Title: **Short-term outcomes of robotic distal gastrectomy with the "preemptive retropancreatic approach": A propensity score matching analysis**

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Abstract

Purpose

We report the usefulness of the preemptive retropancreatic approach (PRA) in robotic distal gastrectomy (RDG) using multi-jointed forceps. Therefore, this study aimed to compare the short-term outcomes of RDG with PRA and conventional laparoscopic distal gastrectomy using the propensity score matching method.

Methods

A total of 126 patients (RDG = 55; laparoscopic distal gastrectomy [LDG] = 71) were retrospectively enrolled. Patients were matched using the following propensity score covariates: age, sex, body mass index, American Society of Anesthesiologists physical status, the extent of lymph node dissection, and Japanese Classification of Gastric Carcinoma stage. Surgical results and postoperative outcomes were compared.

Results

We identified 28 propensity score-matched pairs. The median operative time and blood loss were comparable (P = 0.272 and P = 0.933, respectively). Regarding postoperative outcomes, the incidence of postoperative complications (Clavien–Dindo classification II [CD ≥II]) was lower in the RDG group than in the LDG group (P = 0.020). No significant differences in the peak C-reactive protein value and length of hospital stay were observed between the two groups (P = 0.391 and P = 0.057, respectively). In addition, no patients had postoperative pancreas-related complications (≥ CD II) in the RDG group.

Conclusions

RDG using PRA seems to be a safe and feasible procedure for gastric cancer because of short-term outcomes and reduction of postoperative complications (especially postoperative pancreas-related complications) as compared to conventional LDG.

Keywords: laparoscopic distal gastrectomy, gastric cancer, postoperative complications, preemptive retropancreatic approach

Declarations

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Authors' contributions

Study conception and design: Yuma Ebihara and Yo Kurashima.

Acquisition of data: Yuma Ebihara

Analysis and interpretation of data: Yuma Ebihara and Yo Kurashima

Drafting of manuscript: Yuma Ebihara.

Critical revision of the manuscript: Yuma Ebihara, Yo Kurashima, Soichi Murakami, Toshiaki Shichinohe, and Satoshi Hirano.

Ethics approval: This study was approved by the Hokkaido University Ethics Committee (No. 021-0022).

Consent to participate: The consent form indicated the aim of the study on the hospital's Website and offered participants the right to decline to participate or opt-out at any time. Comprehensive informed consent to use patient information for this study was obtained from all participants preoperatively.

Consent for publication： All authors（Yuma Ebihara, Yo Kurashima, Soichi Murakami, Toshiaki Shichinohe, and Satoshi Hirano) have consented to be published.

Introduction

Gastric cancer (GC) is the fifth most common cancer worldwide and the third most fatal cancer annually [1]. Recently, the number of robotic minimally invasive surgeries and robotic gastrectomy (RG) for GC has been increasing [2]. In April 2018, RG was approved for the national medical insurance coverage in Japan; since then, the number of RG procedures performed has significantly increased [3]. In RG, high-resolution three-dimensional images and the use of forceps with multi-joint functions eliminate the limitations of conventional laparoscopic gastrectomy and allow the performance of sophisticated procedures [4]. Several studies have compared the safety and feasibility of robotic distal gastrectomy (RDG) and laparoscopic distal gastrectomy (LDG) [5-7]. In particular, improvement in local operability is expected to ensure lymph node dissection for malignant tumor surgery and reduce postoperative complications [2].

However, a risk of serious postoperative pancreatic-related complications exists due to the lack of palpation and pancreatic damage in the arm, which can lead to serious postoperative pancreatic-related complications in RG. We have previously reported the usefulness of our novel "preemptive retropancreatic approach" (PRA) in RDG with multi-jointed forceps [8]. The use of forceps with multi-joint functions in RDG eliminates the limitations of conventional RDG. RDG using PRA is a useful technique that minimizes pancreatic compression and creates a good operative field for suprapancreatic lymphadenectomy. In PRA, minimizing pancreatic compression during suprapancreatic lymphadenectomy may reduce postoperative pancreatic-related complications. Thus, this study aimed to clarify short-term outcomes of RDG with PRA in comparison with conventional LDG using the propensity score matching (PSM) method. This is the first reported retrospective study of the usefulness of PRA.

Material and Methods

Patients

Between July 2014 and August 2020, a total of 126 consecutive patients who underwent curative minimally invasive distal gastrectomy (RDG or LDG) for GC at the Department of Gastroenterological Surgery II of Hokkaido University Hospital (Sapporo, Japan) were enrolled in this study. All patients were diagnosed with GC using endoscopy, computed tomography, or endoscopic ultrasound. All patients provided written informed consent to participate in the study. Specimens were evaluated according to the Japanese Classification of Gastric Carcinoma (JCGC), established by the Japanese Research Society for Gastric Cancer [9].

Data collection

Clinicopathological data, including age, sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA-PS), clinical stage, combined resection of other organs, and lymph node dissection, were collected. Surgical outcomes, such as operative time, estimated blood loss, postoperative complications, and length of postoperative hospital stay, were recorded. Patients were divided into three groups based on the Clavien–Dindo (CD) postoperative complication classification grade [10, 11] and further categorized into the RDG and LDG groups. To evaluate the systemic postoperative inflammatory response, serum C-reactive protein (CRP) levels were measured on postoperative days 1, 3, 5, and 7 in principle, and additional measurements were conducted based on patient condition. The highest serum CRP level from surgery to hospital discharge was defined as CRPmax. The Hokkaido University Hospital institutional review board approved the data collection and analysis (No. 021-0022). This study was performed following the Declaration of Helsinki principles.

Surgical procedure

Patients were placed under general anesthesia in the supine position, as previously reported [8]. For RDG, a 5-trocar system with a Nathanson hook liver retractor is generally used (Yufu Itonaga, Tokyo, Japan). After achieving a 10-mmHg pressure in the carbon dioxide pneumoperitoneum, an electrolaparoscope was introduced through the trocar, and four other trocars were positioned. Robotic second and fourth arms were docked at 8-mm left upper, left lower, and right upper trocars, respectively. The 12-mm left and right lower trocars were placed through the 12-mm trocar, and the assistant surgeon used the right lower trocar. The basic extent of lymph node dissection was D1+ (D1+ No.7, 8a, and 9 lymph nodes) or D2, and lymph node dissection was performed. Lymph node regions and dissections were defined according to JCGC [9]. We generally perform distal gastrectomy with Roux-en-Y reconstruction. When the Roux-en-Y reconstruction could not be used, Billroth I reconstruction was performed. The procedures employed during RDG, except for PRA, were not different from those of the conventional LDG. The surgeons are accredited through the endoscopic surgical skill qualification system of the Japan Society for Endoscopic Surgery (JSES) [12]. When the operating surgeon did not possess this qualification, a qualified surgeon supervised the surgery.

PRA in RDG

Initial dissection of the bilateral retropancreatic space, the adherence between the retroperitoneum surface and the pancreas (fusion fascia) is released, providing a good operative field and hindering contact with the pancreas in the suprapancreatic lymph node dissection during RDG. By dissecting the bilateral retropancreatic space, the adherence between the retroperitoneum and the retropancreatic fascia is released, providing a good operative field and hindering contact with the pancreas in suprapancreatic lymph node dissection as previously reported [8]. RDG using PRA does not require pancreatic compression with gauze using the assistant’s forceps and is useful for minimizing pancreatic compression during suprapancreatic lymphadenectomy (Fig. 1).

Statistical analysis

PSM was performed using a logistic regression model to mitigate the selection bias in this study. The parameters used for PSM were age, sex, BMI, American Society of Anesthesiologists physical status, splenectomy, clinical stage, surgical method, and lymph node dissection. The logit of the propensity score was matched within 0.2 standard deviations of the value based on Austin's recommendations [13]. Categorical variables were analyzed using the chi-squared test before PSM and the McNemar and Wilcoxon signed-rank tests after PSM. Qualitative variables are described as numbers (%) and were compared between the groups using the Pearson's chi-square or Fisher's exact tests. Continuous variables were examined using the unpaired t-test before the PSM and Wilcoxon signed-rank test after PSM. Nonparametric continuous values are expressed as median (interquartile range) and compared using the Mann–Whitney U test. Statistical significance was set at $P < 0.05$. Statistical analysis was performed using the JMP® 15 software (SAS Institute Inc., Cary, NC, USA).

Results

Patient backgrounds

Table 1 shows the clinical characteristics and surgical outcomes of the study population. A total of 126 patients were included, comprising 80 men (63.5%) and 46 women (36.5%), with a median age of 70 (range, 35–88) years and median BMI of 22.2 (range 15.3–33.2) kg/m^2. The ASA-PS was ≥2 in 111 patients (88.1%), clinical JCGC stage was ≥2 in 24 patients (19.9%), D2 lymphadenectomy was performed in 23 patients (18.3%), the median operative time was 311 (range, 163–585) min, the median operative blood loss was 0 (range, 0–255) mL, postoperative complications (CD ≥IIIa) occurred in 13 patients (10.3%), and the median postoperative hospital stay was 11 (range, 6–47) days. After applying our exclusion criteria (resection of other organs and Billroth-I reconstruction), 112 patients were included in the subgroup evaluated for PSM. In total, 28 patients in the RDG group were individually matched to 28 patients in the LDG group (Fig. 2). The clinicopathological characteristics of 112 patients who underwent curative minimally invasive distal gastrectomy and 56 propensity-score-matched patients are shown in Table 2. In the propensity-score-matched patients, as determined by the study design, age, sex, BMI, ASA-PS, the extent of lymph node dissection, and clinical JCGC stage distributions between the RDG and LDG groups were comparable.

Surgical outcomes

The surgical outcomes and postoperative complications of 112 patients who underwent curative minimally invasive distal gastrectomy for GC and propensity score-matched patients are shown in Table 3. In the propensity score-matched group of patients, no significant difference in the operative time and blood loss and the number of harvested lymph nodes were observed. Furthermore, no difference in postoperative hospital stay was observed between the two groups. Table 4 shows the incidence of postoperative complications. Among the total complications (CD ≥II), two patients (7.2 %) incurred complications in the RDG group, as compared to nine patients (32.1 %) who experienced complications in the LDG group (P = 0.020), and severe complications (≥CD IIIa) in one patient (3.6%) for each group. No patients complained of postoperative pancreas-related complications (CD II) in the RDG group. No difference in the maximum CRP levels was observed between the two groups. In the RDG group, no patient had postoperative pancreas-related complications (CD ≥II). None of the patients died intraoperatively or during hospitalization.

Discussion

Our study revealed that our novel PRA reduces postoperative complications (CD II) than the conventional LDG. Minimizing pancreatic compression during suprapancreatic lymphadenectomy may reduce postoperative pancreatic-related complications in RDG using PRA. To the best of our knowledge, this is the first reported retrospective study of PRA.

In 2003, Hashizume et al. [14] reported the world's first robot-assisted gastrectomy for GC. Studies comparing RDG with LDG for GC have mainly been retrospective, with almost all of them reporting prolonged operative time, reduced blood loss, and similar incidence of postoperative complications for RG [6, 7]. In RG, a risk of serious postoperative pancreatic-related complications is observed due to the lack of palpation and pancreatic damage in the arm, which can lead to serious postoperative pancreatic-related complications [8]. Regarding pancreatic juice leakage during gastrectomy, Tsujira et al. [15] reported that pancreatic juice leakage after laparoscopic gastrectomy may be attributable to either operator- or assistant-related causes. The operator can injure the pancreatic tissue by direct cutting or cause thermal injury from energy devices used during the dissection of suprapancreatic lymph nodes. In a study using a swine model, Ida et al. [16] reported that pancreatic compression using the assistant's forceps can contribute to pancreatic juice leakage and that their findings will help improve the procedure for lymph node dissection around the pancreas during laparoscopic gastrectomy. Several studies have similarly reported postoperative pancreatic juice leakage due to pancreatic compression during the surgical field preparation to dissect the suprapancreatic lymph nodes during gastrectomy. Hence, we reported that the maximum avoidance of pancreatic compression may be adopted as a safe and precise standard technique in RDG without tactile sensation.

Several reports have indicated that postoperative complications are associated with the prognosis of patients with GC [17,18]. In our previous multicenter retrospective study on the long-term prognosis of laparoscopic surgery for GC, postoperative complications were also found to be associated with survival [19]. Saito et al. [20] have reported that CRP elevation (CRPmax of ≥12 mg/dl) is a more reliable indicator of survival after a GC surgery than the occurrence of postoperative complications. Surgeons should minimize the postoperative inflammatory response to improve the prognosis. Therefore, ensuring the safety of gastrectomy may be important for short- and long-term outcomes of patients with GC. In this study, there were significantly fewer postoperative complications (CD ≥II) ($P = 0.020$) and no pancreatic-related complications in the RDG group. The number of patients with postoperative inflammatory response (CRPmax ≥12 mg/dl) was also lower in the RDG group, although this difference was not significant. Moreover, no patient had postoperative pancreas-related complications (CD II) in the RDG group. We believe that one cause of postoperative pancreatic-related complications may be pancreatic compression during dissection of the suprapancreatic lymph nodes and intend to further substantiate this approach's usefulness in studies with long-term outcomes.

Gastrointestinal cancer surgery requires en bloc removal of the primary tumor and organ-specific mesentery [21]. Kumamoto et al. [22] reported a systematic mesogastric excision (SME) concept for GC, which is advantageous to the surgical anatomy and achieves en bloc primary tumor removal and gastric mesentery. Our novel PRA can perform the SME concept for GC is advantageous for the surgical anatomy, and achieve en bloc removal of the primary tumor and gastric mesentery. Furthermore, although the number of patients investigated was low, prolonged operative time was not observed in RDG compared to conventional LDG in this study cohort. Reduced operative time due to PRA was noted, indicating its effectiveness.

This study has several limitations. This was a retrospective, observational, and non-experimental study. Furthermore, although PSM was performed, selection bias, such as operator bias, cannot be eliminated. In this study, all RDGs and LDGs were performed by experts as operators or teaching assistants. This study was conducted over a rather long period between 2014 and August 2020, which could have been associated with historical biases regarding the treatment strategy and perioperative management, which might indicate the outcomes after gastrectomy. In the future, we will assess the usefulness of RDG with D2 lymphadenectomy using PRA for advanced GC. Finally, this was a single-center retrospective study; therefore, multicenter randomized controlled trials should be performed to verify the reliability of the results.

Conclusion

Our novel technique employing the PRA in RDG seems to be a safe and feasible procedure for GC in terms of short-term outcomes and reducing postoperative complications (especially postoperative pancreas-related complications) as compared to the conventional LDG.

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Figure captions:

Fig. 1 Operative schema of the suprapancreatic lymph node dissection ("preemptive retropancreatic approach"; PRA). a: Conventional laparoscopic dissection of the suprapancreatic lymph node. Exposure of operative view with pancreatic compression with gauze using the assistant's forceps can contribute to the pancreatic juice leakage. b: Robotic dissection of the suprapancreatic lymph node using PRA. During the retropancreatic space dissection, the adherence between the retroperitoneum surface and retropancreatic facia is released. The mesogastrium (including the suprapancreatic lymph nodes) was lifted forward and provided a good operative field and hindered the contact with the pancreas in suprapancreatic lymph node dissection

CHA, common hepatic artery; SA, splenic artery; SV splenic vein; ＊, retropancreatic space.

Fig. 2 Study enrollment

MIDG, minimally invasive distal gastrectomy; GC, gastric cancer; RDG, robotic distal gastrectomy; LDG, laparoscopic distal gastrectomy.

Table 1. Clinical features and surgical outcomes of the study population

Variable	Overall (n=126)
Gender (M/F)	80/46
Age (year) (median, range)	70 (35-88)
BMI† (kg/m^2) (median, range)	22.2 (15.3-33.2)
ASA-PS* (≥II) (patients,%)	111 (88.1%)
Clinical JCGC stage** (≥II) (patients,%)	24 (19.0%)
Surgical procedure (RDG/LDG) ⁑	55/71
Lymph node dissection (≥D2) (patients,%)	23 (18.3%)
Operation time (min) (median, range)	311 (163-585)
Blood loss (ml) (median, range)	0 (0-255)
Postoperative complication (CD§, ≥IIIa) (patients,%)	13 (10.3%)
Postoperative hospital stays (days) (median, range)	11 (6-47)

† Body mass index, *The American Society of Anesthesiologist's physical status, **According to the Japanese classification of gastric carcinoma: 3rd English edition, ⁑ RDG, robotic distal gastrectomy; LDG, laparoscopic distal gastrectomy, § Clavien-Dindo, classification

Table 2. Patient‘s characteristics who underwent minimally invasive distal gastrectomy before and after propensity score matching

	Unmatched patients (n=112)			Propensity-matched patients (n=56)		
	RDG (n=51)	LDG (n=61)	*p* value	RDG (n=28)	LDG (n=28)	*p* value
	Number	Number		Number	Number	
Age (year) (median, range)	70 (36-85)	69 (35-85)	0.341	72.5 (36-85)	71 (57-85)	0.699
Sex (%)			0.106			1.000
Male	36 (70.6)	34 (55.7)		17 (60.7)	17 (60.7)	
Female	15 (29.4)	27 (44.3)		11 (39.3)	11 (39.3)	
BMI† (kg/m^2), median (range)	22.2 (16.0-28.2)	21.8 (16.4-33.2)	0.453	22.1 (16.0-26.6)	22.2 (16.9-26.1)	0.994
ASA-PS* (≥II) (patients,%)	42 (82.4)	56 (91.8)	0.132	24(85.7)	24(85.7)	1.000
Extent of lymph node dissection			0.448			0.752
D1+ (%)	43 (84.3)	48 (78.7)		22 (78.6)	21 (75.0)	
D2 (%)	8 (15.7)	13 (21.3)		6 (21.4)	7 (25.0)	
Clinical JCGC stage** (%)			0.179			0.807
I	45 (88.3)	47 (77.0)		22 (78.6)	20 (71.4)	
II	5 (9.8)	8 (13.1)		5 (17.8)	7 (25.0)	
III	1 (1.9)	6 (9.9)		1 (3.6)	1 (3.6)	

RDG; robotic distal gastrectomy, LDG; laparoscopic distal gastrectomy, †Body mass index, *The American Society of Anaesthesiologist's physical status, **According to the Japanese classification of gastric carcinoma: 3rd English edition.

Table 3 Surgical outcomes and postoperative course in patients who underwent minimally invasive distal gastrectomy before and after propensity score matching

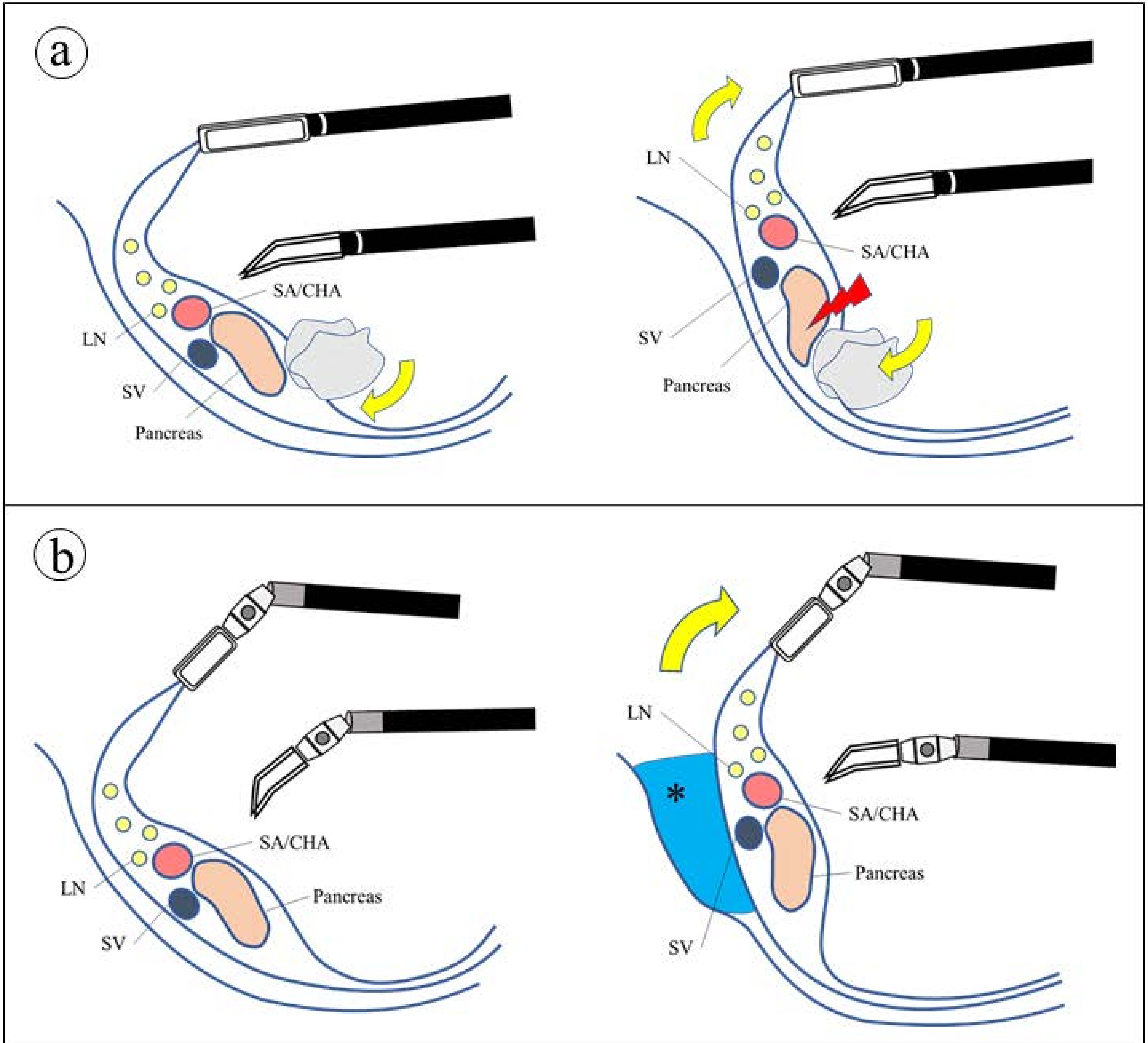
	Unmatched patients (n=112)			Propensity-matched patients (n=56)		
	RDG (n=51) Number	LDG (n=61) Number	*p* value	RDG (n=28) Number	LDG (n=28) Number	*p* value
Operative time (min), median (range)	332 (180-486)	304 (185-511)	0.202	337.5 (180-486)	301 (185-511)	0.272
Blood loss (ml), median (range)	0 (0-255)	0 (0-195)	0.965	0 (0-255)	0 (0-195)	0.933
Number of harvested lymph nodes, median (range)	35 (7-75)	38 (8-114)	0.540	34 (16-75)	36.5 (8-114)	0.486
Pathological JCGC stage* (%)			0.181			0.307
I	37 (72.5)	49 (80.3)		19 (67.9)	22 (78.6)	
II	9 (17.7)	4 (6.6)		6 (21.4)	2 (7.1)	
III	5 (9.8)	8 (13.1)		3 (10.7)	4 (14.3)	
Postoperative hospital stay (day), median (range)	11 (6-36)	12 (6-42)	0.384	10 (6-28)	12 (6-32)	0.057

RDG; robotic distal gastrectomy, LDG; laparoscopic distal gastrectomy, *According to the Japanese classification of gastric carcinoma: 3rd English edition.

Table 4. Postoperative inflammatory response and complications

	RDG (n=28) Number	LDG (n=28) Number	*p* value
Postoperative complication (%)			
≥ CD§ II	2 (7.2)	9 (32.1)	0.020
≥ CD§ III	1 (3.6)	1 (3.6)	1.000
Complications (≥ CD§ II)			
Postoperative bleeding	1	1	
Delayed gastric emptying	0	1	
Pancreatic fistula	0	4	
Pneumonia	1	1	
Urinary tract infection	0	1	
Abdominal abscess	0	1	
CRP max ≥12 mg/dl	7 (25.0)	11 (39.3)	0.391
Mortality	0	0	

RDG; robotic distal gastrectomy, LDG; laparoscopic distal gastrectomy § Clavien-Dindo, classification



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LN
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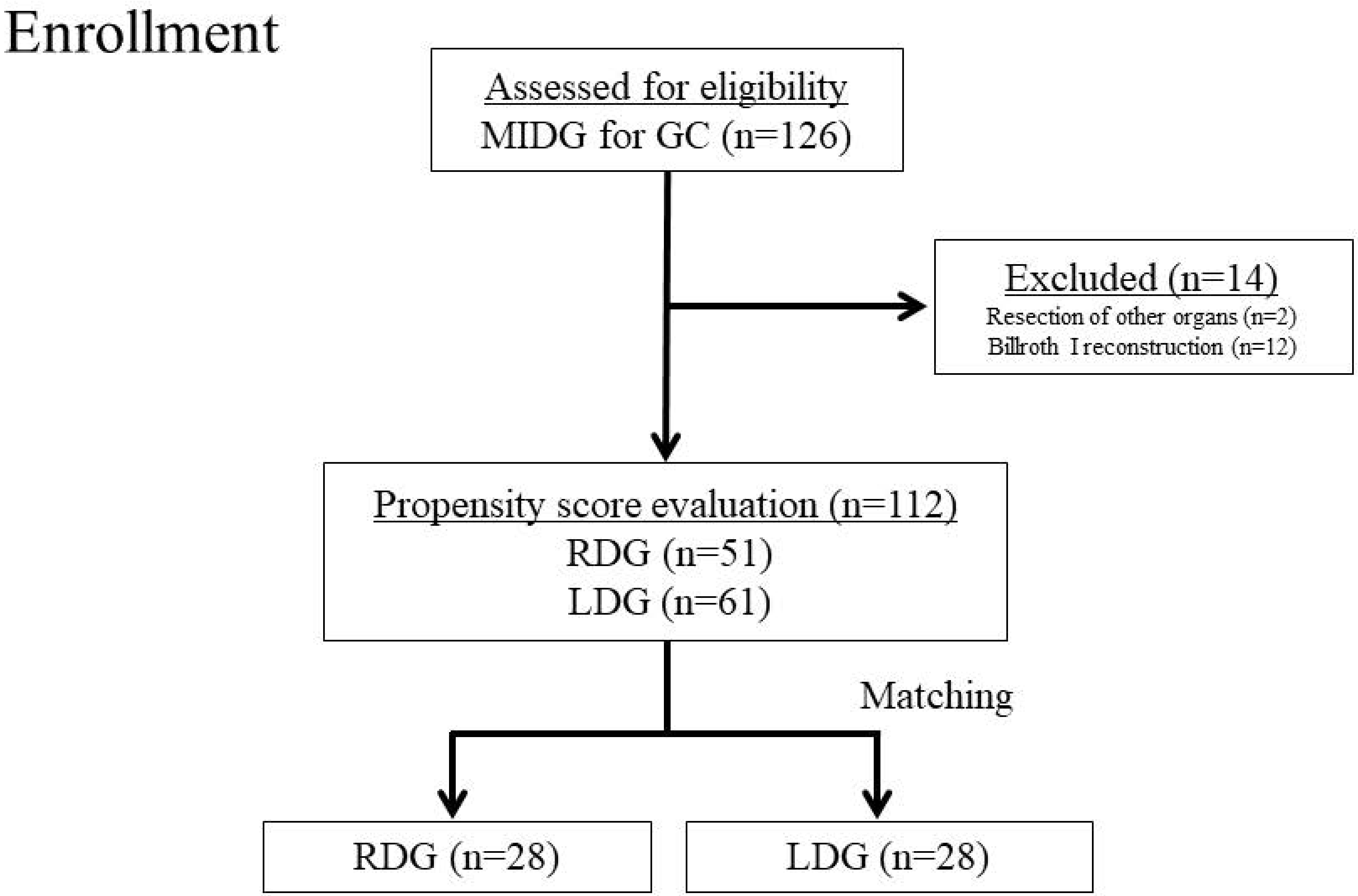
Enrollment
Assessed for eligibility
MIDG for GC (n=126)
Excluded (n=14)
Resection of other organs (n=2)
Billroth I reconstruction (n=12)
Propensity score evaluation (n=112)
RDG (n=51)
LDG (n=61)
Matching
RDG (n=28)
LDG (n=28)