Original Article

Surgical invasiveness and lymphadenectomy in robotic and laparoscopic gastrectomy: A retrospective study with propensity-score matching

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Abstract

Background

There is no consensus amongst comparative studies about the advantages of robotic over laparoscopic surgeries for gastric cancer (GC). We compared invasiveness and lymph node dissection between robotic and laparoscopic gastrectomies (RG and LG).

Methods

We retrospectively reviewed the medical records of 215 consecutive patients with GC who underwent RG or LG with lymphadenectomy from January 2011–December 2020. Propensity score matching analysis was performed to control selection bias.

Results

The RG group had less operative blood loss (*P*=0.0005) and higher C-reactive protein levels on postoperative day 1 (*P*=0.0006) than the LG group. When analyzing the specific sites of dissected lymph nodes, station groups of supra-pancreatic and lesser curvature areas accounted for this difference (*P*=0.0073 and 0.0362, respectively).

Conclusions

RG demonstrated lesser intraoperative bleeding, less of a postoperative inflammatory response, and a higher proportion of lymph node removal than LG, suggesting that it is a better surgical and oncological procedure.

Keywords: robotic surgical procedures, laparoscopy, gastrectomy, gastric cancer, lymph node dissection

Introduction

Gastric cancer (GC) remains the fourth leading cause of cancer-related mortality worldwide, and over one million new cases occurred in 2018.[1] Recently, the use of robotic surgery as a minimally invasive treatment for GC has become widespread, and the number of patients treated for this morbidity has increased.[2] Several studies have compared the short-term results of robotic gastrectomy (RG), laparoscopic gastrectomy (LG), and open gastrectomy (OG),[3,4] and revealed less bleeding and lower complications rates in RG than in LG.[5-7] However, it is still unclear whether RG has an advantage over LG regarding minimal invasiveness and lymph node (LN) dissection techniques. Therefore, we compared the short-term outcomes and site-specific LN dissection in RG and in LG using propensity-score matched cohorts.

Methods

Study design and patient selection

In this retrospective cohort study, we collected data from consecutive patients with GC who underwent subtotal or total RG or LG with LN dissection at our institution between January 2011 and December 2020. At our institution, LG was introduced for treating GC in January 2011, while RG was initiated using the da Vinci Si Surgical System^{TM} (Intuitive Surgical, Sunnyvale, CA, USA) in December 2017. Since RG was introduced, all patients were informed about the advantages and disadvantages of RG and LG by the surgeon and were allowed to choose their preferred surgical approach. As an indicator of hospital volume, our institution had more than 40 cases of radical surgery for gastric cancer per year throughout this period. This study was approved by the

Review Board of our institution, and the study complied with the guidelines stipulated in the Declaration of Helsinki. Informed consent was obtained from all eligible patients who agreed to participate. This study is being reported in line with the STROCSS 2019 Guideline.

The exclusion criteria were residual GC, neoadjuvant chemotherapy, conversion to open surgery before LN dissection completion, LN D1 dissection, proximal gastrectomy, and incomplete clinical data. Cases with residual GC were excluded. Overall, 215 patients (44 and 171 underwent RG and LG, respectively) were eligible for analysis.

Disease assessment and variable definition

The age, sex, body mass index (BMI), and American Society of Anesthesiologists Physical Status (ASA-PS) were recorded. In all cases, GC diagnosis and staging were performed using thoracoabdominal contrast-enhanced computed tomography (CT), upper gastrointestinal endoscopy with biopsy, ultrasound endoscopy, and positron emission tomography (PET)-CT for patients with advanced GC. After tumor staging was performed, all LNs were eliminated by the operating surgeons (Figure 1) according to the Japanese classification of gastric carcinoma: 3rd English edition.[8] Surgical complications were classified according to the Clavien–Dindo system.[9] Postoperative pancreatic fistula was defined as an abdominal drainage fluid with amylase activity three times higher than the upper normal limit of the serum value; grading was based on the updated consensus of the International Study Group on Pancreatic Surgery.[10]

Surgical procedures and lymph node classification

The standard procedure at our institution was a distal or total gastrectomy with D1+ or D2 regional LN dissection, according to the Japanese Gastric Cancer Treatment Guidelines.[11] In clinical stage I tumors, LG with D1+ LN dissection was performed. LNs from the resected specimen were sent for pathological examination for diagnosis of metastases. All LG and RG procedures were performed or guided by Endoscopic Surgical Skill Qualification System (ESSQS)-qualified surgeons. ESSQS was launched in 2004 by the Japanese Society for Endoscopic Surgery to develop a tool to reliably evaluate trainees' surgical techniques.[12] Moreover, RG was performed by surgeons certified to operate a da Vinci Surgical Sysyem (DVSS) console who were ESSQS qualified and certified by the Japanese Society of Gastroenterological Surgery.

Laparoscopic gastrectomy

Six ports were used, and the left liver lobe was elevated as previously described.[13] First, the omentum of the greater curvature was resected using an ultrasonically activated incision device (Harmonic Scalpel™, Echicon Endo-Surgery, Cincinnati, OH, USA). Then, the left gastroepiploic artery was dissected proximal to the first branch, clipped, and ligated. The omentum was opened to reach the gastrocolic trunk, and the right gastroepiploic vein and artery were clipped and ligated at their root. The duodenum was dissected using a Signia™ tri-stapling system (Covidien Japan, Tokyo, Japan). The root of the right gastric artery was exposed and ligated, and LNs at station 5 were dissected. While dissecting the supra-pancreatic LNs (stations 8a, 9, and 11p), the assistant carefully manipulated the pancreas caudally using gauze to prevent damage. Subsequently, the left gastric artery and vein were isolated, ligated, and sectioned at their root, and LNs at station 9 were dissected. Additionally, during the dissection of LNs at station 11p, the body and tail of the pancreas were rolled and protected with a gauze while sealing the bottom of the LNs. For LN dissection near the lesser curvature, the assistant grasped the lymphoid tissue from the ventral side applying tension, and the surgeon resected the LNs. The oral side of the stomach or abdominal esophagus were also dissected in the proper position using a Signia™ tri-stapling system, and the specimen was removed through a small incision wound above the umbilicus.

For reconstruction, Roux-en-Y (R-Y) anastomosis was performed for total gastrectomy. For distal gastrectomy, R-Y anastomosis was selected in the following cases: tumor close to the duodenum; the remaining stomach was < 1/3rd; or there was hiatal hernia. In all other cases, B-I reconstruction was selected. With the exception of the jejunojejunostomy in R-Y anastomosis, all reconstructions were performed laparoscopically. Jejunojejunostomy was performed approximately 30 cm distal to the ligament of Treitz through a small laparotomy (3–4 cm) from which the specimen was removed.

Robotic gastrectomy

All RGs were performed using the da Vinci Si™. The robot was inserted at 0° (aligned with the body’s sagittal axis) for distal gastrectomies and at 15° to the left for total gastrectomies. A Harmonic Scalpel™ or monopolar curved scissors, fenestrated bipolar forceps, and Cadiere forceps were used on the first, second, and third arms, respectively. The assistant’s 12-mm port was implanted to the right of the umbilicus, and pneumoperitoneum was created at 10 mmHg using AirSeal™ (SurgiQuest, Orange CT, USA).

The basic procedures in RG and LG have the following differences. First, the suprapancreatic LNs dissection in RG did not require the assistant to manipulate the pancreas. The gauze was placed on the dorsal side of stomach, and the third arm was used to elevate the gastro-pancreatic folds. Although the pancreas was not mobilized, the operative field remained wide because the robot elevated each port. Second, in RG, when dissecting the left gastric vein, scissors with articulated function attached to the first arm were used for sectioning, thus preventing thermal damage to the pancreas and sparing the need for pancreatic protection. Additionally, since dissection of station 11p was performed using monopolar curved scissors, rolling of the body and tail of the pancreas was not necessary. However, to prevent lymphatic fistula at the base of station 11p, Harmonic Scalpel^{TM} was used. Third, the dissected tissue was grasped by the assistant in LG, but in RG, the third arm of the robot grasped, fixed, and towed the tissue.

Propensity score matching

Propensity score matching (PSM) analysis was performed to reduce potential selection bias using the following covariates: age, sex, BMI, operation method, LN dissection (D1+ or D2), and pathological stage. Then, the two groups were matched using the nearest-neighbor matching algorithm (ratio=1:1 without replacement) with a caliper width of 0.1 of the standard deviation of the propensity score logit. After PSM, 68 patients (34 patients in each of the RG and LG groups) were eligible for analysis.

Statistical analysis

Statistical analyses were performed using the Fisher's exact test or the Mann-Whitney U-test, as appropriate. Statistical calculations were performed using the Statistical Package for the Social Sciences for Mac (version 22.0, IBM Institute, Armonk, NY, USA) and GraphPad Prism version 8.0 (GraphPad Software, San Diego, CA, USA). The Kaplan–Meier method was used to calculate overall survival (OS) and relapse-free survival (RFS), and differences between the survival curves were assessed using the log-rank test. Multivariate analyses for survival were performed using the Cox proportional hazard model. OS was calculated from date of surgery to the date of all-cause death. RFS was calculated from date of surgery until recurrence and censored at death. For all analyses, differences were considered statistically significant when P-value was < 0.05.

Results

Baseline characteristics

Table 1 presents a comparison of baseline characteristics between the two groups before and after PSM. Prior to PSM, the cancer stage was significantly higher in the RG group than in the LG group (P<0.0001); therefore, the percentage of D2 dissection was also significantly higher in the RG group (P<0.0001). After PSM, both groups were comparable in terms of age, sex, BMI, cancer stage, and ASA-PS.

Surgical characteristics and perioperative outcomes

Table 2 shows a comparison of surgical details and outcomes between the two groups before and after PSM. Prior to PSM, there was no difference between groups in the type of operative procedure (distal or total gastrectomy), operative time, postoperative complications, length of stay, or mortality. There was no difference in the number of ESSQS-certified surgeons who performed the surgeries. Laboratory data revealed that blood leukocyte count and drainage fluid amylase levels were comparable among the groups; C-reactive protein (CRP) levels on postoperative day 1 were higher in the RG group than in the LG group (P=0.0004). Additionally, the RG group had less blood loss (P<0.0001) and a higher number of LNs retrieved (P=0.0200) than the LG group.

A significantly larger number of LNs were retrieved in the RG group than in the LG group from the area of stations 7, 8a, 9 and 11p, when examining dissections by site (Table 3 left).

After PSM, a significant reduction in intraoperative blood loss was observed in the RG group compared to the LG group (*P*=0.0005). Additionally, the incidence of postoperative complications, length of stay, or mortality, the RG group had significantly lower CRP levels on postoperative day 1 (*P*=0.0006) (Table 2).

Moreover, the number of LNs retrieved remained significantly higher in the RG group than in the LG group (*P*=0.015). Specifically, LNs retrieved from the station groups of supra-pancreatic (7,8a,9 and 11p) and lesser curvature (1, 3a, 3b and 5) areas accounted for this difference (*P*=0.0073 and 0.0362, respectively) (Table 3).

Survivals

The median follow-up periods were 1842 (range 271–2763) days for LG and 850 (range 142–1501) days for RG, respectively. Figure 2 shows the Kaplan-Meier curves for patients undergoing RG and LG after PSM. There were no significant differences between the LG and RG groups in both OS (log-rank *P*=0.46; Figure 2A) and RFS (log-rank *P*=0.46; Figure 2B), although the survival of RG tended to be higher than that of LG.

Discussion

In this study, we compared the short-term outcomes of RG and LG for GC and found that the RG was associated with less bleeding, lower CRP levels at postoperative day 1, and a higher number of dissected LNs, suggesting that a randomized controlled trial is worth conducting to confirm that RG is less invasive and has oncological advantages.

The use of RG for GC has been increasing since Hashizume first performed it in Japan in 2003.[14] Two large-scale multi-institutional prospective studies, one conducted in Japan[2] and the other in Korea,[15] have compared robotic and laparoscopic approaches for GC. Many smaller studies comparing short- and long-term outcomes have also been reported. Among them, two randomized controlled trials have reported significantly less blood loss with RG than with LG or OG in the short term.[16] In our study, RG resulted in less intraoperative bleeding and a lower CRP value on the first day after surgery compared to LG. RG may be a minimally invasive surgery that causes mild postoperative inflammation.

Many studies have shown that the number of dissected LNs determines the quality of cancer surgery.[17-22] Lymphadenectomy is an important part of GC surgery because the number of dissected LNs may influence the prognosis of patients.[23] In this regard, our study showed that RG could be used to retrieve a significantly increased number of LNs in specific areas compared with LG, suggesting that RG may be a superior surgical technique for LNs dissection. However, survival-based assessments such as OS and RFS are needed to show the oncological superiority of surgery. In this study, RG was superior to LG in terms of OS and RFS, but no significant difference was established; however, this might be due to the small number of cases and the short observation period. Therefore, a large prospective study that includes many cases is needed for the oncological evaluation of RG for GC.

Postoperative pancreas-related complications results can help to examine the superiority of RG over LG in LN dissection. The rates of pancreatic fistula after RG have been reported to be lower (approximately 0%–0.9%) than those of LG (0.5%–5%).[24-27] The reasons for a higher incidence of this complication after LG may include the use of straight forceps and the fact that the pancreas needs to be mobilized with gauze. Additionally, Ojima *et al.*[28] reported that supra-pancreatic LN dissection without manipulating the pancreas is possible in RG. They have found that the number of dissected LNs was higher and the postoperative day 1 drain amylase levels were lower in RG than in LG. Additionally, they demonstrated that the robot had a stable traction force and the articulated monopolar curved scissors could dissect LNs without compressing the pancreas. To evaluate the surgical superiority of the number of resected LNs, we conducted a detailed study by comparing the number of LNs at specific areas, which is a previously unreported method. As a result, RG could remove significantly more LNs in the supra-pancreatic area (stations 7, 8a, 9 and 11p) than LG, but there was no increase in postoperative drain amylase levels.

Considering the reports on the frequency of pancreas-related complications, the reasons for the surgical advantage of RG regarding LN dissection may include the following: 1) all the ports in RG were lifted up ventrally by the robot to keep the intra-abdominal cavity wide and to prevent interference between the pancreas and forceps; 2) a strong and stable third arm could hold the pedicle of the left gastric artery, and the Harmonic Scalpel™ was actively used for supra-pancreatic LN dissection, taking advantage of its sealing effect.

Although the number of LNs obtained was based on the surgical procedure using PSM analysis, the following selection biases still existed when interpreting this result. First, regarding the supra-pancreatic LN dissection of distal gastrectomy, the main difference between D1+ and D2 dissection is whether or not the No.11p LN was retrieved. Due to the high visibility and maneuverability of the RG, the No. 11p LNs may have been unintentionally removed beyond the range defined as D1+. Therefore, such excess excised LNs might have been included in the number of supra-pancreatic areas. Second, there was a significant difference between RG and LG in terms of the number of LN dissections on the lesser curvature areas, which may be difficult to explain by the difference in surgical procedures. Many surgeons in our study performed the LN removals from the resected specimens after gastrectomy. Therefore, surgeon bias may have affected the number of LNs extracted from the resected specimens. After these biases are taken into account, it may be considered that performing RG for LN dissection in the supra-pancreatic areas is not inferior to LG, but rather has an advantage equal to or higher than that of LG. Therefore, a more detailed study—with limited cases involving D2 LN dissection and inclusion of cases with PSM of surgeons who remove the LNs from the specimen—is warranted.

In this retrospective analytical study, we performed PSM which demonstrated the potential benefit of RG over LG in terms of the number of LNs removed, suggesting that RG has a potential advantage in resection in GC surgery. However, one of the problems with this is the difference in the timing of LG and RG. LG began seven years before RG, and RG started after LG technique became stable. Thus, some of the initial LG data may be more susceptible to the learning curve than those of RG. Another problem is the potential bias in the proficiency of surgeons who performed LG or RG. For LG in this study, four ESSQS-qualified surgeons ensured the quality of surgery as an operator or as a supervisor, while only two of the four ESSQS-qualified surgeons exclusively performed RG. The surgeon bias could not be adjusted for using PSM. Therefore, a randomized controlled trial should be conducted to verify the superiority of surgery performed only by skilled surgeons who have reached the learning curve plateau.

This study has some limitations. First, this was a single-center study. The number of cases was subjectively selected by surgeons, and since RG is newer than LG, the number of patients undergoing this procedure was smaller. However, it was possible to confirm the difference by matching the background factors with PSM to compensate for the small sample size. Second, this was a retrospective study. The surgical approach was determined by the operator and patient. Although our results suggest that RG was associated with superior outcomes, these should be validated in a randomized controlled trial. Additionally, future studies may obtain results that are more reliable by increasing the sample size in both groups and comparing outcomes in multi-center settings.

Conclusion

RG resulted in less intraoperative bleeding and lower CRP levels on the first day after surgery compared with LG, indicating that the former is less invasive. Moreover, RG resulted in more effective LN dissection in the supra-pancreatic region than LG, suggesting that it also has the potential to grow into an oncologically better surgical procedure than LG.

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Data Statement: The data that support the findings of this study are openly available in Mendeley Data at "https://data.mendeley.com/drafts/f5kxv6hbx9".

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Figure legends

Figure 1. Lymph node stations, as defined by the Japanese classification of gastric carcinoma (3rd English edition) were classified into the following three areas: 1) greater curvature area, 2) lesser curvature area and 3) supra-pancreatic area.

Figure 2. Kaplan-Meier estimates of (A) overall survival and (B) relapse-free survival probability after the cohort was propensity-score-matched.

Table 1 Patients' characteristics

	Before PSM					After PSM				
	RG (n= 44)		LG (n= 171)		*P* value	RG (n= 34)		LG (n= 34)		*P* value
Age, years, median [range]	71	[24 - 86]	69	[30 - 90]	0.357	69	[24 - 86]	69	[30 - 82]	0.367
Sex					0.381					1.0
Male (%)	25	(56.8)	111	(64.9)		19	(55.9)	18	(52.9)	
Female (%)	19	(43.2)	60	(35.1)		15	(44.1)	16	(47.1)	
Body Mass Index (kg/m^2) [range]	22.4	[16.1 - 32.0]	22.6	[15.1-30.7]	0.46	23.1	[16.1 - 32.0]	23.2	[19.2-29.9]	0.189
cStage†					<0.0001					1.0
IA	30	(68.2)	161	(94.1)		30	(88.2)	29	(85.3)	
IB	4	(9.1)	8	(4.7)		2	(5.9)	3	(8.8)	
>II	10	(22.7)	2	(1.2)		2	(5.9)	2	(5.9)	
Lymph node dissection					<0.0001					>0.999
D1+	30	(68.2)	161	(94.1)		30	(88.2)	29	(85.3)	
D2	14	(31.8)	10	(5.9)		4	(11.8)	5	(14.7)	
ASA-PS‡					0.71					0.94
1	5	(11.4)	25	(14.6)		5	(14.7)	5	(14.7)	
2	36	(81.8)	130	(76.0)		25	(73.4)	24	(70.6)	
3	3	(6.8)	16	(9.4)		4	(11.8)	5	(14.7)	

Data are expressed as median (interquartile) or number of patients (percentage).

†: According to the 15th Japanese Classification of Gastric Carcinoma. ‡ASA-PS:American Society of Anesthetists Physical Status

Table 2 Intraoperative outcomes and surgical procedures

	Before PSM					**After PSM**				
	RG (n= 44)		LG (n= 171)		*P* value	RG (n= 34)		LG (n= 34)		*P* value
Operative procedure					0.53					0.79
Distal gastrectomy, n (%)	34	(77.2)	139	(81.3)		25	(73.5)	24	(70.6)	
Total gastrectomy, n (%)	10	(22.8)	34	(18.7)		9	(26.5)	10	(29.4)	
Operation time, min, median [range]	408	[234 - 639]	384	[209 - 931]	0.94	363	[234 - 639]	396	[226 - 638]	0.72
Blood loss, ml, median [range]	17	[0 - 251]	100	[0 - 4394]	<0.0001	11	[0 - 251]	100	[0 - 960]	0.0005
Retrieved lymph nodes, number, median [range]	39	[7 - 95]	31	[9 - 68]	0.02	42	[19 - 81]	31	[13 - 61]	0.015
Any complication Clavien-Dindo Grade >2, n (%)	1	(2.2)	8	(4.6)	0.69	1	(2.9)	3	(8.8)	0.61
Hospital stay, days, median [range]	11	[7 - 30]	11	[7 - 108]	0.56	11	[7 - 30]	12	[7 - 65]	0.33
Amylase level in drainage fluid on POD1, IU/L, median [range]	503	[83 - 4080]	391	[35 - 26876]	0.27	471	[83 - 4080]	502	[88 - 26729]	0.83
Amylase level in drainage fluid on POD2, IU/L, median [range]	246	[37 - 2085]	211	[19 - 8130]	0.79	254	[37 - 2085]	250	[60 - 4301]	0.79
Amylase level in drainage fluid on POD3, IU/L, median [range]	158	[30 - 2154]	131	[31 - 3434]	0.59	158	[30 - 2154]	195	[30 - 809]	0.84
WBC on POD 1, /μL, median [range]	9200	[4100 - 14400]	9100	[4000 - 20500]	0.56	9250	[4100 - 14400]	8600	[4300 - 16400]	0.61
CRP on POD 1, mg/dL, median [range]	5.6	[0.2 - 9.8]	6.7	[2.3 - 18.3]	0.0004	5.1	[0.6 - 9.6]	7	[3.4 - 18.3]	0.0006
pStage†					<0.001					0.94
IA	28	(63.6)	150	(87.7)		25	(73.5)	24	(70.6)	
IB	5	(11.4)	12	(7.0)		5	(14.7)	5	(14.7)	
>II	11	(25.0)	9	(5.3)		4	(11.8)	5	(14.7)	
Mortality, n (%)	0		0		n.s.	0		0		n.s.
ESSQS-qualified Surgeons, No	2		4		n.s.	2		4		n.s.

Data are expressed as median (interquartile) or number of patients (percentage).

CRP = C reactive protein, n.s. = not significant, WBC = white blood cell, POD = postoperative day, RG = robotic gastrectomy, LG = laparoscopic gastrectomy, ESSQS = Endoscopic Surgical Skill Qualification System.

†: According to the 15th Japanese Classification of Gastric Carcinoma.

Table 3 Comparison of the number of lymph node dissections by site

	Before PSM			**After PSM**		
	RG (n= 44)	LG (n= 171)	*P* value	RG (n= 34)	LG (n= 34)	*P* value
#1,3a,3b,5	11 [2 - 34]	10 [1 - 31]	0.2617	12 [5 - 36]	9 [0 - 26]	0.0362
#4d,6	10 [1 - 33]	9 [0 - 33]	0.2883	11 [3 - 31]	10 [0 - 24]	0.0989
#7,8a,9,11p	12 [0 - 35]	10 [0 - 29]	0.0213	14 [5 - 35]	9 [0 - 23]	0.0073
total	39 [7 - 95]	31 [9 - 68]	0.02	42 [19 - 81]	31 [13 - 61]	0.015

Data are expressed as median [interquartile].

#LNs numbers are according to the 15th Japanese Classification of Gastric Carcinoma.

Figure 1

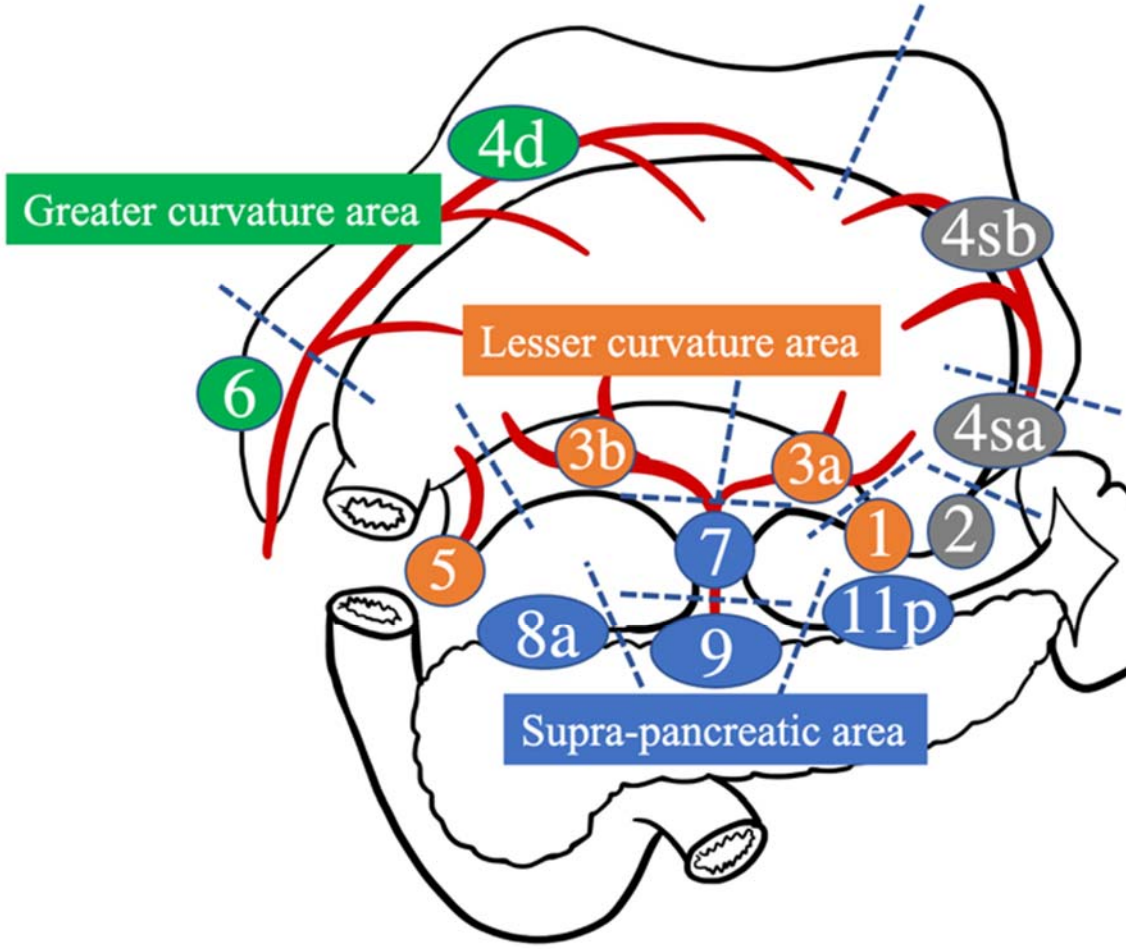
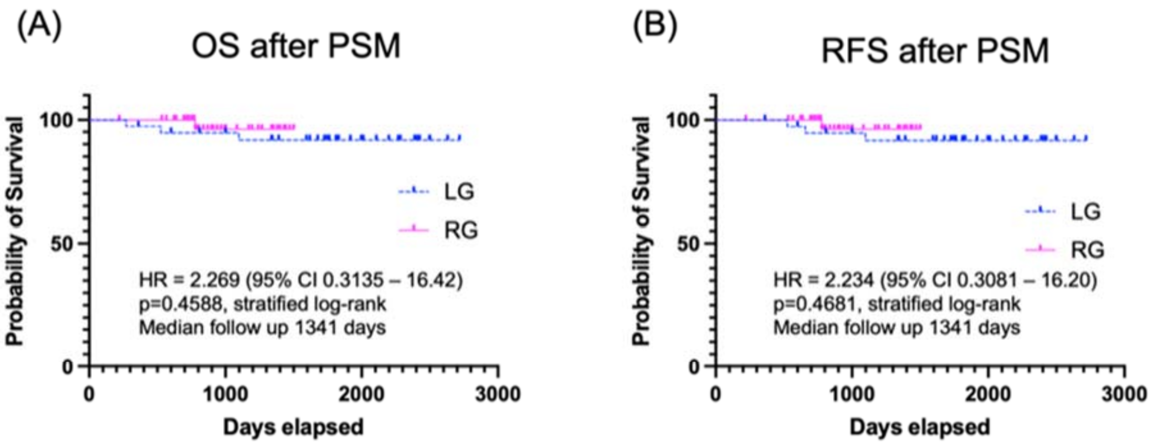

4d
Greater curvature area
4sb
Lesser curvature area
6
4sa
3b
3a
1
2
7
5
8a
9
11p
Supra-pancreatic area

Figure 2



(A)
OS after PSM
Probability of Survival
100
50
0
0
1000
2000
3000
Days elapsed
LG
RG
HR = 2.269 (95% CI 0.3135 – 16.42)
p=0.4588, stratified log-rank
Median follow up 1341 days
(B)
RFS after PSM
Probability of Survival
100
50
0
0
1000
2000
3000
Days elapsed
LG
RG
HR = 2.234 (95% CI 0.3081 – 16.20)
p=0.4681, stratified log-rank
Median follow up 1341 days