

Comparison of minimally invasive surgery with open surgery for remnant gastric cancer: A Multi-institutional Cohort Study

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Synopsis

We conducted a multi-institutional cohort study and compared minimally invasive surgery (MIS) with open surgery for remnant gastric cancer (RGC). This study demonstrated that the MIS for RGC had favorable short- and long-term outcomes compared to open surgery.

Abstract

Background

Despite growing evidence of the effectiveness of minimally invasive surgery (MIS) for primary gastric cancer, MIS for remnant gastric cancer (RGC) remains controversial due to the rarity of the disease. This study aimed to evaluate the surgical and oncological outcomes of MIS for radical resection of RGC.

Methods

Patients with RGC who underwent surgery between 2005 and 2020 at 17 institutions were included and a propensity score (PS) matching analysis was performed to compare the short- and long-term outcomes of MIS with open surgery.

Results

A total of 327 patients were included in this study and 186 patients were analyzed after matching. The risk ratios for overall and severe complications were 0.76 (95% confidence interval [CI]: 0.45, 1.27) and 0.65 (95% CI: 0.32, 1.29), respectively. The MIS group had significantly less blood loss (mean difference [MD], -409 mL; 95% CI: -538, -281) and a shorter hospital stay (MD, -6.5 days; 95% CI: -13.1, 0.1) than the open surgery group. The median follow-up duration of this cohort was 4.6 years, and the 3-year overall survival were 77.9% and 76.2% in the MIS and open surgery groups, respectively (hazard ratio [HR], 0.78; 95% CI: 0.45, 1.36). The 3-year relapse-free survival were 71.9% and 62.2% in the MIS and open surgery groups, respectively (HR, 0.71; 95% CI: 0.44, 1.16).

Conclusions

MIS for RGC showed favorable short- and long-term outcomes compared to open surgery. MIS is a promising option for radical surgery for RGC.

Keywords

remnant gastric cancer, minimally invasive surgery, laparoscopic gastrectomy, robotic gastrectomy

INTRODUCTION

Gastric cancer is one of the most common malignancies in the world.¹ On the other hand, remnant gastric cancer (RGC) is rare and accounts for only 1-8% of all gastric cancers,^{2,3} which is defined as cancer arising in the remnant stomach after initial gastrectomy regardless of the previous disease or surgical procedure.^{4,5} Owing to the early detection of primary gastric cancer and its intensive follow-up, the proportion of resectable RGC cases is increasing nowadays.^{2,6}

Surgical resection is the main treatment strategy for RGC. Compared with open surgery, minimally invasive surgery (MIS) such as laparoscopic and robotic resection for primary gastric cancer is reported to have several short-term advantages, including less blood loss, earlier recovery of bowel function, shorter hospital stay, and better cosmetic results with non-inferior oncological outcomes.⁷⁻¹² However, it is unclear whether the advantages of MIS in primary gastrectomy are present even in gastrectomy for RGC. MIS for RGC demands advanced techniques, because RGC resection has peculiar characteristics such as adhesion and anatomical changes due to previous gastrectomy and its subsequent reconstruction. On the other hand, a magnified view of the MIS may be useful for identifying the optimal surgical plane. Thus, the advantages and safety of MIS for RGC need to be assessed. To our knowledge, only single-center studies with small number of patients have reported the short- and long-term outcomes of MIS for RGC.¹³⁻¹⁶ In this study, we investigated the advantage of MIS for RGC using a multi-institutional cohort with a substantial number of patients.

METHODS

Study design and patients

We conducted a retrospective cohort study of patients who underwent surgical resection for RGC with curative intent between 2005 and 2020 at 17 institutions included in the Kyoto Esophageal and Gastric Surgery Study Group (KEGG). The study protocol was approved by the institutional review board of Kyoto University (R2765) and each participating hospital. The study design and preparation of our original manuscript were performed according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

reporting guideline.

Patients who had undergone surgical resection with curative intent for histologically proven adenocarcinoma in the remnant stomach were selected for this study, and patients with distant metastasis and those who required palliative resection were excluded. Treatment intent was based on the judgment of the local multidisciplinary team.

Study outcomes

The primary outcome was overall postoperative complications which were defined as the Clavien–Dindo classification¹⁷ grade II or higher. Secondary outcomes were severe (grade III or higher) postoperative complications, 3-year overall survival (OS), and 3-year relapse-free survival (RFS). OS was calculated as the time from the date of operation to death due to any cause or to the latest date of follow-up. RFS was calculated as the time from the date of operation to disease relapse, to death due to any cause, or to the latest date of follow-up. Patients were regularly followed up every 3 to 6 months for the first 5 years. Disease relapse was diagnosed using computed tomography (CT), magnetic resonance imaging, or positron emission tomography with CT. In addition, we evaluated the surgical outcomes, including operative time, blood loss, number of lymph nodes retrieved, time to first solid food intake, and length of postoperative hospital stay.

Statistical analysis

Descriptive statistics are reported as median (interquartile range [IQR]) for continuous variables, while categorical variables are reported as absolute numbers with percentages. All tests were 2-sided, and statistical significance was set at $P < 0.05$.

Propensity score (PS) matching is a method used to minimize the treatment selection bias when comparing two procedures.¹⁸ In our analysis, propensity scores were developed accounting for all potential confounding and prognostic factors which reflect previous research findings and our clinical knowledge.¹⁹ Accordingly, individual propensity scores were estimated through a logistic regression model based on the following 16 variables: age (≤ 75 year, > 75 year), sex, body mass index (BMI: $\leq$ first quartile [18.7 kg/m^2], $>$ first quartile

and <third quartile [22.6 kg/m²], ≥third quartile), American Society of Anesthesiologists-Physical Status (ASA-PS) (≤2, ≥3), history of small bowel obstruction, past smoking history, medication for diabetes mellitus, anti-thrombotic therapy, oral steroid use, the reason for previous gastrectomy (malignant, benign disease), the approach of previous gastrectomy (open, MIS), reconstruction used in previous gastrectomy (distal gastrectomy with Billroth-I reconstruction, distal gastrectomy with Billroth-II or Roux-en-Y reconstruction, non-distal gastrectomy), histology (differentiated, undifferentiated), clinical T classification (≤T1b, ≥T2), clinical node involvement (negative, positive), and a hospital volume. Using the third quartile (>70 and ≤70 cases, Supplemental Figure 1), we categorized the institutions into two groups, high-volume hospitals (HVHs) and non-HVHs, based on the annual caseload of gastrectomy in each institution. All patients in the MIS group were then paired 1:1 on propensity scores using greedy nearest-neighbor (NN) matching algorithm without replacement.^{20,21} A standard caliper size of 0.2 standard deviation of PS was used. Absolute Standardized differences (ASDs) of all covariates were calculated before and after matching, and an ASD of ≥0.1 was considered indicative of imbalance.²²

All outcomes were evaluated in the matched samples. For the primary outcome, we calculated the risk differences (RDs) and the relative risks of postoperative complications. The risk ratios (RRs) were calculated using the modified Poisson regression model with robust variance because we presumed that the incidence of postoperative complication would be more than 10% and odds ratios overestimate the risk ratio for common outcomes.^{23,24} In addition, we explored several secondary outcomes. For surgical outcomes, mean differences (MDs) of continuous variables were calculated using the generalized linear model with Gaussian distribution, and categorical variables were compared using the Fisher's exact test. Survival probability was estimated using the Kaplan–Meier method and compared using the log-rank test. The hazard ratios (HRs) of survival outcomes were calculated using the Cox proportional hazard regression model. All statistical analyses were performed with R version 3.6.2. [“MICE”, “MatchIt” and “MatchThem” packages, R Core Team (2019), Vienna, Austria].

Sensitivity analyses

We additionally performed full matching algorithm because the NN matching algorithm without replacement effectively reduces the sample size due to removing unmatched patients from the analysis.²⁵ Moreover, we used multiple imputation (MI) technique to account for the missing values.²⁶ Missing data were treated as missing at random. In summary, we performed NN matching algorithm in patients with complete data as the main analysis, and performed additional NN and full matching analysis with or without MI. In MI, 30 multiply imputed datasets were generated and matching analyses were performed for each dataset, and finally the treatment effect estimates were pooled.

We performed further NN matching algorithm using three different cohort definitions. First, we excluded patients who underwent combined organ resection. Second, we excluded patients who underwent surgery before 2009. Third, MIS cases with intraoperative conversion to the open approach were classified into the open group.

RESULTS

Patient characteristics, previous gastrectomy, and clinical findings

A total of 369 patients underwent gastrectomy for RGC during the study period, and all of them were Asian races. Board-certified surgeons participated in every operation as the main operators or leading assistants. Patients with cStage IV cancer (n=31), palliative resection (n=6), or double cancer (n=5) were excluded; finally, 327 patients were included in the study. MIS and open surgery were performed in 132 (40.4%) and 195 (59.6 %) patients, respectively (Figure 1). After PS matching, 186 patients were included in the main analysis. All ASDs were <0.1 after matching, indicating that all covariates were well balanced (Table 1). Details of unmatched population after the main analysis (NN matching in patients with complete data) are described in Supplemental Table1.

Operative procedures and pathological findings

In the matched cohort, 86 patients (92.5%) in the MIS group and 80 (86.0%) in the open surgery group underwent total gastrectomy. Subtotal gastrectomy was performed only in patients with early-stage cancers (seven patients in the MIS group and 13 patients in the open surgery group). Thirteen patients (14.0%) in the MIS group converted to the open approach during surgery. Combined resection of the gallbladder (5.3% in the MIS group and 32.3% in the open surgery group) and spleen (4.3% in the MIS group and 14.0% in the open surgery group) was more often performed in the open surgery group. For esophagojejunal anastomosis, 69.9% of the MIS group employed the functional end-to-end anastomosis (FEEA)²⁷ or overlap method²⁸, whereas 78.5% of the open surgery group used a circular stapler. The pathological stages I, II, and III were present in 54 (58.1%), 26 (27.9%), and 13 (14.0%) patients in the MIS group and 58 (62.4%), 20 (21.5%), and 15 (16.1%) patients in the open surgery group, respectively (Table 2). Adjuvant chemotherapy was administered to 20.4% of patients in the MIS group and 10.8% of those in the open surgery group.

Surgical outcomes

After matching, the MIS group had significantly less blood loss than the open surgery group (MD [95% CI], -409 mL [-538, -281]; $P<0.001$), while the operative time was longer (MD [95% CI], 62 min [35, 91]; $P<0.001$). The number of retrieved lymph nodes (MD [95% CI], 4.0 [0.3, 7.7]; $P=0.038$) was larger in the MIS group. The time to first food intake (MD [95% CI], -3.0 [-6.2, 0.2]; $P=0.071$) and postoperative hospital stay (MD [95% CI], -6.5 days [-13.1, 0.1]; $P=0.055$) were shorter in the MIS group, although not significant (Table 3).

Postoperative complications

In the matched cohort, the overall complications occurred in 28.0% of the MIS group and 36.6% of the open surgery group (RD [95% CI], -8.6% [-22.1, 4.8]; $P=0.192$, RR [95% CI], 0.76 [0.45, 1.27]; $P=0.198$). Severe complications developed in 14.0% of patients in the MIS group and 21.5% of those in the open surgery group (RD [95% CI], -7.5% [-18.5, 3.5]; $P=0.192$, RR [95% CI], 0.65 [0.32, 1.29]; $P=0.199$). Esophagojejunostomy

leakage occurred in 8.6% of the patients in both groups. The rate of overall intra-abdominal infection (IAI), defined as the development of pancreatic fistula and intra-abdominal abscess other than that from anastomotic leakage, was similar in both groups (8.6% in the MIS group and 9.7% in the open surgery group); however, the rate of severe IAI was higher in the open surgery group (1.1% in the MIS group and 6.5% in the open surgery group). Postoperative bleeding occurred only in the open surgery group (6.5%). Two patients in the open surgery group died during their hospital stay due to bleeding and stroke (Table 4).

Long-term prognosis

The median follow-up time was 4.6 years in the total cohort: 3.7 years in the MIS group and 5.2 years in the open surgery group. In the matched cohort, the 3-year OS were 77.9% and 76.2% in the MIS and open surgery groups, respectively (HR [95% CI], 0.78 [0.45, 1.36]; P=0.400), while the 3-year RFS were 71.9% in the MIS group and 62.2% in the open surgery group (HR [95% CI], 0.71 [0.44, 1.16]; P=0.200) (Figure 2). In patients with recurrences, locoregional recurrence occurred in 3.2% (3/93) of the MIS group and 4.3% (4/93) of the open surgery group, which were similar. No differences were observed in the other patterns of recurrence between the groups (Table 5).

Sensitivity analyses

Patient characteristics, surgical outcomes, and details of postoperative complications are described in Supplemental Table 2, 3, and 4. RR for postoperative complications and HR for long-term prognosis were all consistent with the main results (Supplemental Figure 2, 3).

DISCUSSION

Although the number of gastrectomy is decreasing nowadays,²⁹ the proportion of RGC resection in gastrectomy is increasing.^{2,6} MIS for primary gastric cancer has been proven to be feasible and widely

employed in general practice.³⁰⁻³² However, there is little evidence of the effectiveness of MIS for RGC due to the rarity of the disease. In RGC resection, the remnant stomach often adheres densely to the lateral segment of the liver, and the anastomosis sites may strongly adhere to the pancreatic head after Billroth I reconstruction. In addition, it is often difficult to discriminate between adhesion and tumor invasion in patients with advanced cancer. Therefore, MIS for RGC is technically challenging. However, fewer adhesions can be expected in recent RGC cases because the use of MIS for primary gastrectomy has been increasing, and a magnified view of the MIS may be helpful in resection. To the best of our knowledge, this is the first multi-institutional study with the largest cohort to evaluate the feasibility and oncological safety of MIS for RGC using a statistical method to adjust for confounding factors.

The incidence of postoperative complications in the MIS group in this study (overall: 28.0%, severe: 14.0%) was consistent with previous reports (overall: 38.2%, severe: 14.5%),^{13,14} but was higher than that of laparoscopic total gastrectomy for primary gastric cancer reported in previous literature (overall: 17.8–27.7%, severe: 7.2–8.6%).³³⁻³⁵ In the present study, there was a trend in favor of MIS both in postoperative complications and long-term outcomes. Moreover, intraoperative blood loss was significantly less in the MIS group, and the time to first food intake and postoperative hospital stay were also better in the MIS group, although they were not statistically significant. Similar to surgery for primary gastric cancer, patients with RGC could benefit from MIS in terms of postoperative recovery. Thus, MIS is a favorable option for RGC.

The rate of esophagojejunostomy leakage found in this study (overall: 8.6% in both groups) was consistent with previous studies on RGC (10.0–11.1%),^{13,14} but was higher than that of primary total gastrectomy (1.8–5.7%).³³⁻³⁵ Esophagojejunostomy following gastrectomy for RGC might be more difficult than primary total gastrectomy because of the low mobility of the elevated jejunum due to adhesions.

Overall IAI occurred in 8.6% of the patients in the MIS group and 9.7% in the open surgery group, which was not different. However, severe IAI occurred only in 1.1% of the MIS group, while 6.5% of the open surgery group. In the present study, there were no relationships between IAI and previous reconstruction (especially, Billroth-I) or splenic and pancreatic combined resection. A magnified view of the MIS enabled us to

distinguish pancreatic tissues, resulting in fewer pancreatic fistulas.

Notably, postoperative bleeding occurred only in the open surgery group in this study (overall: 6.5%; severe: 3.2%). The bleeding sites were all intra-abdominal and none of the patients were on antithrombotic medication. Among them, only one patient underwent combined resection (spleen). This difference might be attributable to the magnified view in MIS, which enabled us to operate more precisely.

Conversion from MIS to open surgery was observed in 13 cases (14.0%), and all of them used laparoscopic approaches. The conversion rate in this study was higher than that of laparoscopic total gastrectomy for primary gastric cancers in previous literature (1.3%–1.8%),^{35,36} but similar to previous reports for RGC (13%).¹⁴ In our study, only two of the 13 patients underwent combined resection and almost half (6/13) experienced postoperative complications. The reasons for conversion varied, and it was difficult to define contraindications for MIS. However, those who require open conversion should be regarded as having a high risk of postoperative complications.

There was no difference in the overall rates and patterns of recurrence between the groups, suggesting that the surgical approach did not affect disease recurrence. Although combined organ resection was less frequently performed in MIS, the extent of resection in MIS was sufficient for local control, which may be attributable to the magnified view in MIS.

Hospital volume is reported to be associated with postoperative complications after gastrectomy.^{37,38} Thus we also assessed the surgical outcomes according to the hospital volume. In the MIS group, hospital volume was not associated with short- or long-term outcomes. (Supplemental Table 5a, Supplemental Figure 4) One possible reason is that the hospital volumes of all institutions that participated in this study were relatively high compared with those in previous reports,^{37,38} and another possible reason is that surgical concepts and technical principles of our study group (KEGG) have been shared and standardized in biannual video conferences since 2005.^{34,39-41} On the other hand, in the open surgery group, HVHs had a higher rate of postoperative complications and worse prognosis (Supplemental table 5a, Supplemental figure 4), which may be attributable to a higher T stage. (Supplemental Table 5b)

Three sensitivity analyses using different cohort definitions were performed. In the PS matching analysis, we considered covariates that existed before treatment. Table 1 shows that the covariates included in the matching analysis were well-balanced. In contrast, the combined organ resection and adjuvant chemotherapy in the two groups were not well balanced. We believed that these differences could affect postoperative complications and long-term prognosis. Therefore, in the first sensitivity analysis, we excluded patients who underwent combined organ resection. Second, we excluded cases before 2009, because adjuvant chemotherapy has been recommended since 2010 in Japan. Third, we reclassified the conversion cases into the open surgery group. In all sensitivity analyses including full matching and MI, results were all consistent with the main result and we could confirm the robustness.

The present study has some limitations. First, the study design was retrospective, and the PS matching method was employed to adjust for measurable confounding factors. We could not control the unmeasured confounding factors such as surgeons' skills and advancement in surgical devices during the study period. Second, our findings cannot be applied directly to robotic resection because only seven cases of the robotic approach were included in this study. However, laparoscopic and robotic approaches for RGC have been reported to be feasible.^{13,14}

In conclusion, MIS for RGC showed favorable short- and long-term outcomes compared with open surgery. MIS is a promising option for radical surgery for RGC.

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Table 1. Patient characteristics, previous gastrectomy, and clinical findings

		Overall cohort (N=327)			Matched cohort (N=186)		
		MIS (n=132)	Open (n=195)	ASD	MIS (n=93)	Open (n=93)	ASD
Age	(years)	72 (66-77)	71 (64-79)	0.16	72 (67-77)	73 (64-79)	0.02
Sex	Male	113 (85.6%)	157 (80.5%)	0.25	79 (84.9%)	78 (83.9%)	0.03
BMI	(kg/m ²)	21.0 (18.7-23.0)	20.5 (18.6-22.4)	0.12	20.5 (18.6-22.7)	20.1 (18.8-22.2)	0.01
ASA.PS	≥3	19 (14.4%)	20 (10.3%)	0.17	11 (11.8%)	8 (8.6%)	0.09
Smoking		80 (60.6%)	81 (41.5%)	0.33	56 (60.2%)	57 (61.3%)	0.02
DM		15 (11.4%)	19 (9.7%)	0.05	11 (11.8%)	11 (11.8%)	0
Anti-thrombotic		27 (20.5%)	41 (21.0%)	0.04	17 (18.3%)	18 (19.4%)	0.03
Steroid		2 (1.5%)	2 (1.0%)	0.03	1 (1.1%)	0	0.08
SBO		7 (5.3%)	14 (7.2%)	0.05	5 (5.4%)	6 (6.5%)	0.05
Institution	HVH	49 (37.1%)	39 (20%)	0.46	29 (31.2%)	25 (26.9%)	0.09
Reason for previous gastrectomy	Benign	52 (39.4%)	75 (38.5%)	0.00	41 (44.1%)	43 (46.2%)	0.04
	Malignant	79 (59.8%)	114 (58.5%)		52 (55.9%)	50 (53.8%)	
Previous approach	MIS	31 (23.5%)	14 (7.2%)	0.38	13 (14.0%)	11 (11.8%)	0.05
	Open	101 (76.5%)	178 (91.3%)		80 (86.0%)	82 (88.2%)	
Previous reconstruction	DG_B-I	51 (38.6%)	88 (45.1%)	0.11	33 (35.5%)	37 (39.8%)	0.05
	DG_B-II/RY	68 (51.5%)	76 (39.0%)		53 (57.0%)	42 (45.2%)	
	Non DG	10 (7.6%)	20 (10.3%)		7 (7.5%)	14 (15.0%)	
Histology	Undifferentiated	41 (31.1%)	74 (37.9%)	0.21	33 (35.5%)	35 (37.6%)	0.05
Clinical T classification	≤T1b (SM)	78 (59.1%)	84 (43.1%)	0.29	52 (55.9%)	54 (58.1%)	0.04
	T2 (MP)	27 (20.5%)	43 (22.1%)		22 (23.6%)	17 (18.3%)	
	T3 (SS)	18 (13.6%)	37 (19.0%)		12 (12.9%)	11 (11.8%)	
	T4a (SE)	7 (5.3%)	23 (11.8%)		5 (5.4%)	11 (11.8%)	
	T4b (SI)	2 (1.5%)	7 (3.6%)		2 (2.2%)	0	
Clinical N involvement	Positive	15 (11.4%)	23 (11.8%)	0.01	11 (11.8%)	10 (10.8%)	0.03

Continuous variables are presented as median (interquartile range).

Categorical variables are presented as numbers (%).

BMI, body mass index; DM, diabetes mellitus; SBO, small bowel obstruction; HVH, high volume hospital; MIS, minimally invasive surgery; DG, distal gastrectomy; B-I, Billroth-I reconstruction; B-II, Billroth-II reconstruction; RY, Roux en Y reconstruction; ASD, absolute standardized difference.

Table 2. Operative procedures and pathological findings

		Matched cohort (N=186)	
		MIS (n=93)	Open (n=93)
Gastrectomy	Total	86 (92.5%)	80 (86.0%)
	Subtotal	7 (7.5%)	13 (14.0%)
Conversion	(+)	13 (14.0%)	-
Combined resection	None	80 (86.0%)	44 (47.3%)
	Gallbladder	5 (5.3%)	30 (32.3%)
	Pancreas	2 (2.2%)	2 (2.2%)
	Colon	4 (4.3%)	2 (2.2%)
	Liver	2 (2.2%)	4 (4.3%)
	Spleen	4 (4.3%)	13 (14.0%)
	Esophagojejunostomy		
	Circular	15 (16.1%)	73 (78.5%)
	FEEA	51 (54.8%)	6 (6.5%)
	Over-Lap	14 (15.1%)	2 (2.2%)
	Hand sewn	0	3 (3.2%)
Histology	Differentiated	47 (50.5%)	52 (55.9%)
	Undifferentiated	46 (49.5%)	39 (41.9%)
Pathological T classification	≤T1b (SM)	42 (45.2%)	50 (53.8%)
	T2 (MP)	14 (15.1%)	11 (11.8%)
	T3 (SS)	20 (21.5%)	15 (16.1%)
	T4a (SE)	11 (11.8%)	11 (11.8%)
	T4b (SI)	6 (6.5%)	6 (6.5%)
Pathological N stage	N0	76 (81.7%)	71 (76.3%)
	N1	6 (6.5%)	14 (15.1%)
	N2	2 (2.2%)	4 (4.3%)
	N3a	5 (5.4%)	3 (3.2%)
	N3b	4 (4.3%)	1 (1.1%)
Pathological stage*	IA	40 (43.0)	50 (53.8%)
	IB	14 (15.1%)	8 (8.6%)
	IIA	15 (16.1%)	10 (10.8%)
	IIB	11 (11.8%)	10 (10.8%)
	IIIA	4 (4.3%)	7 (7.5%)
	IIIB	5 (5.4%)	7 (7.5%)
	IIIC	4 (4.3%)	1 (1.1%)

Variables are presented as numbers (%).

* According to the Japanese Classification of Gastric Carcinoma [The 15th edition].

FEEA, functional end-to-end anastomosis; MIS, minimally invasive surgery.

Table 3. Surgical outcomes

	Matched cohort (N=186)		Mean difference (95%CI)
	MIS (n=93)	Open (n=93)	
Blood loss (ml)	50 (10-190)	361 (230-780)	-409 (-538, -281)
Operative time (min)	344 (286-408)	273 (232-349)	62 (35, 91)
R0	91 (97.8%)	89 (95.7%)	0.682*
R1	2 (2.2%)	4 (4.3%)	
R2	0 (0%)	0 (0%)	
LNs retrieved (number)	14 (6-22)	10 (5-20)	4.0 (0.3, 7.7)
Peak CRP (mg/dl)	10.7 (7.3-14.4)	11.4 (7.5-17.0)	-1.2 (-3.1, 0.8)
Time to first food (days)	4 (4-6)	5 (4-7)	-3.0 (-6.2, 0.2)
Hospital stay (days)	13 (12-22)	16 (13-23)	-6.5 (-13.1, 0.1)

Continuous variables are presented as median (interquartile range).

Categorical variables are presented as numbers (%).

MIS, minimally invasive surgery; LNs, lymph nodes; CRP, C-reactive protein.

*: P value

Table 4. Postoperative complications

	Overall complications			Severe complications		
	MIS (n=93)	Open (n=93)	<i>P value</i>	MIS (n=93)	Open (n=93)	<i>P value</i>
EJ leakage	8 (8.6%)	8 (8.6%)		4 (4.3%)	4 (4.3%)	
Duodenal stump leakage	0	0		0	0	
IAI	8 (8.6%)	9 (9.7%)		1 (1.1%)	6 (6.5%)	
Wound infection	3 (3.2%)	0		2 (2.2%)	0	
Bleeding	0	6 (6.5%)		0	3 (3.2%) ^a	
Stenosis	2 (2.2%)	0		1 (1.1%)	0	
SBO/ Ileus	2 (2.2%)	1 (1.1%)		2 (2.2%)	1 (1.1%)	
Pulmonary	2 (2.2%)	3 (3.2%)		0	1 (1.1%)	
Cardiovascular	0	0		0	0	
Stroke	0	1 (1.1%)		0	1 (1.1%) ^a	
Thrombosis	0	1 (1.1%)		0	0	
Others ^b	9 (9.7%)	9 (9.7%)		4 (4.3%)	5 (5.4%)	
Total	26 (28.0%)	34 (36.6%)		13 (14.0%)	20 (21.5%)	
Risk difference (95%CI)	-8.6% (-22.1, 4.8)		0.192	-7.5% (-18.5, 3.5)		0.192
Risk ratio (95% CI)	0.76 (0.45, 1.27)		0.198	0.65 (0.32, 1.29)		0.199

Variables are presented as numbers (%).

^aTwo patients died during their hospital stay due to bleeding and stroke, respectively.

^bCholangitis, cholecystitis, liver abscess, urinary tract infection, catheter infection.

Overall complication: Clavien-Dindo classification Grade II or higher.

Severe complication: Clavien-Dindo classification Grade III or higher.

EJ, esophagojejunostomy; IAI, intra-abdominal infection; SBO, small bowel obstruction; MIS, minimally invasive surgery.

Table 5. Type of the first recurrence

	MIS (n=93)	Open (n=93)
Locoregional	3 (3.2%)	4 (4.3%)
Peritoneal	4 (4.3%)	6 (6.5%)
Distant lymph node	7 (7.5%)	10 (10.8%)
Hematogenous	6 (6.5%)	9 (9.7%)
Others	1 (1.1%) ^a	1 (1.1%) ^b
Total	19 (20.4%)	27 (29.0%)

Variables are presented as numbers (%).

Overlapping distribution.

MIS, minimally invasive surgery.

a Lymphangitis carcinomatosa, b Malignant pleural effusion

Figure 1. Flowchart of patient enrollment

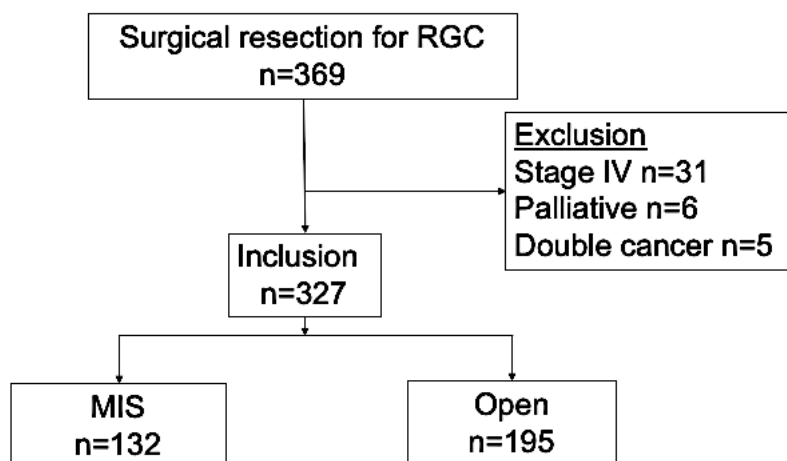
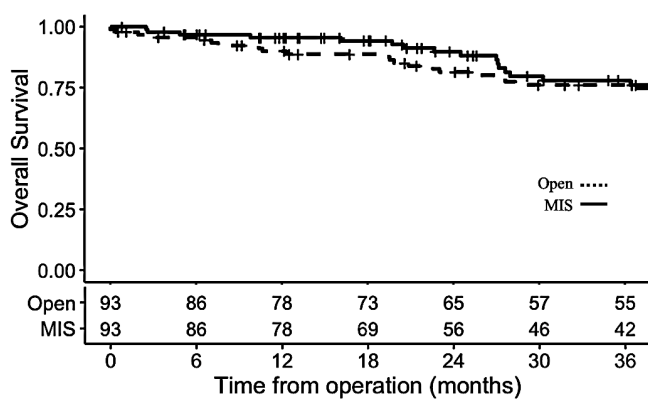


Figure 2. Survival curves after matching.

(a) Overall survival



(b) Relapse-free survival

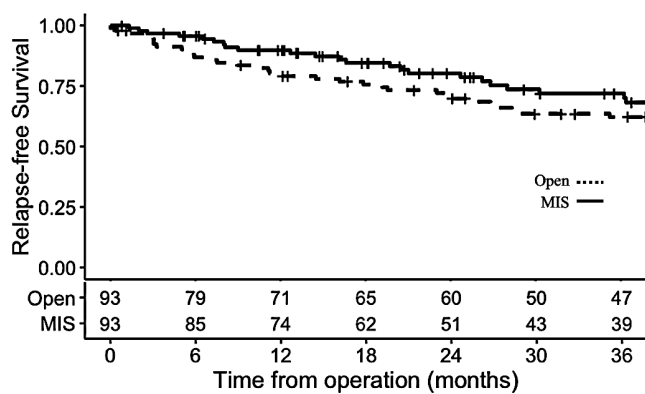


Figure legends

Figure 1. A flowchart of patient enrollment

Figure 2. Survival curves after matching

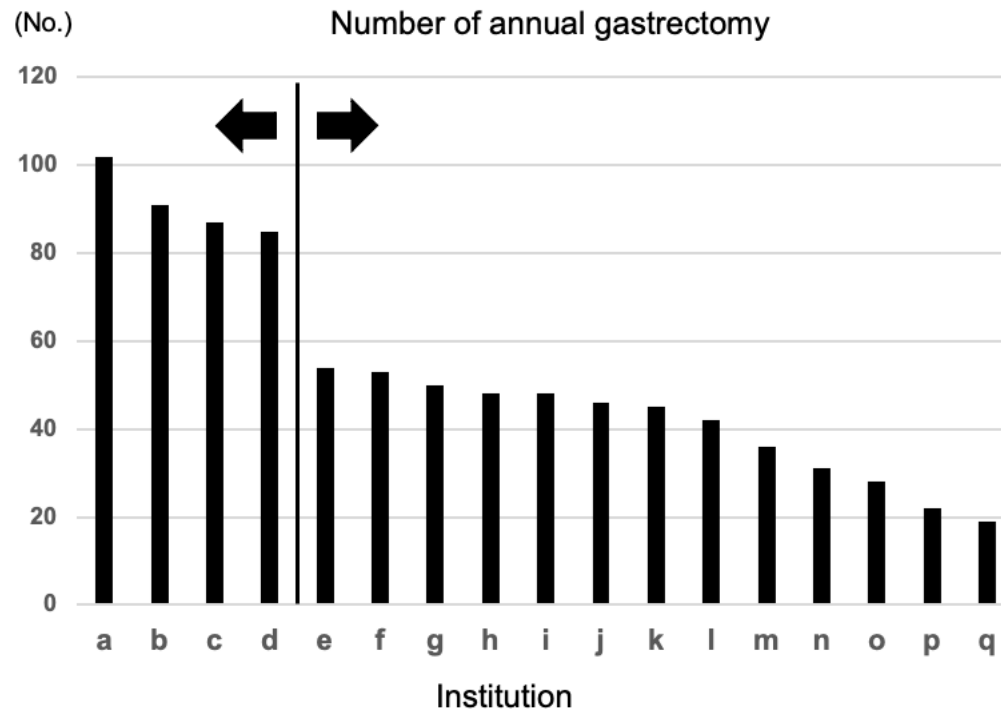
(a). Overall survival (HR [95% CI], 0.78 [0.45, 1.36]; P=0.400).

(b). Relapse-free survival (HR [95% CI], 0.71 [0.44, 1.16]; P=0.200).

HR, hazard ratio; CI, confidence interval

Supplemental figure 1

Number of annual gastrectomy in each institution

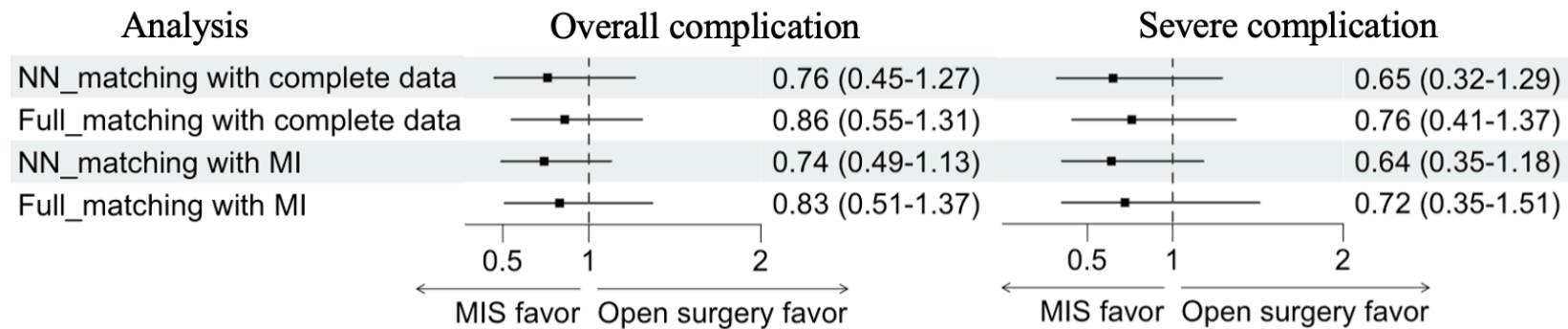


Institution was divided into 2 groups using the third quartile of annual gastrectomy (>70 cases, ≤ 70 cases), and then included in the analysis.

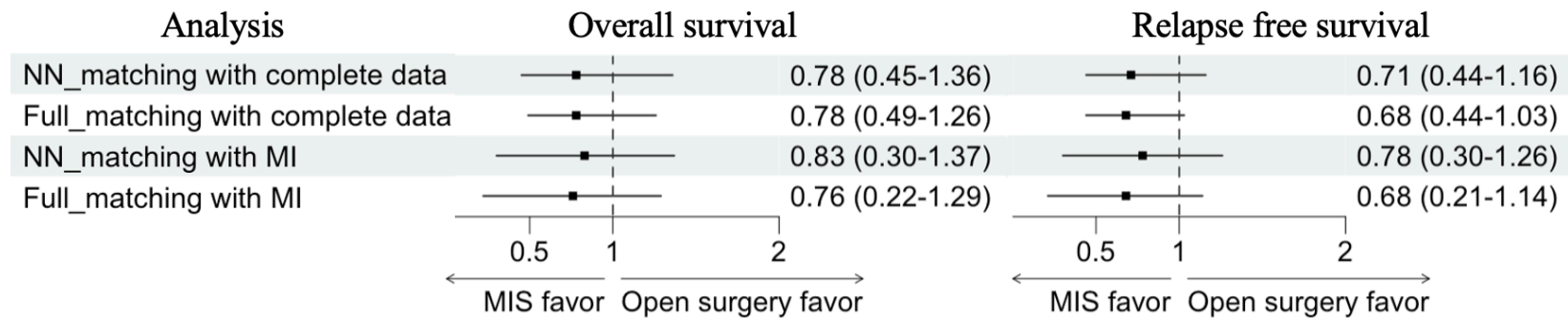
Supplemental figure 2

Results from additional matching analysis (with multiple imputation)

(a) Risk ratios (95% CI) for postoperative complications



(b) Hazard ratios (95%CI) for long-term prognosis

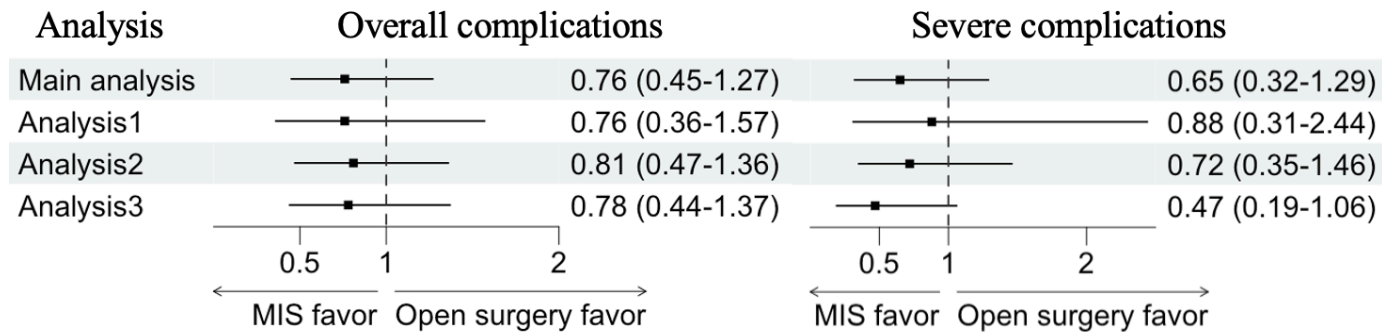


MIS, Minimally invasive surgery; NN matching, nearest neighbor matching; MI, multiple imputation; CI, Confidence interval.

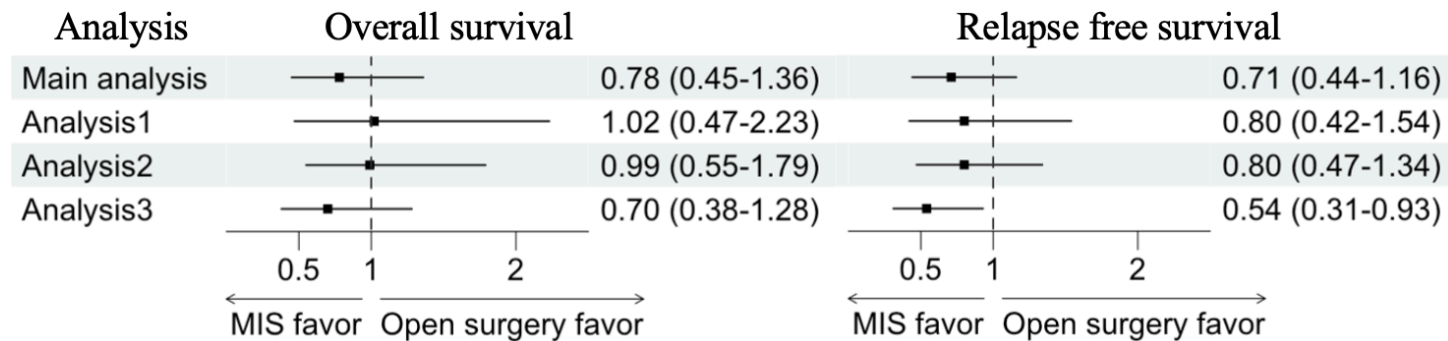
Supplemental figure 3

Results from sensitivity analyses using different cohort definitions

(a) Risk ratios (95% CI) for postoperative complications



(b) Hazard ratios (95%CI) for long-term prognosis



MIS, Minimally invasive surgery; CI, confidence interval.

Analysis 1; Excluding cases of combined organ resection.

Analysis 2; Excluding cases of surgery before 2009.

Analysis 3; Classifying conversion cases into the open group.

(Supplemental table1) Patient characteristics

		unmatched cohort					
		Overall cohort (N=327)		NN matched cohort (N=186)		Unmatched cohort (N=98)	
		MIS (n=132)	Open (n=195)	MIS (n=93)	Open (n=93)	MIS (n=29)	Open (n=69)
Age	(years)	72 (66-77)	71 (64-79)	72 (67-77)	73 (64-79)	71 (67-77)	69 (62-77)
Sex	Male	113 (85.6%)	157 (80.5%)	79 (84.9%)	78 (83.9%)	27 (93.1%)	49 (71.0%)
BMI	(kg/m ²)	21.0 (18.7-23.0)	20.5 (18.6-22.4)	20.5 (18.6-22.7)	20.1 (18.8-22.2)	21.0 (19.0-22.3)	20.4 (18.3-22.5)
ASA.PS	≥3	19 (14.4%)	20 (10.3%)	11 (11.8%)	8 (8.6%)	8 (27.5%)	7 (10.1%)
Smoking		80 (60.6%)	81 (41.5%)	56 (60.2%)	57 (61.3%)	20 (69.0%)	18 (26.1%)
DM		15 (11.4%)	19 (9.7%)	11 (11.8%)	11 (11.8%)	3 (10.3%)	5 (7.2%)
Anti-thrombotic		27 (20.5%)	41 (21.0%)	17 (18.3%)	18 (19.4%)	9 (31.0%)	14 (20.3%)
Steroid		2 (1.5%)	2 (1.0%)	1 (1.1%)	0	1 (3.4%)	2 (2.9%)
SBO		7 (5.3%)	14 (7.2%)	5 (5.4%)	6 (6.5%)	2 (6.9%)	5 (7.2%)
Institution	High volume*	49 (37.1%)	39 (20%)	29 (31.2%)	25 (26.9%)	18 (62.1%)	1 (1.4%)
Reason for previous gastrectomy	Benign	52 (39.4%)	75 (38.5%)	41 (44.1%)	43 (46.2%)	7 (24.1%)	21 (30.4%)
	Malignant	79 (59.8%)	114 (58.5%)	52 (55.9%)	50 (53.8%)	22 (75.9%)	48 (69.6%)
Previous approach	MIS	31 (23.5%)	14 (7.2%)	13 (14.0%)	11 (11.8%)	15 (51.7%)	0
	Open	101 (76.5%)	178 (91.3%)	80 (86.0%)	82 (88.2%)	14 (48.3%)	69 (100%)
Previous reconstruction	DG_B-I	51 (38.6%)	88 (45.1%)	33 (35.5%)	37 (39.8%)	16 (55.2%)	42 (60.9%)
	DG_B-II/RV	68 (51.5%)	76 (39.0%)	53 (57.0%)	42 (45.2%)	10 (34.5%)	25 (36.2%)
	Non DG	10 (7.6%)	20 (10.3%)	7 (7.5%)	14 (15.0%)	3 (10.3%)	2 (2.9%)
Histology	Undifferentiated	41 (31.1%)	74 (37.9%)	33 (35.5%)	35 (37.6%)	6 (20.7%)	33 (47.8%)
Clinical T classification	≤T1b (SM)	78 (59.1%)	84 (43.1%)	52 (55.9%)	54 (58.1%)	21 (72.5%)	20 (29.0%)
	T2 (MP)	27 (20.5%)	43 (22.1%)	22 (23.6%)	17 (18.3%)	4 (13.8%)	16 (23.2%)
	T3 (SS)	18 (13.6%)	37 (19.0%)	12 (12.9%)	11 (11.8%)	3 (10.3%)	20 (29.0%)
	T4a (SE)	7 (5.3%)	23 (11.8%)	5 (5.4%)	11 (11.8%)	1 (3.4%)	8 (11.6%)
	T4b (SI)	2 (1.5%)	7 (3.6%)	2 (2.2%)	0	0	5 (7.2%)
Clinical N involvement	Positive	15 (11.4%)	23 (11.8%)	11 (11.8%)	10 (10.8%)	3 (10.3%)	8 (11.6%)

Patients with missing values are not included in the NN matched and unmatched cohort.

Continuous variables are presented as median (interquartile range).

Categorical variables are presented as numbers (%).

*High volume center: annual caseload of gastrectomy (>70 cases)

BMI, body mass index; DM, diabetes mellitus; SBO, small bowel obstruction; MIS, minimally invasive surgery; DG, distal gastrectomy; B-I, Billroth-I reconstruction; B-II, Billroth-II reconstruction; RY, Roux en Y reconstruction; MIS, minimally invasive surgery; ASD, absolute standardized difference, NN matched, nearest neighbor matched; MI, multiple imputation.

(Supplemental table 2a) Patient characteristics

Nearest neighbor matching (with multiple imputation)

		Overall cohort (N=327)			NN matched cohort (N=186)			NN matched cohort with MI (N=220)		
		MIS (n=132)	Open (n=195)	ASD	MIS (n=93)	Open (n=93)	ASD	MIS (n=110)	Open (n=110)	ASD
Age	(years)	72 (66-77)	71 (64-79)	0.16	72 (67-77)	73 (64-79)	0.02	72 (66-77)	73 (64-79)	0.07
Sex	Male	113 (85.6%)	157 (80.5%)	0.25	79 (84.9%)	78 (83.9%)	0.03	92 (83.6%)	92 (83.6%)	0.04
BMI	(kg/m ²)	21.0 (18.7-23.0)	20.5 (18.6-22.4)	0.12	20.5 (18.6-22.7)	20.1 (18.8-22.2)	0.01	20.5 (18.7-22.7)	20.2 (18.8-22.6)	0.12
ASA/PS	≥3	19 (14.4%)	20 (10.3%)	0.17	11 (11.8%)	8 (8.6%)	0.09	15 (13.6%)	14 (12.7%)	0.05
Smoking		80 (60.6%)	81 (41.5%)	0.33	56 (60.2%)	57 (61.3%)	0.02	62 (56.4%)	66 (60.0%)	0.07
DM		15 (11.4%)	19 (9.7%)	0.05	11 (11.8%)	11 (11.8%)	0	13 (11.8%)	11 (10.0%)	0.04
Anti-thrombotic		27 (20.5%)	41 (21.0%)	0.04	17 (18.3%)	18 (19.4%)	0.03	21 (19.1%)	22 (20.0%)	0.05
Steroid		2 (1.5%)	2 (1.0%)	0.03	1 (1.1%)	0	0.08	1 (0.9%)	1 (0.9%)	0.02
SBO		7 (5.3%)	14 (7.2%)	0.05	5 (5.4%)	6 (6.5%)	0.05	6 (5.5%)	6 (5.5%)	0.03
Institution	High volume*	49 (37.1%)	39 (20%)	0.46	29 (31.2%)	25 (26.9%)	0.09	37 (33.6%)	35 (31.8%)	0.05
Reason for previous gastrectomy	Benign	52 (39.4%)	75 (38.5%)	0.00	41 (44.1%)	43 (46.2%)	0.04	46 (41.8%)	50 (45.5%)	0.08
	Malignant	79 (59.8%)	114 (58.5%)		52 (55.9%)	50 (53.8%)		64 (58.2%)	60 (54.5%)	
Previous approach	MIS	31 (23.5%)	14 (7.2%)	0.38	13 (14.0%)	11 (11.8%)	0.05	18 (16.4%)	14 (12.7%)	0.08
	Open	101 (76.5%)	178 (91.3%)		80 (86.0%)	82 (88.2%)		92 (83.6%)	96 (87.3%)	
Previous reconstruction	DG_B-I	51 (38.6%)	88 (45.1%)	0.11	33 (35.5%)	37 (39.8%)	0.05	41 (37.3%)	44 (40.0%)	0.13
	DG_B-II/RY	68 (51.5%)	76 (39.0%)		53 (57.0%)	42 (45.2%)		60 (54.5%)	50 (45.5%)	
	Non DG	10 (7.6%)	20 (10.3%)		7 (7.5%)	14 (15.0%)		9 (8.2%)	16 (14.5%)	
Histology	Undifferentiated	41 (31.1%)	74 (37.9%)	0.21	33 (35.5%)	35 (37.6%)	0.05	36 (32.7%)	40 (36.4%)	0.08
Clinical T classification	≤T1b (SM)	78 (59.1%)	84 (43.1%)	0.29	52 (55.9%)	54 (58.1%)	0.04	60 (54.5%)	58 (52.3%)	0.08
	T2 (MP)	27 (20.5%)	43 (22.1%)		22 (23.6%)	17 (18.3%)		25 (22.7%)	24 (21.8%)	
	T3 (SS)	18 (13.6%)	37 (19.0%)		12 (12.9%)	11 (11.8%)		17 (15.5%)	14 (12.7%)	
	T4a (SE)	7 (5.3%)	23 (11.8%)		5 (5.4%)	11 (11.8%)		6 (5.5%)	12 (10.9%)	
	T4b (SI)	2 (1.5%)	7 (3.6%)		2 (2.2%)	0		2 (1.8%)	2 (1.8%)	
Clinical N involvement	Positive	15 (11.4%)	23 (11.8%)	0.01	11 (11.8%)	10 (10.8%)	0.03	13 (11.8%)	12 (10.9%)	0.05

Continuous variables are presented as median (interquartile range).

Categorical variables are presented as numbers (%).

*High volume center: annual caseload of gastrectomy (>70 cases)

BMI, body mass index; DM, diabetes mellitus; SBO, small bowel obstruction; MIS, minimally invasive surgery; DG, distal gastrectomy; B-I, Billroth-I reconstruction; B-II, Billroth-II reconstruction; RY, Roux en Y reconstruction; MIS, minimally invasive surgery; ASD, absolute standardized difference, NN matched, nearest neighbor matched; MI, multiple imputation.

(Supplemental table 2b) Patient characteristics

Full matching (with multiple imputation)

		Overall cohort (N=327)			Full matched cohort (N=284)			Full matched cohort with MI (N=327)		
		MIS (n=132)	Open (n=195)	ASD	MIS (n=122)	Open (n=162)	ASD	MIS (n=132)	Open (n=195)	ASD
Age	(years)	72 (66-77)	71 (64-79)	0.16	72 (66-77)	73 (64-78)	0.03	72 (65-77)	71 (63-79)	0.13
Sex	Male	113 (85.6%)	157 (80.5%)	0.25	106 (86.9%)	140 (86.6%)	0.01	113 (85.6%)	166 (85.3%)	0.04
BMI	(kg/m ²)	21.0 (18.7-23.0)	20.5 (18.6-22.4)	0.12	20.5 (18.6-22.6)	19.7 (18.8-21.1)	0.02	20.5 (18.6-23.0)	20.2 (18.7-22.7)	0.26
ASA/PS	≥3	19 (14.4%)	20 (10.3%)	0.17	19 (15.6%)	22 (13.6%)	0.06	19 (14.4%)	24 (12.3%)	0.06
Smoking		80 (60.6%)	81 (41.5%)	0.33	76 (62.3%)	109 (67.4%)	0.11	81 (61.0%)	122 (62.3%)	0.08
DM		15 (11.4%)	19 (9.7%)	0.05	14 (11.5%)	19 (11.5%)	0.00	15 (11.4%)	27 (14.0%)	0.11
Anti-thrombotic		27 (20.5%)	41 (21.0%)	0.04	26 (21.3%)	31 (19.4%)	0.05	27 (20.5%)	35 (17.8%)	0.07
Steroid		2 (1.5%)	2 (1.0%)	0.03	2 (1.6%)	0	0.12	2 (1.5%)	1 (0.4%)	0.01
SBO		7 (5.3%)	14 (7.2%)	0.05	7 (5.7%)	12 (7.3%)	0.07	7 (5.3%)	13 (6.9%)	0.07
Institution	High volume*	49 (37.1%)	39 (20%)	0.46	47 (38.5%)	62 (38.1%)	0.01	49 (37.1%)	69 (35.6%)	0.09
Reason for previous gastrectomy	Benign	52 (39.4%)	75 (38.5%)	0.00	48 (39.3%)	80 (49.4%)	0.21	53 (39.9%)	83 (42.8%)	0.11
	Malignant	79 (59.8%)	114 (58.5%)		74 (60.7%)	82 (50.6%)		79 (60.1%)	112 (57.2%)	
Previous approach	MIS	31 (23.5%)	14 (7.2%)	0.38	28 (23.0%)	34 (20.8%)	0.05	31 (23.5%)	47 (24.0%)	0.08
	Open	101 (76.5%)	178 (91.3%)		94 (77.0%)	128 (79.2%)		101 (76.5%)	148 (76.0%)	
Previous reconstruction	DG_B-I	51 (38.6%)	88 (45.1%)	0.11	49 (40.2%)	57 (35.1%)	0.16	52 (39.4%)	79 (40.7%)	0.34
	DG_B-II/RY	68 (51.5%)	76 (39.0%)		63 (51.6%)	84 (52.0%)		69 (52.4%)	84 (42.7%)	
	Non DG	10 (7.6%)	20 (10.3%)		10 (8.2%)	21 (12.9%)		11 (8.2%)	32 (16.6%)	
Histology	Undifferentiated	41 (31.1%)	74 (37.9%)	0.21	39 (32.0%)	42 (26.0%)	0.13	42 (31.6%)	61 (31.5%)	0.07
Clinical T classification	≤T1b (SM)	78 (59.1%)	84 (43.1%)	0.29	73 (59.9%)	86 (53.1%)	0.14	78 (59.1%)	109 (55.9%)	0.16
	T2 (MP)	27 (20.5%)	43 (22.1%)		26 (21.3%)	34 (21.2%)		27 (20.5%)	39 (20.1%)	
	T3 (SS)	18 (13.6%)	37 (19.0%)		15 (12.3%)	14 (8.7%)		18 (13.6%)	20 (10.1%)	
	T4a (SE)	7 (5.3%)	23 (11.8%)		6 (4.9%)	27 (16.6%)		7 (5.3%)	25 (13.0%)	
	T4b (SI)	2 (1.5%)	7 (3.6%)		2 (1.6%)	7 (0.4%)		2 (1.5%)	2 (1.1%)	
Clinical N involvement	Positive	15 (11.4%)	23 (11.8%)	0.01	14 (11.5%)	23 (14.1%)	0.08	15 (11.4%)	25 (12.7%)	0.11

(Supplemental table 3a) Surgical outcomes

Nearest neighbor matching (with multiple imputation)						
	NN matched cohort (N=186)			NN matched cohort with MI (N=220)		
	MIS (n=93)	Open (n=93)	Mean difference (95%CI)	MIS (n=110)	Open (n=110)	Mean difference (95%CI)
Blood loss (ml)	50 (10-190)	361 (230-780)	-409 (-538, -281)	60 (10-215)	380 (214-692)	-364 (-489, -239)
Operative time (min)	344 (286-408)	273 (232-349)	62 (35, 91)	346 (286-430)	275 (233-340)	66 (38, 93)
R0	91 (97.8%)	89 (95.7%)	0.682*	108 (98.2%)	107 (97.3%)	1.0*
R1	2 (2.2%)	4 (4.3%)		2 (1.8%)	3 (2.7%)	
R2	0 (0%)	0 (0%)		0	0	
LNs retrieved (number)	14 (6-22)	10 (5-20)	4.0 (0.3, 7.7)	13 (5-23)	10 (5-20)	3.1 (-0.5, 6.7)
Peak CRP (mg/dl)	10.7 (7.3-14.4)	11.4 (7.5-17.0)	-1.2 (-3.1, 0.8)	11.1 (7.3-15.7)	11.1 (7.7-16.0)	-0.2 (-2.3, 2.0)
Time to first food (days)	4 (4-6)	5 (4-7)	-3.0 (-6.2, 0.2)	4 (4-6)	5 (4-7)	-2.0 (-5.0, 0.9)
Hospital stay (days)	13 (12-22)	16 (13-23)	-6.5 (-13.1, 0.1)	14 (12-22)	17 (13-28)	-5.8 (-12.2, 0.6)

Continuous variables are presented as median (interquartile range).

Categorical variables are presented as numbers (%).

MIS, minimally invasive surgery; LNs, lymph nodes; CRP, C-reactive protein.

*: P value

(Supplemental table 3b) Surgical outcomes

Full matching (with multiple imputation)						
	Full matched cohort (N=288)			Full matched cohort with MI (N=327)		
	MIS (n=122)	Open (n=162)	Mean difference (95%CI)	MIS (n=132)	Open (n=195)	Mean difference (95%CI)
Blood loss (ml)	54 (10-187)	280 (146-583)	-282 (-380, -183)	57 (10-195)	312 (179-661)	-344 (-519, -169)
Operative time (min)	343 (284-408)	260 (223-326)	75 (53, 97)	343 (282-422)	270 (225-329)	70 (40, 100)
R0	120 (98.4%)	159 (98.3%)	1.0*	129 (97.7%)	192 (98.5)	0.689*
R1	2 (1.6%)	3 (1.7%)		3 (2.3%)	3 (1.5%)	
R2	0	0		0	0	
LN's retrieved (number)	11 (4-21)	10 (4-21)	2.2 (-0.6, 5.0)	11 (4-22)	9 (4-19)	2.6 (-1.3, 6.5)
Peak CRP (mg/dl)	10.4 (7.3-14.6)	11.1 (7.0-14.9)	0.2 (-1.4, 1.7)	10.5 (7.3-15.3)	10.6 (7.1-14.8)	0.1 (-2.2, 2.3)
Time to first food (days)	4 (3-5)	5 (3-6)	-0.9 (-2.9, 1.0)	4 (3-5)	5 (4-6)	-1.2 (-4.0, 1.5)
Hospital stay (days)	13 (10-21)	15 (12-21)	-4.0 (-8.5, 0.6)	13 (10-21)	15 (12-23)	-4.4 (-11.8, 3.0)

(Supplemental table 4a) Postoperative complications

Full matching without multiple imputation						
	Overall complications			Severe complications		
	MIS (n=122)	Open (n=162)	<i>P value</i>	MIS (n=122)	Open (n=162)	<i>P value</i>
EJ leakage	11 (9.0%)	26 (16.0%)		8 (6.6%)	13 (8.0%)	
Duodenal stump leakage	2 (1.6%)	0		0	0	
IAI	10 (8.2%)	21 (13.0%)		9 (7.4%)	18 (11.1%)	
Wound infection	3 (2.5%)	0		2 (1.6%)	0	
Bleeding	0	6 (3.7%)		0	2 (1.2%)	
Stenosis	2 (1.6%)	0		1 (0.8%)	0	
SBO/ Ileus	3 (2.5%)	0		2 (1.6%)	1 (0.6%)	
Pulmonary	2 (1.6%)	1 (0.6%)		0	0	
Cardiovascular	0	0		0	0	
stroke	0	0		0	1 (0.6%)	
Thrombosis	0	0		0	0	
Others	10 (8.2%)	9 (5.6%)		4 (3.3%)	5 (3.1%)	
Total	34 (27.9%)	53 (32.7%)		17 (13.9%)	30 (18.5%)	
Risk difference (95%CI)	-4.6% (-15.4, 6.2)		0.569	-4.3% (-13.0, 4.4%)		0.591
Risk ratio (95% CI)	0.86 (0.55, 1.31)		0.551	0.76 (0.41, 1.37)		0.566

Variables are presented as numbers (%).

a Two patients died during their hospital stay due to bleeding and stroke, respectively.

b Cholangitis, cholecystitis, liver abscess, urinary tract infection, catheter infection

Overall complication: Clavien-Dindo classification Grade $\geq$ II

Severe complication: Clavien-Dindo classification Grade $\geq$ III

EJ, esophagojejunostomy; IAI, intra-abdominal infection; SBO, small bowel obstruction; MIS, minimally invasive surgery

(Supplemental table 4b) Postoperative complications

Nearest neighbor matching with multiple imputation

	Overall complications			Severe complications		
	MIS (n=110)	Open (n=110)	<i>P value</i>	MIS (n=110)	Open (n=110)	<i>P value</i>
EJ leakage	11 (10.0%)	9 (8.2%)		7 (6.4%)	5 (4.5%)	
Duodenal stump leakage	0	0		0	0	
IAI	9 (8.2%)	15 (13.6%)		1 (0.9%)	11 (10.0%)	
Wound infection	3 (2.7%)	2 (1.8%)		2 (1.8%)	2 (1.8%)	
Bleeding	1 (0.9%)	6 (5.5%)		0	4 (3.6%)	
Stenosis	2 (1.8%)	1 (0.9%)		1 (0.9%)	0	
SBO/ Ileus	2 (1.8%)	1 (0.9%)		2 (1.8%)	1 (0.9%)	
Pulmonary	2 (1.8%)	5 (4.5%)		0	1 (0.9%)	
Cardiovascular	0	0		0	0	
stroke	0	1 (0.9%)		0	0	
Thrombosis	0	1 (0.9%)		0	0	
Others	19 (17.3%)	10 (9.1%)		4 (3.6%)	5 (4.5%)	
Total	31 (28.2%)	42 (38.2%)		16 (14.5%)	25 (22.7%)	
Risk difference (95%CI)	-9.8% (-23.4, 3.7)		0.153	-8.1% (-19.0, 2.8)		0.143
Risk ratio (95% CI)	0.74 (0.49, 1.13)		0.159	0.64 (0.35, 1.18)		0.151

(Supplemental table 4c) Postoperative complications

Full matching with multiple imputation

	Overall complications			Severe complications		
	MIS (n=132)	Open (n=195)	<i>P value</i>	MIS (n=132)	Open (n=195)	<i>P value</i>
EJ leakage	14 (10.6%)	15 (7.7%)		9 (6.8%)	9 (4.6%)	
Duodenal stump leakage	0	0		0	0	
IAI	11 (8.3%)	26 (13.3%)		2 (1.5%)	20 (10.3%)	
Wound infection	3 (2.3%)	2 (1.0%)		2 (1.5%)	2 (1.0%)	
Bleeding	1 (0.8%)	9 (4.6%)		0	5 (2.6%)	
Stenosis	2 (1.5%)	1 (0.5%)		1 (0.8%)	0	
SBO/ Ileus	3 (2.3%)	2 (1.0%)		2 (1.5%)	2 (1.0%)	
Pulmonary	2 (1.5%)	8 (4.1%)		0	1 (0.5%)	
Cardiovascular	0	0		0	0	
stroke	0	1 (0.5%)		0	0	
Thrombosis	0	1 (0.5%)		0	0	
Others	11 (8.3%)	14 (7.2%)		4 (3.0%)	7 (3.6%)	
Total	37 (28.0%)	66 (33.8%)		18 (13.6%)	37 (19.0%)	
Risk difference (95%CI)	-5.6% (-21.1, 10.0)		0.477	-5.5% (-18.6, 7.5)		0.402
Risk ratio (95% CI)	0.83 (0.51, 1.37)		0.473	0.72 (0.35, 1.51)		0.379