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Diagnostic Accuracy of T and N Stages With Endoscopy, Stomach Protocol CT, and Endoscopic Ultrasonography in Early Gastric Cancer

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Background: Preoperative accurate diagnosis of the T and N stages in early gastric cancer (EGC) is important in determining the application of various limited treatments. The aim of this study is to analyze the accuracy of T and N staging of EGC with esophagogastroduodenoscopy (EGD), Stomach protocol CT (S-CT), and endoscopic ultrasonography (EUS), and the factors influencing the accuracy.
Methods: Four hundred and thirty-four patients preoperatively diagnosed as EGC using EGD or S-CT and undergoing curative gastrectomy at Seoul National University Hospital in 2005 were included. The T and N stage reviewed by experienced personnel were compared with the surgical pathology.
Results: The predictive values for EGC of EGD, S-CT, and EUS were 87.4%, 92.2%, and 94.1%, respectively. The predictive values for node negativity of S-CT, and EUS were 90.1% and 92.6%, respectively. The factors leading to underestimation of T stage with EGD were the upper third location, the size greater than 2 cm, and diffuse type of tumor. Those with S-CT were female sex, the upper third location and lesion size greater than 2 cm.
Conclusions: Before applying limited treatment for EGC, a surgeon should consider the risk factors of underestimation of T stage with EGD or S-CT.
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KEY WORDS: early gastric cancer; diagnostic accuracy; limited treatment; endoscopy; endoscopic ultrasonography; computed tomography

INTRODUCTION

In far-east Asia, including Korea and Japan, the proportion of cases of gastric cancer detected at an early-stage has recently increased. Early gastric cancer (EGC) accounts for about 50% of all cases of gastric cancer in Korea [1] and more than 50% in Japan. The proportion of gastric cancer patients older than 70 years has been increasing, which has contributed to an increase in mortality and morbidity. These two trends have lead to the advent of various limited treatment options such as endoscopic submucosal dissection, function preserving gastrectomy, and laparoscopic gastrectomy. In addition to the extent of gastrectomy, Korean or Japanese surgeons usually decide the extent of lymphadenectomy (D1 or D2) according to T and N stage [2]. To facilitate the choice of optimal therapeutic approach and the prediction of prognosis, the preoperative differentiation of EGC from AGC and node-negative cancer (N−) from node-positive cancer (N+) is important. Therefore, the aim of this study was to evaluate the accuracy of preoperative T and N staging in patients with preoperative EGC, using esophagogastroduodenoscopy (EGD), stomach protocol-CT (S-CT) and endoscopic ultrasonography (EUS), and to analyze the clinicopathological factors leading to underestimation of T stage.

METHODS

From January to December 2005, 448 patients were examined with EGD and S-CT and diagnosed as EGC by means of EGD or S-CT before curative gastrectomy at the Department of Surgery, Seoul National University Hospital (tertiary referral center). Among them, 14 patients who received endoscopic submucosal dissection before the surgery or underwent gastrectomy without lymph node dissection were excluded because of their inaccuracy of pathologic stage. Therefore, these 434 patients were included to calculate the predictive values and the overall accuracy of T and N stages of each preoperative study. In addition, to calculate the sensitivity, 17 patients who were diagnosed as AGC by both EGD and S-CT and finally diagnosed as pathologic EGC were included. Among 434 patients who were examined with EGD and S-CT, 71 patients were also examined with EUS to get more information about T and N stages. All endoscopies and EUS were performed by a single experienced endoscopist (Kim SG), and evaluated blindly by another endoscopist (Im JP). Final endoscopic diagnosis was made with agreement by two endoscopists because of the variation between endoscopists. All the S-CT images were reviewed by a single experienced radiologist, a specialist in abdominal imaging (Kim SH). In case of S-CT, well-documented criteria of T and N staging were used to minimize inter-observer variation, as described below in detail. The endoscopists and the radiologist were blinded to each other's findings. The preoperative variables (sex, age, location of tumor, gross type of EGC, histology) and the postoperative pathology

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(tumor size, Lauren classification) were analyzed to determine the factors influencing the underestimation of T stage. Histology was recorded according to the World Health Organization (WHO) classification, and was divided into differentiated histology (papillary, well differentiated, and moderately differentiated carcinoma) and undifferentiated histology (poorly differentiated, mucinous adenocarcinoma, and signet ring cell carcinoma).

EGD and EUS were performed after inducing oropharyngeal anesthesia by gargling 10 mL of 2% lidocaine. Before EUS, 3 mg of midazolam and 2 mL of hyoscine-N-butyl bromide (Buscopan; Boehringer Ingelheim, Korea) were administered intravenously. The endoscopes and the echoendoscopes used in this study were the GIF-H260 (Olympus, Tokyo, Japan) and the GF-UM 2000 (Olympus). EUS was performed with a radial scanning echoendoscope system at 12-MHz for T staging and at 5-MHz for N staging. The gross type of EGC was recorded according to the Japanese Classification of Gastric Carcinoma [3] and divided into the elevated type (I, IIa, IIb) and the depressed type (IIc, III). Lesions were staged according to the 6th UICC TNM staging system [4]. The assessment of T stage with EGD was based on the gross findings (Fig. 1a,b) [5,6]. In EGC (T1 lesions), mucosal lesions were elevated small lesions with a smooth surface, or small, slightly depressed lesions without an uneven surface, fold convergence or dam formation. And submucosal lesions were lesions with a more rigid base and irregularly shaped nodules on the margin, or lesions with interrupted and enlarged folds. AGC (T2, T3, and T4) were ulcerative lesions surrounded by a tumorous bank (dam formation) showing no distention after air inflation. The assessment of T stage with EUS was based on the generally accepted 5-layer sonographic structure of the gastric wall (Fig. 1e,f). In EGC, mucosal lesions showed disruption of the first two layers and submucosal lesions showed tumor invasion to the third layer. AGC (T2, T3, and T4 lesions) showed tumor invasion to the fourth of fifth layer. The assessment of N stage with EUS was based on the number of metastatic perigastric lymph nodes. The existence of lymph node metastasis was established if the node met two or more of the following criteria; (1) size more than 5 mm, (2) round shape, (3) hypoechoic pattern, and (4) smooth border (Fig. 2) [7,8].

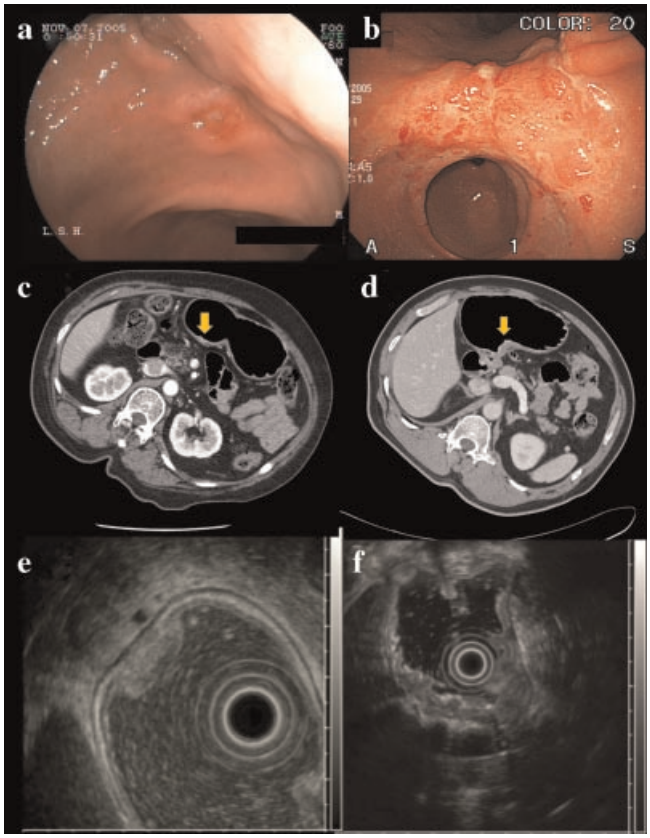

Fig. 1. T staging using EGD, S-CT and EUS. **a**: T1 lesion on EGD: a small depressed lesion with irregular nodules on the margin (pT1(m)). **b**: ≥T2 lesion on EGD: a dam formation and no distension after air inflation (pT2). **c**: T1 lesion on S-CT: an enhancing wall thickening (open arrow) preserving of the low-attenuation stripe indicating submucosal layer (pT(sm)). **d**: ≥T2 lesion on S-CT: an enhancing wall thickening with disruption of the low-attenuation stripe or full-thickness enhancing wall without perigastric fat infiltration (open arrow) (pT2). **e**: T1 lesion on EUS: disruption of sonographic layers 1 to 3 (pT1(sm)). **f**: ≥T2 lesion on EUS: disruption of sonographic layers beyond 4 (pT2). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

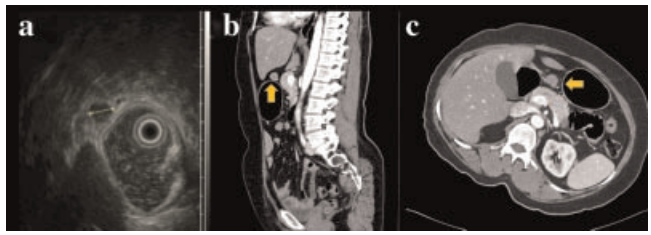

Fig. 2. N staging using S-CT and EUS. **a**: A metastatic lymph node on EUS, which was round, larger than 5 mm, and had hypoechoic pattern and smooth border. **b**: A metastatic lymph node (arrowhead) on sagittal MPR image of S-CT and (**c**) a metastatic lymph node (arrowhead) on axial image of S-CT, which were round, larger than 8 mm in the short axis, and showed necrosis and enhancement on contrast-enhanced CT. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

S-CT was performed with a 16 row multi-detector row computed tomography (MDCT) scanner (Sensation 16, Siemens Medical Systems, Germany) after administration of 10 mg of butyl scopolamine (Buscopan, Boehringer Ingelheim, Korea) and two packs of effervescent granules [9]. We used MDCT because it allowed thinner collimation and faster scanning, which markedly improve the scanning resolution and enable rapid and easy handling of reconstruction of the obtained images and generation of virtual endoscopy and cross-sectional transverse and multiplanar reformation. The scanning protocol we used was as follows: 16×0.75 mm detector configuration; rotation time of 0.5 sec; slice thickness of 1 mm; a pitch of 1.25; kVp and mAs of 120 and 200. Images were reconstructed at an interval of 0.7 mm for 3D imaging and 3 mm for clinical interpretation. CT images were obtained 70 sec after injection of 120 mL of nonionic contrast material (iopromide, Ultravist370, Schering) at a rate of 3–4 mL/sec. During CT scanning, the patients were asked to be in 30° left posterior oblique position to obtain a better distension for the lower half of the stomach. After obtaining CT scan in a left posterior oblique position, the patients changed their postures to right decubitus position to achieve an appropriate distension for the upper half of the stomach. CT images were then reconstructed using coronal and sagittal multiplanar reformation as well as axial images and 3D surface-shaded volume-rendering techniques. The radiologists used reconstructed images as well as transverse 2D images for the interpretation of T and N stages. The T staging criteria of our institution were defined based on the literature (Fig. 1c,d) [10–12]. The indication of EGC (T1 lesions) was the presence of gastric wall thickening with enhancement in the inner surface but the preservation of the low-attenuation stripe, corresponding to the submucosal layer, at the base of the lesion. If the radiologist was not able to delineate the submucosal layer on CT, the enhancement of the lesion confined to the inner half of gastric wall was

considered as EGC. In addition, for 3D surface-shaded volume-rendering images, the radiologist used the same criteria to that of endoscopy. AGC (T2, T3, and T4 lesions) was indicated by a thickened and enhancing gastric wall with disruption of the low-attenuation stripe, perigastric fat infiltration or direct invasion into a contiguous organ or structure. If the radiologist was not able to delineate submucosal layer on CT, the enhancement of the lesion invaded into the outer half of gastric wall was considered to be AGC. N stage was assessed by the Japanese anatomic classification [3] of metastatic perigastric lymph nodes. Lymph node metastasis was established if the node met two or more of the following criteria: (1) $\geq$8 mm diameter on the short-axis and round shape, (2) enhancement on contrast-enhanced CT, (3) necrosis (Fig. 2b,c).

We calculated the predictive value for EGC (number of patients with EGC by the relevant examination and pathology/number of patients with EGC by the relevant examination), the predictive value for N(−) (number of patients with negative metastasis of lymph node by the relevant examination and pathology/number of patients with negative lymph node by the relevant examination), and the overall accuracy (number of patients with pathology identical to the result of the examination/number of patients who were examined). We also calculated the sensitivity for EGC (number of patients with EGC by the relevant examination and pathology/number of patients with EGC by pathology) and the sensitivity for N(−) (number of patients with negative lymph node by the relevant examination and pathology/number of patients with negative metastasis of lymph node by pathology).

For statistical analysis, the chi square test or Fisher's exact test, the independent *t*-test or Mann–Whitney test and the binary logistic regression were used. A *P*-value of less than 0.05 was considered statistically significant. We used SPSS version 12.0 (SPSS, Chicago, IL) for all statistical analysis.

This study was approved by The Institutional Review Board of Seoul National University Hospital.

RESULTS

The Diagnostic Accuracy in the Patients With Preoperative EGC

The study group consisted of 278 men and 156 women with a mean age of 55.9 (11.6, SD) years. Of 434 patients with preoperative EGC, 363 patients (83.6%) were diagnosed as EGC by both EGD and S-CT, 51 (11.8%) patients by only EGD and 20 patients (4.6%) by only S-CT. Three-hundred and eighty-two patients (88.5%) were finally revealed as pathologic EGC (pT1), and 387 patients (89.2%) were revealed as node-negative case (pN0). The clinicopathological features of the patients are summarized in Table I. Fifty laparoscopy-assisted gastrectomies (11.5%) and 20 function-preserving gastrectomies (4.6%) were performed.

Table II shows the T stage determined by EGD, S-CT and EUS and the N stage determined by S-CT and EUS. Four-hundred and fourteen patients (95.4%) were diagnosed as EGC with EGD and the predictive value and the overall accuracy for EGC with EGD were 87.4% (362/414) and 83.4% (362/434), respectively. Three-hundred and eighty-three patients (88.2%) were diagnosed as EGC with S-CT and the predictive value and the overall accuracy for EGC with S-CT were 92.2% (353/383) and 86.4% (375/434), respectively. And the predictive value and the overall accuracy for EGC with EUS were 94.1% (64/68) and 90.1% (64/71). The number of patients who were diagnosed as EGC with both EGD and S-CT was 363 and the predictive value and the overall accuracy for EGC were 91.7% (333/363) and 81.8% (355/434), respectively. The number of patients who were diagnosed as EGC with a combination of all three examinations in 71 patients was 58 and the predictive value and the overall accuracy for EGC were 96.7% (58/60) and 84.5% (60/71) respectively. With the use of an increasing number of tests to examine the patients, the predictive value increased but the overall accuracy decreased (Table II). After including 17 patients with pathologic EGC, the sensitivity for EGC with EGD, S-CT and EUS were 90.8% (365/402), 88.3% (355/402) and 95.7% (66/69), respectively. Those with EGD plus S-CT and all three exams were 83.5% (333/399) and 84.1% (58/69), respectively.

TABLE I. Clinicopathological Features of 434 Patients

Variables	N	(%)
Sex		
M:F	278:156	(1.78:1)
Age		
Mean (SD), year	55.9	(11.6)
Preoperative diagnosis		
EGC only by EGD	51	11.8
EGC only by S-CT	20	4.6
EGC by both EGD and S-CT	363	83.6
Location		
Upper	39	9.0
Middle	81	18.7
Lower	311	71.7
Entire	3	0.7
Histology		
Differentiated (Pap, WD, MD)	247	56.9
Undifferentiated (PD, Mucin, SRC)	187	43.1
Tumor size		
Mean (SD), cm	3.1	(2.1)
Lauren classification		
Intestinal	246	56.7
Diffuse	149	34.3
Mixed	39	9.0
Operation		
Subtotal gastrectomy	354	81.6
Pylorus-preserving gastrectomy	4	0.9
Proximal gastrectomy	16	3.7
Total gastrectomy	60	13.8
Approach		
Open	384	88.5
Laparoscopy-assisted	50	11.5
T status		
T1	382	88.0
T2, 3	52	12.0
N status		
N(−)	387	89.2
N(+)	47	10.8
TNM stage		
I	410	94.5
II	19	4.4
III	5	1.2

With regard to N stage, 394 patients (90.8%) were diagnosed as node negative with S-CT and the predictive value and the overall accuracy for N(−) were 90.1% (355/394) and 83.6% (363/434), respectively. The predictive value and the overall accuracy for N(−) with EUS were 92.6% (63/68) and 90.1% (64/71), respectively. The surgical pathology revealed that no metastatic lymph node found in 59 (95.2%) of 62 patients who were diagnosed as N(−) with both S-CT and EUS.

Clinicopathological Factors Affecting the Underestimation of AGC to EGC

We analyzed the features of 52 patients with pathologically confirmed AGC who were preoperatively underestimated to EGC with EGD (Table III). The underestimation with EGD had statistically significant relationships with patient's age ($P = 0.001$), and with

TABLE II. The Results of EGD, S-CT, and EUS

Study	Result	Pathology		Total	Predictive value for EGC (%)	Overall accuracy for EGC (%)
		EGC	AGC			
T stage of EGD, S-CT and EUS						
EGD	EGC	362	52	414	87.4	83.4
	AGC	20	0	20		
S-CT	EGC	353	30	383	92.2	86.4
	AGC	29	22	51		
EUS	EGC	64	4	68	94.1	90.1
	AGC	3	0	3		
EGD plus S-CT	EGC	333	30	363	91.7	81.8
	AGC	49	22	71		
EGD plus EUS	EGC	63	4	67	94.0	88.7
	AGC	4	0	4		
EUS plus S-CT	EGC	59	2	61	96.7	85.9
	AGC	8	2	10		
EGD, S-CT plus EUS	EGC	58	2	60	96.7	84.5
	AGC	9	2	11		

Study	Result	Pathology		Total	Predictive value for N(−) (%)	Overall accuracy for N(−) (%)
		N(−)	N(+)			
N stage of S-CT and EUS						
S-CT	N(−)	355	39	394	90.1	83.6
	N(+)	32	8	40		
EUS	N(−)	63	5	68	92.6	90.1
	N(+)	2	1	3		
S-CT plus EUS	N(−)	59	3	62	95.2	87.3
	N(+)	6	3	9		

longitudinal location ($P < 0.001$), histology ($P = 0.004$), pathologic size ($P < 0.001$) and Lauren classification ($P < 0.001$) of tumor. Multivariate analysis showed that pathologic AGC located in the upper third of stomach ($P < 0.001$), of size larger than 2 cm ($P = 0.009$) or of the diffuse type ($P = 0.001$) had tendency to be preoperatively underestimated to EGC. There were 14 patients with endoscopic EGC located in the upper third, of size larger than 2 cm and of the diffuse type, of whom nine patients (64.3%) had pathologically confirmed AGC (Table IV and Fig. 3).

The underestimation of T stage with respect to S-CT was significantly associated with patient's sex ($P = 0.005$), and with longitudinal location ($P = 0.001$), histology ($P = 0.012$), pathological size ($P = 0.002$) and Lauren classification ($P = 0.001$) of tumors (Table V). Multivariate analysis showed that the probability of underestimation of pathological AGC was higher in female patients ($P = 0.024$) or those with tumor located in the upper third of the stomach ($P < 0.001$) or of size lager than 2 cm ($P = 0.036$). With S-CT, eight female patients were diagnosed as EGC located in the upper third and of size larger than 2 cm, and 6 patients (75.0%) had pathologically confirmed AGC.

When EGC was preoperatively diagnosed by both EGD and S-CT, the underestimation of T stage was significantly associated with patient's sex ($P = 0.031$), and with tumor's longitudinal location ($P = 0.002$), and pathological size ($P = 0.025$) in multivariate analysis (Table VI). With both EGD and S-CT, eight female patients were diagnosed as EGC located in the upper third and of size larger than 2 cm, and six patients (75.0%) had pathologically confirmed AGC (Table VII).

DISCUSSION

Many methods have been used to preoperatively evaluate T and N stages of gastric cancers. EGD is the established primary diagnostic investigation for patients suspected to have gastric malignancy. EGD has the advantages of simplicity, availability, rapid evaluation, and relatively low cost in Korea. The ability to determine the exact location of the lesion, appreciate its gross morphology and extent, and obtain biopsy specimens make EGD an essential preoperative evaluation method despite many technological advances [13]. However, EGD has limitations in the accurate determination of the depth of tumor invasion and has no ability to evaluate nodal stage. For these reasons, EUS has been used since the early 1980s, and is currently established as the reliable method for preoperative staging of gastric cancer. EUS has the advantage of placing the transducer close to the lesion without interference from fat, bowel gas or bone, and being able to detect nodes and ascitic fluid within the range of the transducer [13,14]. However, EUS has not replaced CT in preoperative staging of gastric cancer, because of its operator dependency and limitations with regard to M staging. The introduction of MDCT, which is able to make thin sections in a short time and has a good diagnostic performance, has raised renewed interest in using it to evaluate gastric abnormalities.

With the introduction of limited surgery for EGC, diagnostic accuracy has considerable clinical importance. There have been many reports about diagnostic accuracy of EGD, MDCT, and EUS. The reported predictive value for EGC with EGD, MDCT, and EUS were 67.3–92.4% [5,15], 76.5–100.0% [12,13,16–18], 57.1–100.0% [13,19–23], respectively in various studies. The overall accuracy for EGC of EGD, MDCT and EUS were 83.6–96.8% [5,6,15,24], 77.8–94.1% [12,13,16–18,25], 76.2–95.6% [7,13,19–22,26,27], respectively. The values in this study were relatively higher than the results from other studies. Our department had annually over 700 cases with gastric cancer more than 10 years and endoscopists and radiologists had a lot of experiences to analyze the preoperative examinations, which could account some part of the relatively high accuracy of this study. Furthermore high performance of CT for T stage may be caused by high-end CT scanner like MDCT and meticulous method for vigorous gastric distension with gas and water [16,28].

TABLE III. The Clinicopathological Features of Patients With Pathological AGC who were Preoperatively Diagnosed as EGC With EGD

N = 414	AGC	*P*-value
Univariate analysis		
Age		
<50 years	27/127 (21.3%)	0.001
≥50 years	25/287 (8.7%)	
Sex		
M	27/266 (10.2%)	0.063
F	25/148 (16.9%)	
Longitudinal location		
Lower	28/295 (9.5%)	<0.001
Middle	8/79 (10.1%)	
Upper	15/38 (39.5%)	
Circular location		
Lesser curvature	21/163 (12.9%)	0.761
Greater curvature	9/67 (13.4%)	
Anterior wall	8/87 (9.2%)	
Posterior wall	14/94 (14.9%)	
EGC gross type		
Elevated (I, IIa, IIb)	8/111 (7.2%)	0.064
Depressed (IIc, III)	44/303 (14.5%)	
Histology		
Differentiated	20/236 (8.5%)	0.004
Undifferentiated	32/178 (18.0%)	
Pathologic Size		
≤2 cm	8/166 (4.8%)	<0.001
>2 cm	44/248 (17.7%)	
Lauren classification		
Intestinal	14/233 (6.0%)	<0.001
Diffuse	32/144 (22.2%)	
Mixed	6/37 (16.2%)	

			95% CI for Exp(B)	
	Sig.	Exp(B)	Lower	Upper
Multivariate analysis				
Age (<50 years)	0.083	1.803	0.925	3.511
Location	<0.001			
Middle	0.682	0.834	0.350	1.987
Upper	<0.001	4.797	2.114	10.882
Histology	0.186	0.540	0.217	1.347
Pathologic size (>2 cm)	0.009	3.053	1.329	7.014
Lauren classification	0.006			
Diffuse	0.001	5.146	1.886	14.046
Mixed	0.103	2.729	0.816	9.126

With respect to the N stage, the reported predictive value for N(−) of MDCT and EUS were 66.7–85.7% [11,13,16,18] and 54.8–95.0% [11,13,19–23,29], respectively, and the overall accuracy for N(−) were 68.9–85.5% [11,13,16,18] and 65.9–98.0% [7,11,13,20–23,27], respectively, similar to those observed in this study. The relatively low predictive value of N(−) was due to the lack of reliable CT and EUS criteria for metastatic nodes. Furthermore, EUS does not permit the assessment of tissue beyond a depth of about 5–6 cm, such as in the para-aortic area and the celiac trunk area, because of the limited depth of the transducer and unsatisfactory visualization of distant lymph nodes.

Accurate pre-treatment diagnosis of T stage is very important for definite cure and therefore should be given priorities. The deeper a tumor infiltrates, the more frequently dose it metastasize to lymph

TABLE IV. The Proportion of the Patients With Pathological AGC in the Patients Diagnosed as EGC With EGD According to Clinicopathological Factors

	Lower	Middle	Upper
Intestinal			
≤2 cm	0/97 (0.0%)	0/14 (0.0%)	0/4 (0.0%)
>2 cm	11/82 (13.4%)	0/22 (0.0%)	3/13 (23.1%)
Diffuse			
≤2 cm	5/26 (19.2%)	0/11 (0.0%)	1/2 (50.0%)
>2 cm	10/68 (14.7%)	7/23 (30.4%)	9/14 (64.3%)

Fig. 3. AGC preoperatively diagnosed as EGC with EGD. **a**: The tumor was larger than 2 cm, located in the upper third and of the intestinal type (pT3). **b**: The tumor was larger than 2 cm, located in the upper third and of the diffuse type (pT2). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

nodes s and the more frequently can it develop recurrence [30,31], which makes further radical treatment essential. With the application of limited treatments, preoperative underestimation of the tumor invasion depth of gastric cancer inevitably leads to an additional definite therapeutic procedure or more frequent surveillance.

In this study, pathological AGC was preoperatively underestimated to EGC with EGD when the tumor was located in the upper third of the stomach, was larger than 2 cm or was of the diffuse type. With S-CT, the tumor was more often preoperatively underestimated when the patient was female or the tumor was located in the upper third of the stomach. There have few studies about the factors leading to the preoperative underestimation of T stage. Sano et al. [5] reported that 14 lesions among the 15 lesions underestimated with EGD were depressed, and Yanai et al. [6] reported that EGD had a tendency to underestimate T stage of tumors in the gastric body-cardia and suggested that this may be due to a forward viewing endoscope. Saito et al. [19] reported that EUS had a tendency to underestimate the depth of cancer invasion more frequently in tumors with some thickened or irregular layers than in mass-forming tumors with relatively clear

TABLE V. The Clinicopathological Features of the Patient With Pathological AGC Who were Preoperatively Diagnosed as EGC With S-CT

N = 383	AGC	*P*-value
Univariate analysis		
Age		
<50 years	14/116 (12.1%)	0.060
≥50 years	16/267 (6.0%)	
Sex		
M	12/246 (4.9%)	0.005
F	18/137 (13.1%)	
Longitudinal location		
Lower	16/275 (5.8%)	0.001
Middle	4/74 (5.4%)	
Upper	10/32 (31.3%)	
Circular location		
Lesser curvature	14/157 (8.9%)	0.770
Greater curvature	5/60 (8.3%)	
Anterior wall	7/80 (8.8%)	
Posterior wall	4/79 (5.1%)	
EGC gross type		
Elevated (I, IIa, IIb)	4/94 (4.3%)	0.128
Depressed (IIc, III)	26/269 (9.7%)	
Histology		
Differentiated	10/215 (4.7%)	0.012
Undifferentiated	20/168 (11.9%)	
Pathologic Size		
≤2 cm	4/155 (2.6%)	0.002
>2 cm	26/228 (11.4%)	
Lauren classification		
Intestinal	8/217 (3.7%)	0.001
Diffuse	20/133 (15.0%)	
Mixed	2/33 (6.1%)	

			95% CI for Exp(B)	
	Sig.	Exp(B)	Lower	Upper
Multivariate analysis				
Sex (F)	0.024	2.678	1.140	6.291
Location	0.001			
Middle	0.600	0.733	0.230	2.340
Upper	0.000	6.332	2.364	16.955
Histology	0.783	0.854	0.278	2.623
Pathologic size (>2 cm)	0.036	3.360	1.084	10.414
Lauren classification	0.124			
Diffuse	0.065	3.117	0.932	10.423
Mixed	0.911	1.107	0.186	6.589

TABLE VI. The Clinicopathological Features of the Patient With Pathological AGC Who were Preoperatively Diagnosed as EGC With Both EGD and S-CT

N = 363	AGC	*P*-value
Univariate analysis		
Age		
<50 year	14/108 (13.0%)	0.039
≥50 year	16/255 (6.3%)	
Sex		
M	12/234 (5.1%)	0.005
F	18/129 (14.0%)	
Longitudinal location		
Lower	16/259 (6.2%)	<0.001
Middle	4/72 (5.6%)	
Upper	10/31 (32.3%)	
Circular location		
Lesser curvature	14/148 (9.5%)	0.790
Greater curvature	5/57 (8.8%)	
Anterior wall	7/77 (9.1%)	
Posterior wall	4/78 (5.1%)	
EGC gross type		
Elevated (I, IIa, IIb)	4/94 (4.3%)	0.128
Depressed (IIc, III)	26/269 (9.7%)	
Histology		
Differentiated	10/204 (4.9%)	0.012
Undifferentiated	20/159 (12.6%)	
Pathologic Size		
≤2 cm	4/153 (2.6%)	0.001
>2 cm	26/210 (12.4%)	
Lauren classification		
Intestinal	8/204 (3.9%)	0.001
Diffuse	20/128 (15.6%)	
Mixed	2/31 (6.5%)	

			95% CI for Exp(B)	
	Sig.	Exp(B)	Lower	Upper
Multivariate analysis				
Age (<50 years)	0.893	1.063	0.435	2.597
Sex (F)	0.031	2.631	1.094	6.328
Location	0.002			
Middle	0.534	0.691	0.215	2.217
Upper	0.000	6.083	2.221	16.657
Histology	0.765	0.838	0.264	2.666
Pathologic size (>2 cm)	0.025	3.647	1.173	11.335
Lauren classification	0.149			
Diffuse	0.073	3.090	0.899	10.626
Mixed	0.891	1.134	0.189	6.787

margins. Kim et al. reported histological differentiation affected the underestimation by EUS. According to Bhandari et al. [13], the understaging by MDCT is largely caused by the presence of focal microscopic submucosal invasion. In our study, poor distension of the stomach in the cardia cancer, and the tendency of diffuse type cancers to spread in the submucosal layer may account for the underestimation by CT. The features leading to the underestimation of T stage in female patients probably may be related to of relatively thin visceral fat and needs further investigation.

As for lymph node metastasis, this study showed relatively low predictive value, sensitivity and overall accuracy of N(−) despite of the introduction of MDCT. Furthermore the sensitivity for lymph node

TABLE VII. The Proportion of the Patients With Pathological AGC in the Patients Diagnosed as EGC With Both EGD and S-CT According to Clinicopathological Factors

	Lower	Middle	Upper
Male			
≤2 cm	1/86 (1.2%)	0/16 (0.0%)	0/3 (0.0%)
>2 cm	8/87 (9.2%)	0/23 (0.0%)	3/18 (16.7%)
Female			
≤2 cm	2/35 (5.7%)	0/10 (0.0%)	1/2 (50.0%)
>2 cm	5/51 (9.8%)	4/23 (17.4%)	6/8 (75.0%)

metastasis was very low (8/47 = 17.0%, Table II). Surgeons should consider the possibility of overlooking nodal metastasis by S-CT as well as the possibility of underestimating tumor invasion depth.

A proper treatment for EGC should be decided carefully on the basis of preoperative stage because there are so many treatment options such as endoscopic submucosal dissection, function preserving gastrectomy, laparoscopic gastrectomy, standard open gastrectomy and D1 or D2 lymphadenectomy. A combination of various diagnostic tests including MDCT and EUS may be helpful to increase the predictive value for EGC, although not all patients in this study were examined with EUS. If any one of the tests suggests that the possibility of AGC, surgeon should reconsider the limited treatment for EGC and radical surgery may be a more preferred option. However, the pathological diagnosis of the preoperative EGC with both EGD and S-CT was AGC in more than 70% of female patients with the tumor located in the upper third of stomach and larger than 2 cm in this study. If anyone of these risk factors is satisfied, surgeons should be careful to perform limited treatment and inform to patients with preoperative EGC with both EGD and S-CT. Thus, surgeons must consider a combination of diagnostic tests and consider the risk factors of underestimation before choosing the appropriate treatment for doubtful EGC.

Our study had a few limitations as not all the patients were examined with EUS. The extent of the lesion was determined by pathological size, and not by endoscopic size. The larger the pathological size of the lesion was, the greater the number of patients with endoscopic EGC that were subsequently diagnosed as AGC by pathology. Therefore, to obtain an accurate preoperative diagnosis of T stage, a study with tumor size determined by endoscopy is needed. Another limitation may be that the removed lymph nodes were not mapped in a one-to-one correspondence by site to correlate with the findings at CT and EUS.

In conclusion, the distinction of EGC from AGC by means of EGD, S-CT or EUS was reliable and the combination of diagnostic tests appears to be useful for more accurate diagnosis. When surgeons choose a limited treatment for EGC, they should consider that EGD has a risk of understaging lesions which are located in the upper third of the stomach, are larger than 2 cm, or are of the diffuse type. Furthermore CT has a risk of underestimating lesions, especially in female patients or in the tumor located upper third of the stomach or larger than 2 cm.

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