Original Article

National validation of laparoscopic approach for locally advanced gastric cancer: Comparison of a randomized controlled trial and real-world practice results

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Abstract

Objective: The laparoscopic approach for locally advanced gastric cancer has recently been adopted based on the results of several randomized controlled trials (RCTs). However, findings from RCTs have not been examined at the national level. This study aimed to investigate the external validity of the Korean Laparoscopic Gastrointestinal Surgery Study-02 (KLASS-02) trial involving 13 tertiary hospitals, using data from the Korean Gastric Cancer Association (KGCA)-led nationwide survey involving 68 tertiary or general hospitals.

Methods: Data on patients who underwent laparoscopic or open distal gastrectomy for pathological stage IB–IIIC gastric cancer under the same conditions were collected from the KLASS-02 trial and the KGCA nationwide survey datasets. Surgical outcomes were assessed for each dataset and multivariable analyses were performed to examine the effect of the laparoscopic approach on surgical outcomes.

Results: The laparoscopic group had a lower overall complication rate than the open group in both KLASS-02 and KGCA datasets (16.1% *vs*. 23.5% for the KLASS-02 and 12.6% *vs*. 19.6% for the KGCA). Moreover, the laparoscopic group had fewer wound problems, and fewer grade II, IIIa, and IV complications than the open group in the KGCA data (0.8% *vs*. 3.4%, 5.8% *vs*. 10.4%, 2.3% *vs*. 3.7%, and 0.5% *vs*. 1.4%, respectively), which were not observed in the KLASS-02 data. Multivariable analyses revealed that the laparoscopic approach was not associated with overall complications, but reduced wound problems and more harvested lymph nodes in the KGCA survey data (adjusted odds ratios, 0.19 for wound problems, adjusted β coefficient 4.39 for number of harvested lymph nodes), which were not shown in the KLASS-02 data.

Conclusions: The safety and feasibility of the laparoscopic approach for locally advanced gastric cancer were

validated at a national level. The laparoscopic approach for locally advanced gastric cancer can be implemented in the Republic of Korea.

Keywords: Advanced gastric cancer; laparoscopy; complication; trial; national survey

Submitted Sep 17, 2024. Accepted for publication Dec 04, 2024.
doi: 10.21147/j.issn.1000-9604.2024.06.11
View this article at: https://doi.org/10.21147/j.issn.1000-9604.2024.06.11

Introduction

Recently, several large-scale randomized controlled trials (RCTs) demonstrated the surgical safety and oncological feasibility of the laparoscopic approach for locally advanced gastric cancer (1-5). In two randomized trials, the 30-d morbidity and mortality rates did not differ significantly between the laparoscopic and open approach groups (3,5). In the Korean Laparoscopic Gastrointestinal Surgery Study-02 (KLASS-02) trial, the morbidity rate was lower in the laparoscopic approach group than in the open approach group (1). Non-inferiority of long-term survival in the laparoscopic group compared with that in the open group was also demonstrated using the 3-year or 5-year overall survival rates (2,4,5). Based on these results, laparoscopic distal gastrectomy has become a standard treatment option for locally advanced gastric cancers located in the middle or lower third of the stomach (6-8).

However, the safety and feasibility of the laparoscopic approach for locally advanced gastric cancer have only been proven by qualified surgeons. To participate in the KLASS-02 trial, surgeons were required to have at least 50 of each laparoscopic and open gastrectomy cases, and five expert peers reviewed three unedited videos of each laparoscopic and open distal gastrectomy with D2 lymphadenectomy (9). In the Chinese Laparoscopic Gastrointestinal Surgical Study-01 (CLASS-01) and Japanese Laparoscopic Surgery Study Group-0901 (JLSSG0901) trials, intraoperative photographs that identified specific surgical fields were reviewed and feedback was regularly provided to the surgeons (3,5). Thus, the positive outcomes of the laparoscopic approach could result from these surgical quality controls, and there is still a lack of evidence regarding whether the laparoscopic approach for locally advanced gastric cancer can be performed in real-world general practice.

This study aimed to investigate the external validity of the KLASS-02 trial using the Korean Gastric Cancer Association (KGCA) nationwide survey dataset regarding whether laparoscopic distal gastrectomy for locally advanced gastric cancer can be conducted nationally in the Republic of Korea (10).

Materials and methods

Datasets

This study used the KLASS-02 trial dataset and KGCA nationwide survey dataset. The KLASS-02 trial is a prospective, multicenter, RCT conducted by the KLASS group, which included 20 researchers from 13 tertiary hospitals in the Republic of Korea (2). Patients with clinical stage T2–4a gastric cancer suitable for curative resection by distal gastrectomy were eligible for the KLASS-02 trial. The enrolled patients were randomly assigned to undergo laparoscopic or open surgery in a 1:1 ratio, and 1,050 patients were recruited between November 2011 and April 2015.

A nationwide survey conducted by the KGCA collected data on patients who underwent surgical treatment for gastric cancer in 2019 (10). The purpose of this nationwide survey was to determine the overall status of gastric cancer surgeries performed in 2019, and it sought to collect as many cases as possible without any restrictions on patients' demographics, clinicopathological factors, or surgical methods. A case report form consisting of 54 items was sent to a representative of each hospital via e-mail, and 14,076 patient data from 68 hospitals were collected between March 2020 and February 2021.

Among the KLASS-02 trial and the nationwide survey data, we selected data from patients who underwent laparoscopic or open distal gastrectomy for pathological stage IB–IIIC gastric cancer from two datasets. The nationwide data did not include any patients enrolled in the KLASS-02 trial due to differences in timing of surgery.

KGCA data were provided by the Information Committee of the KGCA (No. KGCA2023IC2) with the approval of a nationwide survey project. This study was

also approved by the Institutional Review Board of the National Cancer Center, the Republic of Korea (No. NCC 2023-0105).

Clinicopathological factors

The patients' physical status was assessed using the American Society of Anesthesiologists (ASA) classification: 1) normal healthy patient; 2) mild systemic disease; 3) severe systemic disease; and 4) severe systemic disease that is a constant threat to life (11). The pathological staging system was initially different between the two datasets (seventh edition for the KLASS-02 trial and eighth edition for the KGCA survey dataset), and staging was unified into the eighth edition of the American Joint Committee on Cancer tumor-node-metastasis (TNM) classification (12).

Outcomes

Regarding intra-operative surgical quality, omentectomy, D2 lymph node dissection, R0 resection, number of harvested lymph nodes, operating time, and blood loss were assessed. Postoperative surgical outcomes include hospital stay and postoperative complications. The severity of postoperative complications was determined according to the Clavien-Dindo classification (13).

Statistical analysis

Continuous variables are presented as means with standard deviations or medians with interquartile ranges according to normality. Categorical variables were presented as numbers with percentages. The normality of continuous variables was evaluated using the Shapiro-Wilk test. Statistical differences between the two groups were determined using the Student's *t*-test or Wilcoxon-rank sum test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables.

Multivariable logistic regression analyses were performed to assess the effect of the surgical approach (laparoscopy *vs*. open surgery) on surgical outcomes, while adjusting for patient demographics (age, sex, body mass index, number of comorbidities, and ASA score), tumor factors (pathological stage), and surgical factors (extent of lymph node dissection, omentectomy, and combined resection). Multiple linear regression analyses were used for continuous outcomes such as the number of harvested lymph nodes, operating time, estimated blood loss, and hospital stay.

Statistical analyses were performed using SAS (Version 9.4; SAS Institute Inc., Cary, NC, USA) and R (Version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at P<0.05.

Results

Patients

From the KLASS-02 data, patients who did not undergo gastrectomy, those with pathological IA (T1N0M0) or stage IV gastric cancer, and those who underwent total or proximal gastrectomy were excluded (*Figure 1*). Additionally, 23 patients who switched to another approach (open to laparoscopy, n=10; laparoscopy to open, n=13) were included in the groups based on the approach received. Finally, 379 and 395 patients were included in the laparoscopic and open surgery groups, respectively.

Regarding the KGCA data, patients with pathological stages IB–IIIC were selected, and those who met the KLASS-02 exclusion criteria were excluded: those who underwent total, proximal, or pylorus-preserving gastrectomy or robotic gastrectomy, and those with insufficient data. Consequently, 1,631 and 1,107 patients were included in the laparoscopic and open surgery groups, respectively (*Figure 2*).

Baseline characteristics of patients

According to KLASS-02 data, most patient demographics and pathological characteristics were not significantly different between the laparoscopic and open surgery groups. However, the KGCA data showed significant differences between the two groups for all baseline characteristics. The laparoscopic group had a lower proportion of males (67.0% *vs*. 72.5%, P=0.002), higher proportion of ASA score 1 (24.3% *vs*. 20.3%, P=0.015), more comorbidities (66.5% *vs*. 61.2%, P=0.034), lower proportion of upper-third tumor location (5.8% *vs*. 17.4%, P<0.001), and higher proportions of early stage tumors, including T and N classifications and stage (all P<0.001) (*Table 1*).

Surgical outcomes

According to the KLASS-02 trial protocol, D2 lymph node dissection and total omentectomy were performed in nearly all the patients in the KLASS-02 dataset. In contrast, in the KGCA dataset, the proportions of D2 lymph node dissections in the laparoscopic and open surgery groups were 71.1% and 94.8%, respectively (P<0.001). Total omentectomy was performed in 22.6% and 86.4% of the patients in the laparoscopic and open groups, respectively

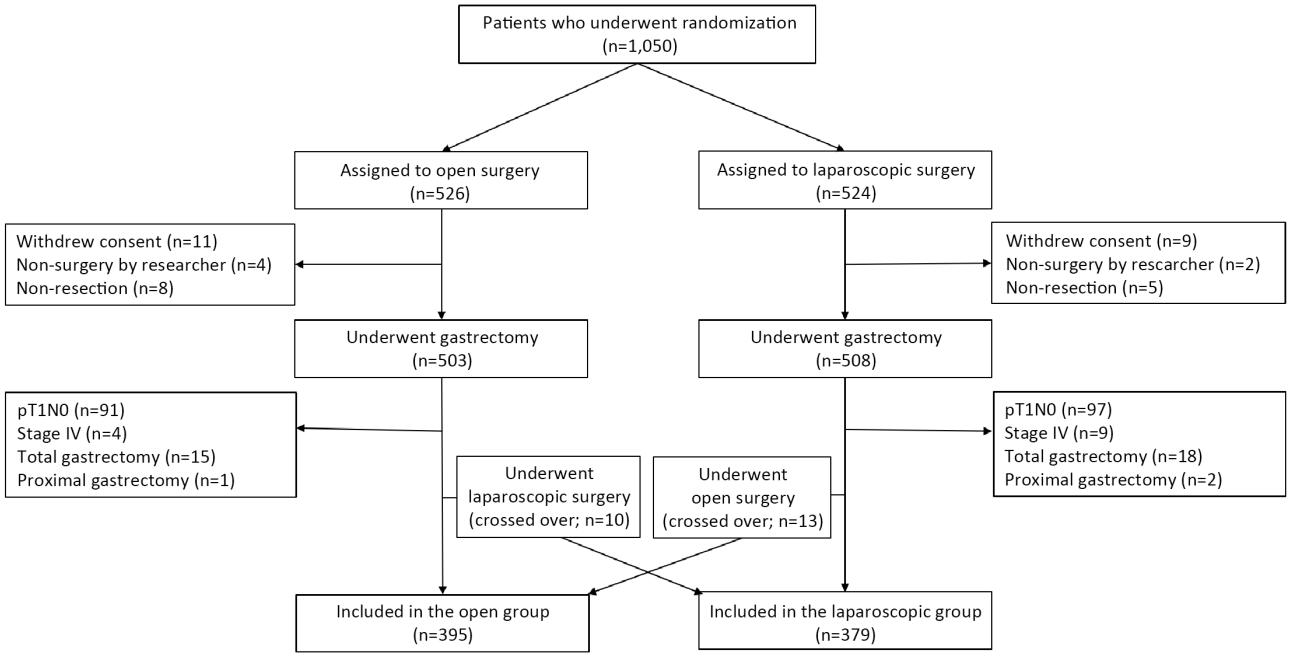

Figure 1 Flowchart for patient selection from KLASS-02 trial dataset. KLASS-02, Korean Laparoscopic Gastrointestinal Surgery Study-02.

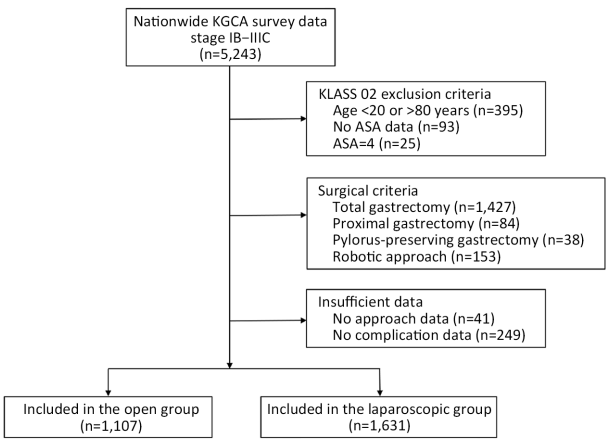

Figure 2 Flowchart for patient selection from KGCA survey dataset. KGCA, Korean Gastric Cancer Association; ASA, American Society of Anesthesiologists.

(P<0.001). Moreover, the laparoscopic group had a lower proportion of combined resections and a higher proportion of R0 resections in the KGCA dataset (P<0.001 and P=0.002, respectively), which were not observed in the KLASS-02 dataset. A similar number of harvested lymph nodes, longer operating time, less estimated blood loss, and shorter hospital stay in the laparoscopic group than in the open group were common in both datasets (*Table 2*).

Postoperative complications

In the KLASS-02 dataset, the overall complication rate was significantly lower in the laparoscopic group than that in the open group (16.1% *vs*. 23.5%, P=0.010). However, no significant difference was observed in any specific complication or Clavien-Dindo grade between the two groups. In the KGCA dataset, the laparoscopic group had a lower rate of wound problems, overall complications, Clavein-Dindo grade II, IIIa, IV, and III or more than those in the open group (P<0.001, <0.001, <0.001, =0.035, =0.015, and =0.012, respectively) (*Table 3*).

Multivariable analysis for effect of laparoscopic approach on surgical outcomes

Multivariable analysis of the KLASS-02 dataset demonstrated reduced overall complications with the laparoscopic approach (OR=0.59; 95% CI: 0.41–0.86) and no effect on the number of harvested lymph nodes and specific complications such as wound, ileus, and cardiac problems. Conversely, the laparoscopic approach did not reduce the overall complication rate, but reduced wound problems (OR=0.19; 95% CI: 0.08–0.44) compared with the open approach in the multivariable analysis of the KGCA dataset (*Table 4*). Moreover, the laparoscopic approach was associated with a higher number of harvested lymph nodes (coefficient, 4.39; 95% CI: 2.61–6.17). Longer operating time, lesser estimated blood loss, and shorter hospital stay were common effects of the laparoscopic approach in both datasets (*Table 5*).

Table 1 Patient demographics and clinicopathologic characteristics from KLASS-02 and KGCA survey datasets

Variables	KLASS-02			KGCA survey		
	Laparoscopic (N=379) [n (%)]	Open (N=395) [n (%)]	P	Laparoscopic (N=1,631) [n (%)]	Open (N=1,107) [n (%)]	P
Age (year) ($\bar{x}\pm s$)	59.7±10.9	59.3±11.5	0.607	62.4±11.6	63.4±10.6	0.029
Sex			0.292			0.002
Male	275 (72.6)	273 (69.1)		1,092 (67.0)	803 (72.5)	
Female	104 (27.4)	122 (30.9)		539 (33.0)	304 (27.5)	
BMI (kg/m^2) ($\bar{x}\pm s$)	23.6±2.9	26.6±3.2	0.899	24.3±3.5	23.5±3.5	<0.001
ASA score			0.952			0.015
1	181 (47.8)	191 (48.4)		397 (24.3)	225 (20.3)	
2	179 (47.2)	186 (47.1)		935 (57.3)	693 (62.6)	
3 or more	19 (5.0)	18 (4.6)		299 (18.3)	189 (17.1)	
Comorbidity[a]			0.338			0.034
No	213 (56.2)	214 (54.2)		507 (33.5)	402 (38.8)	
One	113 (29.8)	135 (34.2)		557 (36.8)	360 (34.7)	
Two	46 (12.1)	36 (9.1)		288 (19.0)	186 (18.0)	
Three or more	7 (1.8)	10 (2.5)		160 (10.6)	88 (8.5)	
Tumor location[b]			0.841			<0.001
Upper third	5 (1.3)	3 (0.8)		94 (5.8)	193 (17.4)	
Middle third	110 (29.0)	122 (30.9)		559 (34.3)	265 (23.9)	
Lower third	251 (66.2)	257 (65.1)		972 (59.6)	642 (58.0)	
Combined	13 (3.4)	13 (3.3)		5 (0.3)	7 (0.6)	
T classification			0.795			<0.001
T1	40 (10.6)	35 (8.9)		426 (26.1)	112 (10.1)	
T2	103 (27.2)	114 (28.9)		521 (31.9)	228 (20.6)	
T3	126 (33.2)	137 (34.7)		444 (27.2)	384 (34.7)	
T4	110 (29.0)	109 (27.6)		240 (14.7)	383 (34.6)	
N classification			0.342			<0.001
N0	117 (30.9)	128 (32.4)		530 (32.5)	315 (28.5)	
N1	89 (23.5)	102 (25.8)		517 (31.7)	246 (22.2)	
N2	87 (23.0)	70 (17.7)		329 (20.2)	228 (20.6)	
N3	86 (22.7)	95 (24.1)		255 (15.6)	318 (28.7)	
Stage			0.222			<0.001
IB	80 (21.1)	75 (19.0)		576 (35.3)	187 (16.9)	
IIA/B	139 (36.7)	169 (42.8)		650 (39.9)	392 (35.4)	
IIIA/B/C	160 (42.2)	151 (38.2)		405 (24.8)	528 (47.7)	

KLASS-02, Korean Laparoscopic Gastrointestinal Surgery Study-02; KGCA, Korean Gastric Cancer Association; BMI, body mass index; ASA, American Society of Anesthesiologists. Missing data for each variable in the KGCA survey dataset: [a], 190 cases; [b], 1 case.

Discussion

In this study, the surgical outcomes of the laparoscopic approach for locally advanced gastric cancer were assessed at the national level and compared with those of a RCT. After adjusting for differences in patient and tumor characteristics, the laparoscopic approach had no effect on the occurrence of postoperative complications in the KGCA survey data. However, it was associated with a reduction in the overall complication rate in the KLASS-02

Table 2 Surgical outcomes from KLASS-02 and KGCA survey datasets

Variables	KLASS-02			KGCA survey		
	Laparoscopic (N=379) [n (%)]	Open (N=395) [n (%)]	P	Laparoscopic (N=1,631) [n (%)]	Open (N=1,107) [n (%)]	P
LN dissection[a]			0.500			<0.001
D1 or D1+	0 (0)	2 (0.5)		470 (28.9)	58 (5.2)	
D2	379 (100)	393 (99.5)		1,159 (71.1)	1,049 (94.8)	
Omentectomy[b]			0.057			<0.001
Partial	4 (1.1)	0 (0)		1,186 (77.4)	144 (13.6)	
Total	375 (98.9)	395 (100)		346 (22.6)	914 (86.4)	
Combined resection[c]			0.384			<0.001
No	368 (97.1)	379 (95.9)		1,512 (92.8)	957 (87.2)	
Yes	11 (2.9)	16 (4.1)		117 (7.2)	141 (12.8)	
Curability[d]			NA			0.002
R0	379 (100)	395 (100)		1,624 (99.6)	1,088 (98.6)	
R1/2	0 (0)	0 (0)		6 (0.4)	16 (1.4)	
No. of harvested LNs [median (IQR)]	43 (34–55)	45 (36–56)	0.158	39 (29–51)	38 (28–50)	0.251
Operating time (min) [median (IQR)][e]	225 (180–265)	160 (135–195)	<0.001	180 (141–223)	160 (127–204)	<0.001
Estimated blood loss (mL) [median (IQR)][f]	100 (50–180)	184 (100–297)	<0.001	50 (25–100)	100 (80–200)	<0.001
Hospital stay (d) [median (IQR)][g]	7 (6–8)	7 (7–9)	<0.001	7 (6–8)	8 (7–10)	<0.001

KLASS-02, Korean Laparoscopic Gastrointestinal Surgery Study-02; KGCA, Korean Gastric Cancer Association; LN, lymph node; IQR, interquartile range; NA, not available; Missing data for each variable in the KGCA survey dataset: [a], 2 cases; [b], 148 cases; [c], 11 cases; [d], 4 cases; [e], 145 cases; [f], 636 cases; [g], 4 cases.

trial. The benefits of the laparoscopic approach included a decrease in wound problems and an increase in harvested lymph nodes based on nationwide data, which were not observed in the KLASS-02 trial. A longer operation time, less estimated blood loss, and shorter hospital stays after the laparoscopic approach were still valid in the national data.

The significance of this study lies in its external validation in a RCT using national data. RCTs have provided high-level evidence, and the results have been adopted in treatment guidelines. The laparoscopic approach was only recommended for early gastric cancer a few years ago. However, the recommendation was expanded to advanced gastric cancer after the results of pivotal RCTs were published (6-8). Notably, each pivotal trial established a surgical quality control system before trial commencement, and only qualified surgeons participated in the trials. Compliance with D2 lymphadenectomy has been reported to be insufficient in many studies, and substantial experience in laparoscopic handling is required to achieve complete lymph node dissection (14-17). Therefore, a national verification of the safety and feasibility of the laparoscopic approach is necessary before generalizing the laparoscopic approach. A previous study on minimally invasive esophagectomy showed discrepancies in postoperative complications between a RCT and the national data (18).

This study revealed that the laparoscopic approach for locally advanced gastric cancer is safe and feasible at the national level as well as in a RCT. The laparoscopic approach did not increase overall postoperative complications or reduce wound complications. The benefits of the laparoscopic approach, such as reduced blood loss and rapid recovery, were also observed in national data (19). Therefore, the laparoscopic approach for locally advanced gastric cancer can generally be performed in the Republic of Korea.

The KGCA data demonstrated a significant reduction in wound problems in the laparoscopic group, which could be associated with the absence of mini-laparotomy wounds. In the KLASS-02 trial, most patients in the laparoscopic group underwent laparoscopy-assisted distal gastrectomy,

Table 3 Postoperative complications from KLASS-02 and KGCA survey datasets

Variables	KLASS-02			KGCA survey		
	Laparoscopic (N=379) [n (%)]	Open (N=395) [n (%)]	P	Laparoscopic (N=1,631) [n (%)]	Open (N=1,107) [n (%)]	P
Local complications						
Wound	15 (4.0)	25 (6.3)	0.136	13 (0.8)	38 (3.4)	<0.001
Fluid collection/abscess	10 (2.6)	20 (5.1)	0.081	36 (2.2)	32 (2.9)	0.259
Intra-abdominal bleeding	2 (0.5)	4 (1.0)	0.687	10 (0.6)	9 (0.8)	0.536
Intra-luminal bleeding	2 (0.5)	2 (0.5)	≥0.999	9 (0.6)	3 (0.3)	0.381
Ileus	8 (2.1)	10 (2.5)	0.698	30 (1.8)	32 (2.9)	0.070
Anastomosis stricture	0 (0)	1 (0.3)	≥0.999	16 (1.0)	4 (0.4)	0.062
Anastomosis leakage	7 (1.8)	5 (1.3)	0.513	24 (1.5)	22 (2.0)	0.303
Pancreas fistula	6 (1.6)	4 (1.0)	0.539	4 (0.2)	3 (0.3)	≥0.999
Systemic complications						
Pulmonary	12 (3.2)	16 (4.1)	0.510	36 (2.2)	27 (2.4)	0.691
Cardiac	0 (0)	0 (0)	NA	4 (0.2)	8 (0.7)	0.079
Cerebrovascular	0 (0)	0 (0)	NA	1 (0.1)	1 (0.1)	≥0.999
Others	15 (4.0)	21 (5.3)	0.370	53 (3.2)	72 (6.5)	<0.001
Overall complications	61 (16.1)	93 (23.5)	0.010	206 (12.6)	217 (19.6)	<0.001
Clavien-Dindo grade						
I	10 (2.6)	19 (4.8)	0.112	38 (2.3)	35 (3.2)	0.185
II	32 (8.4)	44 (11.1)	0.208	94 (5.8)	115 (10.4)	<0.001
IIIa	20 (5.3)	26 (6.6)	0.443	38 (2.3)	41 (3.7)	0.035
IIIb	4 (1.1)	10 (2.5)	0.123	25 (1.5)	16 (1.4)	0.853
IV	3 (0.8)	2 (0.5)	0.681	8 (0.5)	15 (1.4)	0.015
V	1 (0.3)	2 (0.5)	0.999	4 (0.2)	4 (0.4)	0.722
III or more	25 (6.6)	36 (9.1)	0.194	73 (4.5)	74 (6.7)	0.012

KLASS-02, Korean Laparoscopic Gastrointestinal Surgery Study-02; KGCA, Korean Gastric Cancer Association; NA, not available.

Table 4 Multivariable logistic regression analyses for effect of laparoscopic approach on surgical outcomes

Categorical outcomes	KLASS-02			KGCA survey		
	Adjusted OR	95% CI	P	Adjusted OR	95% CI	P
Overall complications	0.59	0.41, 0.86	0.005	0.79	0.59, 1.05	0.103
CD grade 3 or more	0.67	0.40, 1.13	0.131	1.22	0.78, 1.92	0.379
Wound	0.64	0.34, 1.19	0.156	0.19	0.08, 0.44	<0.001
Ileus	0.79	0.33, 1.89	0.592	1.26	0.66, 2.39	0.487
Cardiac	NA	NA	NA	0.48	0.13, 1.72	0.260

CD, Clavien-Dindo; OR, odds ratio; 95% CI, 95% confidence interval. Open group was set as reference for comparison with laparoscopic group. Adjusted OR: Corrected for: age, sex, body mass index, number of comorbidities, ASA score, pathological stage, extent of lymph node dissection, omentectomy, and combined resection; NA, not available.

and extra-corporeal anastomoses were performed via mini-laparotomy. However, in the KGCA data, a totally laparoscopic approach was used in 93.1% (1,519/1,631) of the patients in the laparoscopic group, and intra-corporeal anastomosis was performed without mini-laparotomy. Thus, the KGCA data showed that a totally laparoscopic approach with intra-corporeal anastomosis significantly reduced wound problems compared to the open approach.

Another benefit of the laparoscopic approach in the national data is the higher number of harvested lymph

Table 5 Multivariable linear regression analyses for effect of laparoscopic approach on surgical outcomes

Continuous outcomes	KLASS-02			KGCA survey		
	Adjusted β	95% CI	P	Adjusted β	95% CI	P
No. of harvested LNs	−1.23	−3.57, 1.12	0.305	4.39	2.61, 6.17	<0.001
Operating time	56.22	48.30, 64.14	<0.001	41.92	35.97, 47.87	<0.001
Estimated blood loss	−71.28	−105.78, −36.78	<0.001	−88.70	−106.48, −70.91	<0.001
Hospital stay	−1.35	−2.35, −0.35	0.008	−1.12	−1.82, −0.41	0.002

LN, lymph node; 95% CI, 95% confidential interval. Open group was set as reference for comparison with laparoscopic group. Adjusted β: Corrected for: age, sex, body mass index, number of comorbidities, ASA score, pathological stage, extent of lymph node dissection, omentectomy, and combined resection.

nodes. In the KLASS-02 data, the number of harvested lymph nodes showed no difference between the laparoscopic and open approaches, which was consistent with the CLASS trial (3). One contributing factor to the higher number of harvested lymph nodes may be fluorescence image-guided surgery, which was recently introduced and has rapidly expanded worldwide. Indocyanine green visualizes lymphatic channels and facilitates dedicated lymph node dissection. Many experienced surgeons may have performed fluorescence image-guided surgery and harvested more lymph nodes during laparoscopic gastrectomy. Late operation period of KGCA data might also be related to the higher number of harvested lymph nodes. As time passes, the overall experiences of the operators would have accumulated, and the laparoscopic surgical instruments would have further developed.

Understanding the characteristics of the two datasets and their corresponding analysis methods is crucial. In the KLASS-02 trial, all data were prospectively collected according to the protocol and monitored by an independent research organization. Data errors were reported regularly and corrected using query management. However, KGCA data were collected retrospectively at a specific time point, and meticulous data management could not be performed. Considerable data were missing, and sending queries, supplementing data, and corrections were limited to critical errors in KGCA data. Therefore, a direct comparison of surgical outcomes between the two datasets would be inappropriate. Instead, we compared the outcomes between the laparoscopic and open groups in each dataset because the data characteristics were consistent within each dataset.

Another notable finding of this study was the determination of the real-world status of laparoscopic procedures for locally advanced gastric cancer using the KGCA data. Since the introduction of laparoscopic procedures, surgeons have become familiar with partial omentectomy and D1+ lymph node dissection. Thus, the proportion of patients who underwent D2 lymph node dissection was approximately 70% in the laparoscopic group, and more than 90% of patients underwent D2 lymph node dissection in the open group. Additionally, total omentectomy was performed less often in the laparoscopic group than in the open group (22.6% *vs.* 86.4%), which may have narrowed in recent years as surgeons have become more experienced in laparoscopic procedures. However, several studies have shown no clinical advantage of omentectomy for advanced gastric cancer, and a RCT is currently underway to compare the long-term outcomes between omentectomy and non-omentectomy groups (20-23). In the future, compliance with omentectomy would be affected by the results of this ongoing study.

This study has some limitations. First, the inclusion criteria were not identical for the two datasets. In the KLASS-02 trial, patients were preoperatively enrolled, and their clinical stage and Eastern Cooperative Oncology Group (ECOG) performance status were used for screening. However, these were unavailable in the KGCA data, and pathological stage was used as an inclusion criterion. Although we attempted to match the patient conditions of the two groups as equally as possible, they were not identical. Second, this study showed only short-term outcomes and not long-term survival outcomes, because there were no long-term data in the KGCA dataset. However, the number of harvested lymph nodes has been demonstrated to be associated with long-term survival in previous studies and could be a surrogate marker of overall survival (24,25). In this study, the number of harvested lymph nodes was not significantly different between the two groups in the KGCA dataset, and long-term outcomes were expected to be similar. Third, the timing of surgery differed between the two datasets. In

KLASS-02, surgery was performed between 2011 and 2015, whereas it was performed in 2019 using KGCA data. Although we adjusted for the detailed surgical method in the multivariable analyses, the surgeons' experiences and advances in surgical skills could have induced some bias.

Conclusions

The laparoscopic approach for locally advanced gastric cancer had no negative effect on overall postoperative complications and was associated with a reduction in wound problems and an increase in harvested lymph nodes in real-world national practice. Other outcomes of the laparoscopic approach, including longer operation time, lower estimated blood loss, and shorter hospital stay, remain valid at the national level. Therefore, a laparoscopic approach to locally advanced gastric cancer can be implemented in the Republic of Korea.

Acknowledgements

This study was supported by a grant from the Patient-Centered Clinical Research Coordinating Center (PACEN) funded by the Ministry of Health & Welfare, Republic of Korea (No. RS-2020-KH095827).

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Eom BW, Han M, Yoon HM, Hyung WJ, Yang HK, Park YK, Lee HJ, An JY, Kim W, Kim HI, Kim HH, Ryu SW, Hur H, Kim MC, Kong SH, Cho GS, Kim JJ, Park DJ, Kim YW, Kim JW, Lee JH, Han SU, Ryu KW, the information committee of the Korean Gastric Cancer Association. National validation of laparoscopic approach for locally advanced gastric cancer: Comparison of a randomized controlled trial and real-world practice results. Chin J Cancer Res 2024;36(6):742-751. doi:10.21147/j.issn.1000-9604.2024.06.11

