J Gastric Cancer. 2024 Apr;24(2):210-219
https://doi.org/10.5230/jgc.2024.24.e16
pISSN 2093-582X·eISSN 2093-5641

Journal of Gastric Cancer

Original Article

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Real-world Nationwide Outcomes of Minimally Invasive Surgery for Advanced Gastric Cancer Based on Korean Gastric Cancer Association-Led Survey

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Received: Aug 24, 2023
Revised: Feb 04, 2024
Accepted: Mar 11, 2024
Published online: Mar 18, 2024

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ABSTRACT

Purpose: The study aimed to investigate real-world surgical outcomes of minimally invasive surgery (MIS) for advanced gastric cancer using Korean Gastric Cancer Association (KGCA)-led nationwide data.
Materials and Methods: A nationwide survey of patients who underwent surgical treatment for gastric cancer in 2019 was conducted by the KGCA. A total of 14,076 patients from 68 institutions underwent surgery, and 4,953 patients diagnosed with pathological stages IB-III gastric cancer were included. Among them, 1,689 patients who underwent MIS (MIS group) and 1,689 who underwent the open approach (open group) were matched using propensity score in a 1:1 ratio. Surgical outcomes were compared, and multivariate analysis was performed to identify the independent factors for overall morbidity.
Results: The MIS group had a lower proportion of D2 lymphadenectomy, total omentectomy, and combined resection. However, the number of harvested lymph nodes was higher in the MIS group. Better surgical outcomes, including less blood loss and shorter hospital stay, were observed in the MIS group, and the overall morbidity rate was significantly lower in the MIS group (17.5% vs. 21.9%, P=0.001). The mortality rates did not differ significantly between the 2 groups. In the multivariate analysis, the minimally invasive approach was a significant protective factor against overall morbidity (odds ratio, 0.799; P=0.006).
Conclusions: Based on the Korean nationwide data, MIS for stage IB-III gastric cancer had better short-term outcomes than the open approach, including lower rates of wound complications, intra-abdominal abscesses, and cardiac problems.

Keywords: Stomach neoplasm; Gastrectomy; Laparoscopy; Treatment outcome

INTRODUCTION

Minimally invasive approaches for the treatment of gastric cancer have become popular worldwide. The proportion of minimally invasive surgery (MIS) cases among all gastrectomy cases has increased to over 70% in a 2019 nationwide survey the Republic of Korea [1].

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Funding
This research was supported by a nationwide survey project of the information committee of the Korean Gastric Cancer Association (study number: KGCA2023IC10).

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
Conceptualization: P.S.H., E.B.W.; Data curation: P.S.H., E.B.W.; Formal analysis: P.S.H., H.M.; Investigation: P.S.H., E.B.W.; Methodology: P.S.H., E.B.W.; Project administration: Y.H.M., R.K.W., K.Y.W.; Resources: Information Committee of the Korean Gastric Cancer Association; Writing - original draft: P.S.H.; Writing - review & editing: H.M., R.K.W., E.B.W.

The surgical safety and oncological feasibility of laparoscopic gastrectomy for both early and advanced gastric cancer (AGC) were demonstrated in 2 multicenter randomized controlled trials by the Korean Laparoscopic Gastrointestinal Research Association (KLASS-01 and KLASS-02) [2-5]. In the KLASS-02 trial for AGC, the overall postoperative complication rate was significantly lower in the laparoscopic group than in the open surgery group (16.6% vs. 24.1%, P=0.003), and the long-term survival rates were comparable between the two groups [4,5]. These results have led to the acceptance of the laparoscopic approach as a treatment option for AGC, and laparoscopic gastrectomy is more commonly performed [6].

In the KLASS-02 trial, surgeon quality control and standardization of D2 lymphadenectomy were preceded [7,8]. Unedited videos of both laparoscopic and open gastrostomies were reviewed by peer reviewers, and only the surgeons who passed the assessment participated in the trial. Because of this surgeon quality control, there has been a concern that the favorable results of the KLASS-02 trial might not be generalizable to less-experienced surgeons. The authors reported that laparoscopic gastrectomy for AGC is safer than open gastrectomy when performed by a well-trained surgeon [4]. Therefore, the real-world outcomes of MIS for AGC performed by surgeons with varying levels of experience remain unclear.

This study aimed to evaluate real-world surgical outcomes of MIS for AGC using nationwide survey data. In this study, AGC indicates tumor requiring D2 lymph node dissection, because what makes surgery for AGC different from surgery for early gastric cancer is the extent of lymph node dissection and surgeon quality control was performed for D2 lymphadenectomy in the KLASS-02 trial. Previous gastric cancer treatment guidelines recommended D2 lymph node dissection for N+ or ≥T2 tumors and pathological stage IB-III tumors were included in this study [6,9].

MATERIALS AND METHODS

Data collection

In 2019, the Korean Gastric Cancer Association (KGCA) conducted a nationwide survey of patients who underwent surgery for gastric cancer. Sixty-eight institutions participated in this survey and data from 14,076 patients were collected. In this study, data from 4,953 patients diagnosed with pathological stages IB–III gastric cancer requiring D2 lymph node dissection were selected.

The Information Committee of KGCA reviewed all collected data and filtered for incorrect or missing data. Several queries regarding incorrect data were sent to representatives of each institution, and incorrect data were revised based on the responses. This study was approved by the Institutional Review Boards of National Cancer Center (approval no. NCC 2022-0357). The requirement for patient consent was waived because the researcher extracted anonymized data from the Korean Gastric Cancer Association.

Survey data

This nationwide survey consisted of 54 questions on patient demographics, clinicopathological characteristics, surgical methods, postoperative morbidity, and mortality.

The histological types were categorized according to the 2019 World Health Organization classification [10]. Staging was performed according to the eighth edition of the American

Joint Committee on Cancer tumor-node-metastasis (TNM) classification [11]. Post-operative complications were defined as events that occurred within 30 days of surgery. Mortality included death within 30 days after surgery and death during hospitalization, regardless of the time. The incidence of local and systemic complications was assessed, and the severity of complications was graded using the Clavien-Dindo classification system [12].

Statistical analysis

Continuous variables are presented as means with standard deviations or medians with interquartile ranges, and categorical variables are presented as numbers with proportions. Statistical differences were analyzed using the Student's t-test or Wilcoxon rank-sum test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables.

The baseline clinicopathological characteristics were imbalanced between patients who underwent MIS and those who underwent open gastrectomy. Propensity score matching (PSM) was performed using a multivariate logistic regression model. Potential confounding covariates were age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, pathological TNM stage, and extent of gastric resection. A 1:1 nearest-neighbor matching was used with a caliper of 0.05 without replacement. A standardized mean difference of 10% or less was considered to indicate a well-balanced result.

Univariate and multivariate logistic regression analyses were performed to determine risk factors for postoperative complications. Significant variables (P<0.05) in the univariate analysis were included in the multivariate analysis, and the results of the logistic regression model were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was set at P<0.05. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R software version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) for the PSM.

RESULTS

Clinicopathological characteristics of all included patients and matched cohorts

Among the 4,953 patients diagnosed with pathological stages IB–III gastric cancer, 2,719 underwent minimally invasive gastrectomy (2,503 laparoscopic and 216 robotic approaches), and 2,234 underwent open gastrectomy (**Fig. 1**). Most baseline clinicopathological characteristics, except for age, were significantly different between the two groups (**Table 1**). After PSM, each group included 1,689 patients. The MIS group comprised 1,564 laparoscopic and 125 robotic cases. Age, sex, BMI, ASA, extent of gastric resection, and pathological TNM stage were balanced. However, the MIS group had more comorbidities, a lower proportion of neoadjuvant chemotherapy, and fewer tumors in the upper third of the stomach.

Operative outcomes

The proportions of D2 lymphadenectomy, total omentectomy, and combined resection were significantly lower in the MIS group than those in the open group (76.0% vs. 94.1%, 30.8% vs. 86.3%, and 8.2% vs. 16.4%, respectively; all P<0.001) (**Table 2**). However, the number of harvested lymph nodes was significantly higher in the MIS group than in the open surgery group (41 vs. 38, P<0.001). The MIS group had a longer operating time (193 vs. 167 minutes, P<0.001), lesser blood loss, and shorter hospital stay than the open group (all P<0.001).

https://doi.org/10.5230/jgc.2024.24.e16

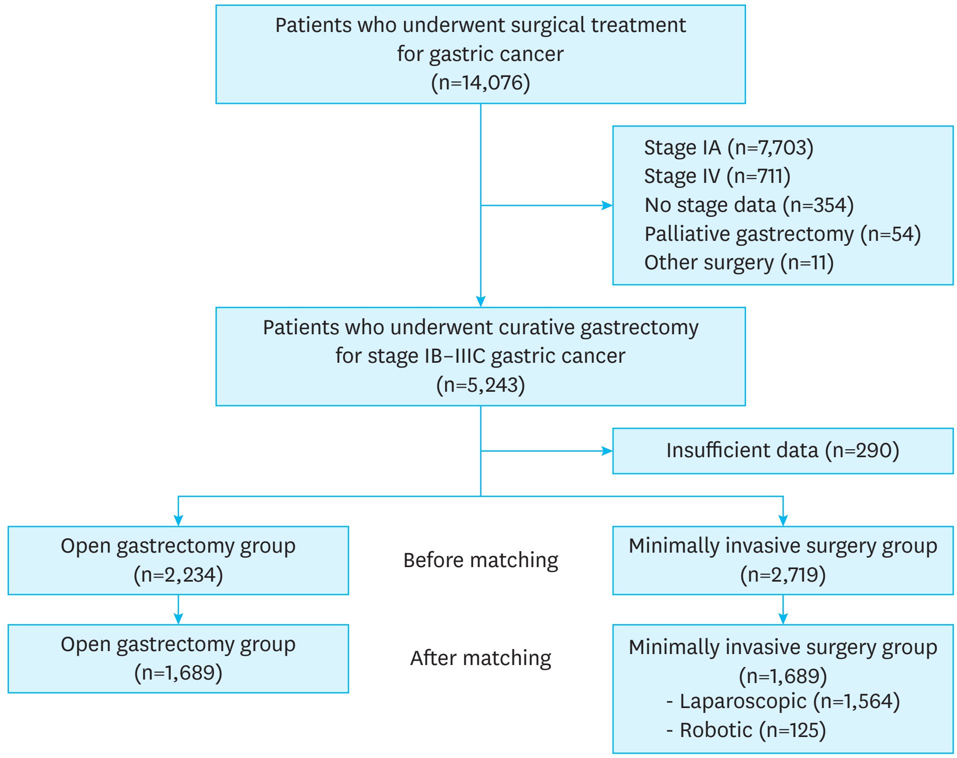

Fig. 1. Flowchart of the study.

Postoperative complications

The 30-day overall complication rate was significantly lower in the MIS group than in the open surgery group (17.5% vs. 21.9%, P=0.001) (**Table 3**). In terms of local complications, wound complications, and intra-abdominal abscesses occurred less frequently in the MIS group (1.2% vs. 3.7% and 2.5% vs. 4.2%, P<0.001 and P=0.006). In contrast, the anastomotic stricture rate was higher in the MIS group than in the open surgery group (1.4% vs. 0.4%, P=0.001). With regard to systemic complications, the incidence of cardiac problems was lower in the MIS group than in the open group (0.2% vs. 0.7%, P=0.045). According to the Clavien-Dindo classification, the incidences of grade II, IIIA, and IV complications were significantly lower in the MIS group than in the open surgery group (8.7% vs. 11.0%, 3.7% vs. 5.1%, and 0.9% vs. 1.7%, P=0.028, P=0.044, and P=0.046, respectively). The 30-day postoperative mortality rate was 1.3% (22/1,689) in the MIS group and 1.5% (26/1,689) in the open surgery group, with no significant difference (P=0.561).

Risk factors for the overall complication

In the multivariate logistic regression analysis, the minimally invasive approach was a significant protective factor against overall complications (OR, 0.799; P=0.006). Age, sex, ASA classification, pathological TNM stage, extent of gastric resection, and combined resection were independent factors associated with overall complications (all P<0.05) (**Table 4**).

DISCUSSION

The present study evaluated the surgical outcomes of MIS for IB-III gastric cancer using the KGCA nationwide survey data. According to the annual report on gastric cancer adequacy

Table 1. Clinicopathological characteristics of the patients before and after propensity score matching

Variable	Before matching			After matching		
	MIS (n=2,719)	Open (n=2,234)	P-value	MIS (n=1,689)	Open (n=1,689)	P-value
Age (yr)	63.8±12.5	64.3±11.8	0.130	64.5±12.3	64.2±11.9	0.466
Sex			<0.001			0.825
Male	1,777 (65.4)	1,573 (70.4)		1,142 (67.6)	1,148 (68.0)	
Female	942 (34.6)	661 (29.6)		547 (32.4)	541 (68.0)	
BMI(kg/m^2)*	24.1±12.5	23.4±3.5	<0.001	23.7±3.2	23.6±3.5	0.527
ASA score†			0.021			0.784
1	591 (22.3)	425 (19.3)		326 (19.3)	342 (20.2)	
2	1,541 (58.2)	1,370 (62.2)		1,015 (60.1)	1,020 (60.4)	
3	499 (18.8)	389 (17.7)		336 (19.9)	315 (18.7)	
4 or 5	19 (0.7)	19 (0.9)		12 (0.7)	12 (0.7)	
Comorbidity‡			<0.001			0.001
No	789 (31.4)	779 (37.4)		489 (31.3)	583 (36.9)	
One	976 (38.9)	693 (33.3)		602 (38.9)	529 (33.5)	
Two	480 (19.1)	417 (20.0)		292 (18.7)	317 (20.1)	
Three or more	267 (10.6)	193 (9.3)		178 (11.4)	150 (9.5)	
Neoadjuvant chemotherapy§			<0.001			<0.001
No	2,645 (97.3)	2,078 (93.0)		1,639 (97.0)	1,564 (92.6)	
Yes	73 (2.6)	156 (7.0)		50 (3.0)	125 (7.4)	
Tumor location‖			<0.001			<0.001
Upper third	547 (20.1)	691 (31.0)		414 (24.5)	469 (27.8)	
Middle third	869 (32.0)	596 (26.7)		522 (30.9)	425 (25.2)	
Lower third	1,276 (46.9)	840 (37.7)		729 (43.2)	736 (43.6)	
Combined	26 (1.0)	103 (4.6)		24 (1.4)	58 (3.4)	
Extent of gastric resection			<0.001			0.970
DG/PG/PPG	2,148 (79.0)	1,249 (55.9)		1,159 (68.6)	1,158 (68.6)	
TG	571 (21.0)	985 (44.1)		530 (31.4)	531 (31.4)	
Pathological T category			<0.001			<0.001
T1	597 (22.0)	168 (7.5)		237 (14.0)	156 (9.2)	
T2	839 (30.9)	391 (17.5)		426 (25.2)	363 (21.5)	
T3	789 (29.0)	802 (35.9)		604 (35.8)	609 (36.1)	
T4	494 (18.2)	873 (39.1)		422 (25.0)	561 (33.2)	
Pathological N category			<0.001			0.014
N0	954 (35.1)	658 (29.5)		485 (28.7)	563 (33.3)	
N1	800 (29.4)	474 (21.2)		428 (25.3)	386 (22.9)	
N2	494 (18.2)	435 (19.5)		354 (21.0)	312 (18.5)	
N3	471 (17.3)	667 (29.9)		422 (25.0)	428 (25.3)	
TNM stage			<0.001			0.512
I	893 (32.8)	314 (14.1)		329 (19.5)	304 (18.0)	
II	1,087 (40.0)	805 (36.0)		670 (39.7)	673 (39.8)	
III	739 (27.2)	1,115 (49.9)		690 (40.9)	712 (42.2)	

Values are presented as number (%) or mean ± standard deviation.
MIS = minimally invasive surgery; BMI = body mass index; ASA = American Society of Anesthesiologists; DG = distal gastrectomy; PG = proximal gastrectomy; PPG = pylorus-preserving gastrectomy; TG = total gastrectomy; TNM = tumor-node-metastasis.
Missing data for each variable before propensity score matching: *3 cases; †100 cases; ‡359 cases; §1 case; ‖5 cases.

evaluation by the Korean Health Insurance Review and Assessment Service, the number of patients surgically treated for gastric cancer was 14,451 in 2019 [13]. The KGCA nationwide survey data included 14,076 patients, accounting for 97.4% of all surgically treated cases in Korea. Thus, the results of this study can be considered to represent real-world outcomes in South Korea. In this study, the MIS group demonstrated better results, including less blood loss, shorter hospital stays, and lower overall morbidity rates than the open group. Postoperative mortality was comparable between the two groups, and multivariate analysis identified the minimally invasive approach as a significant protective factor against overall morbidity. In terms of short-term outcomes, the minimally invasive approach had greater benefits than the open approach for AGC.

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Table 2. Surgical outcomes in propensity score-matched patients

Surgical outcome	MIS (n=1,689) (%)	Open (n=1,689) (%)	P-value
Lymph node dissection*			<0.001
≤D1	21 (1.2)	19 (1.1)	
D1+	384 (22.8)	81 (4.8)	
D2	1,280 (76.0)	1,589 (94.1)	
Omentectomy†			<0.001
Total	487 (30.8)	1,388 (86.3)	
Partial	1,094 (69.2)	221 (13.7)	
Combined resection‡			<0.001
No	1,548 (91.8)	1,398 (83.6)	
Yes	138 (8.2)	274 (16.4)	
Radicality§			0.043
R0	1,673 (99.2)	1,657 (98.3)	
R1	11 (0.7)	24 (1.4)	
R2	2 (0.1)	5 (0.3)	
Number of harvested LNs‖	41 (30–54)	38 (29–51)	<0.001
Operating time(min)¶	193 (145–243)	167 (130–209)	<0.001
Estimated blood loss(mL)**	50 (30–100)	100 (80–250)	<0.001
Length of hospital stay (days)††	7 (6–10)	8 (7–11)	<0.001

Values are presented as number (%) or median (interquartile range).
MIS = minimally invasive surgery; LN=lymph node.
Missing data for each variable: *4 cases; †188 cases; ‡20 cases; §6 cases; ¶1 case; ¶1 case; **804 cases; ††8 cases.

Table 3. Postoperative complications in propensity score-matched patients

Complication	MIS (n=1,689)	Open (n=1,689)	P-value
Overall complication			0.001
Absence	1,394 (82.5)	1,319 (78.1)	
Presence	295 (17.5)	370 (21.9)	
Local complication			
Wound complication	20 (1.2)	63 (3.7)	<0.001
Fluid collection	10 (0.6)	3 (0.2)	0.052
Intra-abdominal abscess	42 (2.5)	71 (4.2)	0.006
Intra-abdominal bleeding	12 (0.7)	16 (0.9)	0.448
Intra-luminal bleeding	9 (0.5)	3 (0.2)	0.083
Ileus	40 (2.4)	44 (2.6)	0.659
Anastomotic stricture	24 (1.4)	6 (0.4)	0.001
Anastomotic leakage	45 (2.7)	39 (2.3)	0.507
Pancreatic fistula	7 (0.4)	9 (0.5)	0.616
Systemic complication			
Pulmonary	63 (3.7)	58 (3.4)	0.643
Cardiac	4 (0.2)	12 (0.7)	0.045
Cerebrovascular	1 (0.1)	1 (0.1)	1.000
Others	68 (4.0)	109 (6.5)	0.002
Clavien-Dindo grade			
I	43 (2.5)	54 (3.2)	0.257
II	147 (8.7)	185 (11.0)	0.028
IIIA	62 (3.7)	86 (5.1)	0.044
IIIB	28 (1.7)	25 (1.5)	0.678
IV	15 (0.9)	28 (1.7)	0.046
V	6 (0.4)	6 (0.4)	1.000
Mortality	22 (1.3)	26 (1.5)	0.561

MIS = minimally invasive surgery.

A notable finding of this study was that the overall morbidity of the nationwide survey data was not different from that of a multicenter trial (KLASS-02 trial) [4]. The overall morbidity of the minimally invasive approach was lower than that of open surgery in both the nationwide survey and the KLASS-02 trial. Lower estimated blood loss and shorter lengths of hospital stay in the MIS group were also common findings in both datasets. Estimated blood loss is an important indicator of the quality of surgery and surgeon proficiency. The length

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Table 4. Multivariate analysis for morbidity

Variable	OR (95% CI)	P-value
Age	1.016 (1.009–1.023)	<0.001
Sex		0.003
Male	1 (ref)	
Female	0.779 (0.660–0.919)	
ASA		<0.001
1	1 (ref)	
2	0.989 (0.805–1.215)	
≥3	1.474 (1.150–1.888)	
TNM stage		0.001
I	1 (ref)	
II	0.994 (0.809–1.223)	
III	1.340 (1.092–1.644)	
Surgical approach		0.006
Open	1 (ref)	
MIS	0.799 (0.681–0.936)	
Extent of gastric resection		<0.001
DG/PG/PPG	1 (ref)	
TG	1.560 (1.331–1.829)	
Combined resection		0.001
No	1 (ref)	
Yes	1.407 (1.144–1.729)	

OR = odds ratio; CI = confidence interval; ASA = American Society of Anesthesiologists; MIS = minimally invasive surgery; DG = distal gastrectomy; PG = proximal gastrectomy; PPG = pylorus preserving gastrectomy; TG = total gastrectomy.

of hospital stay is directly associated with the occurrence of complications. Therefore, in this study, the advantages of MIS were demonstrated using nationwide data from 68 institutions across the country, including relatively inexperienced surgeons, and a multicenter clinical trial research group composed exclusively of well-trained surgeons.

Furthermore, the nationwide survey data showed better MIS outcomes for specific complications, such as wound problems, fluid collection, and cardiac complications. Fewer wound complications are a clear advantage of the minimally invasive approach, and fluid collection is closely related to MIS. The lower incidence of local complications in the MIS group may have resulted in shorter hospital stays.

Another notable finding of this study was that the MIS group had a higher number of harvested lymph nodes than the open group (41 vs. 38). Previous multicenter trials showed no difference in the number of harvested lymph nodes between the two groups [4,14,15]. However, in the present study, the number of harvested lymph nodes was higher in the MIS group than in the open group, although the proportion of D2 lymphadenectomies was lower in the MIS group. This may be related to the magnified view of the laparoscope, fluorescence image-guided lymph node dissection in some MIS cases, and the fact that more experienced surgeons perform MIS [16]. Moreover, the number of harvested lymph nodes is linked to the quality of lymphadenectomy and curability. Thus, favorable long-term outcomes were expected in the MIS group [17-19]. Further research is required to confirm the long-term oncological safety of MIS in patients with AGC.

The MIS group had lower proportions of D2 lymphadenectomies, total omentectomies, and combined resections of other organs than the open group. D2 lymphadenectomy is a standard procedure for stage IB-III tumors [6,9,20], and 94.1% of the patients underwent D2 lymphadenectomy in the open group. However, it was performed in 76% of patients in the MIS group, which may be associated with a lower rate of morbidity [21-23]. Intra-abdominal abscesses that may occur after deep lymph node dissection developed less frequently in the MIS group than in the open group. Total omentectomy is recommended for cT3-T4 gastric cancer [9], and 86.3% of the patients in the open group underwent total omentectomy. However, only 30.8% of the patients in the MIS group underwent total omentectomy. The surgeons were likely familiar with D1+ lymphadenectomy and partial omentectomy in the laparoscopic setting and may have performed these procedures in some early-stage cases. Laparoscopic total omentectomy requires considerable time and effort and some surgeons may be reluctant to perform the procedure. In addition, combined resection of multiple organs is known to be associated with complications after gastrectomy [24-26], and the lower rate of combined resection in the MIS group might have contributed to the lower morbidity compared to that in the open group.

Another unfavorable outcome of minimally invasive gastrectomy was the high incidence of anastomotic strictures. This result differs from those of previous multicenter trials that showed no significant differences in anastomotic strictures between the two groups [4,14]. Several factors may have contributed to this result, such as the anastomotic approach, method, and surgeon's experience. All patients underwent extracorporeal anastomosis in a Japanese trial [27], and in most cases in the KLASS-02 trial [4]. However, intracorporeal anastomosis was primarily performed in this nationwide survey (**Supplementary Tables 1** and **2**). Although very few cases of total gastrectomy have been included in previous multicenter trials [4,14,28], 31.4% of the patients in this study underwent total gastrectomy. All surgeons were qualified in previous trials; however, their initial experience with intracorporeal anastomosis may have been included in this study.

There was no significant difference in the postoperative mortality rates between the two groups. However, the overall mortality rate in this study was somewhat higher than those reported in previous multicenter trials (1.4% vs. <1% in this study and previous multicenter trials, respectively) [4,14,28]. This nationwide survey included not only deaths within 30 days after surgery but also deaths during hospitalization, regardless of the time of mortality. It was not clear whether death during hospitalization was related to gastrectomy, which could have resulted in an overestimation of mortality. In addition, the greater number of total gastrectomy cases, inexperienced surgeons, a relatively disorganized intensive care system, and lack of critical care personnel in the small hospitals included in this survey might be associated with a higher mortality rate [29,30].

The present study had several limitations. First, data were retrospectively collected, and considerable missing data were observed, particularly for comorbidities, omentectomy, and estimated blood loss. This may have led to biased results. As it was not practical to send queries for all missing data, the results of this study may differ from the actual results. Second, there were differences in patient selection and surgical methods according to surgeons and institutions. The surgical approach and detailed surgical method were decided by the surgeon's criteria and the institution's practice, which are characteristic of real-world data. Third, the definition and grading of each complication may differ depending on the surgeon's opinion or institutional practice. Unlike prospective studies, retrospective studies do not have a predefined protocol, and the interpretation of complications is based entirely on the surgeon's decision. Finally, this study did not assess the long-term outcomes. Oncological outcomes should also be confirmed before the acceptance of a minimally invasive approach in practice. Therefore, further studies are needed to assess survival outcomes such as overall survival and recurrence rates.

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In conclusion, based on the nationwide survey data, MIS for stage IB-III gastric cancer had better short-term outcomes than the open approach. In particular, MIS was associated with lower rates of wound complications, intraabdominal abscesses, and cardiac complications. Therefore, MIS for AGC, including different patient selection and surgical methods, is acceptable for short-term outcomes in most hospitals in Korea that perform gastrectomies. Further studies are needed to verify the long-term oncological outcomes of MIS for AGC in a nationwide practice.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Details of extent of gastric resection and anastomotic method after propensity score matching

Supplementary Table 2

Comparison of surgical details according to anastomotic stricture

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