Int Surg 2016;**101:**562–569
DOI: 10.9738/INTSURG-D-15-00245.1

Clinically Early Gastric Cancer: Features and Treatment Strategy

Si-Hak Lee[1], Cheol Woong Choi[2], Su Jin Kim[2], Dae-Hwan Kim[3], Chang In Choi[3], Tae-Yong Jeon[3], Dong-Heon Kim[3], Sun Hwi Hwang[1]

[1]*Department of Surgery, Pusan National University Yangsan Hospital, South Korea*

[2]*Department of Internal Medicine, Pusan National University Yangsan Hospital, South Korea*

[3]*Department of Surgery, School of Medicine, Pusan National University, South Korea*

This study aimed to clarify the clinicopathologic features and explore treatment strategies for patients with pathologically confirmed advanced gastric cancer (AGC) diagnosed as clinically early gastric cancer (cEGC) before surgery. We included 955 patients who were treated by curative gastrectomy between 2008 and 2013; 42 patients had cEGC. The clinicopathologic features of the patients with cEGC were compared with those of patients with early gastric cancer (EGC); AGC; cancer of the muscularis propria (MP cancer, gastric cancer invading the muscularis propria of the stomach); or SM3 cancer (gastric cancer invading all 3 parts of the submucosal layer). Patients with cEGC had more tumor lymph node metastasis; more lymphatic invasion; and more perineural invasion (all $P < 0.001$) compared with those with EGC. Patients with cEGC had more tumor lymph node metastasis ($P = 0.017$) than did patients with SM3. Compared with patients with AGC or MP cancer, patients with cEGC were more likely to be operated on using a laparoscopic procedure and less likely to receive lymph node dissection. Multivariate analysis showed that gross type III [odds ratio (OR), 12.92; $P < 0.001$] and tumor location (middle body, OR, 2.691; $P = 0.009$) were significant predictors of cEGC before surgery. Although patients with cEGC had clinicopathologic features similar to those of patients with MP cancer, they were treated like patients with SM3 cancer (*e.g.*, limited use of lymphadenectomy). These findings suggest that patients with cEGC should be given a more aggressive treatment strategy.

Key words: Clinicopathologic feature – cEGC – Risk factor

Corresponding author: Sun-Hwi Hwang, 20 Geumo-ro, Moolgeum-eup, Yangsan-si, Kyungsangnam-do, Korea.
Tel.: +82-55-360-2124; Fax: +82-55-360-2154; E-mail: hwangsh@pusan.ac.kr

The increased interest in cancer screening and the development of endoscopic techniques have enabled early detection of gastric cancer. Early gastric cancer (EGC) is defined as cancer confined to the mucosal or submucosal layers of stomach regardless of whether there is lymph node (LN) metastasis or not, and advanced gastric cancer (AGC) is gastric cancer extending into or beyond the proper muscle layer.[1]

Minimally invasive treatment, such as laparoscopic gastrectomy with limited LN dissection, is the operation of choice for patients with EGC in South Korea and Japan wishing to maintain their quality of life after surgery.[2–4] Despite the development of new diagnostic and treatment methods, we often treat patients with a preoperative diagnosis of clinically early gastric cancer (cEGC), which is pathologically confirmed AGC after operation (Fig. 1). The prognostic factors for gastric cancer are influenced by the depth of tumor invasion, LN metastasis, and complete tumor removal.[5–7]

Radical gastrectomy with systemic D2 LN dissection is the standard operation in the treatment of AGC. Even with laparoscopic gastrectomies, standard D2 LN dissection should be conducted in case of AGC.[8–10] However, patients diagnosed with cEGC might undergo operation with limited LN dissection despite of their advanced stage. Thus, accurately predicting the tumor invasion depth before surgery is critical for deciding the range of the operation.

In this study, we evaluated the clinicopathologic characteristics of patients with cEGC and developed a method to predict cEGC preoperatively to provide useful information for selecting the optimal therapeutic strategy.

Materials and Methods

Patients

A total of 955 patients with gastric cancer who were treated by curative gastrectomy between December 2008 and December 2013 were included in this study. They were diagnosed with EGC or AGC preoperatively by imaging studies such as esophagogastroduodenoscopy, computed tomography, or endoscopic ultrasound (EUS). Among the 626 patients preoperatively diagnosed with EGC, 42 (6.7%) had cEGC that was confirmed pathologically as AGC after resection (Fig. 2). The demographic and clinicopathological characteristics were analyzed for each group. These included sex, age, tumor location, operative method, tumor size, gross type, invasion depth, LN metastasis, Lauren classification, lymphatic invasion, vascular invasion, and perineural invasion. These analyses were applied to

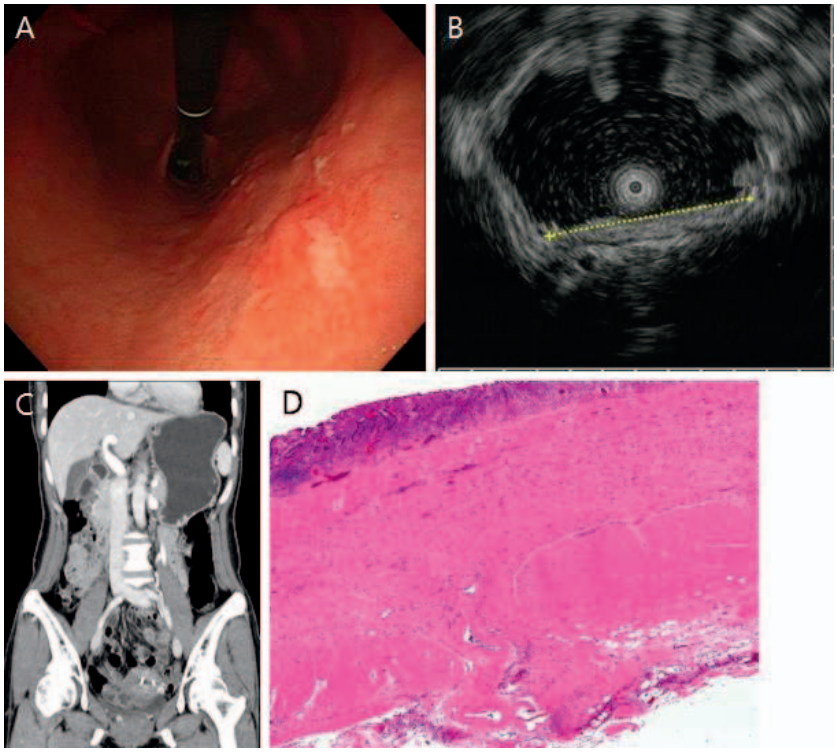

Fig. 1 Images obtained from a 47-year-old woman with advanced gastric cancer that was preoperatively diagnosed as cEGC. (A) Endoscopic image: EGC gross type IIb with irregular margin on the midbody lesser curvature. (B) Endoscopic ultrasound image: hypoechoic disruption of the superficial and deep mucosal layers is noted. The lesion invaded further into, but not through, the third (submucosal) layer. (C) Abdominal computed tomography: no evidence of focal wall thickening or a mass in the stomach. (D) Histological findings: cancer cells had invaded the subserosal layer (hematoxylin and eosin stain, ×40).

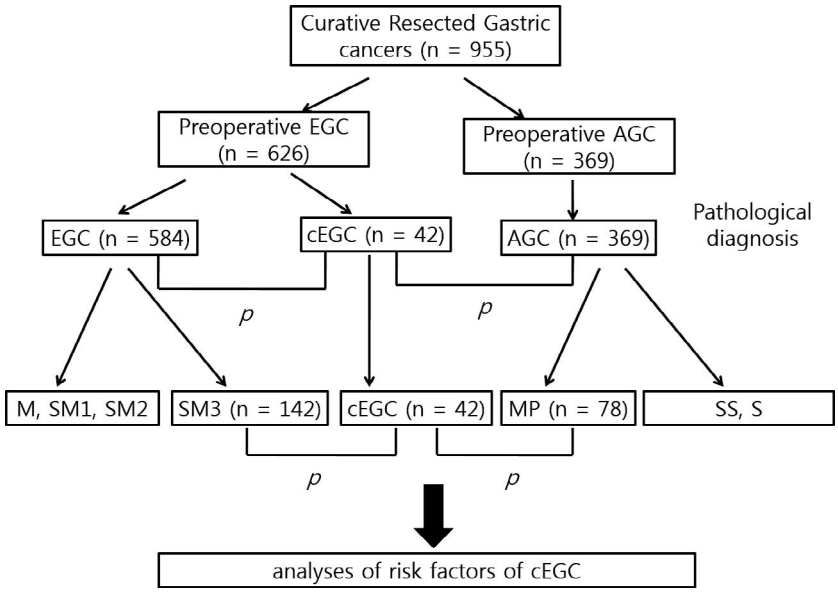

Fig. 2 Flow chart for this study. Among the 626 patients with EGC, 42 patients (6.7%) were diagnosed with cEGC before surgery, which was confirmed pathologically as AGC after resection. The clinicopathologic features of the cEGC group were compared with those of patients with EGC, AGC, MP cancer (gastric cancer invading the muscularis propria), or SM3 cancer (gastric cancer invading all 3 parts of the submucosal layer). M, mucosal gastric cancer; SM1, gastric cancer invading the first submucosal layer; SM2, gastric cancer invading the second submucosal layer; SS, subserosal gastric cancer; S, serosal gastric cancer.

patients with gastric cancer invading all 3 parts of the submucosal layer (SM3 cancer) or cancer of the muscularis propria (MP cancer).

The stomach can be divided anatomically into 3 portions: the upper body (UB), middle body (MB), and lower body (LB), by lines connecting the trisected points on the lesser and greater curvatures. The tumor location was described by the parts involved. There were 3 gross types of EGC: type I (protruded), type II (superficial), and type III (excavated), according to the Japanese classification of gastric carcinoma.[8] The degree of differentiation was classified into 2 groups: differentiated type, which included papillary, well differentiated, or moderately differentiated; and undifferentiated type, which included poorly differentiated, signet ring cell carcinoma, or mucinous carcinoma.

Prognostic factors associated with the recurrence of gastric cancer

A disease-free survival (DFS) curve was prepared to identify the most significant prognostic factors for gastric cancer in our hospital based on recurrence, and these factors were compared with the clinicopathologic characteristics of the patients with cEGC to determine the appropriate treatment. The DFS curve was prepared to compare the rate of recurrence between patients with cEGC, SM3 cancer, and MP cancer. The diagnosis of recurrence was confirmed by radiologic findings, computed or positron emission tomography, and by endoscopic biopsy histopathologic findings.

Risk factors for predicting cEGC

Univariate and multivariate analyses were performed to identify risk factors for predicting cEGC. The aim of these analyses was to determine whether these factors could be detected preoperatively.

Statistical analysis

All statistics were conducted using statistical software (SPSS ver. 21, IBM Corp, Armonk, New York). The χ^2 test or Fisher's exact test was used to compare differences in categorical variables, and the Student's *t*-test was used for continuous variables. Independent risk factors associated with cEGC were analyzed by logistic regression analysis. ORs were estimated with 95% confidence intervals (CIs). DFS curves were plotted using the Kaplan–Meier method, and the log-rank test was used to analyze the univariate risk factors for recurrence. The Cox proportional-hazards regression model (F test) was used to identify the independent risk factors for recurrence. Values of $P < 0.05$ were considered significant for all statistical analyses.

Results

Among the 626 patients with preoperative EGC, 42 patients (6.7%) had cEGC that was confirmed pathologically as AGC after resection. The tumor invasion depths were as follows: 30 cases (71.4%) involved invasion of the muscularis propria, 6 cases (14.3%) involved invasion of the subserosa, and 6 cases (14.3%) involved invasion of the serosa.

Comparisons between the cEGC, EGC, and AGC groups

No significant differences were observed for sex, age, tumor size, Lauren classification, extension of LN dissection, or vascular invasion between the cEGC and EGC groups. The cEGC group had a higher percentage of patients with cancer located above the MB ($P = 0.007$). Near-total gastrectomy or proximal gastrectomy was performed more often ($P < 0.001$) in the cEGC group compared with the EGC group. A higher percentage of patients in the cEGC group had gross type III cancer, whereas a higher percentage in the EGC group had type II cancer ($P < 0.001$).

The cEGC group had a higher percentage of patients with LN metastasis ($P < 0.001$); undifferentiated type ($P = 0.019$); lymphatic invasion ($P < 0.001$); and perineural invasion ($P < 0.001$) compared with the EGC group. The cEGC group was operated on more often with a laparoscopic procedure ($P < 0.001$); had smaller tumors ($P < 0.001$); less LN dissection ($P < 0.001$); less LN metastasis ($P < 0.001$); less vascular invasion ($P = 0.011$); and less perineural invasion ($P < 0.001$) compared with the AGC group.

Notably, compared with the EGC group, the cEGC group had more advanced pathologic characteristics, such as tumor depth of invasion and more patients with LN metastases, whereas they were more likely to have received a laparoscopic procedure with limited LN dissection (Table 1).

Comparisons between the cEGC, SM3 cancer, and MP cancer groups

Significant differences were observed in the clinicopathological features between the cEGC and SM3 groups. A higher percentage of patients in the cEGC group had gross type III cancer ($P < 0.001$); LN metastasis ($P = 0.017$); undifferentiated type ($P = 0.01$); and diffuse type according to Lauren classification ($P = 0.026$), but other features were fairly similar.

By contrast, the cEGC group patients were more often operated on with a laparoscopic procedure ($P < 0.001$); had smaller tumors ($P = 0.036$); less LN dissection ($P < 0.001$); and less perineural invasion ($P = 0.045$) compared with the MP group.

Interestingly, the cEGC group had similar pathologic characteristics to the MP group, but the cEGC group received many more laparoscopic procedures with limited LN dissection, and those patients were thus treated similarly to patients with SM3 cancer (Table 2).

Univariate and multivariate analyses of risk factors for cEGC

LN metastasis, gross type (type III), location (above the MB), undifferentiated histological type, extracellular mucin pool, lymphatic invasion, and perineural invasion were significantly associated with cEGC in the univariate analysis. Of these variables, gross type (type III: OR, 12.92; 95% CI, 5.765–28.93); location (above the MB: OR, 2.691; 95% CI, 1.280–5.660); lymphatic invasion (OR, 2.63; 95% CI, 1.022–6.769); and perineural invasion (OR, 5.8; 95% CI, 2.146–6.769) were independent predictors of cEGC in the multivariate analysis (Table 3).

Prognostic factors associated with recurrence of gastric cancer

The 3-year DFS rates were 85% for cEGC, 98% for SM3, and 93% for MP cancer. However, no significant difference was observed (Fig. 3). The univariate analysis showed that tumor size, T stage, N stage, range of LN dissection, Lauren classification, World Health Organization (WHO) classification, lymphatic invasion, vascular invasion, and perineural invasion correlated significantly with gastric cancer recurrence in all patients who were treated by curative gastrectomy at our hospital (Table 4). However, only T and N stages were independent prognostic factors for gastric cancer recurrence in the multivariate analysis (Table 4).

Discussion

The degree of inaccuracy in predicting tumor depth of invasion is reported to be 5.9% to 22.2% preoperatively in patients with cEGC, whereas we found a rate of 6.7%.[11–13]

The main purpose of this study was to determine whether the current cEGC treatment is appropriate for achieving curative resection and whether it is possible to predict cEGC before operation to allow the surgeon to select the best operative method. We compared the clinicopathologic characteristics between patients with cEGC, EGC, or AGC. Although obvious differences were observed between groups, the treatment, such as laparoscopic gastrectomy with limited LN dissection, was similar in the cEGC and EGC groups. Thus, we compared the characteristics between the cEGC, SM3, and MP cancer groups because these groups were expected to have similar clinicopathologic characteristics.

The characteristics of the cEGC group did not differ significantly from those of the MP group except

Table 1 Clinicopathologic comparison between groups

	EGC (n = 584)	*P*	cEGC (n = 42)	*P*	AGC (n = 369)
Sex, male/female (%)	379/205 (64.9/35.1)	0.39	30/12 (71.4/28.6)	0.58	248/121 (67.2/32.8)
Age, y	59.5 ± 10.81	0.248	61.5 ± 10.77	0.957	61.6 ± 10.97
BMI	23.86 ± 3.1	0.722	24.04 ± 3.64	0.089	23 ± 3.76
Location, UB/MB/LB (%)	60/125/399 (10.3/21.4/68.3)	0.007	10/12/20 (23.8/28.6/47.6)	0.301	92/69/208 (24.9/18.7/56.4)
Operation method, TG/NTG/STG/PG (%)	52/106/420/6 (8.9/18.2/71.9/1)	<0.001	5/13/20/4 (11.9/31/47.6/9.5)	<0.001	112/48/207/2 (30.4/13/56.1/0.5)
Gastrectomy, open/laparoscopic, (%)	166/418 (28.4/71.6)	0.726	13/29 (31/69)	<0.001	318/51 (86.2/13.8)
Size	3.22 ± 2.17	0.312	3.57 ± 2.14	<0.001	6.28 ± 3.27
Gross type in EGC, I/II/III (%)	29/524/31 (5/89.7/5.3)	<0.001	2/22/18 (4.8/52.4/42.9)		
Depth, T1/T2/T3/T4 (%)			0/30/6/6 (0/71.4/14.3/14.3)	<0.001	0/78/142/149 (0/21.1/38.5/40.4)
N stage, N0/N1/N2/N3 (%)	534/30/14/6 (91.4/5.1/2.4/1)	<0.001	27/5/10/0 (64.3/11.9/23.8/0)	<0.001	121/79/63/106 (32.8/21.4/17.1/28.7)
Resected LNs	33.6 ± 12.5	0.399	35.3 ± 13.5	0.012	41.5 ± 15.3
Node dissection, less than D2/more than D2 (%)	393/191 (67.3/32.7)	0.097	23/19 (54.8/45.2)	<0.001	27/342 (7.3/92.7)
Node metastasis, +/− (%)	50/534 (8.6/91.4)	<0.001	15/27 (35.7/64.3)	<0.001	248/121 (67.2/32.8)
Extracellular mucin pool, +/− (%)	17/567 (2.9/97.1)	0.002	5/37 (11.9/88.1)	0.747	38/331 (10.3/89.7)
Lauren classification, intestinal/diffuse (%)	319/265 (54.6/45.4)	0.076	17/25 (40.5/59.5)	0.533	168/201 (45.5/54.5)
WHO classification, differentiated/undifferentiated (%)	290/294 (49.7/50.3)	0.019	13/29 (31/69)	0.292	145/224 (39.3/60.7)
Lymphatic invasion, +/− (%)	49/535 (8.4/91.6)	<0.001	14/28 (33.3/66.7)	0.179	163/206 (44.2/55.8)
Vascular invasion, +/− (%)	13/571 (2.2/97.8)	0.266	2/40 (4.8/95.2)	0.011	76/293 (20.6/79.4)
Perineural invasion, +/− (%)	25/559 (4.3/95.7)	<0.001	11/31 (26.2/73.8)	<0.001	236/133 (64/36)

NTG, near-total gastrectomy; PG, proximal gastrectomy; STG, subtotal gastrectomy; TG, total gastrectomy.

Table 2 Clinicopathologic comparison between groups

	SM3 cancer (n = 142)	*P*	cEGC (n = 42)	*P*	MP cancer (n = 78)
Sex, male/female (%)	97/45 (68.3/31.7)	0.701	30/12 (71.4/28.6)	0.847	57/21 (73.1/26.9)
Age	62 ± 11.61	0.798	61.5 ± 10.77	0.556	62.7 ± 10.61
BMI	23.91 ± 3.58	0.834	24.04 ± 3.64	0.726	23.8 ± 3.6
Location, UB/MB/LB (%)	20/31/91 (14.1/21.8/64.1)	0.138	10/12/20 (23.8/28.6/47.6)	0.484	23/15/40 (29.5/19.2/51.3)
Operation method, TG/NTG/STG/PG (%)	15/20/104/3 (10.6/14.1/73.2/2.1)	0.005	5/13/20/4 (11.9/31/47.6/9.5)	0.041	21/13/42/2 (26.9/16.7/53.8/2.6)
Surgery, open/laparoscopic (%)	57/85 (40.1/59.9)	0.281	13/29 (31/69)	<0.001	51/27 (65.4/34.6)
Size	3.69 ± 2.06	0.747	3.57 ± 2.14	0.036	5.02 ± 3.18
Gross type in EGC, I/II/III (%)	13/112/17 (9.2/78.9/12)	<0.001	2/22/18 (4.8/52.4/42.9)		
N stage, N0/N1/N2/N3 (%)	116/16/8/2 (81.7/11.3/5.6/1.4)	0.005	27/5/10/0 (64.3/11.9/23.8/0)	0.072	42/21/11/4 (53.8/26.9/14.1/5.1)
Resected LNs	33.3 ± 13	0.397	35.3 ± 13.5	0.492	37.1 ± 13.9
Node dissection, less than D2/more than D2 (%)	69/73 (48.6/51.4)	0.482	23/19 (54.8/45.2)	<0.001	11/67 (14.1/85.9)
Node metastasis, +/− (%)	26/116 (18.3/81.7)	0.017	15/27 (35.7/64.3)	0.27	36/42 (46.2/53.8)
Extracellular mucin pool, +/− (%)	11/131 (7.7/92.3)	0.401	5/37 (11.9/88.1)	0.782	8/70 (10.3/89.7)
Lauren classification, intestinal/diffuse, %	85/57 (59.9/40.1)	0.026	17/25 (40.5/59.5)	0.126	43/35 (55.1/44.9)
WHO classification, differentiated/undifferentiated (%)	76/66 (53.5/46.5)	0.01	13/29 (31/69)	0.06	38/40 (48.7/51.3)
Lymphatic invasion, +/− (%)	33/109 (23.2/76.8)	0.188	14/28 (33.3/66.7)	0.663	23/55 (29.5/70.5)
Vascular invasion, +/− (%)	11/131 (7.7/92.3)	0.736	2/40 (4.8/95.2)	0.492	7/71 (9/91)
Perineural invasion, +/− (%)	20/122 (14.1/85.9)	0.066	11/31 (26.2/73.8)	0.045	35/43 (44.9/55.1)

Table 3 Univariate and multivariate analyses of risk factors for cEGC

Pathological factor	Univariate analysis			Multivariate analysis		
	P value	95% CI	OR	*P* value	95% CI	OR
LN metastasis	<0.001	2.963–11.88	5.933	0.084		
EGC type I and II versus type III	<0.001	6.577–27.22	13.38	<0.001	5.765–28.93	12.92
Lower body versus middle body	0.006	1.263–4.455	2.372	0.009	1.280–5.660	2.691
Differentiated versus undifferentiated	0.019	1.121–4.317	2.2	0.203		
Extracellular mucin pool	0.002	1.575–12.89	4.507	0.189		
Lymphatic invasion	<0.001	2.697–11.05	5.459	0.045	1.022–6.769	2.63
Perineural invasion	<0.001	3.579–17.59	7.934	0.001	2.146–6.769	5.8

Logistic regression analysis; $P < 0.10$.

for size and perineural invasion. By contrast, there were more differences between the cEGC and SM3 groups, such as a higher percentage of patients in the cEGC group with LN metastasis, undifferentiated type, diffuse type, and Lauren classification. This result is consistent with that of other studies and suggests that cEGC tends to have more invasive tumor features, such as deeper invasion and more LN metastasis.[14] However, laparoscopic gastrectomy with limited LN dissection was the treatment of choice for cEGC, similar to the treatment for SM3 cancer.

The Japanese Gastric Cancer Association recommends that nonearly, potentially curable gastric cancer should be treated with D2 lymphadenectomy. D1 or D1+ is an option for T1 tumors. D1+ can be substituted for D2 in a poor-risk patient or when D2 cannot be performed safely.[8] In other words, gastrectomy with D2 lymphadenectomy is recognized as the best and standard treatment for AGC. A D2 lymphadenectomy leads to a better prognosis, but the necessity for an additional lymphadenectomy has not been demonstrated. Thus, in this study, the appropriateness of the cEGC treatments was evaluated by analyzing prognostic factors related to gastric cancer recurrence. The univariate analysis showed that tumor size, T stage, N stage, range of LN dissection, Lauren classification, WHO classification, lymphatic invasion, vascular invasion, and perineural invasion correlated significantly with gastric cancer recurrence in all patients treated by curative gastrectomy at our hospital. However, only T and N stages were identified as independent prognostic factors for gastric cancer recurrence in the multivariate analysis. It is well known that prognostic factors for gastric cancer are influenced by tumor invasion depth, LN metastasis, and complete tumor removal.[5–7]

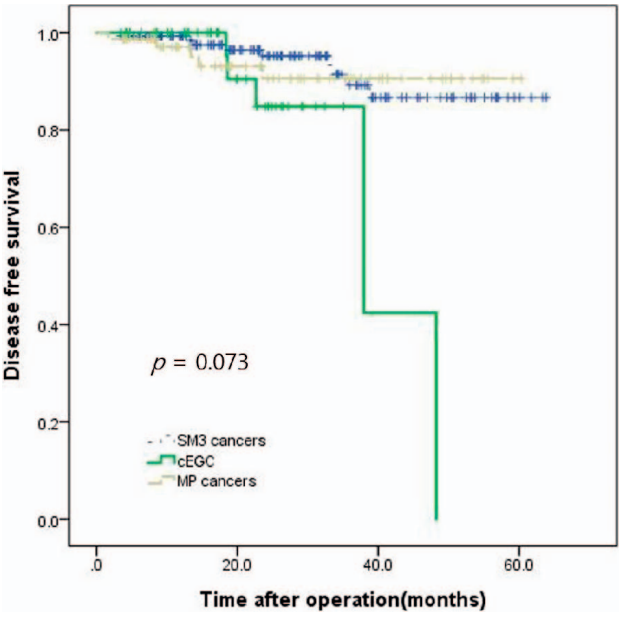

Fig. 3 Disease-free survival curves using the Kaplan–Meier method for cEGC, SM cancer, and MP cancer.

Our results show clearly that the choice of cEGC treatment should be gastrectomy with D2 lymphadenectomy, because cEGC has more aggressive characteristics in the T and N stages than do EGC and SM3 cancer. We reasoned that more rigorous treatment could be given at the time of the operation rather than performing additional surgery if cEGC could be predicted before surgery. Thus, we evaluated the risk factors for cEGC and potential preoperative factors that could predict cEGC.

The risk factors for cEGC in the univariate analysis were LN metastasis, gross type, location, undifferentiated, extracellular mucin pool, lymphatic invasion, and perineural invasion. The multivariate analysis showed that gross type, location, lymphatic invasion, and perineural invasion were independent factors. In particular, gross type (*e.g.*, type III EGC) and location (*e.g.*, above the MB) can be detected preoperatively.

The accuracy of endoscopic staging tends to be lower in the flat/depressed configuration, and type

Table 4 Prognostic factors for DFS in patients with curative gastric cancer

Factor	Number	DFS time, mo	Univariate analysis		Multivariate analysis		
			95% CI	*P* value	OR	95% CI	*P* value
Lesion				0.031			
Upper body	162	50.92	47.50–54.32				
Middle body	206	51.31	47.97–54.64				
Lower body	627	67.1	63.81–67.30				
Size				<0.001			
<4.5 cm	618	67.71	65.93–69.50				
≥4.5 cm	377	58.83	55.42–62.25				
T stage				<0.001			0.004
T1	584	71.95	70.41–73.49		1		
T2	108	55.74	52.48–58.99		1.57	0.59–4.15	0.363
T3	148	52.51	48.33–56.70		2.39	1.03–5.55	0.042
T4	155	37.8	33.46–42.16		4.51	1.86–10.86	0.001
N stage				<0.001			0.001
N0	682	70.89	69.33–72.45		1		
N1	114	52.59	48.74–56.43		1.16	0.54–2.46	0.708
N2	87	49.75	44.78–54.72		1.38	0.65–2.90	0.395
N3	112	33.6	28.42–38.78		3.27	1.68–6.37	<0.001
Extracellular mucin pool				0.183			
Absent	935	65.9	64.10–67.70				
Present	60	47.32	41.49–53.14				
LN dissection				<0.001			
Limited LN dissection	443	70.42	68.91–71.93				
Extended LN dissection	552	60.46	57.69–63.18				
Lauren classification				0.004			
Intestinal	504	67.53	65.23–69.84				
Diffuse	401	54.66	52.52–56.81				
WHO classification				<0.001			
Papillary	11	55.68	47.27–64.09				
Well differentiated	124	71.18	67.41–74.95				
Moderately differentiated	313	55.84	53.51–58.17				
Poorly differentiated	260	51.66	48.44–54.88				
Mucinous	20	39.36	32.48–46.21				
Signet ring cell	267	67.28	64.44–70.11				
Lymphatic invasion				<0.001			
Absent	769	69.56	67.92–71.20				
Present	226	44.96	41.20–48.72				
Vascular invasion				<0.001			
Absent	904	67.68	65.99–69.37				
Present	91	44.15	38.98–49.40				
Perineural invasion				<0.001			
Absent	723	70.02	68.32–71.71				
Present	272	47.22	43.87–50.57				

Patients were evaluated by univariate analysis using the Kaplan–Meier method and log-rank test and multivariate analysis using the Cox proportional-hazard model.

III EGC has more tumor invasion depth preoperatively than the other types.[13,15] The findings in our study may have resulted from differences in stomach wall thickness according to tumor location. Several studies have reported similar findings. The proximal part of the stomach has a thinner wall than the distal stomach, and cancer cells may penetrate the layers of the stomach wall more easily and extensively, and this effect may lead to the underdiagnosis of AGC as EGC, namely cEGC diagnosed during preoperative endoscopy.[16,17] Other studies have reported that tumor location is the only prognostic factor for stage IB gastric cancer. These results suggest that type III EGC and EGC located above the MB should be treated with caution when selecting the curative resection method, such as gastrectomy with D2 lymphadenectomy.

Several limitations in this study should be mentioned. First, EUS was not performed in all patients because it has a lower diagnostic accuracy, particularly

for deeper gastric cancer, and requires an experienced endoscopist, additional time, and cost.[18–20] Another limitation was the short follow-up after gastrectomy, which meant that it was not possible to evaluate the accuracy of the gastric cancer prognoses. However, we expect that patients with cEGC may have a poorer prognosis because they have similar clinicopathological characteristics as do patients with MP cancer, but they are treated by limited LN dissection similar to the treatment of patients with EGC. Despite these limitations, this is the first study to identify risk factors for cEGC. We suggest that further studies are required to confirm the validity of these characteristics as predictors of cEGC.

Conclusion

It is important to predict the tumor invasion depth preoperatively to select the optimum gastric cancer therapeutic strategy, particularly in terms of LN dissection. We found that type III EGC and EGC located above the MB are preoperative predictive risk factors for cEGC. Caution should be taken when selecting the curative resection method, such as gastrectomy with D2 lymphadenectomy, for cEGC patients.

References

1. Katai H, Sano T. Early gastric cancer: concepts, diagnosis, and management. *Int J Clin Oncol* 2005;**10**(6):375–383
2. Lee JH, Han HS, Lee JH. A prospective randomized study comparing open vs laparoscopy-assisted distal gastrectomy in early gastric cancer: early results. *Surg Endosc* 2004;**19**(2):168–173
3. Kitano S, Shiraishi N, Fujii K, Yasuda K, Inomata M, Adachi Y. A randomized controlled trial comparing open vs laparoscopy-assisted distal gastrectomy for the treatment of early gastric cancer: An interim report. *Surgery* 2002;**131**(1):S306–S311
4. Kim HH, Hyung WJ, Cho GS, Kim MC, Han SU, Kim W *et al*. Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer: an interim report–a phase III multicenter, prospective, randomized Trial (KLASS Trial). *Ann Surg* 2010;**251**(3):417–420
5. Lo SS, Wu CW, Chen JH, Li AF, Hsieh MC, Shen KH *et al*. Surgical results of early gastric cancer and proposing a treatment strategy. *Ann Surg Oncol* 2006;**14**(2):340–347
6. Shiraishi N, Sato K, Yasuda K, Inomata M, Kitano S. Multivariate prognostic study on large gastric cancer. *J Surg Oncol* 2007;**96**(1):14–18
7. Kim DH, Kim SM, Hyun JK, Choi MG, Noh JH, Sohn TS *et al*. Changes in postoperative recurrence and prognostic risk factors for patients with gastric cancer who underwent curative gastric resection during different time periods. *Ann Surg Oncol* 2013;**20**(7): 2317–2327
8. Sano T, Aiko, T. New Japanese classifications and treatment guidelines for gastric cancer: revision concepts and major revised points. *Gastric Cancer* 2011;**14**(2):97–100
9. Tokunaga M, Hiki N, Fukunaga T, Nohara K, Katayama H, Akashi Y *et al*. Laparoscopy-assisted distal gastrectomy with D2 lymph node dissection following standardization—a preliminary study. *J Gastrointest Surg* 2009;**13**(6):1058–1063
10. Song KY, Kim SN, Park CH. Laparoscopy-assisted distal gastrectomy with D2 lymph node dissection for gastric cancer: technical and oncologic aspects. *Surg Endosc* 2007;**22**(3):655–659
11. Ganpathi IS, So JB-Y, Ho KY. Endoscopic ultrasonography for gastric cancer: does it influence treatment? *Surg Endosc* 2006; **20**(4):559–562
12. Saito N, Takeshita K, Habu H, Endo M. The use of endoscopic ultrasound in determining the depth of cancer invasion in patients with gastric cancer. *Surg Endosc* 1991;**5**(1):14–19
13. Sun Z, Wang ZN, Zhu GL, Huang BJ, Li K, Xu Y *et al*. Advanced gastric cancer with early cancer macroscopic appearance: is it worthy of D2 lymphadenectomy? *Ann Surg Oncol* 2010;**17**(5):1278–1290
14. Lee SY, Han HS, Lee KY, Hwang TS, Kim JH, Sung IK *et al*. Sonic hedgehog expression in gastric cancer and gastric adenoma. *Oncol Rep* 2007;**17**(5):1051–1015
15. Choi J, Kim SG, Im JP, Kim JS, Jung HC, Song IS. Endoscopic prediction of tumor invasion depth in early gastric cancer. *Gastrointest Endosc* 2011;**73**(5):917–927
16. Pickhardt PJ, Asher DB. Wall thickening of the gastric antrum as a normal finding: multidetector CT with cadaveric comparison. *AJR Am J Roentgenol* 2003;**181**(4):973–979
17. Park HS, Lee SY, Hong SN, Kim JH, Sung IK, Park JS *et al*. Early gastric cancer-like advanced gastric cancer versus advanced gastric cancer-like early gastric cancer. *Clin Endosc* 2013;**46**(2):155–160
18. Hizawa K, Iwai K, Esaki M, Matsumoto T, Suekane H, Iida M. Is endoscopic ultrasonography indispensable in assessing the appropriateness of endoscopic resection for gastric cancer? *Endoscopy* 2002;**34**(12):973–978
19. Yanai H, Noguchi T, Mizumachi S, Tokiyama H, Nakamura M, Tada M *et al*. A blind comparison of the effectiveness of endoscopic ultrasonography and endoscopy in staging early gastric cancer. *Gut* 1999;**44**(3):361–365
20. Kwee RM, Kwee TC. The accuracy of endoscopic ultrasonography in differentiating mucosal from deeper gastric cancer. *Am J Gastroenterol* 2008;**103**:1801–1809