

Review Article



Comparison of the Clinical Outcomes of Reconstruction Methods After Distal Gastrectomy: A Systematic Review and Meta-Analysis Based on Randomized Controlled Trials

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ABSTRACT

Background: To analyze the short- and long-term clinical outcomes of 2 reconstruction methods after distal gastrectomy for gastric cancer.

Methods: Three keywords, “gastric neoplasm,” “distal gastrectomy,” and “reconstruction,” were used to search PubMed. We selected only randomized controlled trial that compared the anastomosis methods. A total of 11 papers and 8 studies were included in this meta-analysis. All statistical analyses were performed using the R software.

Results: Among short-term clinical outcomes, a shorter operation time, reduced morbidity, and shorter hospital stay were found for Billroth type I (B-I) than for Roux-en-Y (RNY) reconstruction in the meta-analysis ($P<0.001$, $P=0.048$, $P<0.001$, respectively). When comparing Billroth type II (B-II) to RNY, the operation time was shorter for B-II than for RNY ($P<0.019$), but there were no differences in morbidity or length of hospital stay ($P=0.500$, $P=0.259$, respectively). Regarding long-term clinical outcomes related to reflux, there were significantly fewer incidents of reflux esophagitis, reflux gastritis, and bile reflux ($P=0.035$, $P<0.001$, $P=0.019$, respectively) for RNY than for B-I in the meta-analysis, but there was no difference between the 2 methods in residual food ($P=0.545$). When comparing B-II to RNY, there were significantly fewer incidents of reflux gastritis ($P<0.001$) for RNY than for B-II, but the amount of residual food and patient weight gain showed no difference.

Conclusion: B-I had the most favorable short-term outcomes, but RNY was more advantageous for long-term outcomes than for other methods. Surgeons should be aware of the advantages and disadvantages of each type of anastomosis and select the appropriate method.

Keywords: Gastric neoplasms; Distal gastrectomy; Reconstruction

INTRODUCTION

According to the Global Cancer Statistics in 2020, based on GLOBOCAN produced by the International Agency for Research on Cancer, an estimated 769,000 deaths occurred due to gastric cancer, with over one million new cases in 2020. Gastric cancer ranks fourth in

Conflict of Interest

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

Author Contributions

Conceptualization: M.J.S., J.S.H., S.K.W.;
Investigation: M.J.S., J.S.H., K.R.B.;
Methodology: M.J.S., K.R.B., J.S.H.; Project
administration: M.J.S., J.S.H.; Resources:
M.J.S., J.S.H., K.R.B.; Writing - original draft:
M.J.S., J.S.H.; Writing - review & editing:
M.J.S., J.S.H., S.K.W., K.R.B.

mortality and fifth in global incidence [1]. The incidence rates of gastric cancer are highest in Eastern Asia and Eastern Europe [2]. In accordance with the Korea Central Cancer Registry report, 12.0% of the total cancer incidence in Korean people was newly diagnosed with gastric cancer in 2018 [3]. Recently, the Information Committee of the Korean Gastric Cancer Association reported that the proportion of early gastric cancer (EGC) in 2019 was 67.9%, an increase of 10% over the past 10 years (even though the survey included only patients who underwent gastrectomy) [4]. Additionally, a noticeable change was observed in the surgical approach used for gastric cancer treatment. The proportion of laparoscopic approaches for gastrectomy increased from 6.6% in 2004 to 64.9% in 2019, whereas the proportion of open surgery decreased from 80.8% to 27.6% [4]. Additionally, the committee identified that a shift in the surgical approach influenced the reconstruction method. Most Billroth type I (B-I) reconstructions in the past were recently reversed to the preferred Billroth type II (B-II) or Roux-en-Y (RNY) reconstructions. This trend is presumed to reflect the current era of increasing incidence of EGC and the use of laparoscopic gastrectomy. Laparoscopic distal gastrectomy (DG) exhibits benefits compared with open surgery, such as less wound pain, faster recovery, and a lower complication rate [5].

Some meta-analyses have been previously reported; however, they included studies of all designs in addition to randomized controlled trials (RCTs). Most studies that do not include RCTs are likely to have biases and errors in the confirmation of accurate results. Therefore, we conducted a meta-analysis that included only RCTs to minimize bias. This meta-analysis aimed to examine various anastomosis methods after DG. We sought to identify the strengths and weaknesses of each method after DG for gastric cancer by analyzing the clinical course and short- and long-term clinical outcomes for each anastomosis method.

MATERIALS AND METHODS

Search scheme & selection of studies

The flow diagram of the meta-analysis search scheme is shown in **Fig. 1**. Three keywords, “gastric neoplasm,” “distal gastrectomy,” and “reconstruction,” were used to search PubMed. In total, 653 studies were conducted in November 2021. Among them, 629 non-RCTs were excluded and 24 RCTs were included. Based on the titles and abstracts of the 24 RCTs, 13 RCTs on reconstruction during gastric neoplasm and DG were selected. Two of these studies were comparative studies on the use of hand-sewn sutures or staples in B-I reconstruction, and another study compared intracorporeal and extracorporeal anastomoses. Since this meta-analysis compared the advantages and disadvantages of each reconstruction method, these papers were excluded. In addition, since 3 studies analyzed the same RCT cohort, a total of 11 papers and 8 studies were used for this meta-analysis. One of the 8 studies compared the anastomosis methods of B-I and B-II with the Braun anastomosis and RNY. Five studies compared B-I and RNY, and 2 studies compared B-II and RNY with B-II and uncut RNY. These studies were analyzed using a forest plot chart, and the results are reported herein.

Statistical analysis of data

We performed pairwise meta-analyses comparing B-I and RNY for 3 different surgical outcomes (operative time, complication events, and days of hospital stay) and endoscopic findings 1 year after surgery. The between-group effect size was computed as the occurrence of complications and endoscopic abnormalities between the groups by calculating the pooled odds ratio (OR) and 95% confidence interval (CI). Operative time and days of hospital stay

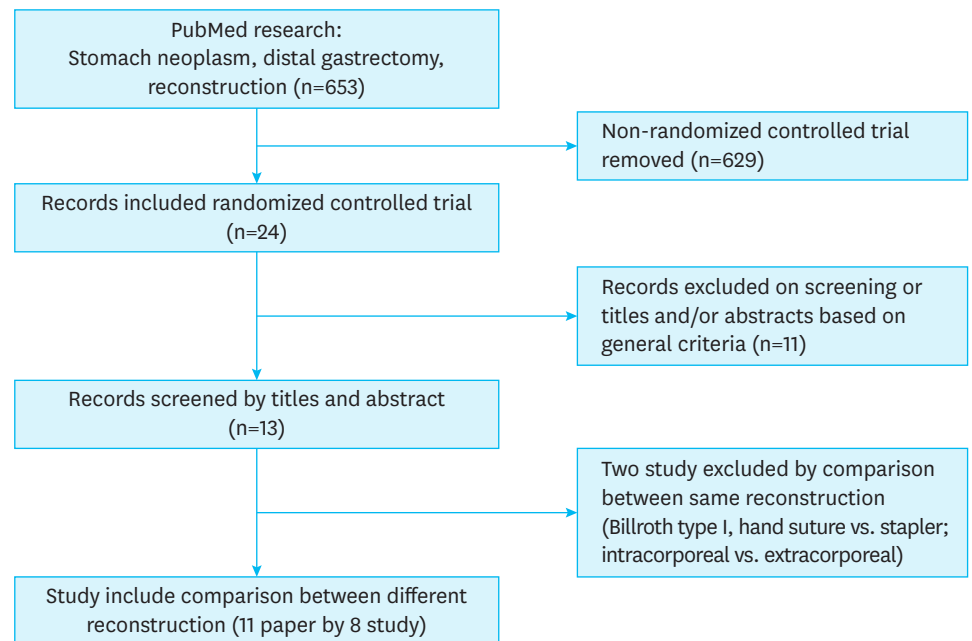


Fig. 1. Flow chart of study selection.

were calculated as the pooled mean difference (MD) and 95% CI. If a study did not report an OR, we used the available data to calculate the effect size. Effect sizes for dichotomous outcomes were computed according to the intention-to-treat principle by reporting the observed number of participants with an outcome event to the total number of individuals randomized to that group. Means and standard deviations were used to compute effect sizes for continuous data, which were subsequently converted to MDs between groups.

Effect sizes were pooled using common- or random-effects models with a generic invariance method to incorporate the heterogeneity of differences across the studies. The between-study quantification of heterogeneity was measured using I-square statistics, and heterogeneity was tested using Cochran's Q. As a result, we adopted a random-effects model when the I-square values were more than 50% and the P-value of Cochran's Q was less than 0.1; otherwise, a common (fixed) effects model was adopted. Sensitivity analyses were performed by serially excluding each study (leave-one-out method) to assess the implications of each study on the pooled effect size (**Supplementary Fig. 1**). Publication bias was assessed using funnel plots and tested for asymmetry using the Egger test (**Supplementary Fig. 2**). All statistical analyses were performed using the metafor (meta-regression) and mice (multiple imputation by chained equations) packages in the R software, version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria). Statistical tests were 2-sided for the ORs and 1-sided for the Egger test, with a significance threshold of $P < 0.05$.

RESULTS

Clinical course and morbidity between B-I and RNY in the RCTs

The operation time for RNY was longer than that for B-I in all RCTs [6-11], except for one [12] (**Fig. 2, Table 1**). There was also a significant difference in the meta-analysis results, with a value of $P < 0.001$ (**Fig. 2A**; MD, -37.5; 95% CI, -52.0, -23.1).

Clinical Outcome of Reconstruction After DG

Table 1. Summary of clinical course with morbidity between B-I and RNY reconstruction methods after distal gastrectomy

Publication	First author/Reference number	Cases	Approach method	Type of reconstruction	Op time B-I (min)	Op time RNY (min)	Morbidity B-I	Morbidity RNY	Hospital stay B-I (day)	Hospital stay RNY (day)
2012	Lee et al. [8]	159	Open + LADG	B-I (49) vs. B-II + Braun (52) vs. RNY (47)	163.4±45.1	228.4±52.2	4	6	9.2±3.1	10.8±7.7
2005	Ishikawa et al. [12]	50	Open	B-I (26) vs. RNY (24)	250±79	260±68	1	2	19.0±6.2	31.8±21.7
2012–2013	Takiguchi et al. [10], Imamura et al. [7], Hirao et al. [6]	332	Open (270) + Laparo (62)	B-I (132) vs. RNY (136)	180±48	214±44	14	23	14.1±6.5	16.4±10.4
2016	Nakamura et al. [9]	122	Open (118) + Laparo (82)	B-I (60) vs. RNY (62)	222.1±64.3	255.4±77.9	4	9	11 (7–63)	11 (7–88)
2017	Choi et al. [13]	40		B-I (20) vs. RNY (20)			2	2	6.7±1.0	7.1±1.1
2017	Yang et al. [11]	140	Open (104) vs. Laparo (36)	B-I (70) vs. RNY (70)	239.4±40.8	271.2±39.2	13	18	9.6±1.2	10.3±3.7

B-I = Billroth type I; RNY = Roux-en-Y.

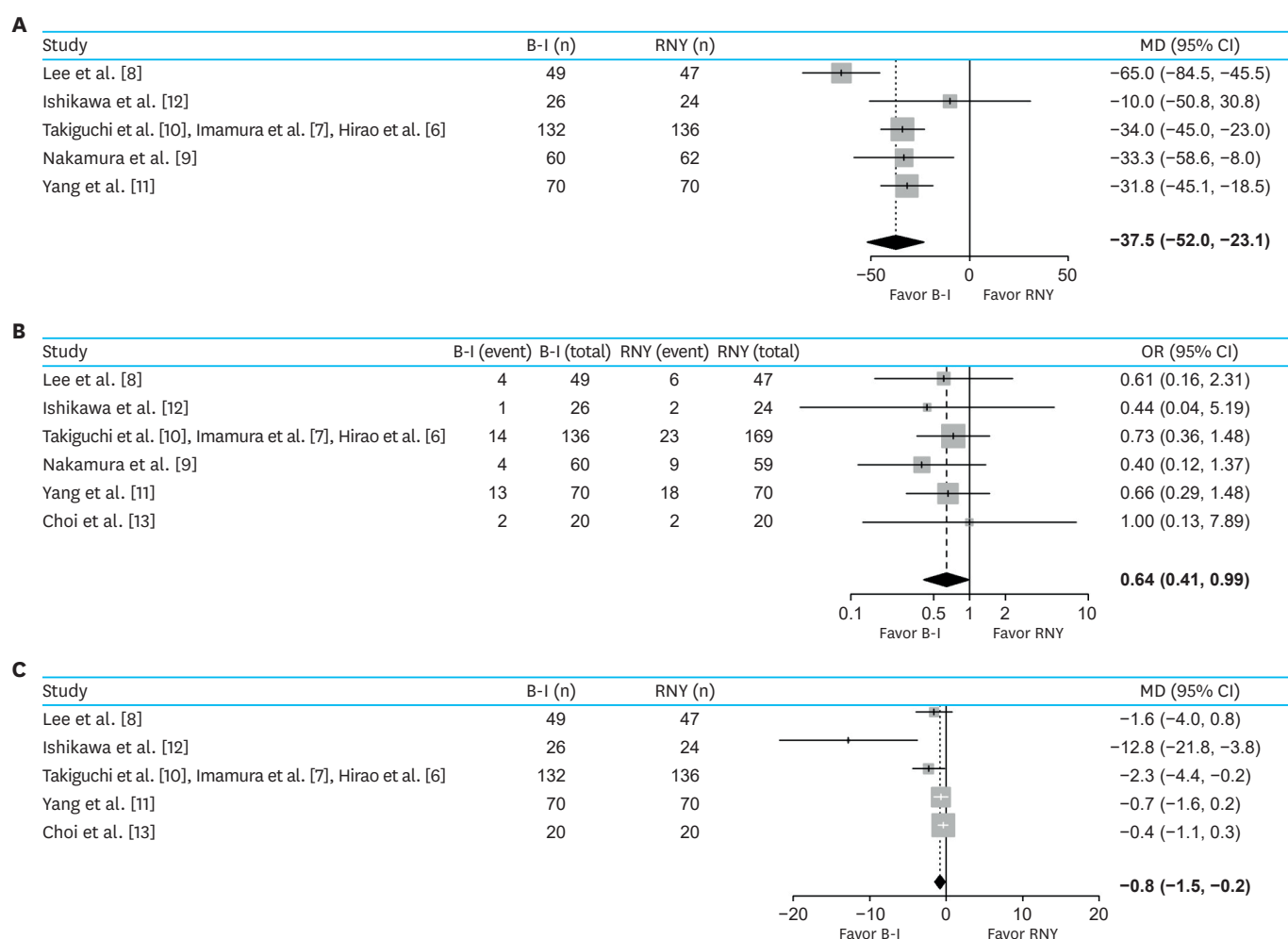


Fig. 2. Comparison of clinical course with morbidity between B-I and RNY. (A) Operation time; (B) Postoperative complications; (C) Hospital stay. B-I = Billroth type I; RNY = Roux-en-Y; MD = mean difference; CI = confidence interval.

The results of the 6 RCTs comparing postoperative complications between B-I and RNY are shown in **Fig. 2B** [6-13]. Overall, the analysis showed a preference for B-I over RNY. There was no difference in the total incidence of postoperative complications between each RCT; however, there was a significant difference in the preference for B-I compared to RNY in the meta-analysis (P=0.048; OR, 0.64; 95% CI, 0.41, 0.99).

For hospital stay, 2 RCTs [10,12] showed a significant difference among the 5 studies comparing B-I and RNY; however, there was no significant difference in the other 3 RCTs [8,11,13] (**Fig. 2C**). However, in the meta-analysis, RNY had a significantly longer hospital stay than BI ($P<0.001$; MD, -0.8 ; 95% CI, $-1.5, -0.2$).

Clinical course and morbidity between B-II and RNY or uncut RNY in the RCTs

One RCT [14] reported that the operation time was significantly shorter for B-II than for RNY (B-II vs. RNY, 247.3 ± 56.7 minutes vs. 269.5 ± 58.7 minutes, $P<0.019$). There was no difference between the 2 groups in terms of postoperative complications (B-II vs. RNY, 28.4% vs. 33.8%, $P=0.500$). Additionally, there was no difference in the median length of hospital stay between the 2 groups (B-II vs. RNY, 9 days [7–12], 8 days [7–11], $P=0.259$).

In addition, another RCT presented similar results when comparing B-II and uncut RNY. Yang et al. [15] reported that the operation time was significantly longer for uncut RNY than for B-II (uncut RNY vs. B-II, 154.8 ± 17.8 minutes vs. 145.5 ± 15.1 minutes, $P=0.001$). However, there was no significant difference in postoperative morbidity between the 2 groups (uncut RNY vs. B-II, 7.6% vs. 10.1%, $P=0.576$). Only one RCT reported the clinical course and morbidity between B-II and RNY or uncut RNY; therefore, a meta-analysis could not be conducted.

Long-term clinical outcomes related to reflux between B-I and RNY in RCTs

The meta-analysis of endoscopic findings performed 1 year after surgery for patients who underwent B-I and RNY anastomoses is discussed below and presented in **Fig. 3** and **Table 2**. The occurrence of reflux esophagitis was analyzed in 4 RCTs (**Fig. 3A**). Two RCTs [6,8] reported that RNY showed a significantly lower occurrence of reflux esophagitis than B-I. In contrast, the other 2 RCTs [9,12] did not show any difference in postoperative reflux esophagitis. However, the present meta-analysis indicated that the occurrence of reflux esophagitis was significantly lower with RNY than with B-I ($P=0.035$).

Additionally, these 4 RCTs reported data on reflux gastritis (**Fig. 3B**). In all 4 RCTs, the incidence of reflux gastritis was significantly lower for RNY than for B-I, and the meta-analysis showed a significantly lower incidence of RNY than of B-I ($P<0.001$).

Bile reflux was analyzed in 2 RCTs (**Fig. 3C**). In one RCT, the incidence of bile reflux was lower in the RNY group than in the B-I group ($P=0.012$) [9]. In another RCT, there was no significant difference in the incidence between B-I and RNY ($P=0.144$) [11]. In the present meta-analysis, the incidence of postoperative bile reflux was significantly lower in the RNY group than in the B-I group ($P=0.019$).

Table 2. Summary of long-term clinical outcomes related to reflux between B-I and RNY reconstruction methods after distal gastrectomy

Publication	First author/ Reference number	Cases	Approach method	Type of reconstruction	Reflux esophagitis B-I	Reflux esophagitis RNY	Reflux gastritis B-I	Reflux gastritis RNY	Residual food B-I	Residual food RNY	Bile reflux B-I	Bile reflux RNY
2012	Lee et al. [8]	159	Open + LADG	B-I (49) vs. RNY (47)	12	4						
2005	Ishikawa et al. [12]	50	Open	B-I (26) vs. RNY (24)	7	8	16	7				
2012–2013	Hirao et al. [6]	332	Open (270) + Laparo (62)	B-I (132) vs. RNY (136)	26	10	71	44	47	37		
2016	Nakamura et al. [9]	122	Open (118) + Laparo (82)	B-I (60) vs. RNY (62)	8	10	35	15	11	14	14	0
2017	Yang et al. [11]	140	Open (104) vs. Laparo (36)	B-I (70) vs. RNY (70)			38	27	12	13	9	4

B-I = Billroth type I; RNY = Roux-en-Y.

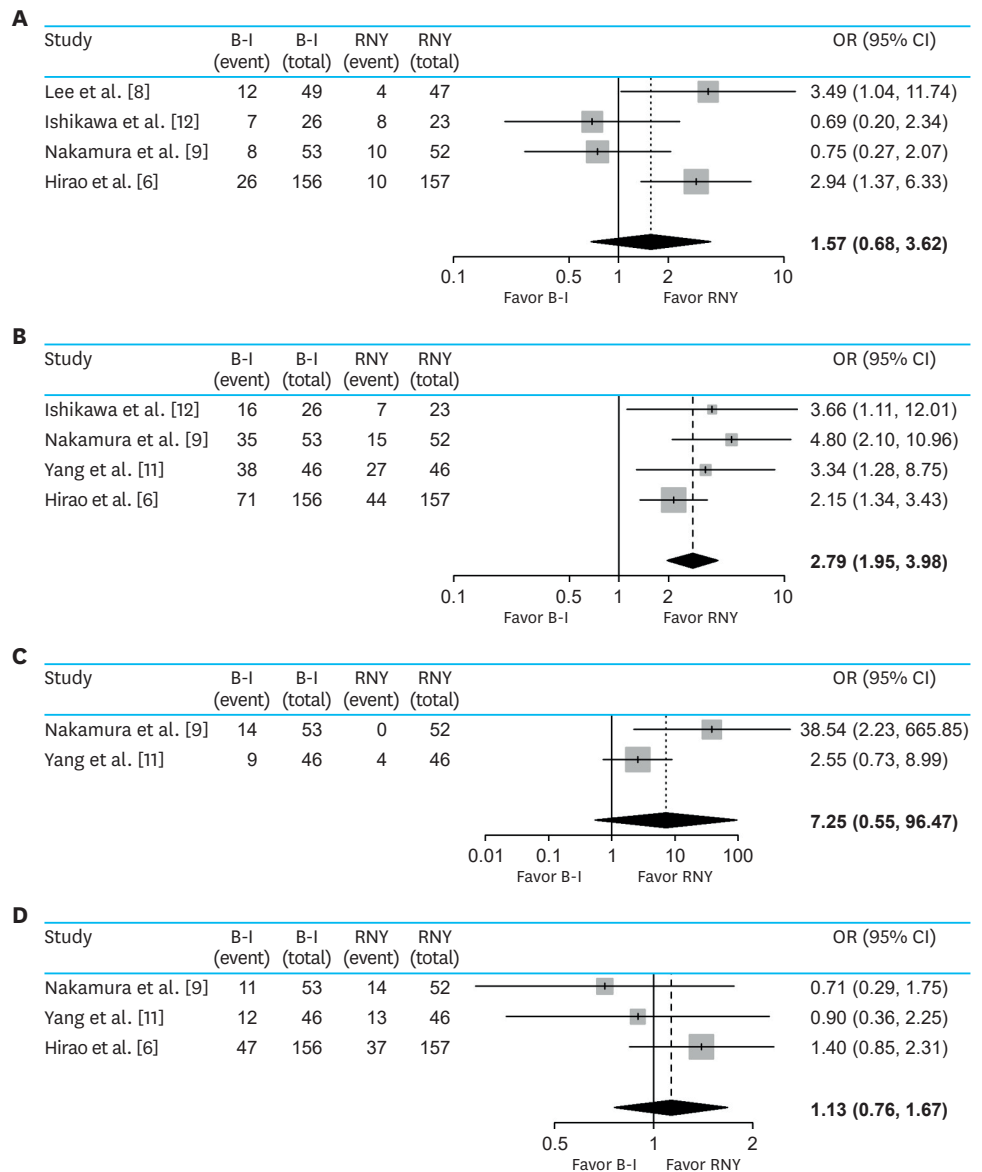


Fig. 3. Endoscopic findings comparing B-I and RNY. (A) Reflux esophagitis; (B) Reflux gastritis; (C) Bile reflux; (D) Residual food.

B-I = Billroth type I; RNY = Roux-en-Y; OR = odds ratio; CI = confidence interval.

Three RCTs reported endoscopic findings of residual food (**Fig. 3D**). All 3 RCTs showed no difference in residual food between the 2 types of anastomoses [6,9,11]. The present meta-analysis revealed similar results (P=0.545).

Long-term clinical outcomes related to reflux between B-II and RNY or uncut RNY in RCTs

One RCT reported that the median endoscopic grade for gastritis with RNY was significantly lower than that with B-II one year after surgery (MD, 1.32; 95% CI -1.67, -0.98; P<0.001) [14].

In another RCT, the occurrence of bile reflux significantly increased in B-II compared with uncut RNY one year postoperatively (B-II vs. uncut RNY, 60.9% vs. 90.3%, P<0.001) [15].

Additionally, the occurrence of alkaline gastritis notably increased with B-II (B-II vs. uncut RNY, 72.2% vs. 55.1%, $P < 0.05$). However, histopathological examination using endoscopy did not show a significant difference in the diagnosis of gastritis ($P = 0.278$). In addition, the amount of residual food and patient weight gain were not significantly different between the B-II and RNY groups.

DISCUSSION

The present meta-analysis compared and analyzed the clinical course and short- or long-term clinical outcomes of reconstruction methods after DG in patients with gastric cancer. Unlike other meta-analyses, this study only included RCTs on anastomotic methods. The results indicated that B-I or B-II was better than RNY, with fewer complications, shorter operation times, and shorter hospital stays. Regarding long-term clinical outcomes, RNY was significantly better than B-I or B-II for reflux esophagitis, reflux gastritis, and bile reflux after DG.

When DG is performed to treat gastric cancer, anastomosis methods mainly consist of B-I, B-II, and RNY. In the case of RNY, uncut RNY was included. B-I (gastroduodenostomy) anastomosis is most closely associated with Theodor Billroth; however, it was first described by Polish surgeon Ludwik Rydygier [16]. B-I anastomosis preserves the duodenal and jejunal continuity by anastomosing the remnant stomach to the duodenal stump in a primary end-to-end fashion, which could be conducted for lower-third gastric cancers [17]. The advantages of B-I include a shorter operation time than that of other methods, avoidance of problems with the afferent and efferent small bowel limb, easier performance of endoscopic retrograde cholangiopancreatography, and endoscopic examination after gastrectomy. The disadvantage of B-I is the retrograde reflux of biliary contents into the stomach, which causes alkaline gastritis. The incidence of bile reflux has been reported to be 29%–48% after B-I and 40%–85% after B-II [8,18-20]. Hori et al. [21] compared stapler usage ($n=92$) and hand-sewn suturing ($n=95$) in 187 gastric cancer patients who underwent open DG with B-I; they reported no difference in complications, and the stapler group was revealed to have a significantly shorter operation time than the hand-sewn suturing group (stapler usage vs. hand-sewn suturing, 14 vs. 25 min, $P=0.02$). Hosoda et al. [22] reported no significant difference in the amount of analgesia with intracorporeal (delta-shaped) anastomosis compared to extracorporeal (circular stapler) anastomosis during the recovery period after laparoscopic DG with B-I ($P=0.91$). Additionally, there was no difference in the overall proportion of B-II or B-III in-hospital surgical complications (11% for intracorporeal anastomosis and 14% for extracorporeal anastomosis).

B-II indicates gastrojejunostomy anastomosis. Von Hacks first mentioned B-II anastomosis after partial gastrectomy at the Billroth Clinic in 1885 [23]. The advantage of B-II is that it is applicable in cases of middle- or upper-third gastric cancers with a more extended DG. Additionally, B-II is an easy-to-implement technique that can add biliary drainage via Braun (jejunojejunostomy) anastomosis. The disadvantage of B-II is that it has a higher incidence than RNY for the following issues: remnant gastritis, reflux esophagitis due to bile reflux, and dumping syndrome [24]. To reduce bile reflux, Braun anastomosis is sometimes performed to bypass bile juice after B-II; however, the effectiveness of the bypass is still controversial. Lindecken et al. [25] examined the residual stomach using hepatobiliary sequence scintigraphy and identified bile reflux in 53% (16/30) of patients after B-II anastomosis. Lee et al. [8] showed that bile reflux occurred in approximately 75% of cases involving B-II

with hand-sewn Braun anastomosis, which was significantly higher than the 3.7% found for RNY. A meta-analysis conducted by Tersmette et al. [26] demonstrated that the incidence of remnant gastric cancer at 15–20 years after B-II was significantly higher than that after B-I (B-II [OR, 1.6] vs. B-I [OR, 1.2]).

The term RNY is derived from the name of the surgeon who first described it (César Roux) [27] and the stick-figure representation. The advantage of RNY gastrojejunostomy is that it diverts bilious drainage away from the gastric remnant [17,28]. Therefore, RNY has a lower occurrence of reflux symptoms, remnant gastritis, and reflux esophagitis than B-II [24]. However, the disadvantages of RNY are that there are a relatively high number of parts connected to the anastomosis; therefore, the operation time is longer than that of other anastomotic methods (e.g., B-I or B-II), and internal hernia can easily occur. If vagotomy is not performed at the time of RNY anastomosis, a jejunal ulcer may develop near the gastric jejunostomy site. In addition, Roux stasis syndrome may develop after RNY [29]. This can be the result of gastric stasis or atony, and this adverse effect of jejunal transection contributes to a syndrome of abdominal pain and vomiting known as Roux syndrome or Roux stasis syndrome. The cause of this syndrome is disordered motility of the Roux loop with propulsive activity toward, instead of away from, the remnant stomach. When patients are suspected of having Roux stasis syndrome, evaluations involving upper gastrointestinal series, endoscopy, and nuclear medicine gastric emptying studies are recommended. Medical treatment for Roux stasis syndrome consists of the intake of prokinetic agents such as metoclopramide, erythromycin, and azithromycin. When medical therapy fails, surgical treatment can be considered to resect the Roux limb with a new reconstruction. To prevent recurrence of Roux stasis after surgical treatment, further resection of the remnant stomach, such as near-total gastrectomy, is required. Patients with severe Roux stasis syndrome may require a completion gastrectomy [17].

To prevent Roux stasis syndrome, uncut RNY is used to minimize injury to the jejunal mesenteric nervous system. According to a study by Park et al., the incidence of Roux stasis syndrome decreased and gastric stasis decreased with uncut RNY compared to RNY. The authors used 3- and 6-row staplers during uncut RNY. The recanalization rate was 6.9% for the 6-row linear stapler, which was low compared with 30.6% for the 3-row linear stapler [30].

The current meta-analysis had some limitations. Among the studies of various anastomosis methods after DG, 6 RCTs compared B-I and RNY, thus they could be compared sufficiently. However, there were not enough additional comparative studies to perform meta-analyses. For example, no RCTs compared B-I and B-II, one RCT compared B-I and B-II with Braun and RNY, one RCT compared B-II and RNY, and one RCT compared B-II and uncut RNY.

In the sensitivity analysis, the short-term outcome (operation time, morbidity, and hospital stay) results among the studies were uniform, and the same results were obtained even when approximately one result was omitted. However, in the case of long-term results, the number of studies was relatively small (2 to 4 studies), and the uniformity of the results decreased. There was no difference in the sensitivity test in the case of reflux gastritis (**Supplementary Fig. 1E**); however, when studies of Ishikawa et al. [12] and Nakamura et al. [9] were omitted, the OR difference in the meta-analysis decreased from approximately 2 times to 1.2 times in reflux esophagitis analysis. For bile reflux, the OR difference between studies of Nakamura et al. [9] and Yang et al. [11] was 2.5 times and 38 times, respectively, favoring RNY; however, the difference was large. For residual food (**Supplementary Fig. 1G**), when Hirao et al. [6] was omitted, there was a large difference among the studies, with the OR favoring B-I over

RNY. Regarding publication bias, all of the studies except study of Ishikawa et al. [12] were uniformly distributed toward B-I, and both morbidity and hospital stay were uniformly distributed toward B-I over RNY. However, in the long-term outcome results, reflux gastritis was uniformly distributed (**Supplementary Fig. 2E**), and reflux esophagitis (**Supplementary Fig. 2D**) in previous studies [6, 8, 9] and Ishikawa et al. [12] had a wide distribution. In addition, for bile reflux, the distribution was contradictory, and for residual food, studies of Nakamura et al. [9] and Yang et al. [11] showed contrasting results to those of Hirao et al.'s study [6] (**Supplementary Fig. 2F and G**). Nevertheless, to the best of our knowledge, no study has conducted a meta-analysis based only on RCT results thus far; therefore, this meta-analysis is the first to analyze anastomosis methods after DG.

In conclusion, there are specific strengths and weaknesses of each anastomosis method after DG in patients with gastric cancer. Surgeons should accurately identify the advantages and disadvantages of each anastomosis and select a method appropriate for each patient's characteristics.

SUPPLEMENTARY MATERIALS

Supplementary Fig. 1

Sensitivity analysis between B-I and RNY. (A) Operation time; (B) Postoperative complications; (C) Hospital stay; (D) Reflux esophagitis; (E) Reflux gastritis; (F) Bile reflux; (G) Residual food.

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Supplementary Fig. 2

Analysis of publication bias of B-I and RNY. (A) Operation time; (B) Postoperative complications; (C) Hospital stay; (D) Reflux esophagitis; (E) Reflux gastritis; (F) Bile reflux; (G) Residual food.

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