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ORIGINAL REPORT

Long-Term Results of Laparoscopic Gastrectomy for Gastric Cancer: A Large-Scale Case-Control and Case-Matched Korean Multicenter Study

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ABSTRACT

Purpose
The oncologic outcomes of laparoscopy-assisted gastrectomy for the treatment of gastric cancer have not been evaluated. The aim of this study is to validate the efficacy and safety of laparoscopic gastrectomy for gastric cancer in terms of long-term survival, morbidity, and mortality retrospectively.

Patients and Methods
The study group comprised 2,976 patients who were treated with curative intent either by laparoscopic gastrectomy (1,477 patients) or open gastrectomy (1,499 patients) between April 1998 and December 2005. The long-term 5-year actual survival analysis in case-control and case-matched population was conducted using the Kaplan-Meier method. The morbidity and mortality and learning curves were evaluated.

Results
In the case-control study, the overall survival, disease-specific survival, and recurrence-free survival (median follow-up period, 70.8 months) were not statistically different at each cancer stage with the exception of an increased overall survival rate for patients with stage IA cancer treated via laparoscopy (laparoscopic group; 95.3%, open group: 90.3%; $P < .001$). After matching using a propensity scoring system, the overall survival, disease-specific survival, and recurrence-free survival rates were not statistically different at each stage. The morbidity of the case-matched group was 15.1% in the open group and 12.5% in the laparoscopic group, which also had no statistical significance ($P = .184$). The mortality rate was also not statistically significant (0.3% in the open group and 0.5% in the laparoscopic group; $P = 1.000$). The mean learning curve was 42.

Conclusion
The long-term oncologic outcomes of laparoscopic gastrectomy for patients with gastric cancer were comparable to those of open gastrectomy in a large-scale, multicenter, retrospective clinical study.

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INTRODUCTION

Despite a decrease in its incidence, gastric cancer is still the second most common cancer worldwide.[1] In Eastern Asian countries, particularly Korea and Japan, gastric cancer is still the most prevalent malignancy, and the proportion of early gastric cancer has increased as a result of the nationwide improved surveillance of gastric cancer in both countries.[2,3] Currently, surgical resection using gastrectomy and proper perigastric lymphadenectomy is the only treatment option to enhance the survival rate of patients with gastric cancer.[4] Although most early-stage gastric cancer requires surgical resection, a limited use of gastrectomy and lymphadenectomy is sufficient to provide a cure in these patients.

In 1999, Ohgami et al[5] published the first instance of a laparoscopic wedge resection for a patient with early-stage gastric cancer. Since then, laparoscopic surgery has become one of the general modalities to manage patients with early-stage gastric cancer. Moreover, a recent meta-analysis for early-stage gastric cancer showed a superior postoperative recovery in patients treated with laparoscopic surgery compared with those treated using an open, conventional surgery.[6,7] In other studies, laparoscopic gastrectomy with extended lymph node dissection for gastric cancer was shown to provide comparable outcomes with those from open surgery

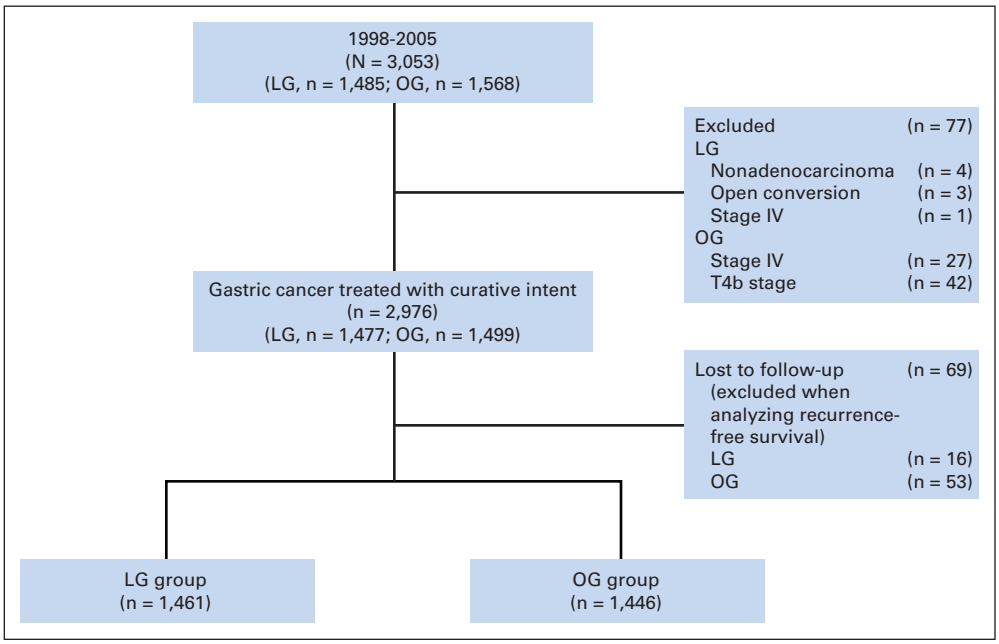

Fig 1. CONSORT diagram. LG, laparoscopic group; OG, open gastrectomy group.

in a single-center, retrospective analysis.[8,9] In addition, another small-sized, single-center, randomized clinical trial reported that the outcomes from laparoscopic surgery for all stages of gastric cancer were not inferior to those from open surgery.[10] However, because of a lack of large-scale data concerning the long-term outcomes for these patients, the use of laparoscopic gastrectomy for the treatment of gastric cancer is still a contentious issue.

The Korean laparoscopic gastrointestinal surgical society (KLASS) recently completed the enrollment of patients involved in a multicenter, randomized controlled clinical trial (KLASS-01, NCT00452751) to compare laparoscopic and open conventional surgery in the treatment of patients with early-stage gastric cancer. Although an interim analysis already shows that morbidity and mortality of laparoscopic surgery for gastric cancer were not inferior to those results from open surgery,[11] the confirmed results, including the oncologic outcomes, are still awaiting. This delay, however, hampers the advancement and expanded use of the laparoscopic approach in the treatment of more advanced stages of gastric cancer. Thus, before laparoscopy can become a universally applicable surgery for most patients with gastric cancer, the analysis of the long-term outcomes using multicenter data for a large-scale trial is required.

Before the KLASS-01 clinical trial, preliminary tests were undertaken by 10 of the participating surgeons using retrospectively reviewed laparoscopic and open procedures, conducted between April 1998 and December 2005. The aim of this study was to verify the long-term safety of laparoscopic gastrectomy for gastric cancer as compared with open conventional gastrectomy by analyzing the long-term follow-up data of a large number of patients across multiple institutions. This article reports the findings of this long-term follow-up.

PATIENTS AND METHODS

Study Design and Patients

To provide background data for the KLASS-01 clinical trial, 10 surgeons participating in this trial retrospectively collected data from their gastric cancer surgeries, including laparoscopic and open procedures, from the date of their first laparoscopic surgery for gastric cancer (the earliest was April 1998) until December 2005. Before employing a laparoscopic surgical approach for the treatment of gastric cancer, each hospital demonstrated a history of 80 or more conventional open surgeries per year.

The data collected included clinical, surgical, and long-term follow-up results of all consecutive patients who underwent curative gastrectomy for gastric cancer at the participating institutions. The operative procedures, such as the instruments for dissection and the reconstruction methods used, were not standardized between the various institutions, and the approach (laparoscopic or open) was decided independently according to protocols that were in place at each institution. However, most participating surgeons applied a laparoscopic approach to patients who had a tumor that was defined as clinically infiltrating into the muscularis propria, without metastatic lymph node involvement.

Between April 1998 and December 2005, a total of 3,053 patients, including 1,485 in the laparoscopic group (LG) and 1,568 in the open gastrectomy group (OG), were enrolled in the study. We had to exclude 77 patients from the cohort: four patients did not have adenocarcinoma, three patients had open conversion, one patient represented with stage IV cancer in the LG, 27 patients presented with stage IV cancer, and 42 patients in the OG had a pT4b lesion, which was not present in the LG. Finally, a total of 2,976 patients (1,477 in the LG and 1,499 in the OG) were enrolled to analyze the actual 5-year overall survival rate for patients treated with each procedure. When we analyzed the actual recurrence-free survival, we excluded an additional 16 patients in the LG and 53 patients in the OG because these patients were lost to follow-up (Fig 1).

To eliminate confounding variables induced by the different indications for a particular surgical method between the two groups, we performed matched analysis and unmatched analysis. Matched analysis aimed to balance high-dimensional observed covariates, and it was done by propensity score matching using calipers of 0.1 of the standard deviation of the propensity score. A total of 635 patients in each group were extracted from the 2,976 patients after matching by operative procedure (subtotal or total gastrectomy), the extent of lymphadenectomy (D2 or D1+), body mass index, operator, and cancer stage. Unmatched analysis was adjusted for the same variables on which we have matched (Table 1).

Adjuvant Treatment and Follow-Up of Patients

The follow-up schedule and indication for adjuvant treatment were not standardized among the various institutions. However, most patients with cancer at stage II or higher were treated with a fluorouracil-based adjuvant

Table 1. Patients' Stages After Matching by BMI, Operative Methods, Extent of Lymphadenectomy, Operator, and Stage of Cancer

Stage	OG (n = 635)	LG (n = 635)
IA	334	320
IB	130	150
IIA	69	62
IIB	51	50
IIIA	20	21
IIIB	16	23
IIIC	15	9

Abbreviations: BMI, body mass index; LG, laparoscopic gastrectomy; OG, open gastrectomy.

treatment, and follow-up investigations were scheduled at 3-month intervals for the first 2 years, at 6-month intervals for the next 3 years, and then annually until the patient's death. The follow-up program consisted of a physical examination, laboratory blood tests, endoscopy, and ultrasonography or computed tomography. Recurrence was diagnosed from clinical, radiologic, or endoscopic signs of disease.

Data Collection and Statistical Analysis

Data were collected by reviewing the electronic medical records and the prospectively maintained gastric cancer database from each hospital. Data monitoring was performed by a single central research person, who is a medical recorder who has worked in this field for 7 years. The data analysis was performed by a medical statistician.

Statistical analyses were performed using SPSS version 18.0 (SPSS, Chicago, IL) and the R program (R Foundation for Statistical Computing, Vienna, Austria). The χ^2 test and independent t test were used for comparisons between the two groups. The overall and recurrence-free survival rates were estimated using the Kaplan-Meier method and compared with the log-rank test. For the matched analysis, propensity score matching was performed using MatchIt package in the R program. For learning curve analysis, we applied the change point package in the R program to detect changes within a given sequences. A change point was defined as the point that maximized the likelihood of normally distributed observations over all possible change point locations under the alternative hypothesis that a single change point existed. All data were considered statistically significant at $P \leq .05$.

RESULTS

Results From the Case-Control Analysis

The patients' characteristics are summarized in Table 2. The mean age was 59.0 years in the OG and 57.7 years in the LG. For patients in the OG, a distal gastrectomy was performed in 70.6% of patients, a total gastrectomy in 28.3% of patients, and a proximal gastrectomy in 0.7% of patients. Meanwhile, for the LG, a distal gastrectomy was performed in 89.2% of patients, a total gastrectomy in 8.7% of patients, and a proximal gastrectomy in 1.6% of patients. A D2 lymphadenectomy was performed in 83.5% of patients in the OG and 56.1% of patients in the LG. In the OG, a seventh-edition TNM/International Union Against Cancer criteria stage IA cancer was identified in 25.5% of patients, stage IB in 11.2%, stage IIA in 10.4%, stage IIB in 12.5%, stage IIIA in 11.3%, stage IIIB in 11.5%, and stage IIIC in 17.5%. In the LG, a seventh-edition TNM/International Union Against Cancer criteria stage IA cancer was classified in 76.7% of patients, stage IB in 10.7%, stage IIA in 5.2%, stage IIB in 3.6%, stage IIIA in 1.6%, stage IIIB in 1.6%, and stage IIIC in 0.6%. Twelve patients (0.8%) in the OG and nine patients (0.6%) in the LG died within 30 days of surgery. The median survival was 70.8 months across the entire cohort, calculated as 68.8 months for the OG and 72.3 months for the LG.

Table 2. Clinicopathologic Characteristics of Patients in the Two Treatment Groups (n = 2,976)

Characteristic	OG (n = 1,499) No.	OG (n = 1,499) %	LG (n = 1,477) No.	LG (n = 1,477) %	*P*
Age, years					.003
Mean	59.02		57.68		
SD	12.09		12.11		
Sex					< .001
Male	1,044		926		
Female	455		551		
BMI, kg/m^2					.015
Mean	23.06		23.34		
SD	3.20		2.98		
Type of procedure					< .001
Distal gastrectomy	1,059	70.6	1,319	89.3	
Total gastrectomy	424	28.3	128	8.7	
Proximal gastrectomy	11	0.7	24	1.6	
Other	5	0.4	6	0.4	
Lymph node dissection					< .001
< D2	247	16.5	649	43.9	
≥ D2	1,252	83.5	828	56.1	
No. of retrieved lymph nodes					< .001
Mean	39.92		31.76		
SD	16.90		13.50		
Depth of invasion					< .001
Mucosa (T1a)	195	12.9	765	51.7	
Submucosa (T1b)	265	17.7	475	32.2	
Proper muscle (T2)	245	16.3	129	8.7	
Subserosa (T3)	286	19.1	63	4.3	
Serosa exposure (T4a)	509	34.0	46	3.1	
N stage					< .001
N0	666	44.4	1,261	85.4	
N1	225	15.0	122	8.3	
N2	232	15.5	63	4.3	
N3a	213	14.2	25	1.7	
N3b	163	10.9	6	0.4	
Stage					< .001
IA	382	25.5	1,134	76.8	
IB	168	11.2	158	10.7	
IIA	156	10.4	77	5.2	
IIB	188	12.5	52	3.5	
IIIA	170	11.3	23	1.6	
IIIB	173	11.5	24	1.6	
IIIC	262	17.5	9	0.6	
Operative mortality (≤ 30 days)	12	0.8	9	0.6	.532

Abbreviations: BMI, body mass index; LG, laparoscopic gastrectomy; OG, open gastrectomy; SD, standard deviation.

The actual 5-year overall survival rate was 90.3% in the OG and 95.3% in the LG for patients with stage IA, which was statistically significant ($P < .001$). The actual 5-year overall survival rate for patients in stage IB was 92.3% in the OG and 91.8% in the LG; in stage IIA, 84.0% and 85.7%; in stage IIB, 75.0% and 75.5%; in stage IIIA, 68.8% and 56.5%; in stage IIIB, 49.1% and 45.8%; and in stage IIIC, 30.5% and 33.3%, respectively. A comparative analysis of the overall survival showed no statistical significance for any of the stages of

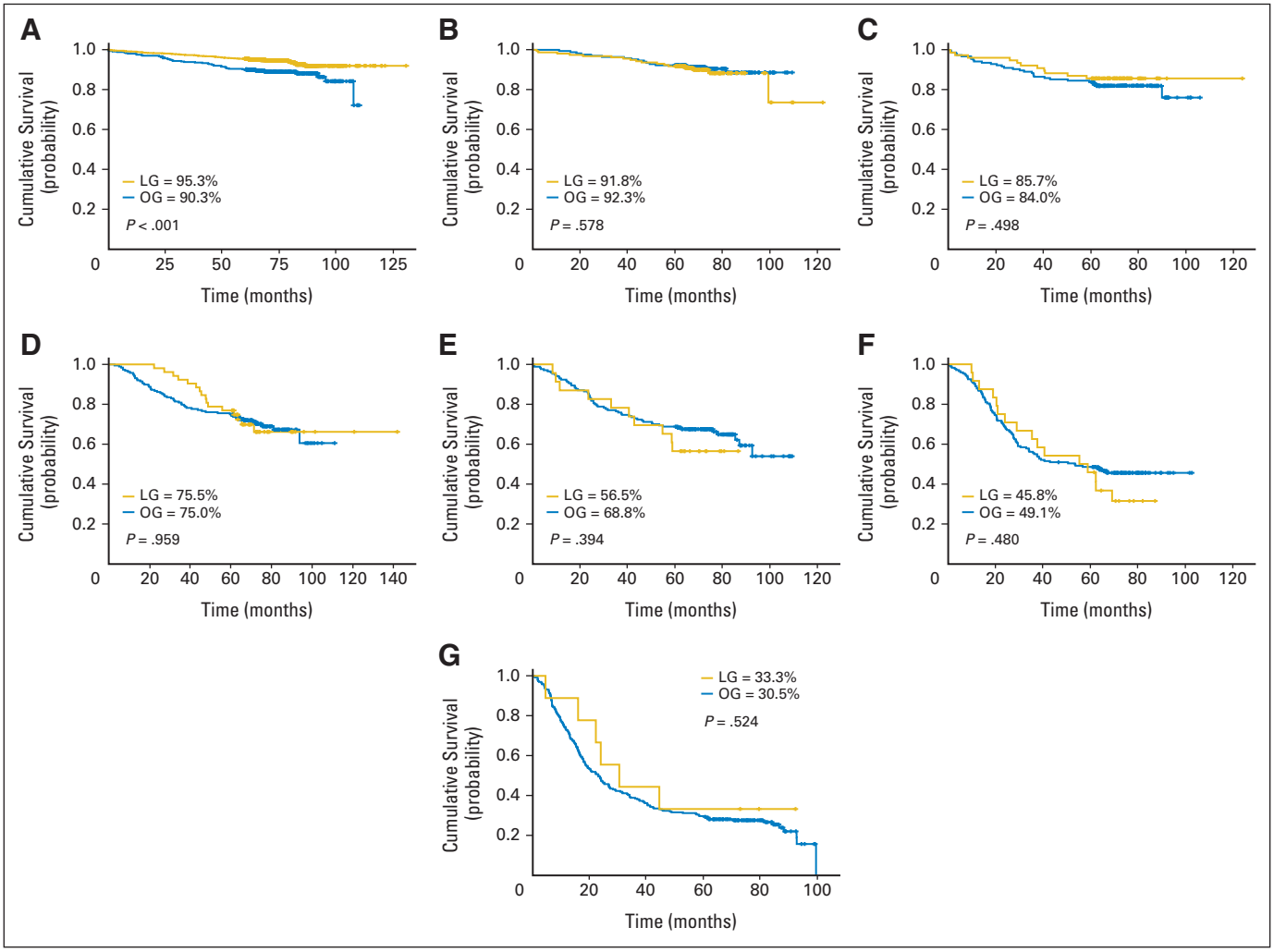

Fig 2. Comparison of overall long-term survival rate between laparoscopic group (LG) and open gastrectomy group (OG) according to stage. (A) stage IA; (B) stage IB; (C) stage IIA; (D) stage IIB; (E) stage IIIA; (F) stage IIIB; (G) stage IIIC.

cancer, with the exception of stage IA, for which a better survival rate was shown for the LG (Fig 2).

Similar findings were observed for the actual 5-year disease-specific survival and the actual 5-year recurrence-free survival. The actual 5-year disease-specific survival was 98.1% in the OG and 98.8% in the LG for patients with stage IA cancer, 98.1% and 96.1% for stage IB, 88.7% and 91.9% for stage IIA, 80.0% and 79.9% for stage IIB, 73.5% and 60.3% for stage IIIA, 52.2% and 53.1% for stage IIIB, and 35.2% and 33.3% for stage IIIC patients, respectively (Data Supplement). The actual 5-year recurrence-free survival was 98.1% in OG and 98.9% in LG for patients with stage IA, 96.3% and 96.8% for stage IB, 88.6% and 93.1% for stage IIA, 78.9% and 74.5% for stage IIB, 73.0% and 66.7% for stage IIIA, 32.8% and 22.2% for stage IIIB, and 45.8% and 24.8% for stage IIIC, respectively (Data Supplement). Comparisons of the disease-specific and recurrence-free survival rates did not show statistical significance for any of the stages of cancer.

Results From the Case-Matched Analysis

After propensity score matching, the actual 5-year overall survival rate was 94.0% for stage IA patients in the OG and 95.6% for patients in the LG, 96.9% and 92.7% for stage IB, 88.4% and 85.5% for stage IIA, 80.3% and 80.0% for stage IIB, 70.0% and 61.9% for stage IIIA, 68.8% and 47.8% for stage IIIB, and 40.0% and 33.3% for stage IIIC, respectively (Fig 3; Data Supplement). The overall survival rate after matching did not show any significant differences between the OG and the LG for all stages of cancer.

Postoperative Morbidity and Mortality

The morbidity of the case-control cohort was 17% in the OG and 13.4% in the LG, which was not statistically significant ($P = .173$). The morbidity of the case-matched group was 15.1% in the OG and 12.5% in the LG, which was also not statistical significance ($P = .184$). The mortality rate of the matched cohort was not statistically significant (0.3% in the OG and 0.5% in the LG; $P = 1.000$; Table 3).

Learning Curve of Laparoscopic Gastrectomy

The mean learning curve was 42, with a range between 4 and 72. Some surgeons had statistically significantly less complication and more numbers of retrieved lymph nodes after their learning curve, but most of them were not significant. So generally there was trend toward less morbidity and more retrieved lymph nodes after learning curve (Table 4).

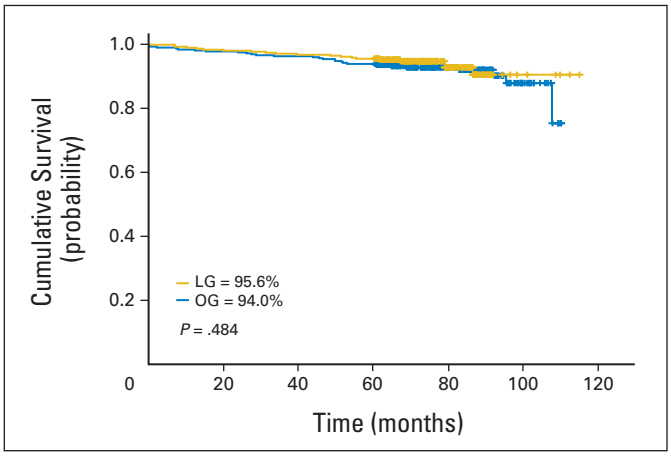

Fig 3. Comparison of overall long-term survival rate between laparoscopic group (LG) and open gastrectomy group (OG) after matching by operation methods and operators: stage IA.

DISCUSSION

Our multicenter, retrospective, comparative study, which assessed the largest patient cohort currently reported in the literature, showed that curative laparoscopic gastrectomy leads to the same long-term oncologic outcomes in patients with all stages of gastric cancer (stages IA through IIIC) as compared with open surgery.

As surgical procedures and equipment improved over time, the methods used to treat early-stage gastric cancer moved away from more radical surgeries with larger incisions to the use of minimally invasive techniques, including endoscopic resection, laparoscopic gastrectomy, sentinel node navigation with limited gastrectomy, robotic gastrectomy, and single-port gastrectomy.[12] Of these modalities, laparoscopic gastrectomy has gained popularity as a tool for surgical resection for gastric cancer in Japan and Korea, particularly after 2005, when patients in Korea could be reimbursed for laparoscopic procedures for gastric cancer. Indeed, according to KLASS records, during 2009, 3,783 patients underwent laparoscopic gastric procedures in Korea, accounting for just less than 26% of all gastric operations.[3] However, controversy still surrounds the use of laparoscopic gastrectomy for the treatment of gastric cancer because of the paucity of concrete evidence in favor of its long-term positive oncologic outcomes. Therefore, although generally accepted for routine early-stage gastric cancer treatment, under the Japanese gastric cancer treatment guidelines, laparoscopic gastrectomy is still classified as an investigational procedure.[13]

Table 3. Postoperative Morbidity and Mortality in Matched Analysis

	OG (n = 635)		LG (n = 635)		
Morbidity and Mortality	No.	%	No.	%	*P*
Complication	96	15.1	79	12.5	.184
Wound problem	40	6.3	30	4.8	
Fluid collection	11	1.7	11	1.7	
Intra-abdominal bleeding	4	0.6	3	0.5	
Intraluminal bleeding	4	0.6	5	0.8	
Intestinal obstruction	3	0.5	2	0.3	
Ileus	6	0.9	1	0.2	
Stenosis	2	0.3	1	0.2	
Leakage	3	0.5	7	1.1	
Fistula	0		1	0.2	
Pancreatitis	1	0.2	1	0.2	
Pulmonary problem	5	0.8	4	0.6	
Urinary problem	2	0.1	1	0.1	
Renal problem	1	0.2	0		
Hepatic problem	0		2	0.3	
Cardiac problem	2	0.3	0		
Others			11	1.7	
Operative mortality	2	0.3	3	0.5	1.000

Abbreviations: LG, laparoscopic gastrectomy; OG, open gastrectomy.

To date, there have been only six prospective randomized controlled clinical trials to assess the clinical value of laparoscopic gastrectomy.[10,11,14-17] Among them, only one clinical trial, performed by Huscher et al,[10] focused on the long-term survival rates of patients with gastric cancer and reported no statistically significant difference in the 5-year overall survival between patients treated with open surgery or laparoscopic surgery (55.4% in the OG and 58.9% in the LG). The patients enrolled in that study were diagnosed with both early and advanced stages of gastric cancer; however, the sample size was too small to provide conclusive evidence for survival. Other prospective studies showed no recurrence in patients who underwent laparoscopic surgery during the follow-up period.[6,7,18] These studies, however, also had a low clinical impact in terms of the long-term oncologic outcomes owing to the relatively short follow-up period of 12 to 39 months and a small sample size that could not reach statistical power. Most of these investigators using a meta-analysis reported the same survival rate between the LGs and OGs, even when a small number of lymph nodes were collected in patients who underwent laparoscopic surgery.[6,7,18] Likewise, two clinical studies from one institution in Korea showed the same 3-year actual overall survival rate for patients with gastric cancer who underwent laparoscopic surgery as those treated with an open approach[19] and a 5-year disease-specific survival rate of 85.6% for patients with advanced gastric cancer that was comparable to the historical survival rates for gastric cancer patients treated via open, conventional surgery.[20] Another retrospective, large-scale, multicenter study from the Japanese Laparoscopic Surgery Study Group found a 5-year disease-free survival rate of 99.8% in patients with stage IA (sixth edition of TNM) cancer, 98.7% in patients with stage IB cancer, and 85.7% in patients with stage II cancer over a median 36 months of follow-up.[21] However, this study had no open control group.

In the present study, we analyzed the multicenter retrospective data for a large cohort of matched cases. The long-term oncologic results showed that the laparoscopic approach was not statistically inferior to the open conventional approach for the treatment of gastric cancer, even in patients with advanced gastric cancer. Although the current indication for laparoscopic surgery for gastric cancer is limited to patients with early-stage gastric cancer, we envision that the results from our study might act as preliminary evidence for a randomized controlled clinical trial investigating the efficacy of laparoscopic surgery in patients with advanced gastric cancer.

Although we showed that the long-term oncologic outcomes were not statistically different between the two groups, we did find one exception in the actual 5-year overall survival for patients with stage IA cancer. In these patients, the long-term overall survival was better for

Table 4. Comparison of Complication Rate and Mean Number of Retrieved Lymph Nodes Before and After Learning Curve

			Complication Rate							Retrieved LNs					Retrieved LNs ≤ 15*						
			Before			After				Before		After			Before			After			
Operator	No. of Operations	Change Point	No.	Total No.	%	No.	Total No.	%	*P*	Mean	SD	Mean	SD	*P*	No.	Total No.	%	No.	Total No.	%	*P*
1	208	53	9	53	17.0	27	155	17.4	.942	26.21	11.33	35.05	13.21	< .001	8	53	15.1	6	155	3.9	.005
2	91	50	8	50	16.0	4	41	9.8	.536	24.38	10.09	28.66	14.36	.100	11	50	22.0	7	41	17.1	.557
3	381	72	10	72	13.9	30	309	9.7	.297	18.01	9.31	35.76	13.54	< .001	33	72	45.8	6	309	1.9	< .001
4	50	38	—			—			—	26.39	11.35	29.58	16.74	.455	5	38	13.2	2	12	16.7	1.000
5	53	35	7	38	18.4	1	15	6.7	.415	45.11	17.34	41.53	8.65	.452	0		35	0	18		—
6	55	4	0	0	4	8	51	15.7	1.000	32.75	11.29	35.43	12.85	.677	0		4	1	50	2.0	1.000
7	75	62	8	62	12.9	1	13	7.7	1.000	29.15	10.52	31.54	12.75	.536	7	62	11.3	0	13		.343
8	110	15	2	15	13.3	12	95	12.6	1.000	23.67	5.82	26.98	6.58	.058	1	15	6.7	1	95	1.1	.255
9	214	29	15	29	51.7	25	185	13.5	< .001	26.31	14.57	28.25	11.26	.497	5	29	17.2	20	185	10.8	.316
10	239	62	7	62	11.3	17	177	9.6	.704	33.85	13.62	36.55	13.22	.179	6	62	9.7	4	177	2.3	.021

Abbreviations: LNs, lymph nodes; SD, standard deviation.
*Retrieved fewer than 15 lymph nodes.

those treated by laparoscopy as compared with those treated using the open method (95.3% *v* 90.3%; $P < .001$). This survival benefit of laparoscopic group probably arose from heterogeneity of two groups. A comparison of the clinical factors between the two groups of stage IA patients showed that elder age, male sex, and location of the cancer were dominant in patients who underwent open conventional surgery. Moreover, we chose open surgery for advanced gastric cancer preoperatively so the OG of stage IA patients had more aggressive clinical nature preoperatively. This asymmetric distribution might be caused by the different indications for selecting each procedure. So far, after tight matching using a propensity scoring system, this benefit of survival disappeared. This limitation in the results for patients with stage IA cancer will be overcome when the long-term survival results of the multicenter randomized controlled clinical trial (registered in as NCT00452751) by surgeons who participated in this retrospective study become available.

Besides this imbalance in the clinical factors between the two groups, a more aggressive surgery, such as total gastrectomy and aggressive lymphadenectomy, was also performed in patients who underwent open conventional surgery. To overcome this asymmetry, we analyzed the data after stage stratification and case matched using the propensity scoring system. However, the number of patients with greater than stage III disease was too small to verify the results decisively. Despite these limitations, our study is the first to show the same long-term oncologic results for laparoscopic procedures as compared with open, radical gastrectomy in a large, multicenter cohort. Therefore, we anticipate a trend for the long-term survival of patients with gastric cancer treated with laparoscopic surgery.

Our KLASS group reported that the morbidity and mortality rate was not statistically different between laparoscopic gastrectomy and open gastrectomy.[11] The present study also showed no significant difference in morbidity and mortality of matching group. It was quite similar to the result of previous reports. Therefore, laparoscopic gastrectomy is as safe as open gastrectomy, even aggressive D2 lymphadenectomy or total gastrectomy, in terms of morbidity and mortality.

We analyzed each surgeon's learning curve, which was defined as change point of operation time within a given sequences. The mean learning curve was 42, with range between 4 and 72. This is as same as previous reports. Some surgeons had less morbidity and more lymph nodes retrieved but this was not universal. However, most surgeons had a trend toward less morbidity and more retrieved lymph nodes after the learning curve. For defining precise lymphadenectomy, we evaluated the number of retrieved lymph nodes at less than 15. After the learning curve, the case of fewer than 15 retrieved lymph nodes was generally decreased in most operators.

In conclusion, the long-term outcomes of laparoscopic gastrectomies for gastric cancer seem comparable to those of open procedures in this large-scale retrospective study. However, this result should be confirmed by well-designed prospective randomized controlled trials.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: Hyung-Ho Kim, Min-Chan Kim, Woo Jin Hyung
Collection and assembly of data: All authors
Data analysis and interpretation: Hyung-Ho Kim, Woo Jin Hyung, Wook Kim
Manuscript writing: All authors
Final approval of manuscript: All authors

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