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Long-term oncological outcomes of laparoscopic gastrectomy for grossly early gastric cancer-mimicking advanced gastric cancer

Propensity score matching analysis

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Abstract

Laparoscopic gastrectomy became an option in the treatment of early gastric cancer (EGC) in clinical practice. However, whether laparoscopic surgery for grossly EGC-mimicking advanced gastric cancer (AGC) patients is oncologically safe long-term is still controversial.

We retrospectively analyzed 472 patients with AGC who were diagnosed as clinical EGC. Patients received laparoscopic or open gastrectomy with standard lymph node (LN) dissection from January 2007 to February 2015. We used a 1:3 propensity score matching method for the analysis. The matching factors were age, sex, body mass index, American Society of Anesthesiologists score and pathologic stage. After the matching process, we evaluated the 5-year overall survival and the cumulative incidence curve of recurrence.

All of the analyzed patients were pathologically diagnosed with AGC after surgery (grossly EGC-mimicking AGC). The median (range) duration of follow-up was 58.0 (0–132) months. After propensity score matching, 31.5% of patients in the laparoscopy group had D1+ LN dissection and 99.2% of patients in the open group had D2 LN dissection. The 5-year overall survival rate between the laparoscopy (n=92) and open groups (n=244) were not significantly different (95.3% versus 91.4%, $P=.224$). There was no significant difference between the cumulative recurrence incidence curves of the matched groups ($P=.319$).

Laparoscopic surgery for grossly EGC-mimicking AGC might be safe in terms of long-term survival outcome. After confirming grossly EGC-mimicking AGC in the final pathology report, no additional surgery might be required.

Abbreviations: AGC = advanced gastric cancer, ASA = American Society of Anesthesiologists, BMI = body mass index, EGC = early gastric cancer, LN = lymph node, OS = overall survival.

Keywords: grossly early gastric cancer-mimicking advanced gastric cancer, laparoscopy, recurrence, survival

1. Introduction

The incidence of gastric cancer worldwide is the highest among all cancers[1] and gastric cancer is the most commonly diagnosed cancer in Korea.[2] Many surgical methods have been developed for the treatment of gastric cancer. Laparoscopic gastrectomy for early gastric cancer (EGC) was first introduced in 1994,[3] and several studies have revealed the benefits of minimal invasive surgery when used for gastric cancer, such as less pain after

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We investigated the long-term survival of patients with grossly early gastric cancer-mimicking advanced gastric cancer who underwent laparoscopic gastrectomy with lymph node (LN) dissection. After propensity score matching, we found that there were no significant differences in the 5-year overall survival and cumulative incidence of recurrence between the laparoscopic group and open surgery group. Limited LN dissection (D1+) may be feasible and no additional surgery might be required after initial curative surgery.

The authors have no conflicts of interest to disclose.

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

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surgery, recovery of bowel movements in a short time and fewer hospitalization days after surgery.[4,5] Based on the long-term results of a randomized clinical trial, laparoscopic assisted distal gastrectomy for EGC has become an alternative to open surgery while maintaining procedural and oncological safety.[6] Therefore, laparoscopic surgery for EGC is largely accepted and increasingly used in Korea.

As surgeons face multiple laparoscopic cases, they gain more experience and better surgical techniques. With the innovative development of laparoscopic devices, the complicated and difficult procedures of laparoscopy have been mastered. In this regard, the expanded use of laparoscopic surgery for advanced gastric cancer (AGC) has been promising; however, the standard extent of lymph node (LN) dissection of AGC is D2[7,8] and the long-term oncologic outcome has not been confirmed.

Some patients who are clinically diagnosed with and treated for EGC show a final pathologic report of AGC. These cancers are defined as grossly EGC-mimicking AGCs.[9] While a randomized clinical trial investigating the long-term survival of patients with AGC who underwent radical laparoscopic surgery is being completed,[10] we conducted this study to determine whether patients diagnosed with grossly EGC-mimicking AGC need additional surgical intervention regarding LN dissection. We compared the overall survival (OS) and cumulative recurrence incidence between the open surgery group and the laparoscopic group after propensity score matching.

2. Materials and methods

We retrospectively reviewed the medical records of 552 patients who were clinically diagnosed with EGC preoperatively (clinical stage, T1) and AGC postoperatively (pathologic stage, T2 or more). All patients had gastrectomy with LN dissection by laparoscopic or open method at Samsung Medical Center (SMC; Seoul, Korea) from January 2007 to February 2015. Patients who were diagnosed with other malignancies (n = 62) or remnant gastric cancer (n = 18) were excluded from this study. The remaining 472 patients were included in this study and their clinicopathologic data were analyzed. The median (range) follow-up duration of the analyzed patients was 58.0 (0–132) months.

Clinical stage was determined based on results of preoperative esophagogastroduodenoscopy and abdomen-pelvis computed tomography. We evaluated sex, age, body mass index (BMI), reconstruction method, American Society of Anesthesiologists (ASA) score, tumor location, tumor size, histologic differentiation, resection margin (proximal and distal), depth of tumor invasion, LN metastasis, number of dissected LNs, extent of LN dissection (D1+ or D2), lymphatic invasion, vascular invasion, perineural invasion, distant metastasis, pathologic stage and adjuvant chemotherapy. Histologic differentiation was categorized as differentiated or undifferentiated. Well or moderately differentiated adenocarcinoma was classified as differentiated, whereas poorly differentiated tubular adenocarcinoma, signet ring cell, and mucinous adenocarcinoma were sorted to the undifferentiated group. We used the 8th edition American Joint Committee on Cancer classification to classify the pathologic stage. We also evaluated the short-term surgical outcomes and postoperative course, which included operation time (min), estimated blood loss (mL), postoperative complications (recorded according to the Clavien–Dindo classification), and the number of hospitalization days after surgery.

Patients were divided according to the method of surgery, as open surgery or laparoscopy, for analysis. We usually recommended adjuvant chemotherapy except for the patients with stage T2N0 cancers. Follow-up of the enrolled patients was performed via outpatient visits with regular esophagoduodenoscopy and computed tomography. Recurrence and survival were confirmed with recent medical records and the National Statistics, Republic of Korea. The study protocol was approved by the institutional review board of SMC (2019-01-100).

2.1. Statistical method

Differences in clinicopathologic parameters between patients who underwent open and laparoscopic surgery were determined by Mann–Whitney test, Wilcoxon rank test, Chi-square test or Fisher exact test. Before and after the matching, the 5-year survival rate was calculated using the Kaplan–Meier method with the log-rank test. The cumulative incidence curve of the recurrence was analyzed with the Fine and Gray model, defining the death event as the competing risk.[11] Logistic regression was used to check the association between surgical method and survival or recurrence. We matched the 2 study groups in a 1:3 ratio (laparoscopy vs. open surgery) with the caliper of 0.20 of propensity score.[12] The matching process was executed using R 3.5.1 (Vienna, Austria http://www.R-project.org/), package 'MatchIt.' The matching variables were sex, age, BMI, ASA score, and pathologic stage. The hazard ratio and 95% confidence interval were calculated. For univariate analysis of survival, the log-rank test was used. The variables with $P < .05$ in univariate analysis were included for multivariate analysis using the Cox proportional hazards model with the backward logistic regression method to identify independent prognostic factors of survival. $P < .05$ was considered statistically significant. All statistical analysis, except propensity score matching, was carried out using the statistical software SAS version 9.4 (SAS Institute, Cary, NC) and SPSS version 25.0 for Windows (SPSS, Chicago, IL).

3. Results

3.1. Patient demographics and comparison of the laparoscopic and open groups

Among the 472 patients, 97 patients (20.6%) had laparoscopic gastrectomy with LN dissection. In the laparoscopic group, there were significantly more proportions of young (< 60 years), female and low BMI (< 23 kg/m^2) patients than the open group (Table 1). Approximately 61.9% of the laparoscopic group underwent Billroth I anastomosis. Regarding the extent of LN dissection, 33.0% of patients in the laparoscopic group had D1+ dissection and 98.9% of patients in the open group had D2 dissection ($P < .001$). Although the number of dissected LNs was significantly lower in the laparoscopic group than in the open group (38 ± 12 versus 46 ± 16; $P < .001$), the pathologic stage including N stage was not significantly different between the 2 groups.

After 1:3 propensity score matching, 92 patients in the laparoscopic group were matched to 244 patients in the open group. The matching factors were age, sex, BMI, ASA score, and pathologic stage, and we confirmed that there were no significant differences in the proportions of the matching factors between the laparoscopic group and the open group (Table 1).

Table 1

Clinicopathologic characteristics of patients in the 2 treatment groups before and after propensity score matching.

Characteristics	Before matching			After matching (1:3)		
	Laparoscopy (n = 97)	Open (n = 375)	*P* value†	Laparoscopy (n = 92)	Open (n = 244)	*P* value†
Age, yr§	50.5 ± 13.4	56.1 ± 12.0	<.001	51.5 ± 13.0	54.2 ± 11.8	.042
Age, yr			.003			.144
≥ 60	24 (24.7)	154 (41.1)		24 (26.1)	84 (34.4)	
< 60	73 (75.3)	221 (58.9)		68 (73.9)	160 (65.6)	
Sex			.001			.410
M	44 (45.4)	237 (63.2)		44 (47.8)	129 (52.9)	
F	53 (54.6)	138 (36.8)		48 (52.2)	115 (47.1)	
BMI (kg/m^2)§	22.4 ± 2.9	23.7 ± 3.1	<.001	22.7 ± 2.7	22.8 ± 2.7	.417
BMI (kg/m^2)			<.001			.237
≥ 23	36 (37.1)	216 (57.6)		36 (39.1)	113 (46.3)	
< 23	61 (62.9)	159 (42.4)		56 (60.9)	131 (53.7)	
ASA score			.345			.625
1	51 (52.6)	177 (47.2)		48 (52.2)	120 (49.2)	
2+	46 (47.4)	198 (52.8)		44 (47.8)	124 (50.8)	
Extent of LN dissection			<.001			<.001
D1+	32 (33.0)	4 (1.1)		29 (31.5)	2 (0.8)	
D2	65 (67.0)	371 (98.9)		63 (68.5)	242 (99.2)	
Reconstruction			<.001			<.001
Billroth I	60 (61.9)	194 (51.7)		57 (62.0)	123 (50.4)	
Billroth II	23 (23.7)	46 (12.3)		22 (23.9)	30 (12.3)	
RY EJ	14 (14.4)	135 (36.0)		13 (14.1)	91 (37.3)	
Adjuvant chemotherapy			.986			.934
No	40 (41.2)	155 (41.3)		38 (41.3)	102 (41.8)	
Yes	57 (58.8)	220 (58.7)		54 (58.7)	142 (58.2)	
Tumor size, cm§	3.7 ± 2.3	4.3 ± 2.5	.004	3.7 ± 2.2	4.3 ± 2.6	.015
Tumor location			<.001			<.001
Lower	56 (57.7)	151 (40.3)		55 (59.8)	86 (35.2)	
Middle	34 (35.1)	123 (32.8)		30 (32.6)	93 (38.1)	
Upper	7 (7.2)	91 (24.3)		7 (7.6)	56 (23.0)	
Whole	0 (0.0)	10 (2.7)		0 (0.0)	9 (3.7)	
PRM, cm§	4.0 ± 2.8	4.0 ± 3.2	.515	4.1 ± 2.8	3.8 ± 3.0	.287
DRM, cm§	6.1 ± 3.9	7.9 ± 4.7	.001	6.2 ± 3.9	8.2 ± 4.6	<.001
Histologic type			.006			.066
Differentiated	16 (16.5)	115 (30.7)		16 (17.4)	66 (27.0)	
Undifferentiated	81 (83.5)	260 (69.3)		76 (82.6)	178 (73.0)	
Lauren type			.027			.133
Intestinal	22 (22.7)	137 (36.5)		22 (23.9)	86 (35.2)	
Diffuse	59 (60.8)	177 (47.2)		55 (59.8)	127 (52.0)	
Mixed & Indeterminate	16 (16.5)	61 (16.3)		15 (16.3)	31 (12.7)	
Depth of invasion			.739			.564
T2	64 (66.0)	257 (68.5)		60 (65.2)	170 (69.7)	
T3	25 (25.8)	95 (25.3)		24 (26.1)	60 (24.6)	
T4	8 (8.2)	23 (6.1)		8 (8.7)	14 (5.7)	
Dissected LN§§	38 ± 12	46 ± 16	<.001	38 ± 13	47 ± 17	<.001
LN metastasis			.113			.126
N0	56 (57.7)	202 (53.9)		52 (56.5)	139 (57.0)	
N1	20 (20.6)	88 (23.5)		19 (20.7)	56 (23.0)	
N2	18 (18.6)	47 (12.5)		18 (19.6)	27 (11.1)	
N3a	3 (3.1)	26 (6.9)		3 (3.3)	17 (7.0)	
N3b	0 (0.0)	12 (3.2)		0 (0.0)	5 (2.0)	
Distant metastasis			1.000‡			N/A
M0	97 (100)	372 (99.2)		92 (100)	244 (100)	
M1	0 (0.0)	3 (0.8)		0 (0.0)	0 (0.0)	
Pathologic stage*			.964‡			.976
I	41 (42.3)	152 (40.5)		38 (41.3)	104 (42.6)	
II	43 (44.3)	163 (43.5)		41 (44.6)	106 (43.4)	
III	13 (13.4)	57 (15.2)		13 (14.1)	34 (13.9)	
IV	0 (0.0)	3 (0.8)		0 (0.0)	0 (0.0)	
Lymphatic invasion			.060			.221
Absent	58 (59.8)	184 (49.1)		54 (58.7)	125 (51.2)	
Present	39 (40.2)	191 (50.9)		38 (41.3)	119 (48.8)	

(*continued*)

Table 2
(continued).

Characteristics	Before matching			After matching (1:3)		
	Laparoscopy (n = 97)	Open (n = 375)	*P* value[†]	Laparoscopy (n = 92)	Open (n = 244)	*P* value[†]
Vascular invasion			.042			.153
Absent	93 (95.9)	334 (89.1)		88 (95.7)	222 (91.0)	
Present	4 (4.1)	41 (10.9)		4 (4.3)	22 (9.0)	
Perineural invasion			.454			.431
Absent	63 (64.9)	228 (60.8)		59 (64.1)	145 (59.4)	
Present	34 (35.1)	147 (39.2)		33 (35.9)	99 (40.6)	

Values in parentheses are percentages. The continuous variables were indicated as mean ± standard deviation.
[*] According to the 8th edition of the American Joint Committee on Cancer classification.
[†] $\chi 2$ test.
[‡] Fisher exact test.
[§] Wilcoxon rank test.
ASA = American Society of Anesthesiologists, BMI = body mass index, DRM = distal resection margin, LN = lymph node, N/A = not applicable, PRM = proximal resection margin, RY EJ = Roux-en Y esophagojejunostomy.

3.2. Short-term surgical outcomes

The short-term surgical outcomes and postoperative course of the matched patients are shown in Table 2. Operation time did not significantly differ between the study groups ($P = .214$). Estimated blood loss during operation was significantly lower ($P < .001$) and the number of hospital days was significantly lower ($P < .001$) in the laparoscopic group than the open group. The postoperative complication rate between the 2 groups was not significantly different ($P = .387$). In the laparoscopic group, 1 patient underwent emergent operation due to anastomosis site leakage. Two patients in the open group underwent re-operation; 1 patient had wound dehiscence and the other patient experienced immediate postoperative bleeding.

3.3. Long-term surgical outcomes

Before patient matching, there was no significant difference in the 5-year OS between the laparoscopic group and open group (95.5% vs 89.6%; $P = .068$; Fig. 1A). The 5-year cumulative recurrence rate between the 2 unmatched groups was also not significant (laparoscopy versus open, 4.5% versus 8.1%; hazard ratio = 0.55, 95% CI = 0.19–1.59, $P = .272$; Fig. 1B). Similar results were observed in the matched groups. The OS rates between the 2 groups were not significantly different (Fig. 2A, $P = .224$); the 5-year OS was 95.3% in the laparoscopic group and 91.4% in the open group. The association between surgical method (laparoscopy versus open) and death event was not

Table 2
Short-term surgical outcomes and postoperative course of the matched patients.

Outcomes	Laparoscopy (n = 92)	Open (n = 244)	*P* value[†]
Operation time (min)	178 ± 55	168 ± 43	.214
Blood loss during operation (ml)	135 ± 100	170 ± 107	<.001
Hospital stay (days)	8 ± 3	9 ± 3	<.001
Postoperative complication (CD classification)			.387[*]
None	74 (80.4)	179 (73.4)	
I	2 (2.2)	17 (7.0)	
II	13 (14.1)	36 (14.8)	
IIIa	2 (2.2)	10 (4.1)	
IIIb	1 (1.1)	2 (0.8)	

Values in parentheses are percentages. The continuous variables are indicated as mean ± standard deviation.
[†] Mann-Whitney test.
[*] Fisher exact test.
CD = Clavien-Dindo.

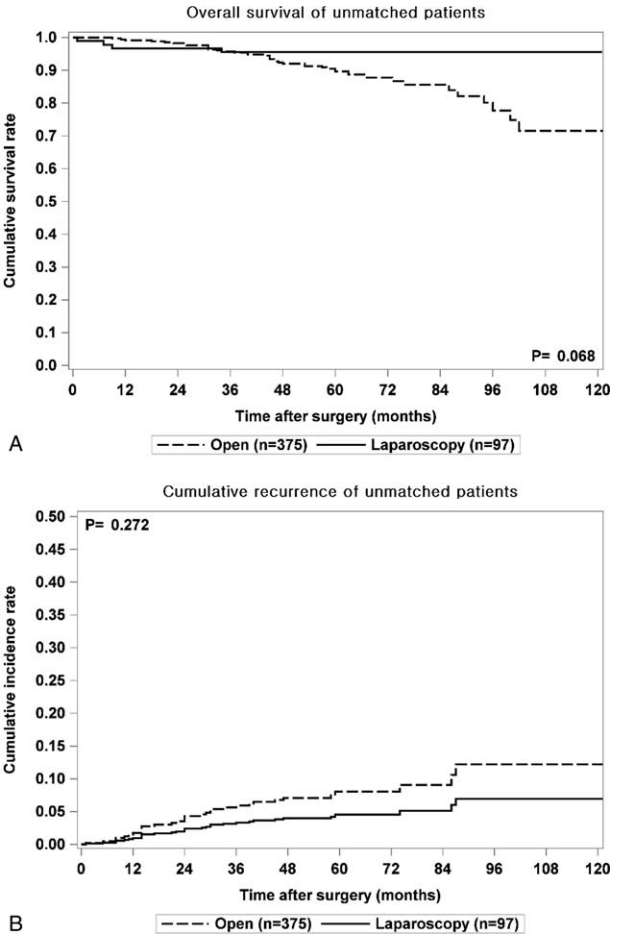

Figure 1. The (A) overall survival curve and (B) cumulative recurrence curve of unmatched patients. The curves were not significantly different ([A] $P = .068$; [B] $P = .272$).

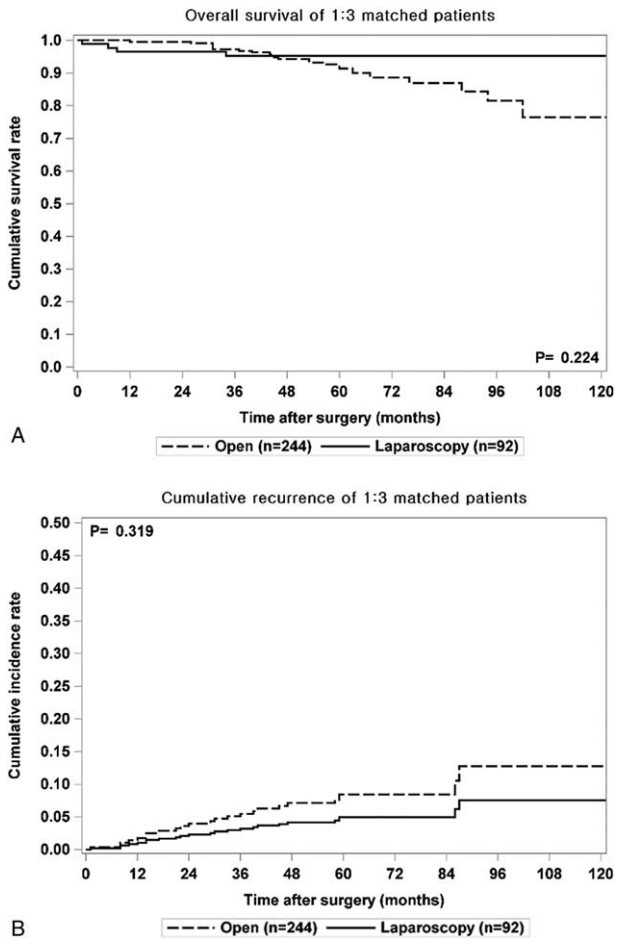

Figure 2. The (A) overall survival curve and (B) cumulative recurrence curve of 1:3 matched patients. The curves were not significantly different ([A] $P = .224$; [B] $P = .319$).

significant ($P = .163$, odds ratio = 0.46, 95% CI 0.15–1.37). The cumulative recurrence incidence was not significantly different between the matched groups (laparoscopy versus open, 5.0% versus 8.4%; $P = .319$; Fig. 2B). In addition, there was no significant association between surgical method and recurrence events ($P = .229$, odds ratio = 0.51, 95% CI 0.17–1.53). In the univariate analysis of OS and recurrence-free survival, the surgical method was not a significant factor (Table 3). In the multivariate analysis of OS, depth of invasion ($P = .002$) and vascular invasion ($P = .018$) were independent prognostic factors. In the case of recurrence-free survival, depth of invasion ($P = .003$), vascular invasion ($P = .003$) and perineal invasion ($P = .018$) were significant factors in multivariate analysis.

4. Discussion

This study investigated the long-term oncological outcome of grossly EGC-mimicking AGC patients who underwent laparoscopic surgery. After matching the patients with propensity score, we compared the 5-year OS and cumulative recurrence incidence of the laparoscopy group and open group and found out that there were no significant differences among those outcomes.

Laparoscopic gastrectomy with D1+ LN dissection is a standard treatment for clinical EGC in clinical practice, but this surgical approach is still insufficient as a standard procedure for advanced disease.[7,8] For establishment of sufficient evidence regarding the oncological and procedural safety of laparoscopic gastrectomy with D2 LN dissection for AGC, there were many published studies for verification.

The prognosis of patients with grossly EGC-mimicking AGC was shown to be better than those with Borrmann type AGC due to fewer LN metastases.[13] In addition, subgroup analysis showed that there was no significant difference in survival between patients who underwent D1+ and D2 LN dissection. In our study, the surgical method (laparoscopic versus open) did not significantly affect the survival of patients with grossly EGC-mimicking AGC. Although there was a significant difference in the proportion of the extent of LN dissection after matching (31.5% of patients in the laparoscopic group underwent D1+ dissection and 99.2% of patients in the open group underwent D2 dissection), the multivariate analysis of OS and disease-free survival showed that the surgical method and the extent of LN dissection were not significant independent prognostic factors. In this regard, laparoscopic gastrectomy with D1+ LN dissection in patients diagnosed with grossly EGC-mimicking AGC might be oncologically safe and there will be no need for additional surgery in these patients.

However, when we consider the laparoscopic surgery of the patients with Borrmann type AGC, the extent of LN dissection is our major concern. In terms of the oncologic safety, abundant dissected LNs collected by standard lymphadenectomy can provide a pathological report with accurate evaluation of disease status.[14] A meta-analysis of 16 studies showed that laparoscopic surgery could achieve the same LN dissection effect as open surgery.[15] A large matched cohort study (n = 186) regarding long-term survival in Japan concluded that the oncological outcomes were comparable between the laparoscopic and open surgery groups.[16] In addition, a case-control study conducted in Korea for comparison of the 5-year survival rate and disease-free survival rate showed that there was no significant difference between the laparoscopic and open surgery groups.[17]

In a randomized clinical trial conducted by experienced surgeons at high volume centers in China, the morbidity and mortality rates between the laparoscopy and the open group (n = 528 in each group) were not statistically different.[18] Among the intraoperative effects of the surgical method, the operation time was significantly longer in the laparoscopic group.[15,18,19] However, the authors concluded that laparoscopic surgery with extended LN dissection for AGC is a feasible and safe procedure when performed by an experienced surgeon. The operation time of the laparoscopic approach will likely decrease as the surgeons experience more difficult and new cases and overcome the learning curve.[20,21]

In our study, the operation time was not significantly different between the laparoscopic and open groups. We preferred to perform laparoscopic gastrectomy with D1+ lymphadenectomy for only clinical EGC patients. The operation time might be reduced due to limited LN dissection. We also found that among unmatched patients, female and low BMI patients underwent laparoscopic surgery more often than open method. As female patients have a relatively large portion of subcutaneous fat compared with visceral fat,[22] this phenomenon might reflect the surgeons' preference of selecting patients for laparoscopic gastrectomy. In fact, the amount of visceral fat requires complex laparoscopic procedures and this might be a barrier for inexperienced surgeons.

Table 3

Univariate and multivariate analysis of overall survival and recurrence-free survival in the matched grossly EGC-mimicking AGC patients.

	Overall survival					Recurrence-free survival				
	Univariate analysis		Multivariate analysis			Univariate analysis		Multivariate analysis		
Variables	**5YOS**	***P* value**	**HR**	**95% CI**	***P* value**	**5YDFS**	***P* value**	**HR**	**95% CI**	***P* value**
Method of operation		.224					.317			
Laparoscopy	95.3					95.3				
Open	91.4					91.3				
Age, years		.164					.951			
≥ 60	89.0					90.3				
< 60	93.8					93.2				
Sex		.729					.125			
M	94.1					95.6				
F	90.4					88.9				
BMI (kg/m^2)		.287					.115			
≥ 23	93.1					95.6				
< 23	91.4					89.6				
ASA score		.073					.631			
1	94.5					91.9				
2	92.3					93.0				
3+	57.1					87.5				
Extent of LN dissection		.144					.145			
D1+	100.0					100.0				
D2	91.7					91.7				
Reconstruction		.007			0.067		.160			
Billroth I	98.0		1.00			96.0				
Billroth II	86.0		3.53	1.22–10.22	0.020	88.5				
RY EJ	85.2		1.93	0.75–4.99	0.175	87.5				
Adjuvant chemotherapy		.366					.038			
No	95.5					96.7				
Yes	90.6					89.8				
Tumor size, cm		.074					.136			
≥ 4	88.1					88.1				
< 4	95.7					95.5				
Tumor location		.096					.835			
Lower	94.9					94.2				
Middle	94.4					92.5				
Upper	88.7					86.4				
Whole	42.9					85.7				
PRM, cm		.326					.843			
≥ 4	94.5					93.6				
< 4	91.0					91.5				
DRM, cm		.780					.922			
≥ 8	95.4					91.9				
< 8	90.1					92.5				
Histologic type		.041					.867			
Differentiated	86.1					92.6				
Undifferentiated	94.2					92.3				
Lauren type		.424					.139			
Intestinal	88.3					95.7				
Diffuse	94.9					92.5				
Mixed & Indeterminate	91.2					80.1				
Depth of invasion		<.001			0.002		<.001			.003
T2	94.7		1.00			95.2		1.00		
T3	93.1		1.15	0.43–3.09	0.785	93.0		0.88	0.30–2.61	.820
T4	64.3		6.50	2.46–17.16	< 0.001	59.4		5.69	1.97–16.45	.001
LN metastasis		.014					<.001			
N0	94.1					94.5				
N1	95.5					97.1				
N2	89.5					91.0				
N3a	81.3					75.0				
N3b	60.0					40.0				
Distant metastasis										
M0	92.4					92.4				
M1	N/A	N/A				N/A	N/A			

(*continued*)

Table 3

(continued).

	Overall survival					Recurrence-free survival				
	Univariate analysis		Multivariate analysis			Univariate analysis		Multivariate analysis		
Variables	5YOS	*P* value	HR	95% CI	*P* value	5YDFS	*P* value	HR	95% CI	*P* value
Pathologic stage*		.072					.003			
I	95.5					95.8				
II	92.7					94.1				
III	82.6					77.8				
Lymphatic invasion		.002					.004			
Absent	97.4		1.00			96.8		1.00		
Present	87.3		2.58	0.93–7.13	0.069	87.8		2.35	0.84–6.59	.104
Vascular invasion		.002					.001			
Absent	93.6		1.00			93.9		1.00		
Present	77.5		3.27	1.23–8.68	0.018	74.5		4.66	1.71–12.68	.003
Perineural invasion		.016					<.001			
Absent	93.8					97.3		1.00		
Present	89.8					84.8		3.48	1.24–9.73	.018

* According to the 8th edition of the American Joint Committee on Cancer classification.

ASA = American Society of Anesthesiologists, BMI = body mass index, CI = confidence interval, DRM = distal resection margin, 5YDFS = 5-year disease free survival, 5YOS = 5-year overall survival, HR = hazard ratio, LN = lymph node, N/A = not applicable, PRM = proximal resection margin, RY EJ = Roux-en Y esophagojejunostomy.

One of the limitations of this retrospective study is that only a small number of patients were analyzed after propensity score matching. With a small number of patients, we could not further categorize the patients according to specific surgical method such as extra- or intra-corporeal anastomosis, number of trocar insertions, and type of stapler. Due to the very low death and recurrence events in the laparoscopic group, the statistic power was low, and this might have resulted in insignificant differences in the outcome between the 2 groups. In this regard, we performed logistic regression to support the results and found that the outcomes were not significantly correlated with the surgical method.

In conclusion, the laparoscopic method for surgical treatment of patients with grossly EGC-mimicking AGC might be feasible in terms of long-term outcomes. Limited LN dissection (D1+) may be effective without the need for additional surgery after initial curative surgery. However, as grossly EGC-mimicking AGC showed less LN metastasis than AGC, this result needs to be interpreted cautiously when we approach patients with AGCs.

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Author contributions

Jun Ho Lee contributed to the conception of this study and provided critical revision of the study. Sung Eun Oh collected and analyzed the data and drafted the work. Ji Yeong An, Min-Gew Choi, Tae Sung Sohn, and Jae Moon Bae ensured that questions related to the accuracy or integrity of all parts of the work were appropriately investigated and resolved. All authors gave final approval of the version to be published.

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