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Research article

Histopathologic diversity of gastric cancers: Relationship between enhancement pattern on dynamic contrast-enhanced CT and histological type

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ABSTRACT

Purpose: To evaluate the diagnostic value of contrast-enhanced computed tomography gastrography (CE-CTG) to predict the histological type of gastric cancer.

Materials and methods: We analyzed 47 consecutive patients with resectable advanced gastric cancer preoperatively evaluated by multiphasic dynamic contrast-enhanced CT. Two radiologists independently reviewed the CT images and they determined the peak enhancement phase, and then measured the CT attenuation value of the gastric lesion for each phase. The histological types of gastric cancers were assigned to three groups as differentiated-type, undifferentiated-type, and mixed-type. We compared the peak enhancement phase of the three types and compared the CT attenuation values in each phase.

Results: The peak enhancement was significantly different between the three types of gastric cancers for both readers (reader 1, $p = 0.001$; reader 2, $p = 0.009$); most of the undifferentiated types had peak enhancement in the delayed phase. The CT attenuation values of undifferentiated type were significantly higher than those of differentiated or mixed type in the delayed phase according to both readers (reader 1, $p = 0.002$; reader 2, $p = 0.004$).

Conclusion: CE-CTG could provide helpful information in diagnosing the histological type of gastric cancers preoperatively.

1. Introduction

Computed tomography (CT) has been a standard imaging modality for preoperative staging for gastric cancers. Recently, multidetector row CT (MDCT) techniques have advanced the accuracy of determinations of depth of invasion at the primary site of gastric cancer (T stage) as well as nodal involvement (N stage) and distant metastasis (M stage) [1–3]. There have also been reports on gastric-cancer analysis using a three-dimensional (3D) CT technique known as CT gastrography (CTG) [2,4–6]. These studies demonstrated that gastric cancer causes wall thickening of the stomach with moderate to marked enhancement in the early phase [6–8]. However, unlike colorectal, esophageal and other gastrointestinal cancers, gastric cancers exhibit diversity in various pathological factors, including histological type, differentiation, stroma, and infiltration patterns. Histological type is one of the most important factors because it has a close relationship to the aggressiveness of the disease or prognosis of patients with gastric cancer [9–11]. It is known that patients with poorly differentiated-type gastric cancers have a worse prognosis than those with well differentiated-type gastric cancers [12]. Endoscopic biopsy is the only way to obtain histological diagnosis of gastric cancer preoperatively. However, the small specimens obtained by endoscopic biopsy allow diagnosis of only a small part of the lesion, and not the whole lesion. Some gastric cancers are of a mixed histological type that includes both differentiated and

Abbreviations: 3D, Three-dimensional; ANOVA, Analysis of variance; CE-CTG, Contrast-enhanced computed tomography gastrography; ICC, Intraclass correlation coefficient; MDCT, Multidetector computed tomography; NPV, Negative predictive value; PPV, Positive predictive value; ROC, Receiver operator characteristics; ROI, Region of interest

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undifferentiated adenocarcinoma. Several authors reported that CT enhancement pattern of gastric cancers would be influenced by histological components [10,13]. We hypothesized that histological feature of whole component of gastric cancer can be preoperatively predictable by CT enhancement pattern.

The purpose of this study was to evaluate the diagnostic value of CE-CTG to predict the histological type of gastric cancer and to compare the diagnostic performance of CTG and endoscopic biopsy.

2. Materials and methods

2.1. Patients

This retrospective study was approved by the institutional review board of our institusion, and informed consent was waived. From January 2013 to December 2015, 142 consecutive patients with gastric cancer were evaluated by gastroscopy and CE-CTG at our institution. All gastric cancer patients at our institution preoperatively underwent CE-CTG to determine clinical stage except for contraindication for intravenous contrast agent such as iodine allergy.

We enrolled 56 patients with advanced gastric cancer (T2-T4) after gastrectomy with pathological confirmation. Patients who underwent chemotherapy or previous gastrectomy were excluded. Patients with poor CT image quality due to artifacts or poor gastric distension were also excluded. Eventually, a total of 47 patients served as our study cohort, whose clinicopathological characteristics are presented in Table 1. Tumor stages were stated on the patients' operation records according to the Japanese Classification of Gastric Carcinoma (3rd English edition)[14].

2.2. CT protocol

CT was performed using two MDCT scanners: a 64-detector row CT (Aquilion 64; Toshiba Medical Systems, Tokyo [n = 21]) and a 320-detector row CT (Aquilion ONE; Toshiba Medical Systems, Tokyo [n = 26]). The scan parameters were as follows: for the 64-detector row CT scanner, rotation time 0.5 s, section thickness and intervals 1 mm, beam collimation 1 mm, pitch 53, 120 kVp, 200 mAs, and matrix 512 × 512; for the 320-detector row CT scanner, rotation time 0.5 s, section thickness and intervals 0.5 mm, 120 kVp, 200 mAs, and matrix 512 × 512. After an overnight fast, each patient ingested 5.25 g of an effervescent agent (Baros Effervescent Granules-S; Horii Pharmaceutical Industries, Saitama, Japan) with a small amount of water just before the scanning to achieve gastric pouch distension. The patient was then given an intramuscular injection of 20 mg of scopolamine (Buscopan; Boehringer Ingelheim, Ingelheim am Rhein, Germany) to suppress peristalsis. The scanning covered the entire stomach during a single breath-hold.

CT images were obtained 40 s (arterial phase), 70 s (portal phase) and 240 s (delayed phase) after an infusion of 2 mL/kg of nonionic contrast material (Iopamiron370; Bayer Health Care, Osaka, Japan) at a rate of 3 mL/s followed by a 20-ml physiological saline flush using an automatic injector. The patient's position was supine in all phases. All CT datasets were transferred to a commercially available workstation equipped with image reconstruction software (Synapse Vincent, Fujifilm, Tokyo).

Table 1
Characteristics of 47 cases of advanced gastric cancers detectable on CT.

Variables	(n = 47)
Sex	
Male	26
Female	21
Mean age (y, ± SD)	65 ± 12
Tumor stage	
T2	14
T3	15
T4	18
Histology, biopsy specimen	
Differentiated	20
Mixed	5
Undifferentiated	22
Histology, surgery specimen	
Differentiated	10
Mixed	20
Undifferentiated	17
Location	
U	12
M	18
L	17
Mean lesion size (mm, ± SD)	59 ± 23

SD standard deviation.

2.3. CT images analysis

Interpretation of CT images was performed by two gastrointestinal abdominal radiologists (M.M. and T.M.) with 17 and 10 years of experience. Both readers were blinded to all clinical and pathologic data except for the endoscopic findings. They independently reviewed and analyzed the CT images on the workstation. They identified the gastric lesion on virtual endoscopy using optical endoscopic findings as a reference. The lesion was determined to be cancerous when the gastric wall showed focal thickening of ≥6 mm on axial images [15]. After localization of the gastric lesion, the radiologists determined the largest tumor section on axial images as a representative.

The image analysis included subjective and objective analyses. For the subjective analysis, the readers determined the "peak enhancement phase" in which the lesion showed the highest attenuation value among the three phases for each case. Then, for the objective analysis, the readers traced the entire tumor as the region of interest (ROI) of the gastric lesion, and measured the CT attenuation value of the ROI for each phase.

2.4. Pathological findings

All cases underwent endoscopic biopsy preoperatively. The endoscopists took one or two pieces of specimen from each lesions using biopsy forceps. The histological types of the biopsy specimens were diagnosed as well or moderately differentiated adenocarcinomas or papillary adenocarcinomas ("differentiated"), or poorly differentiated adenocarcinomas or signet-ring cell carcinomas ("undifferentiated") [15]. After gastrectomy, the pathological diagnosis was confirmed in all cases. All pathological diagnosis was performed by experienced pathologists. The histological types of resected tumors were assigned to three groups as follows: tumors composed of well or moderately differentiated adenocarcinomas or papillary adenocarcinomas were classified as differentiated-type, tumors composed of poorly differentiated adenocarcinomas or signet-ringed cell carcinomas were undifferentiated-type, and tumors composed of both differentiated and undifferentiated types of gastric cancer were considered as mixed-type.

3. Statistical analysis

3.1. Peak enhancement (subjective analysis)

We compared the peak enhancement phase of the three types using Chi-square tests as subjective analyses. The interobserver agreement between the two readers was evaluated using κ statistics. A κ value of 0.00–0.20 indicated poor, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good and 0.81–1.00 excellent agreement.