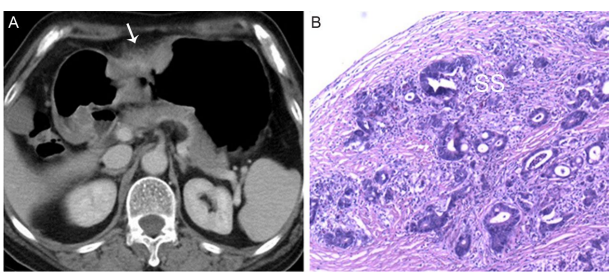

Figure 4 Intestinal-type of gastric cancer (pT3) in a 68-year-old woman. (A) Axial contrast-enhanced CT shows conventional signs of serosa involvement, including the nodular or irregular outer layer of gastric wall and the haziness of the perigastric fat (arrow), but without high enhanced serosa demonstrated; (B) Photomicrograph of corresponding pathologic specimen shows no serosal invasion of cancer. SS, subserosa.

manifested that the fibrosis strands and spiculations near the serosa could hardly distort the outer gastric wall. Therefore the hyperattenuating serosa was seen more specificly in intestinal-type than in diffuse-type. For the cases of mixed-type of gastric cancers, in which both intestinal and diffuse components were histologically shown, the features on CT were seen of both two types, which could explain the diagnostic performance of mixed-type did not show significant difference compared with other two types.

According to Lauren's classification (10), two types of gastric cancer may be distinguished. The intestinal-type of

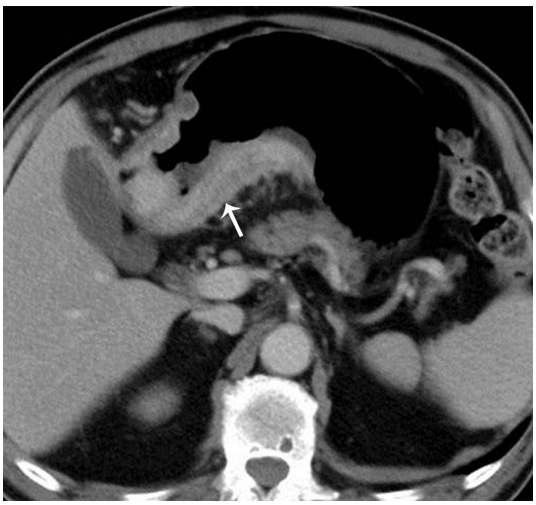

Figure 5 Intestinal-type of gastric cancer (pT4a) in a 71-year-old man. Axial contrast-enhanced CT shows diffuse thickened hyperattenuating outer layer of the gastric wall (arrow).

gastric cancer is characterized by solid components and a glandular structure. Inflammatory cell infiltration due to host reaction occurs, concentrating especially at the margin of tumor spread (*Figure 4B*). This type of gastric cancer is associated with lymphatic or vascular invasion, and the lesions are scattered in distant positions (14). In diffuse gastric cancer, tumor cells lack adhesion and infiltrate the stroma as single cells or small subgroups, leading to a population of non-cohesive, scattered tumor cells. Cells seem to be scattered without forming distinct epithelial cords, with a high percentage of secreting cells and secreted mucus dispersed in the stroma (14,15,17). These tumors do not grow as a well-defined mass and have a wider spread inside the mucosa. Intestinal gastric cancer tends to spread locally, with vascular and other organ invasions. Whereas diffuse gastric cancer tends to spread more diffusely, with lymphatic invasion that can produce peritoneal seeding and ascites (20).

Histologically, a high-attenuating abnormal inner layer corresponded to where cancer cells were closely proliferated, mainly in the mucosal and submucosal layers, whereas a low-attenuating abnormal second layer corresponded to where cancer cells were diffusely scattered, mainly in the proper muscle layer with desmoplastic change and inflammatory reaction (17,18). In addition, the presence of a high-attenuating abnormal third layer on the serosal surface of the gastric wall suggested the serosal infiltration of the tumor because this high-attenuating layer histologically corresponded to a closely linked proliferation of cancer cells from the subserosal layer to the serosa, indicating direct serosal infiltration by the tumor (19).

Some new tools had been recently used to characterize gastric cancer, such as CT texture analysis, which analyses the distribution and relationship of pixel intensities in CT images, it might be able to reveal subtle differences that cannot be recognized by human eyes and to compensate for the shortage of conventional CT imaging. In addition, CT texture analysis provides an assessment of tumor heterogeneity at imaging and indirect information of tumor microenvironment with a range of quantified parameters.

Previous study concluded that the potential benefits of giving chemotherapy before surgery are the downsizing and downstaging of the primary tumor and lymph node metastases, treating micrometastases early in the course of treatment (22). Moreover, multimodal treatment of locally AGC provides reasonable 3-year survival compared with historical data (23).

Our study has excluded patients who underwent pre-operative neoadjuvant therapy, which has been undertaken randomly in patients with AGCs in Peking University Cancer Hospital. Although in some clinical trials, neo-adjuvant chemotherapy is more frequently used in the locally AGC with serosal invasion (22,23). Therefore, the selection of patients had little impact on the population bias.

Lauren classification exhibited a number of distinct clinical and molecular characteristics. Gastric cancer exhibits varied sensitivity to chemotherapy drugs and significant heterogeneity. Therefore, the Lauren classification may provide the basis for individualized treatment for AGC. T4a tumor penetrated the serosa and the potential rate of peritoneum metastasis was increased, which will lead to a poor prognosis. The analysis of CT features might help differentiate T3 from T4 gastric cancers, so that more timely selection of appropriate treatment strategies would be made.

Factors that could impact the analysis of CT images were as follows: 1) Gastric cancers with ulceration may be misdiagnosed in the depth of cancer invasion; 2) The lesions on the angular incisure of stomach, whose CT findings were not typical due to a collapsed gastric lumen; and 3) Cancers of the esophagogastric junction cannot be accurately analyzed because it may invade the gastric bare area without serosa coverage. That may explain why the overall sensitivity (*Table 1*) is low (63.7%–66.1%) in our study. For the T3 tumors whose paragastric inflammatory strands may mimic the cancer infiltration out of the serosa and lead to the overstaging, the high enhanced serosa sign is of important significance.

Our study has several limitations. First, the evaluation of

the hyperattenuating serosa could be subjectively because the CT value of the stratified layers could not be measured precisely. Moreover, some of the CT images appear with reticular or linear soft-tissue density, which may mimic tumor invasion of the perigastric fat, this situation could be improved by the combination of new modalities [spectral CT, diffusion weighted magnetic resonance imaging (MRI), etc.]. Second, all of the cases in our series were resectable. It is unclear whether our results are applicable to unresectable gastric cancers. Third, the retrospective design of our study induced selection bias by limiting our study to patients with gastric cancer who underwent CT and surgery.

In addition, other imaging modalities were also proved of value in differentiation of staging. Several studies have confirmed the value of diffusion-weighted imaging (DWI) in detection (24) and characterization of gastric cancers. A characteristic appearance named "sandwich sign" can be widely and definitely observed on DW images, suggesting a stage ≥pT3 (25). MRI with DWI can increase the sensitivity and accuracy in TNM Classification of Malignant Tumors (TNM) staging of gastric cancers (26,27), especially in T staging (28).

Conclusions

The high enhanced serosa sign on CT is associated with gastric cancer involvement of the serosa. The sensitivity of the judgement of serosa invasion using hyperattenuating serosa sign in diffuse-type was significant higher than that in intestinal-type. The finding could be a key diagnostic feature for differentiating T3 from T4a stage gastric cancers.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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