Propensity-score-matched analysis of a multi-institutional dataset to compare postoperative complications between Billroth I and Roux-en-Y reconstructions after distal gastrectomy

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Received: 3 October 2019 / Accepted: 4 February 2020 / Published online: 17 February 2020
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Abstract

Background Few well-controlled studies have compared postoperative complications between Billroth I (B-I) and Roux-en-Y (R-Y). The aim of the present study was to compare the incidence of overall and severe postoperative complications by reconstruction method after distal gastrectomy.

Methods We performed a multi-institutional dataset study of patients who underwent distal gastrectomy with B-I or R-Y reconstruction from 2010 to 2014. Using propensity scores to strictly balance the significant variables, we compared postoperative complications between the techniques.

Results After matching, we enrolled 1014 patients ($n=507$ in each group). The incidence of postoperative complications in the R-Y group was significantly higher vs the B-I group (29% vs 17%, $P<0.0001$). The incidence of intra-abdominal abscess (4.3% vs 1.8%, $P=0.0177$), bowel obstruction (2.6% vs 0.6%, $P=0.0203$), and delayed gastric emptying (5.3% vs 1.0%, $P<0.0001$) in the R-Y group was significantly higher vs the B-I group, respectively; we saw no significant difference in leakage (3.4% vs 4.1%, $P=0.5084$). The incidence of grade $\geq$ III severe postoperative complications in the R-Y group was significantly higher vs the B-I group (13% vs 7.1%, $P=0.0013$). Multivariable analysis showed that R-Y reconstruction was a strong independent risk factor for overall postoperative complications (odds ratio 1.58, $P=0.0044$) and grade $\geq$ III severe postoperative complications (odds ratio 1.75, $P=0.0127$). A forest plot revealed that R-Y reconstruction was associated with a greater risk of both overall and grade $\geq$ III severe postoperative complications in any subgroups.

Conclusions R-Y reconstruction was associated with increasing overall postoperative complications, as well as severe postoperative complications.

Keywords Gastric cancer · Billroth I · Roux-en-Y · Postoperative complication · Propensity · Score matching

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s10120-020-01048-6>) contains supplementary material, which is available to authorized users.

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Introduction

Distal gastrectomy is the standard treatment for gastric cancer located in the lower two-thirds of the stomach, and there are various types of reconstruction such as Billroth I (B-I), Billroth II, and Roux-en-Y (R-Y) procedures [1]. The reconstruction method is determined based on patients' condition and the surgeon's choice. B-I or R-Y reconstruction are performed often, each with advantages and disadvantages [2, 3], and which is the most successful remains unclear.

B-I reconstruction is the most common reconstruction in Japan because of its technical simplicity and physiological advantages [3, 4]. However, R-Y reconstruction has become popular in Japan because of the benefits of a lower incidence of postoperative complications including anastomotic leakage, less bile reflux, and remnant gastritis, compared with B-I reconstruction [5–10]. Several crucial prospective randomized clinical trials (RCT) compared these two reconstruction methods, and results showed no significant difference in long-term patients' quality of life (QOL) and the incidence of postoperative complications, although a slight difference was reported in short-term QOL and operation time [11–13]. Meta-analyses and systematic reviews also reported R-Y required longer operation time but resulted in less bile reflux and a lower incidence of remnant gastritis [6–8]. However, there have been conflicting opinions regarding incidence of postoperative complications. In the two studies, no significant differences in morbidity rates were found between R-Y and B-I reconstructions [6, 7], while the other one reported B-I reconstruction had a significantly lower rate of postoperative complications compared to R-Y reconstruction [8]. As a limitation, these studies clarified only the difference in the incidence of overall postoperative complications and not the severity. R-Y results in a low incidence of anastomotic leakage, which is a severe postoperative complication, and the main reason the procedure is preferred by surgeons [3].

Basis of the surgeon's choice of reconstruction methods after distal gastrectomy has been changed. Until a decade ago, it mostly depends on patient's condition, such as the extent of gastric resection. However, popularization of surgical devices for anastomosis (e.g. linear and circular staplers) and laparoscopic surgery allow surgeons to select reconstruction methods with their discretion. In addition, worse perioperative course, more postoperative complications, and delayed postoperative adjuvant chemotherapy lead to worse prognosis in patients with gastric cancer [14–17]. Therefore, the clinical importance of preventing postoperative complications is increasing, and it is worthwhile to re-evaluate the differences in postoperative complications by reconstruction method after distal gastrectomy. In single-institutional surveys, the sample size is

limited, the reconstruction method is often biased between institutions because of the surgeon's choice. Moreover, pre-operative conditions, for example age, comorbidities and disease stages, also generate serious selection biases. To overcome these limitations, we performed a multicenter dataset analysis using propensity score matching to strictly balance these significant variables to compare the incidence of overall and severe postoperative complications between R-Y and B-I reconstruction methods.

Patients and methods

Patient selection

We retrospectively reviewed the clinical data from 3484 patients who underwent gastrectomy for gastric cancer between January 2010 and December 2014, as acquired from medical records at nine institutions. We retrieved eligible patients for analysis based on the following criteria: distal gastrectomy with B-I or R-Y reconstruction, pathologically proven gastric adenocarcinoma, no preoperative treatment, R0 resection, no duodenal invasion, and sufficient data for analysis. Patients who underwent concurrent surgical procedures other than cholecystectomy or extended surgery (e.g. combined resection of adjacent involved organs for T4b tumor, para-aortic lymph node dissection) or modified surgery without systemic lymphadenectomy or with insufficient data on postoperative complications from discharge to 90 days after surgery were excluded from the study (Fig. 1).

Definition of postoperative complications

We analyzed data for postoperative complications occurring within 90 days after surgery in accordance with the Clavien–Dindo classification system [18, 19]. We considered Clavien–Dindo grade $\geq$ II postoperative complications clinically relevant, and grade $\geq$ III severe postoperative complications. We categorized complications as intra-abdominal (anastomotic bleeding, anastomotic leakage, anastomotic stricture, anastomotic ulcer, bowel obstruction including ileus, delayed gastric emptying including R-Y stasis, duodenal stump leakage, intra-abdominal abscess, intra-abdominal bleeding, pancreatic fluid leakage, wound infection) or systemic (pneumonia, bacteremia, Enteritis, Cholecystitis, and others). Intra-abdominal abscess and intra-abdominal bleeding accompanying with pancreatic fluid leakage were included in the pancreatic fluid leakage. All data on postoperative complications within 90 days after surgery were collected even for those treated in the outpatient clinics. Adverse effects of postoperative adjuvant chemotherapy was excluded from postoperative complications.

Fig. 1 Flow-chart of patient enrolment

Surgery and patient management

To guarantee the quality of the gastrectomy, systemic lymphadenectomy and reconstruction procedure, we selected institutions that performed more than 50 gastrectomies for gastric cancer each year, according to the Japanese gastric cancer treatment guidelines. Board-certified surgeons from the Japanese Society of Gastroenterological Surgery performed or supervised all surgeries. Because of retrospective study nature, there were no prescriptions for the selection of reconstruction method among the nine participating institutions. Surgeons' consensus was that R-Y reconstruction is preferable for patients with a small remnant stomach, hiatal hernia or reflux esophagitis. A central review was not performed. Clinical stage was classified based on the 14th edition and third English edition of the Japanese Classification of Gastric Carcinoma [20]. Other clinical and histopathological factors were recorded according to the 15th edition of the Japanese Classification of Gastric Carcinoma [21].

Postoperative chemotherapy with S-1 monotherapy has been recommended to all patients with pathological stage II/III except T1 and T3N0 gastric cancer, unless contraindicated by the patient's condition [1]. Patient follow-up was performed in accordance with the Japanese gastric cancer treatment guidelines [1], as follows: physical examinations and laboratory tests were performed every 3 months for the first 3 years and then every 6 months until 5 years after surgery; enhanced CT (chest and abdominal cavity) was conducted every 6 months for 5 years, and endoscopy was performed 1, 3, and 5 years post surgery. Patients were diagnosed with a relapse when signs or symptoms indicated a possible recurrence. During S-1 administration, patients underwent hematologic tests and assessments of clinical symptoms each cycle.

Ethics

This study conformed to the World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects ethical guidelines. Written informed consent for surgery and the use of patients' clinical data were obtained from the patients as required by the Institutional Review Board of each participating institution. We used an opt-out recruitment strategy in accordance with the Japanese government's policy because we performed this clinical research using only retrospective clinical data without intervention. The purpose, design, and objectives of the study were posted on our institutional home web page (https://www.med.nagoya-u.ac.jp/medical_J/ethics/rinsyoukansatsu.html) to provide an opportunity for patients to decline to participate in our study.

Propensity score matching

We used propensity score matching to strictly balance the significant variables in the analyses that follow. Propensity scores were estimated using a logistic regression model according to institution, sex, age, preoperative body mass index, the presence of diabetes mellitus, preoperative Eastern Cooperative Oncology Group Performance Status score, tumor location in preoperative examination, tumor size in preoperative examination, histology in preoperative biopsy findings, surgical approach (open or laparoscopy), intended extent of lymphadenectomy, and clinical stage. One-to-one matching without replacement was performed using a 0.1 caliper width, and the resulting score-matched pairs were used in subsequent analyses.

Statistical analysis

Correlations between each group and the clinicopathological variables were analyzed using the Chi square test or Fisher's exact test for categorical variables and the Mann–Whitney *U* test for continuous variables. We also performed a multivariate analysis using a Cox proportional hazards model and a logistic regression model, after relevant prognostic variables had been defined by the univariate analysis. When calculating disease-specific survival, only gastric cancer-related deaths were counted, and patients who died of other causes were censored. Relapse-free survival was defined as the period between the day of curative gastrectomy and detecting disease recurrence. Data were analyzed using JMP version 14 software (JMP, SAS Institute, Cary, NC, USA). $P < 0.05$ was considered statistically significant.

Results

Patients' characteristics

We included 1820 patients: 1275 patients (70%) underwent B-I reconstruction, and 545 patients (30%) underwent R-Y reconstruction. Patients' clinical and histopathological characteristics are summarized in Table 1. Propensity score matching was performed to minimize selection bias, resulting that the clinicopathological characteristics and institutions of the two groups ($n = 507$ for each group) were then well balanced. We performed further analyses using data for these 1014 patients. The median follow-up period in B-I group was 54.6 months or until death (range 5.7–91.2 months) and in R-Y group, 45.7 months or until death (range 3.4–91.7 months).

Table 1 Patients' characteristics categorized by reconstruction method after distal gastrectomy

	Unmatched comparison			Matched comparison		
	Billroth I (<i>n</i> = 1275)	Roux-en-Y (<i>n</i> = 545)	<i>P</i> value	Billroth I (<i>n</i> = 507)	Roux-en-Y (<i>n</i> = 507)	<i>P</i> value
Institution			<0.0001			0.9972
A	146 (79%)	38 (21%)		35 (49%)	37 (51%)	
B	112 (64%)	63 (36%)		61 (52%)	57 (48%)	
C	86 (54%)	74 (46%)		69 (52%)	63 (48%)	
D	96 (76%)	30 (24%)		27 (49%)	28 (51%)	
E	267 (66%)	141 (34%)		137 (50%)	137 (50%)	
F	160 (85%)	28 (15%)		29 (51%)	28 (49%)	
G	141 (68%)	66 (32%)		61 (50%)	60 (50%)	
H	102 (65%)	56 (35%)		50 (49%)	52 (51%)	
I	165 (77%)	49 (23%)		38 (46%)	45 (54%)	
Sex			0.1235			0.8883
Male	878 (69%)	395 (72%)		368 (73%)	366 (72%)	
Female	397 (31%)	150 (28%)		139 (27%)	141 (28%)	
Age (years)						
Mean ± SD	67.3 ± 10.2	68.3 ± 10.3	0.0656	68.6 ± 9.7	68.1 ± 10.3	0.4327
Preoperative BMI (kg/m ²)						
Mean ± SD	22.2 ± 3.0	22.5 ± 3.3	0.0820	22.4 ± 3.0	22.5 ± 3.3	0.5182
Comorbidities						
Diabetes mellitus	189 (15%)	99 (18%)	0.0736	83 (16%)	89 (18%)	0.6156
Cerebrovascular disease	80 (6%)	41 (8%)	0.3275	34 (7%)	42 (8%)	0.3400
Cardiovascular disease	144 (11%)	70 (13%)	0.3471	63 (12%)	63 (12%)	1.0000
Pulmonary disease	85 (7%)	44 (8%)	0.2841	34 (7%)	37 (7%)	0.7120
Renal dysfunction	51 (4%)	26 (5%)	0.4544	25 (5%)	25 (5%)	1.0000
ECOG-PS			<0.0001			0.3380
0	1113 (87%)	431 (79%)		404 (80%)	416 (82%)	
≥ 1	162 (13%)	114 (21%)		103 (20%)	91 (18%)	
Previous abdominal operation	166 (13%)	76 (14%)	0.5944	63 (12%)	69 (14%)	0.5755
Tumor location			0.1894			0.5273
Lower	630 (49%)	251 (46%)		220 (43%)	230 (45%)	
Middle	645 (51%)	294 (54%)		287 (57%)	277 (55%)	
Surgical approach			0.2199			0.5560
Open	799 (63%)	358 (66%)		329 (65%)	320 (63%)	
Laparoscopy	476 (37%)	187 (34%)		178 (35%)	187 (37%)	
Lymph node dissection			0.0004			0.6148
D1/D1 +	698 (55%)	249 (46%)		235 (46%)	243 (48%)	
≥ D2	577 (45%)	296 (54%)		272 (54%)	264 (52%)	
Histologic type			0.3795			0.9499
Differentiated	686 (54%)	281 (52%)		265 (52%)	264 (52%)	
Undifferentiated	589 (46%)	264 (48%)		242 (48%)	243 (48%)	
cStage (JGCA 14th)			<0.0001			0.8054
IA	668 (52%)	223 (41%)		210 (41%)	223 (44%)	
IB	268 (21%)	93 (17%)		112 (22%)	93 (18%)	
IIA	146 (11%)	64 (12%)		63 (12%)	64 (13%)	
IIB	98 (8%)	57 (11%)		48 (10%)	50 (10%)	
IIIA	89 (7%)	84 (15%)		68 (13%)	70 (14%)	
IIIB	6 (0.5%)	24 (4%)		6 (1%)	7 (1%)	
pT stage			<0.0001			0.8719

Table 1 (continued)

	Unmatched comparison			Matched comparison		
	Billroth I (n = 1275)	Roux-en-Y (n = 545)	P value	Billroth I (n = 507)	Roux-en-Y (n = 507)	P value
T1	686 (54%)	281 (52%)		287 (57%)	276 (54%)	
T2	157 (12%)	74 (14%)		67 (13%)	72 (14%)	
T3	142 (11%)	94 (17%)		76 (15%)	75 (15%)	
T4	133 (10%)	98 (13%)		77 (15%)	84 (17%)	
pN stage			<0.0001			0.3312
N0	896 (70%)	322 (59%)		308 (61%)	317 (63%)	
N1	191 (15%)	92 (17%)		97 (19%)	84 (17%)	
N2	115 (9%)	55 (10%)		53 (11%)	44 (9%)	
N3	73 (6%)	76 (14%)		49 (10%)	62 (12%)	
pStage (JGCA 15th)			<0.0001			0.2900
IA	727 (57%)	240 (44%)		233 (46%)	238 (47%)	
IB	173 (14%)	70 (13%)		75 (15%)	69 (14%)	
IIA	108 (8%)	55 (10%)		46 (9%)	53 (11%)	
IIB	104 (8%)	43 (8%)		56 (11%)	36 (7%)	
IIIA	101 (8%)	67 (12%)		55 (11%)	55 (11%)	
IIIB	48 (4%)	52 (10%)		29 (6%)	41 (8%)	
IIIC	14 (1%)	18 (3%)		13 (3%)	15 (3%)	

SD standard deviation, BMI body mass index, ECOG-PS Eastern Cooperative Oncology Group Performance Status, JGCA Japanese Gastric Cancer Association

Surgical outcomes and postoperative course

Patients' surgical outcomes and postoperative courses are summarized in Table 2. The operation time for the R-Y group (283 ± 72 min) was significantly longer vs the B-I group (246 ± 65 min, $P < 0.0001$); however, the intraoperative blood loss volume in the R-Y group (234 ± 288 ml) was not significantly different vs the B-I group (211 ± 244 ml, $P = 0.1720$). The length of postoperative hospital stays in the R-Y group (18 ± 20 days) was significantly longer vs the B-I group (15 ± 15 days, $P = 0.0070$). The incidence of overall postoperative complications in the R-Y group (148 [29%]) was significantly higher vs the B-I group (88 [17%], $P < 0.0001$), and the incidence of reoperation because of postoperative complications in the R-Y group (17 [3%]) was significantly higher vs the B-I group (4 [0.8%], $P = 0.0041$). Although not significantly different, the incidence of readmission because of postoperative complications within 90 days in the R-Y group (36 [7%]) was higher vs the B-I group (22 [4%], $P = 0.0583$).

Breakdown of each postoperative complications

The breakdown of the incidence of each postoperative complication is summarized in Table 3. The incidence of intra-abdominal postoperative complications in the R-Y group (107 [21%]) was significantly higher vs the B-I group

(59 [12%], $P < 0.0001$); however, the incidence of systemic postoperative complications was not significantly different between the two groups (B-I 29 patients [5.7%]; R-Y 41 patients [8.1%]; $P = 0.1371$).

Regarding each intra-abdominal postoperative complication, we found a significant difference for intra-abdominal abscess (B-I 9 patients [1.8%]; R-Y 22 patients [4.3%]; $P = 0.0177$), bowel obstruction (B-I 3 patients [0.6%]; R-Y 13 patients [2.6%]; $P = 0.0230$) and delayed gastric emptying (B-I 5 patients [1.0%]; R-Y 27 patients [5.3%]; $P < 0.0001$), and no significant difference in anastomotic leakage (B-I 21 patients [4.1%]; R-Y 17 patients [3.4%]; $P = 0.5084$) and pancreatic fluid leakage (B-I 11 patients [2.2%]; R-Y 12 patients [2.4%]; $P = 0.8329$).

Comparison of the severe postoperative complications

Complications graded $\geq$ III according to the Clavien–Dindo classification were regarded as severe postoperative complications. The comparison of each postoperative complication between the two reconstruction methods is summarized in Table 3. The incidence of severe postoperative complications in the R-Y group (67 [13%]) was significantly higher than the B-I group (36 [7.1%], $P = 0.0013$). A significant difference was found in severe intra-abdominal postoperative complications (B-I 31 patients [6.1%]; R-Y 57 patients

Table 2 Patients' surgical outcomes and postoperative courses

	Billroth I (n = 507)	Roux-en-Y (n = 507)	P value
Operation time (min)			
Mean ± SD	246 ± 65	283 ± 72	< 0.0001
Intraoperative blood loss (ml)			
Mean ± SD	211 ± 244	234 ± 288	0.1720
Intraoperative transfusion	19 (4%)	21 (4%)	0.7470
Dissected lymph node			
Mean ± SD	33 ± 14	32 ± 14	0.2475
Combined cholecystectomy	67 (13%)	79 (16%)	0.2831
Hospital stay after surgery (days)			
Mean ± SD	15 ± 15	18 ± 20	0.0070
Postoperative complications ^a			
II	52 (10%)	81 (16%)	
IIIa	30 (6%)	42 (8%)	
IIIb	2 (0.4%)	20 (4%)	
IV	2 (0.4%)	4 (0.8%)	
V	2 (0.4%)	1 (0.2%)	
Total	88 (17%)	148 (29%)	< 0.0001
Reoperation	4 (0.8%)	17 (3%)	0.0041
Readmission within 90 days	22 (4%)	36 (7%)	0.0583
Adjuvant chemotherapy			0.1920
Absent	371 (73%)	389 (77%)	
Present	136 (27%)	118 (23%)	

SD standard deviation

^aAccording to the Clavien–Dindo classification

[11%]; $P=0.0037$), and there was no significant difference in incidence of severe systemic complications (B-I 5 patients [1.0%]; R-Y 10 patients [2.0%]; $P=0.1934$).

Regarding each intra-abdominal postoperative complication, we found a significant difference for intra-abdominal abscess (B-I 4 patients [0.8%]; R-Y 14 patients [2.8%]; $P=0.0177$) and bowel obstruction (B-I 1 patients [0.2%]; R-Y 9 patients [1.8%]; $P=0.0209$), and no significant differences in anastomotic leakage (B-I 11 patients [2.2%]; R-Y 16 patients [3.2%]; $P=0.3294$), pancreatic fluid leakage (B-I 8 patients [1.6%]; R-Y 9 patients [1.8%]; $P=0.8068$), and delayed gastric emptying (B-I 1 patients [0.2%]; R-Y 2 patients [0.4%]; $P=1.0000$).

Oncological outcomes

We compared the overall, disease-specific, and relapse-free survival rates in each group (summarized in Supplemental Figure 1). There was no significant difference between the two groups for overall survival ($P=0.5237$, Supplemental Figure 1A), disease-specific survival ($P=0.3457$, Supplemental Figure 1B), or relapse-free survival rates ($P=0.3552$, Supplemental Figure 1C). We also investigated the patterns of the initial recurrence after surgery and found no significant difference between each pattern (Supplemental Figure 1D).

Table 3 Breakdown of postoperative complications according to the Clavien–Dindo classification

	Billroth I (n = 507)					Roux-en-Y (n = 507)					P value	
	II	IIIa	IIIb	≥ IV	Total (%)	III	IIIa	IIIb	≥ IV	Total (%)	All grade	Grade ≥ III
Intra-abdominal complications, n	28	28	2	1	59 (12)	50	37	18	2	107 (21)	< 0.0001	0.0037
Anastomotic leakage	10	10	0	1	21 (4.1)	0	1	0	0	17 (3.4)	0.5084	0.3294
Duodenal stump leakage	0	0	0	0		1	10	4	1			
Anastomotic stricture	1	2	1	0	4 (0.8)	4	1	2	0	7 (1.4)	0.5466	1.0000
Anastomotic bleeding	0	1	0	0	1 (0.2)	0	0	0	0	0	1.0000	1.0000
Anastomotic ulcer	0	0	0	0	0	0	1	0	0	1 (0.2)	1.0000	1.0000
Intra-abdominal abscess	5	4	0	0	9 (1.8)	8	12	2	0	22 (4.3)	0.0177	0.0294
Pancreatic fluid leakage	3	8	0	0	11 (2.2)	3	8	0	1	12 (2.4)	0.8329	0.8068
Wound infection	2	0	0	0	2 (0.4)	1	0	1	0	2 (0.4)	1.0000	1.0000
Bowel obstruction	2	1	0	0	3 (0.6)	4	2	7	0	13 (2.6)	0.0203	0.0209
Delayed gastric emptying	4	1	0	0	5 (1.0)	25	2	0	0	27 (5.3)	< 0.0001	1.0000
Intra-abdominal bleeding	1	1	1	0	3 (0.6)	4	0	2	0	6 (1.2)	0.5059	1.0000
Systemic complications, n	24	2	0	3	29 (5.7)	31	5	2	3	41 (8.1)	0.1371	0.1934
Pneumonia	9	0	0	0	9 (1.8)	2	0	0	1 ^a	3 (0.6)	0.1436	1.0000
Bacteremia	0	0	0	1 ^a	1 (0.2)	1	0	0	0	1 (0.2)	1.0000	1.0000
Enteritis	3	0	0	0	3 (0.6)	5	0	0	0	5 (1.0)	0.7255	1.0000
Cholecystitis	3	0	0	0	3 (0.6)	4	1	1	0	6 (1.2)	0.5059	0.4995
Others	9	2	0	2 ^a	13 (2.6)	19	4	1	2	26 (5.1)	0.0338	0.5466

^aOne patient with grade V complication (surgical mortality)

Table 4 Potential risk factors for postoperative complications (Clavien–Dindo grade $\geq$ II)

Variables	Univariate			Multivariable		
	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value
Sex						
Male	1.48	1.04–2.12	0.0307	1.23	0.85–1.80	0.2655
Age (years)						
≥ 70	1.45	1.07–1.96	0.0167	1.35	0.98–1.87	0.0654
Preoperative BMI (kg/m ²)						
≥ 22	1.16	0.86–1.57	0.3339			
Comorbidities						
One or more	1.55	1.15–2.10	0.0044	1.33	0.97–1.84	0.0792
Performance status						
≥ 1	1.03	0.70–1.50	0.8954			
Surgical approach						
Open	1.16	0.84–1.59	0.3583			
Lymph node dissection						
$\geq$ D2	0.82	0.61–1.11	0.2093			
Type of reconstruction						
Roux-en-Y	1.69	1.24–2.29	0.0008	1.58	1.15–2.17	0.0044
Anastomotic method						
Hand-sutured	0.90	0.63–1.28	0.5477			
Intraoperative transfusion						
Received	1.83	0.93–3.61	0.0817			
Intraoperative blood loss (ml)						
≥ 200	1.54	1.14–2.09	0.0050	1.44	1.05–1.96	0.0226
Operation time (min)						
≥ 240	1.54	1.12–2.12	0.0079	1.43	1.02–2.00	0.0383
Tumor size (cm)						
≥ 5.0	1.21	0.87–1.69	0.2560			
Macroscopic type						
Type 4/large type 3	1.28	0.65–2.51	0.4693			
T stage						
pT3/4	1.01	0.73–1.40	0.9287			
Lymph node metastasis						
pN0	1.11	0.81–1.51	0.5142			
Pathological stage						
II/III	1.05	0.77–1.43	0.7528			
Histologic type						
Differentiated	1.44	1.06–1.95	0.0190	1.26	0.92–1.76	0.1397

OR Odds ratio, CI confidence interval, BMI body mass index

Risk factors for postoperative complications

First, to investigate the risk factors for postoperative complications, we performed a risk analysis for overall postoperative complications. The univariate and multivariable analysis results are shown in Table 4. The univariate analysis revealed that male sex, age ≥ 70 , one or more comorbidities, R-Y reconstruction, intraoperative blood loss volume ≥ 200 ml, operation time ≥ 240 min, and differentiated histological type were significant risk factors. Moreover, R-Y reconstruction (odds ratio [OR]

1.58; 95% CI 1.15–2.17; $P = 0.0044$), intraoperative blood loss volume ≥ 200 ml (OR 1.44; 95% CI 1.05–1.96; $P = 0.0226$), and operation time ≥ 240 min (OR 1.43; 95% CI 1.02–2.00; $P = 0.0383$) were identified risk factors in the multivariable analysis.

Second, we performed a risk analysis for grade $\geq$ III severe postoperative complications. Multivariable analysis identified the following as significant factors: R-Y reconstruction (OR 1.75; 95% CI 1.13–2.74; $P = 0.0127$) and male sex (OR 1.73; 95% CI 1.01–2.96; $P = 0.0440$, Supplemental Table 1).

Fig. 2 Forest plot evaluating the impact of the reconstruction method on overall postoperative complications after Billroth I vs Roux-en-Y gastric reconstruction

Subgroup analyses

To further evaluate the impact of the reconstruction method on overall postoperative complications, we performed a subgroup analysis. A forest plot revealed that R-Y reconstruction was associated with a greater risk of overall postoperative complications in any subgroups (Fig. 2). The results of the analysis of severe postoperative complications are shown in Supplemental Fig. 2, which showed the same tendency as for the analysis of overall postoperative complications.

Discussion

In this study, we aimed to evaluate differences in postoperative complications by reconstruction methods after distal gastrectomy using propensity score matching, and revealed that both overall and severe postoperative complications in the R-Y group were higher than those in the B-I group. In addition, R-Y reconstruction was a strong independent risk factor for overall and severe postoperative complications.

B-I reconstruction is the most common reconstruction in Japan because of its technical simplicity, the need for only one anastomotic site, and that it restores a physiological path [3, 4]. However, the disadvantage of B-I reconstruction is

that it is not suitable in gastric cancer patients requiring large stomach resection, which is the main reason B-I reconstruction is rarely used in the West [22, 23]. On the other hand, R-Y reconstruction is the most widely used reconstruction method after total gastrectomy because it is the quickest and simplest technique [3, 22] and has become popular even as reconstruction method after distal gastrectomy. R-Y reconstruction has been favored in the prevention of postoperative reflux disease and a decreased probability of remnant gastric cancer [5–10]. However, the disadvantages of R-Y reconstruction are the possible onset of R-Y stasis, increasing the difficulty of approaching the ampulla of Vater endoscopically, and the higher number of anastomosis sites which requires longer operation time [2]. Thus, R-Y reconstruction is selected in cases with a small remnant stomach, hiatal hernia or reflux esophagitis, which is the residual selection bias for the choice of reconstruction method, though we performed propensity score matching to strictly balance the various clinicopathological characteristics of the two groups.

Meta-analyses and systematic reviews indicated that there were no significant differences in the incidence of anastomotic leakage between the R-Y and B-I reconstruction groups [5–7], which is consistent with our findings. Several previous large-scale studies reported that the incidence of

anastomotic leakage after distal gastrectomy was 1.3–2.4% [14, 24–26], if limited to duodenal stump leakage, the incidence were 0–3.2% [11, 12, 27, 28]. The incidence of gastroduodenal anastomosis leakage and duodenal stump leakage in our study were 4.1% and 3.4%, respectively, and were slightly higher than those in the previous studies. One possible reason is that our multicenter dataset included a greater proportion of patients with elder age or comorbidities because it was consisted of data from territorial hospitals in part. Considering that oral intake is contraindicated when gastroduodenal anastomotic leakage occurs after B-I reconstruction, R-Y reconstruction has an advantage during treatment of anastomotic leakage.

The R-Y group was associated with an increased incidence of both overall and grade $\geq$ III severe intra-abdominal abscess. We performed propensity score matching to strictly balance the factors such as tumor location in preoperative examination, tumor size in preoperative examination, intended extent of lymphadenectomy and clinical stage between the two groups, though the confounders such as the length of the resected stomach did not eliminate completely. Contamination by intestinal bacteria when opening the jejunum during the reconstruction procedure and prolonged operation time might increase the intra-abdominal abscess after R-Y reconstruction. A well-designed study analyzing sequential cultures of abdominal fluids is desirable to answer this clinical question.

R-Y stasis, internal hernia, and bowel obstruction are well-known common complications after R-Y reconstruction [2, 3], and Ishikawa et al. reported that hospital stay in the R-Y group was significantly longer compared to the B-I group because of those R-Y specific complications [29]. Large-scale studies reported that the incidence of R-Y stasis was 3.2–9.5% [10–12]; however, a Japanese questionnaire survey reported that 30% of institutions have not experienced this complication [3]. In addition, it is believed that most patients with this complication could be treated conservatively without further severe complications. In our study, R-Y stasis was the most frequent postoperative complication in the R-Y group, with an incidence of 5.3% (27 patients), and most did not develop severe complications, which is consistent with previous studies. However, severe postoperative complications requiring surgical intervention such as bowel obstructions secondary to internal hernia or adhesion, stricture of the jejunojejunostomy, and twisting of the Y-limb, had a higher incidence in the R-Y group. The difficulty in standardization of the reconstruction procedure because of a retrospective multi-institutional study might influence those results.

We have recently reported that postoperative complications and delay in postoperative adjuvant chemotherapy adversely affected the prognosis in patients with gastric cancer [15, 17]. In this study, we compared survivals between

the R-Y and B-I groups. As a result, oncological outcomes were comparable between the two groups. A previous study indicates that postoperative complications have less adverse impact on prognosis of patients who underwent distal gastrectomy than those who underwent total gastrectomy [17].

We performed a risk analysis and found that R-Y reconstruction was an independent risk factor for overall postoperative complications and severe postoperative complications. Kumagai et al. also reported that R-Y was a risk factor for severe postoperative complications [28]. However, Kumagai et al.'s study was limited to laparoscopic surgery only and was not well balanced regarding patients' backgrounds, which are differences compared with our study. To further evaluate the impact of the reconstruction method regarding severe postoperative complications, we performed a subgroup analysis and found that patients undergoing R-Y were at greater risk of developing severe postoperative complications in any subgroups.

There are several possible reasons for the different results between our study and previous studies. First, we analyzed data for postoperative complications within 90 days after surgery because many patients were readmitted with functional or inflammatory postoperative complications even after 30 days from discharge, with a significantly higher incidence in the R-Y group. Second, our study had a multi-institutional design with no uniformity in the surgical procedures, and the R-Y group had a higher incidence of R-Y-specific postoperative complications that required ingenious surgical techniques to prevent. Third, our multicenter dataset included a greater proportion of patients with elder age or comorbidities because it was consisted of data from territorial hospitals in part. Fourth, because the incidence of each postoperative complication was not high, previous relatively small-scale studies may have lacked statistical power. Of note, there have been a meta-analysis and a systematic review demonstrating that B-I reconstruction had a lower rate of postoperative complications compared to R-Y reconstruction [8], though they focused on laparoscopic surgery.

Our study has several limitations. First, although we used propensity score matching to strictly balance the significant patient background factors and institutions, it was impossible to eliminate residual selection bias. RCTs are desirable for further high-quality analysis, and this is a limitation with retrospective studies. Second, the definition of postoperative complication may not be strict because this was a multicenter dataset analysis and we did not perform a central review. To overcome this problem, we collected data for postoperative complications in accordance with the Clavien–Dindo classification system which is the most widely used and reliable data collection method, though it includes a subjective judge. Third, this study included only Japanese data. B-I reconstruction is limited in the West for gastric cancer surgery, with reconstruction performed according

to recommendations in each country. Forth, we included patients who underwent gastrectomy between 2010 and 2014 to avoid a prolonged period of time to acquire data leading to time-dependent transition of standard treatment. Nevertheless, the difficulty in standardization of the allocation of the surgical procedure, device, and perioperative management should be acknowledged as one of limitations of our multicenter retrospective dataset. Finally, we did not compare the long-term benefits with each procedure, such as preventing reflux and remnant gastritis, and the low incidence of remnant gastric cancer, which are advantages of R-Y reconstruction. However, because previous high-quality RCTs investigated patients' long-term QOL [12, 13], this issue has been addressed. Regarding remnant gastric cancer, our follow-up period was too short to investigate this concern.

In conclusion, we compared the incidence of overall and severe postoperative complications between B-I and R-Y, and found that R-Y reconstruction was associated with increased morbidity rates after distal gastrectomy. However, some R-Y-specific postoperative complications could be theoretically prevented by improved surgical techniques, and several such surgical techniques have been introduced. Our results do not apply in all clinical settings, and further adequately powered, well-designed, and technically uniform studies are needed.

Acknowledgements We thank Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval All procedures performed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

- Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric Cancer*. 2017;20:1–19.
- Hoya Y, Mitsumori N, Yanaga K. The advantages and disadvantages of a Roux-en-Y reconstruction after a distal gastrectomy for gastric cancer. *Surg Today*. 2009;39:647–51.
- Kumagai K, Shimizu K, Yokoyama N, Aida S, Arima S, Aikou T, et al. Questionnaire survey regarding the current status and controversial issues concerning reconstruction after gastrectomy in Japan. *Surg Today*. 2012;42:411–8.
- Weil PH, Buchberger R. From Billroth to PCV: a century of gastric surgery. *World J Surg*. 1999;23:736–42.
- Kostakis ID, Alexandrou A, Armeni E, Damaskos C, Kouraklis G, Diamantis T, et al. Comparison between minimally invasive and open gastrectomy for gastric cancer in Europe: a systematic review and meta-analysis. *Scand J Surg*. 2017;106:3–20.
- Xiong JJ, Altaf K, Javed MA, Nunes QM, Huang W, Mai G, et al. Roux-en-Y versus Billroth I reconstruction after distal gastrectomy for gastric cancer: a meta-analysis. *World J Gastroenterol*. 2013;19:1124–34.
- Cai Z, Zhou Y, Wang C, Yin Y, Shen C, et al. Optimal reconstruction methods after distal gastrectomy for gastric cancer: a systematic review and network meta-analysis. *Medicine (Baltimore)*. 2018;97:e10823.
- Kim MS, Kwon Y, Park EP, An L, Park H, Park S. Revisiting laparoscopic reconstruction for Billroth 1 versus Billroth 2 versus Roux-en-Y after distal gastrectomy: a systematic review and meta-analysis in the modern era. *World J Surg*. 2019;43(6):1581–93.
- Kojima K, Yamada H, Inokuchi M, Kawano T, Sugihara K. A comparison of Roux-en-Y and Billroth-I reconstruction after laparoscopy-assisted distal gastrectomy. *Ann Surg*. 2008;247:962–7.
- Nunobe S, Okaro A, Sasako M, Saka M, Fukagawa T, Katai H, et al. Billroth 1 versus Roux-en-Y reconstructions: a quality-of-life survey at 5 years. *Int J Clin Oncol*. 2007;12:433–9.
- Imamura H, Takiguchi S, Yamamoto K, Hirao M, Fujita J, Miyashiro I, et al. Morbidity and mortality results from a prospective randomized controlled trial comparing Billroth I and Roux-en-Y reconstructive procedures after distal gastrectomy for gastric cancer. *World J Surg*. 2012;36:632–7.
- Nakamura M, Nakamori M, Ojima T, Iwahashi M, Horiuchi T, Kobayashi Y, et al. Randomized clinical trial comparing long-term quality of life for Billroth I versus Roux-en-Y reconstruction after distal gastrectomy for gastric cancer. *Br J Surg*. 2016;103:337–47.
- Takiguchi S, Yamamoto K, Hirao M, Imamura H, Fujita J, Yano M, et al. A comparison of postoperative quality of life and dysfunction after Billroth I and Roux-en-Y reconstruction following distal gastrectomy for gastric cancer: results from a multi-institutional RCT. *Gastric Cancer*. 2012;15:198–205.
- Tokunaga M, Tanizawa Y, Bando E, Kawamura T, Terashima M. Poor survival rate in patients with postoperative intra-abdominal infectious complications following curative gastrectomy for gastric cancer. *Ann Surg Oncol*. 2013;20:1575–83.
- Nakanishi K, Kanda M, Ito S, Mochizuki Y, Teramoto H, Ishigure K, et al. Delay in initiation of postoperative adjuvant chemotherapy with S-1 monotherapy and prognosis for gastric cancer patients: analysis of a multi-institutional dataset. *Gastric Cancer*. 2019;22:1215–25.
- Nakanishi K, Kanda M, Kodera Y. Long-lasting discussion: Adverse effects of intraoperative blood loss and allogeneic transfusion on prognosis of patients with gastric cancer. *World J Gastroenterol*. 2019;25:2743–51.
- Kanda M, Ito S, Mochizuki Y, Teramoto H, Ishigure K, Murai T, et al. Multi-institutional analysis of the prognostic significance of postoperative complications after curative resection for gastric cancer. *Cancer Med*. 2019;8(11):5194–201.
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–13.
- Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg*. 2009;250:187–96.
- Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer*. 2011;14:101–12.
- Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma. 15th ed. Tokyo: Kanehara Publisher; 2017.

22. Piessen G, Triboulet JP, Mariette C. Reconstruction after gastrectomy: which technique is best? *J Visc Surg*. 2010;147:e273–e283.
23. Van Cutsem E, Sagaert X, Topal B, Haustermans K, Prenen H. Gastric cancer. *Lancet* (London, England). 2016;388:2654–64.
24. Yoshida K, Honda M, Kumamaru H, Kodera Y, Kakeji Y, Hiki N, et al. Surgical outcomes of laparoscopic distal gastrectomy compared to open distal gastrectomy: A retrospective cohort study based on a nationwide registry database in Japan. *Ann Gastroenterol Surg*. 2018;2:55–64.
25. Kurita N, Miyata H, Gotoh M, Shimada M, Imura S, Kimura W, et al. Risk model for distal gastrectomy when treating gastric cancer on the basis of data from 33,917 Japanese patients collected using a nationwide web-based data entry system. *Ann Surg*. 2015;262:295–303.
26. Kim MC, Kim W, Kim HH, Ryu SW, Ryu SY, Song KY, et al. Risk factors associated with complication following laparoscopy-assisted gastrectomy for gastric cancer: a large-scale korean multicenter study. *Ann Surg Oncol*. 2008;15:2692–700.
27. Ri M, Hiki N, Ishizuka N, Ida S, Kumagai K, Nunobe S, et al. Duodenal stump reinforcement might reduce both incidence and severity of duodenal stump leakage after laparoscopic gastrectomy with Roux-en-Y reconstruction for gastric cancer. *Gastric Cancer*. 2019;22(5):1053–9.
28. Kumagai K, Hiki N, Nunobe S, Jiang X, Kubota T, Aikou S, et al. Different features of complications with Billroth-I and Roux-en-Y reconstruction after laparoscopy-assisted distal gastrectomy. *J Gastrointest Surg*. 2011;15:2145–52.
29. Ishikawa M, Kitayama J, Kaizaki S, Nakayama H, Ishigami H, Fujii S, et al. Prospective randomized trial comparing Billroth I and Roux-en-Y procedures after distal gastrectomy for gastric carcinoma. *World J Surg*. 2005;29:1415–20 **discussion 21**.

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