Systematic Review and Meta-Analysis

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Is Roux-en-Y or Billroth-II reconstruction the preferred choice for gastric cancer patients undergoing distal gastrectomy when Billroth I reconstruction is not applicable? A meta-analysis

Lirong He, MD, Yajie Zhao, MD*

Abstract

Background: Although Billroth II and Roux-en-Y procedures are the two most commonly performed types of reconstruction techniques following distal stomach resection, there is yet no consensus on which reconstruction is the best choice. This meta-analysis aims to compare the perioperative safety and long-term complications of Billroth-II and Roux-en-Y reconstruction.

Method: We searched the databases of the PubMed, the Cochrane Library, Web of Science, EMBASE, and the Chinese Biomedicine Database from January 2000 to January 2018 and included studies that compared Roux-en-Y with Billroth-II reconstruction after distal gastrectomy for gastric cancer. The meta-analyses were performed using RevMan 5.0 software.

Result: Four randomized controlled trials (RCTs) and eight non-randomized observational clinical studies (OCS) were included. Billroth-II anastomosis was more beneficial than Roux-en-Y in reducing the operation time (OR = 34.14, 95%CI = 24.19-44.08, $P < .00001$, $I^2 = 54\%$) and intraoperative blood loss (OR = 54.32, 95%CI = 50.29-58.36, $P < .00001$, $I^2 = 36\%$). However, Roux-en-Y anastomosis was more beneficial than Billroth-II in reducing the incidence of remnant gastritis (OR = 0.12; 95% CI = 0.08-0.17; $P < .00001$; $I^2 = 8\%$), reflux esophagitis (OR = 0.26; 95%CI = 0.15-0.44; $P < .00001$; $I^2 = 0\%$), dumping symptoms (OR = 0.31; 95% CI = 0.13-0.73; $P = .008$; $I^2 = 0\%$), reflux symptoms (OR = 0.20; 95% CI = 0.10-0.42; $P < .0001$; $I^2 = 0\%$). No differences were found between the two groups with respect to anastomotic leakage (OR = 1.56, 95%CI = 0.66-3.64, $P = .59$, $I^2 = 0\%$); postoperative mortality (OR = 1.15, 95%CI = 0.38-3.51, $P = .80$, $I^2 = 0\%$); overall postoperative morbidity (OR = 0.92, 95%CI = 0.6-1.42, $P = .72$, $I^2 = 0\%$); and delayed gastric emptying (OR = 0.84, 95%CI = 0.40-1.77, $P = .65$, $I^2 = 0\%$).

Conclusion: Roux-en-Y reconstruction does not carry greater postoperative complications than the Billroth II reconstruction. Additionally, it can improve the postoperative quality of life owing to less remnant gastritis, reflux esophagitis, dumping symptoms, and reflux symptoms. Considering the long-term postoperative outcomes, Roux-en-Y reconstruction appears to be a better choice following distal stomach resection.

Abbreviations: ERCP = endoscopic retrograde cholangiopancreatography, GC = gastric cancer, MINORS = methodological index for nonrandomized studies, OSC = nonrandomized observational clinical studies, RCT = randomized controlled trial.

Keywords: billroth-II, distal gastrectomy, meta-analysis, roux-en-Y

1. Introduction

Among malignant tumors, gastric cancer (GC) has the fourth highest incidence and is the second leading cause of cancer-related death worldwide.[1] When Billroth I reconstruction is not suitable for distal gastrectomy, Billroth II and Roux-en-Y are the two most commonly used reconstruction techniques. In addition, Billroth II or Roux-en-Y are preferred in patients with a stump stomach or a duodenum shortened by extensive resection to ensure the safety of surgical margins. However, the choice of the best reconstruction method remains controversial. Surgeons in the Asia–Pacific region favor the Billroth II anastomosis, while those in Europe and the United States tend to perform Roux-en-Y anastomosis during distal stomach resection. Some surgeons tend to choose Billroth II reconstruction. This may be because the Roux-en-Y reconstruction, given its complicated nature, is associated with high rates of postoperative complications, whereas the Billroth II reconstruction retains the intestinal continuity.[2,3] However, Billroth II reconstruction has an inevitable structural disadvantage, such as remnant gastritis and reflux esophagitis that result from the intestinal contents'

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Department of Surgical Oncology, Baoji Central Hospital.

** Correspondence: Yajie Zhao, Department of Abdominal Surgical Oncology, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China (e-mail: China.1103831536@qq.com).*

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reflux into the stomach. Furthermore, it results in rapid gastric emptying, ultimately leading to dumping syndrome.[4] In addition, this biliary and duodenal-pancreatic reflux is a potential risk factor for malignant changes in the lower esophagus and remnant stomach.[5,6] Survival in patients with gastric cancer has improved owing to advances in early detection and treatment.[7] and concerns about esophageal reflux have also been strongly considered in the selection of surgical techniques. Control of acid reflux is generally considered a fundamental physiological principle that directly affects the quality of life of patients after surgery.[8] Therefore, it is difficult to choose a specific type of reconstruction. Although some randomized controlled trials and observational clinical studies have addressed this problem, these studies have failed to determine which reconstruction is the best choice after distal gastrectomy. Therefore, the purpose of this meta-analysis was to compare perioperative outcomes and postoperative complications in patients undergoing Roux-en-Y reconstruction and Billroth-II after distal gastrectomy.

1.1. Literature search

We searched the Cochrane Library, PubMed, EMBASE, Science Network, and Chinese Medicine Database for journal articles published between January 2000 and January 2018. The following search terms were used: ("stomach tumor" OR "stomach neoplasm" OR "stomach cancer" OR "cancer of the stomach" OR "gastric neoplasm" OR "gastric cancer") AND ("Billroth-II procedure" OR "Billroth-II operation" OR "Billroth-II gastrectomy" OR "Billroth II resection" OR "Billroth-II anastomosis" OR "Billroth-II reconstruction" OR "Billroth-II" OR "Billroth") AND ("Roux-en-Y anastomosis" OR "Roux-en-Y procedure" OR "Roux-en-Y reconstruction" OR "Roux-en-Y" OR "Roux" OR "Loop") NOT "animals". No language restriction was applied. Researchers performed this search independently, and a third individual was consulted in case of conflicting opinions. These keywords were identified in the medical subject heading, title, or abstract. The results of the search strategy are shown in Table 1. All analyses were based on previous published studies; thus, no ethical approval and patient consent are required.

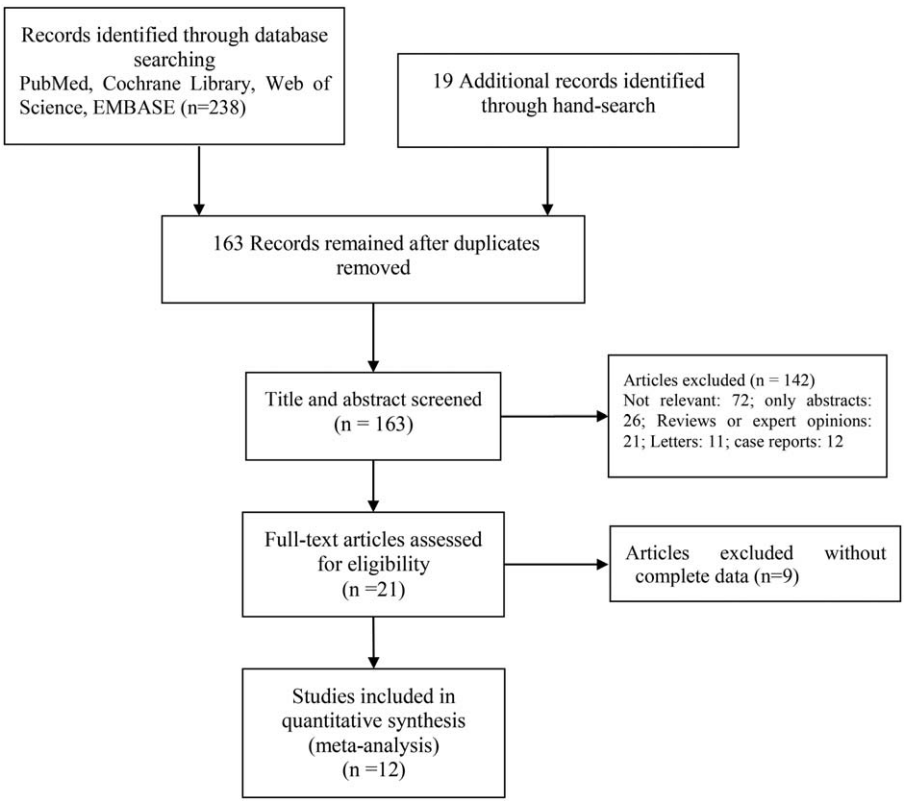
1.2. Inclusion criteria

The following studies were included:

(1) those that compared the perioperative outcomes and postoperative complications between Roux-en-Y and Billroth-II reconstruction after distal gastrectomy;
(2) those that reported at least one of the above outcomes;
(3) those in which all patients underwent follow-up 6 to 9 months postoperatively to evaluate the condition of the remnant gastric mucosa and lower esophagus, and to assess the presence and degree of remnant gastritis and reflux esophagitis;
(4) those that were the latest publication (in case of multiple publications);
(5) those that allowed full-text access.

Table 1

PRISMA flow diagram depicting the selection process.



1.3. Exclusion criteria

The following studies were excluded:

(1) those wherein the detailed surgical type was not reported;
(2) those with no comparison between Roux-en-Y and Billroth-II;
(3) those with incomplete or unavailable data;
(4) all animal studies, abstracts, letters, comments, reviews, and case reports.

1.4. Data extraction and definition

The following detailed data were extracted: population characteristics such as authors, year, country, study type, surgery, mean age, and sex. Outcome indices including:

(1) Operation time—from first skin incision to complete skin closure;
(2) Anastomotic leakage—defined as clinical signs included peritonitis, fever, abdominal pain, pus discharge from the abdominal drain catheter, and/or contrast leakage from a viscus into a body cavity confirmed by a radiographic examination;
(3) Delayed gastric emptying—(a) aspiration ≥ 500 mL/d from nasogastric tube left ≥ postoperative day 10, (b) reinsertion of nasogastric tube, (c) failure of unlimited oral intake by postoperative day 14;
(4) Intraoperative blood loss—volume of blood loss during surgery;
(5) Postoperative mortality—defined as surgery-associated death within 30 days after operation;
(6) Overall postoperative morbidity—defined as any complications occurring within 30 days after operation;
(7) Reflux esophagitis—this was evaluated using the Los Angeles classification [9] and graded as grade 0 (absent) or 1 (present);
(8) Remnant gastritis—evaluated on the basis of residue, gastritis, bile classification (RGB score [10]), normal mucosa (grade 0–grade 4; score > grade 2 were positive findings) as postoperative endoscopic findings 1 year after surgery;
(9) Dumping symptoms—defined as at least one episode of palpitations, suffusion, perspiration, or vertigo after meals at 6 months after surgery; and
(10) Reflux symptoms—defined as at least one episode of heartburn, nausea, or regurgitation more than once a day at 6 months after surgery.

1.5. Quality assessment

Methodological quality of RCTs and OCSs was assessed using the Jadad scoring system and Methodological Index for Nonrandomized Studies (MINORS), respectively.

1.6. Statistical analysis

Review Manager software was used for the meta-analysis. For categorical variables, data were combined and estimated by odds ratio (OR) with corresponding 95% confidence intervals (CIs). Weighted mean difference (WMD) with corresponding 95% CIs were used to analyze the continuous variables. Random model ($I^2 > 50\%$) or fixed model ($I^2 < 50\%$) was used according to the heterogeneity test results. Funnel plots were used to evaluate potential publication bias. $P < .05$ was considered statistically significant.

1.7. Assessment of the risk of bias of RCTs

Assessment of the bias risk of included RCTs. (Fig. 1).

2. Results

2.1. Characteristics of the included studies

Four randomized clinical trials and eight retrospective cohort studies were included. The total number of patients was 1369, of whom 732 underwent Roux-en-Y and 637 underwent Billroth II reconstruction. Characteristics of studies included in the meta-analysis are presented in Table 2. Definition of short-and long-term postoperative complications in the included studies are presented in Table 3.

2.2. Methodological quality assessment

The scores of the study are presented. The 4 RCT studies had a score of 5-7 (Table 4), indicating that they are of high quality; however, two studies not reported the Withdraw and exit. The quality of the included OCSs was assessed using MINORS; scores for most studies ranged from 19 to 22 out of 24 (Table 5).

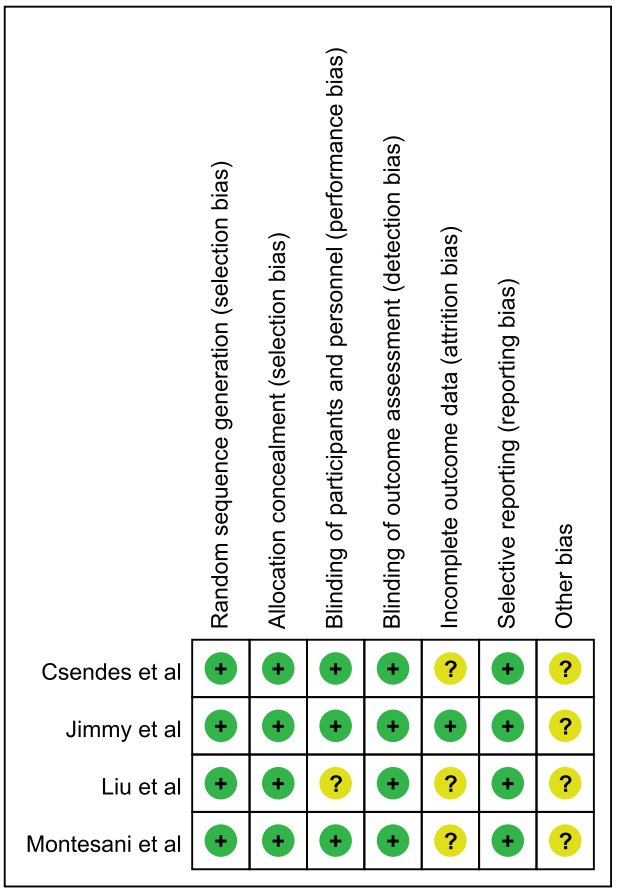


Figure 1. Risk of bias of RCTs: Assessment was based on a quality checklist recommended in the Cochrane Handbook. "Yes" indicated a "low" risk of bias; "unclear," an "uncertain" risk of bias; "no," a "high" risk of bias.

Table 2

The characteristics of all the included studies.

Author	Year	Country	Study Type	Group	Number	Male/Female	Age, y
Jimmy et al[11]	2017	Singapore	RCT	Roux-en-Y	81	46/35	64.5±10.9
				Billroth II	81	45/36	62.0±10.9
Liu et al[12]	2015	China	RCT	Roux-en-Y	93	45/48	63.56±8.45
				Billroth II	93	47/46	62.49±7.32
Csendes et al[13]	2009	Chile	RCT	Roux-en-Y	36	25/8	49.1±1.8
				Billroth II	39	25/8	51.3±3.2
Montesani et al[14]	2002	Italy	RCT	Roux-en-Y	15	–	–
				Billroth II	15	–	–
Cui et al[15]	2017	Korea	OSC	Roux-en-Y	30	22/8	57.6±12.6
				Billroth II	26	15/11	60.1±13.3
Chang et al[16]	2016	Korea	OSC	Roux-en-Y	40	28/12	57.2±10.7
				Billroth II	26	18/8	59.7±9.1
Tran TB et al[17]	2016	USA	OSC	Roux-en-Y	257	147/110	65±13
				Billroth II	190	102/88	67±12
Feng LM [18]	2013	China	OSC	Roux-en-Y	40	18/22	–
				Billroth II	44	25/19	–
Shao ZY[19]	2011	China	OSC	Roux-en-Y	27	–	–
				Billroth II	34	–	–
Osugi et al[20]	2004	Japan	OSC	Roux-en-Y	18	–	60.2
				Billroth II	17	–	64.7
Shinoto et al[21]	2003	Japan	OSC	Roux-en-Y	20	22/16	71 (41–80)
				Billroth II	14	25/22	72 (33–86)
Fukuhara et al[22]	2002	Japan	OSC	Roux-en-Y	68	43/25	62.8±12.2
				Billroth II	65	48/17	62.0±8.9

OSC = nonrandomized observational clinical studies, RCT = randomized controlled trial.

Table 3

Definition of short-and long-term postoperative complications in the included studies.

Author	Anastomotic leakage	DGE	Reflux esophagitis	Remnant gastritis	Dumping symptoms	Reflux symptoms
Jimmy et al[11]	Def A	Def B	–	Def D	–	Def F
Liu et al[12]	Def A	Def B	Def C	Def D	–	–
Csendes et al[13]	–	–	Def C	Def D	Def E	Def F
Montesani et al[14]	–	–	Def C	Def D	–	–
Cui et al[15]	–	–	–	–	–	Def F
Chang et al[16]	–	Def B	Def C	Def D	–	–
Tran TB et al[17]	Def A	–	–	–	–	–
Feng LM [18]	–	–	Def C	Def D	Def E	–
Shao ZY[19]	–	–	Def C	–	Def E	–
Osugi et al[20]	–	–	–	Def D	Def E	Def F
Shinoto et al[21]	–	–	Def C	Def D	–	–
Fukuhara et al[22]	Def A	–	–	–	Def E	Def F

Definition A: defined as clinical signs included peritonitis, fever, abdominal pain, pus discharge from the abdominal drain catheter, and/or contrast leakage from a viscus into a body cavity confirmed by a radiographic examination. Definition B: (1) aspiration ≥ 500 mL/d from nasogastric tube left ≥ postoperative day 10, (2) reinsertion of nasogastric tube, (3) failure of unlimited oral intake by postoperative day 14. Definition C: Reflux esophagitis was evaluated using the Los Angeles classification. Definition D: the degree of remnant gastritis was evaluated according to the RGB (Residue, Gastritis and Bile) classification. When gastritis scored over grade 2, we decided those were positive finding. Definition E: Patient suffer from at least one episode of palpitations suffusion, perspiration or vertigo after meals on six mouth after surgery. Definition F: Patient suffer from at least one episode of heartburn, nausea or regurgitation more than once a day on six mouth after surgery.

However, 2 studies scored <15[18,19] because of missing detailed descriptions of some items (inclusion of consecutive patients; loss to follow-up not exceeding 5%; and statistical analyses adapted to the study design). In all, only 2 studies[15,16] reported unbiased evaluation of endpoints, and none of the OCSs reported prospective calculation of the study size.

3. Meta-analysis

3.1. Operation time

Six studies which reported the operation time were included in this meta-analysis. Using a Random model ($I^2 = 54\%$), the results of meta-analysis indicate that operating time was significantly shorter in Billroth II group (OR = 34.14; 95%CI, 24.19-44.08; $P < .00001$). The result of RCTs and OCS subgroup both reveals that the operating time was significantly shorter in Billroth II group. [RCTs ($I^2 = 81\%$, OR = 34.71; 95%CI, 13.81-55.61; $P < .00001$), OCS ($I^2 = 0\%$, OR = 31.16; 95% CI, 21.08-41.24; $P < .00001$)] (Fig. 2)

3.2. Intraoperative blood loss

Five included studies reported the intraoperative blood loss. Using a fixed model ($I^2 = 36\%$), Billroth II reconstruction was associated with a significant reduction in the intraoperative blood loss (OR = 54.32; 95%CI, 50.29-58.36; $P < .00001$) (Fig. 3)

Table 4

Jadad scale system for randomized controlled trials.

Refs	Randomization	Concealment of allocation	Double blinding	Withdrawals and drop out	Total Score
Jimmy et al	2	2	2	1	7
Liu et al	2	2	1	1	6
Csendes et al	2	2	2	0	6
Montesani et al	2	2	1	0	5

Jadad scale system: The Jadad scale, sometimes known as Jadad scoring or the Oxford quality scoring system, is a procedure to independently assess the methodological quality of a clinical trial. It is the most widely used such assessment in the world. The quality of the RCT studies was evaluated using the Jadad scale. The system was used to assess randomization, concealment of allocation, blinding, and withdrawals in the study. Each item was given a score of 0–2 and 7 score in total. If the total score was ≥4, the RCT was of high quality.

Table 5

Quality Assessment for OCSs Using MINORS.

Refs	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	Total Score
Cui et al	2	2	2	2	2	2	2	2	2	2	0	2	22
Chang et al	2	2	2	2	1	2	2	2	2	2	0	2	21
Tran TB et al	2	2	2	2	0	2	0	2	2	2	0	2	18
Feng LM	2	0	2	2	0	1	1	2	2	2	0	0	14
Shao ZY	2	0	2	2	0	2	1	2	2	1	0	0	14
Osugi et al	2	2	2	2	0	2	2	2	2	2	0	2	20
Shinoto et al	2	2	2	2	0	2	2	2	2	2	0	2	19
Fukuhara et al	2	2	2	2	0	2	1	2	2	2	0	2	19

MINORS criteria include the following items: (1): A stated aim of the study (2): Inclusion of consecutive patients (3):Prospective collection of data (4): Endpoint appropriate to the study aim (5): Unbiased evaluation of endpoints (6): Follow-up period appropriate to the major endpoint (7): Loss to follow up not exceeding 5% (8): A control group having the gold standard intervention (9): Contemporary groups (10): Baseline equivalence of groups (11): Prospective calculation of the sample size (12): Statistical analyses adapted to the study design. Items are scored as follows: 0 (not reported); 1 (reported but inadequate); or 2 (reported and adequate). The ideal global score for comparative studies is 24.

3.3. Anastomotic leakage

Four studies which reported the incidence of anastomotic leakage included in this meta-analysis, using a fixed model ($I^2=0\%$). No significant difference between 2 groups in the incidence of anastomotic leakage (OR = 1.56; 95%CI, 0.66-3.64; $P=.59$). The meta-analysis of RCTs and OCS subgroup both reveals no statically different between two groups in incidence of anastomotic leakage. [RCTs ($I^2=0\%$, OR = 3.07; 95% CI, 0.61-15.41; $P=.67$), OCS ($I^2=0\%$, OR = 1.13; 95% CI, 0.4-3.16; $P=1.13$)] (Fig. 4).

3.4. Postoperative mortality

Five studies which reported the postoperative mortality in this meta-analysis. Using a fixed model ($I^2=0\%$), no significant difference between two groups in the incidence of postoperative mortality (OR = 1.15; 95%CI, 0.38-3.51; $P=.80$) (Fig. 5)

3.5. Overall postoperative morbidity

Seven studies which reported the incidence of overall postoperative morbidity in this meta-analysis. Using a fixed model ($I^2=$

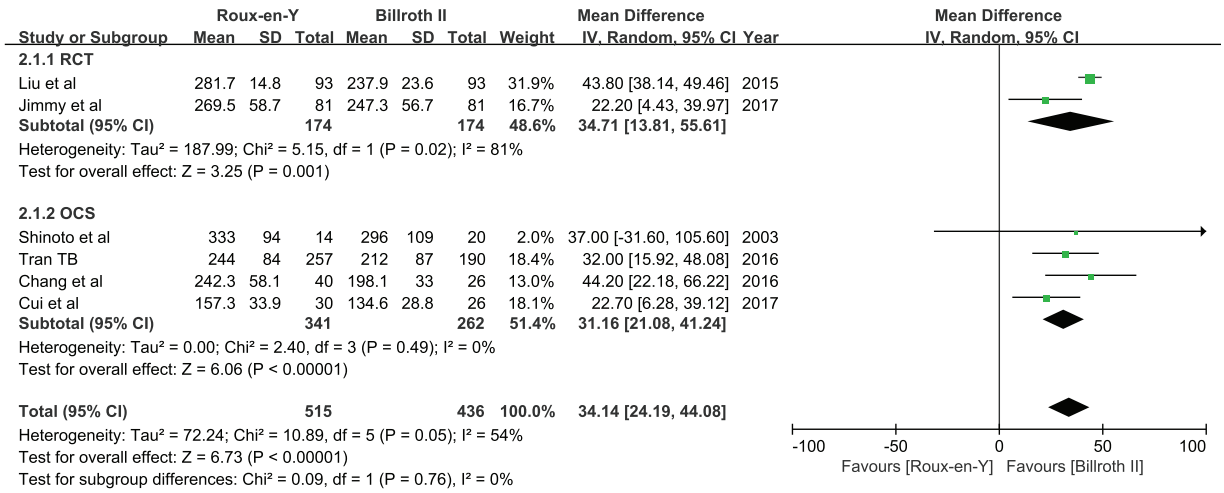


Figure 2. Meta-analysis of operation time.

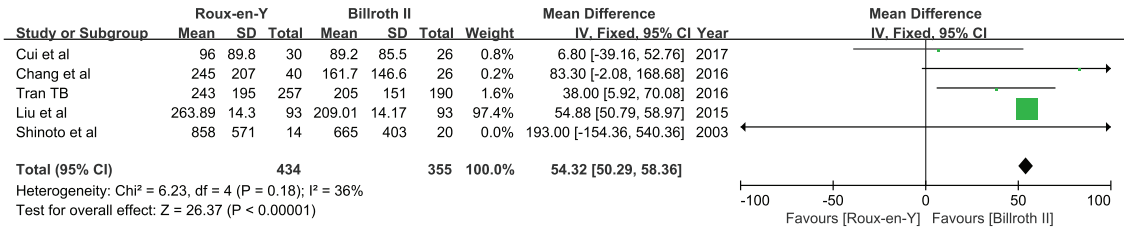


Figure 3. Meta-analysis of intraoperative blood loss.

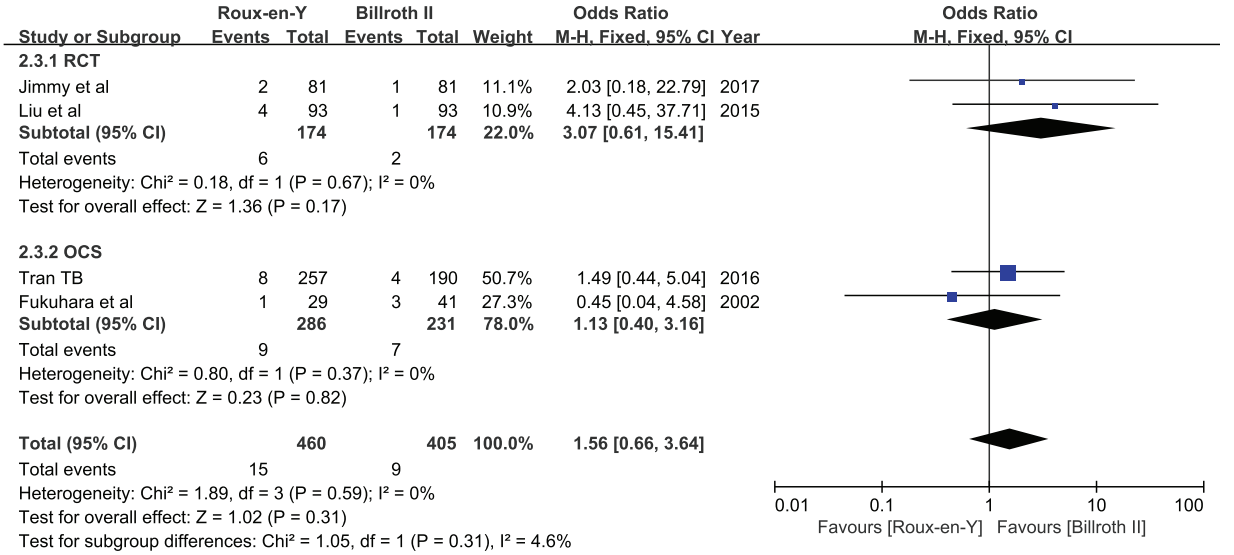


Figure 4. Meta-analysis of incidence of anastomotic leakage.

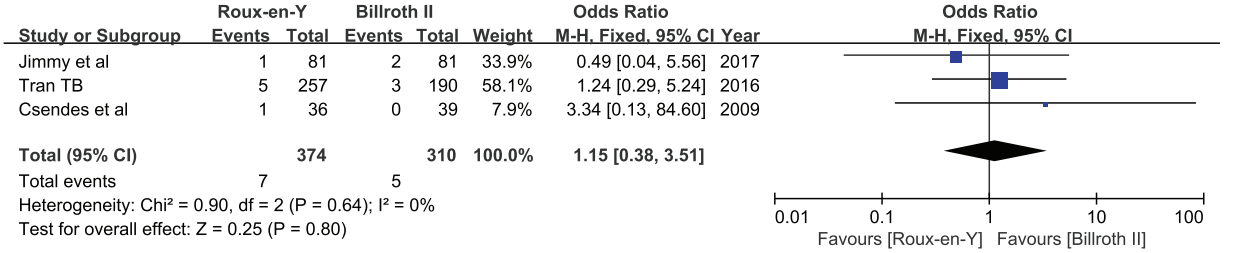


Figure 5. Meta-analysis of incidence of postoperative mortality.

0%), no significant difference between 2 groups in the incidence of overall postoperative morbidity (OR = 0.92; 95%CI, 0.6-1.42; $P = .72$). The meta-analysis of RCTs and OCS subgroup both reveals no statically different between 2 groups in overall postoperative morbidity. [RCTs ($I^2 = 0\%$, OR = 1.22; 95% CI, 0.67-2.23; $P = .51$), OCS ($I^2 = 0\%$, OR = 0.69; 95% CI, 0.37-1.27; $P = .23$)] (Fig. 6).

3.6. Delayed gastric emptying

Three included studies reported the incidence of delayed gastric emptying. Using a fixed model ($I^2 = 0\%$), no significant difference between two groups in the incidence of delayed gastric emptying after operation (OR = 0.84; 95%CI, 0.40-1.77; $P = .65$). (Fig. 7).

3.7. Dumping symptoms

Five included studies reported the dumping symptoms (palpitation, suffusion, perspiration and vertigo) after surgery. Using a fixed model ($I^2 = 0\%$), the results of meta-analysis show that Roux-en-Y reconstruction was associated with a significant reduction in the incidence of dumping symptoms after distal gastrectomy (OR = 0.31; 95% CI, 0.13-0.73; $P = .008$). (Fig. 8).

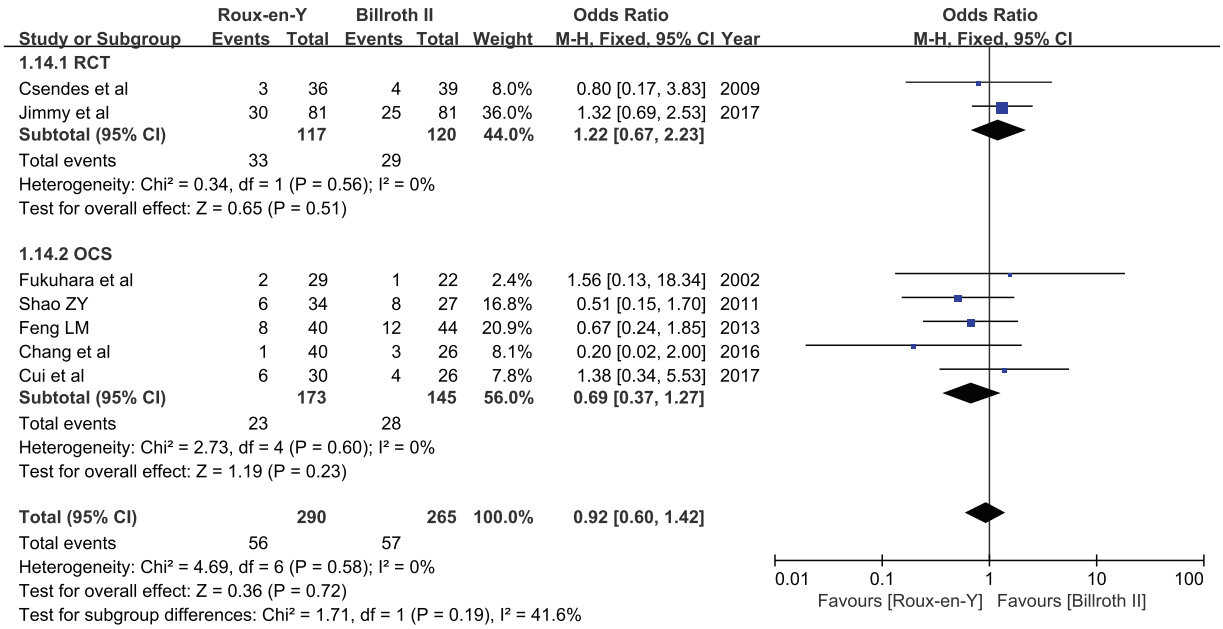


Figure 6. Meta-analysis of incidence of overall postoperative morbidity.

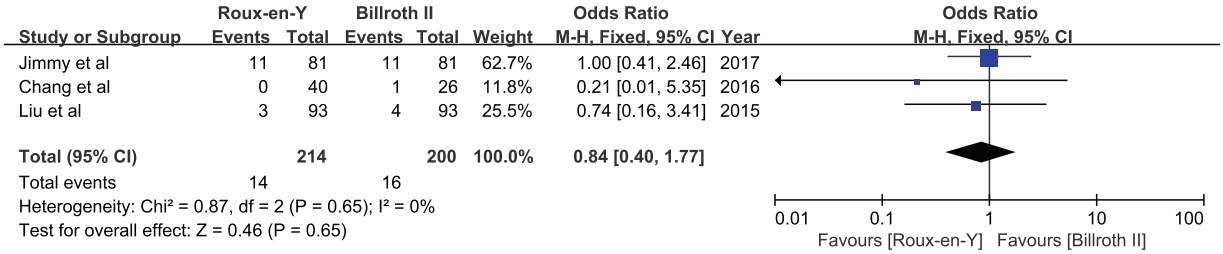


Figure 7. Meta-analysis of incidence of delayed gastric emptying.

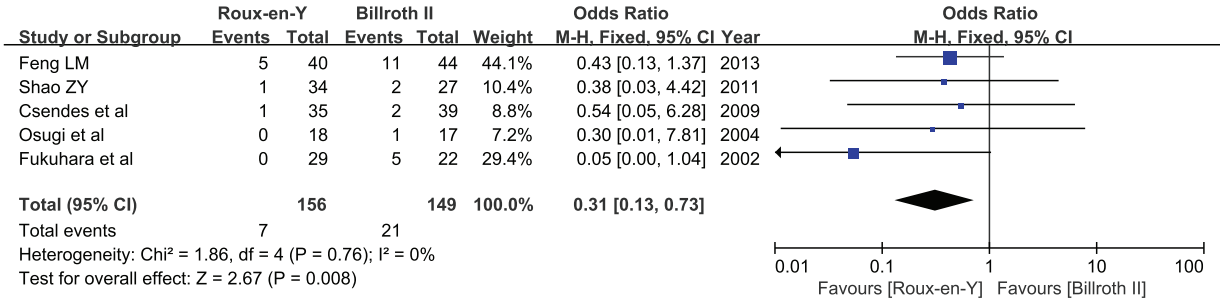


Figure 8. Meta-analysis of dumping symptoms.

3.8. Reflux symptoms

Five included studies reported the reflux symptoms. Using a fixed model ($I^2 = 0\%$), the result of meta-analysis revealed that Roux-en-Y reconstruction was associated with a significant reduction in the incidence of reflux symptoms after distal gastrectomy (OR = 0.20; 95% CI, 0.10-0.42; $P < .0001$). The result of RCTs and OCS subgroup both reveals Roux-en-Y reconstruction had significantly lower incidence of reflux symptoms. [RCTs ($I^2 = 0\%$, OR = 0.13; 95%CI, 0.04-0.46; $P = .001$), OCS ($I^2 = 0\%$, OR = 0.27; 95% CI, 0.11-0.70; $P = .007$)] (Fig. 9).

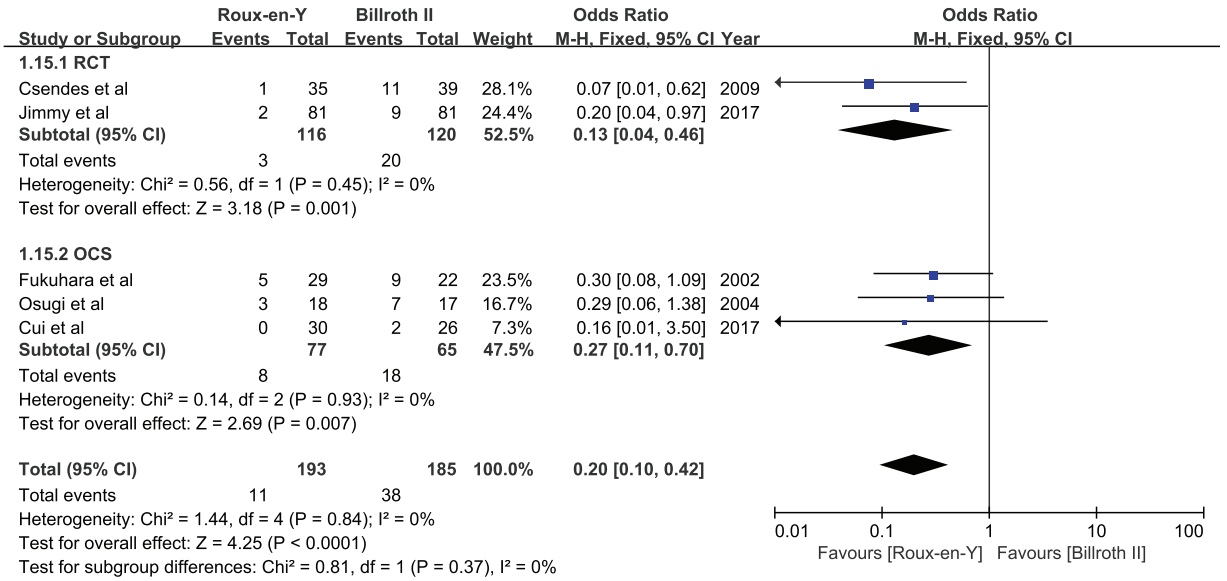


Figure 9. Meta-analysis of reflux symptoms.

3.9. Remnant gastritis

Seven included studies reported the incidence of remnant gastritis. Using a fixed model ($I^2=8\%$), the results of meta-analysis show that Roux-en-Y reconstruction was associated with a significant reduction in the incidence of remnant gastritis (OR = 0.12; 95% CI, 0.08-0.17; $P<.00001$). The result of RCTs and OCS subgroup both reveals that Roux-en-Y reconstruction had significantly lower incidence of remnant gastritis. [RCTs ($I^2=38\%$, OR = 0.14; 95%CI, 0.09-0.22; $P<.00001$), OCS ($I^2=0\%$, OR = 0.07; 95% CI, 0.03-0.17; $P<.0001$)] (Fig. 10).

3.10. Reflux esophagitis

Six included studies reported the incidence of reflux esophagitis. Using a fixed model ($I^2=0\%$), the results of meta-analysis show that Roux-en-Y reconstruction was associated with a significant reduction in the incidence of reflux esophagitis (OR = 0.26; 95% CI, 0.15-0.44; $P<.00001$). The result of RCTs and OCS subgroup both reveals Roux-en-Y reconstruction had significantly lower incidence of reflux esophagitis. [RCTs ($I^2=0\%$, OR = 0.28; 95%CI, 0.13-0.63; $P=.002$), OCS ($I^2=0\%$, OR = 0.24; 95% CI, 0.12-0.49; $P<.0001$)] (Fig. 11).

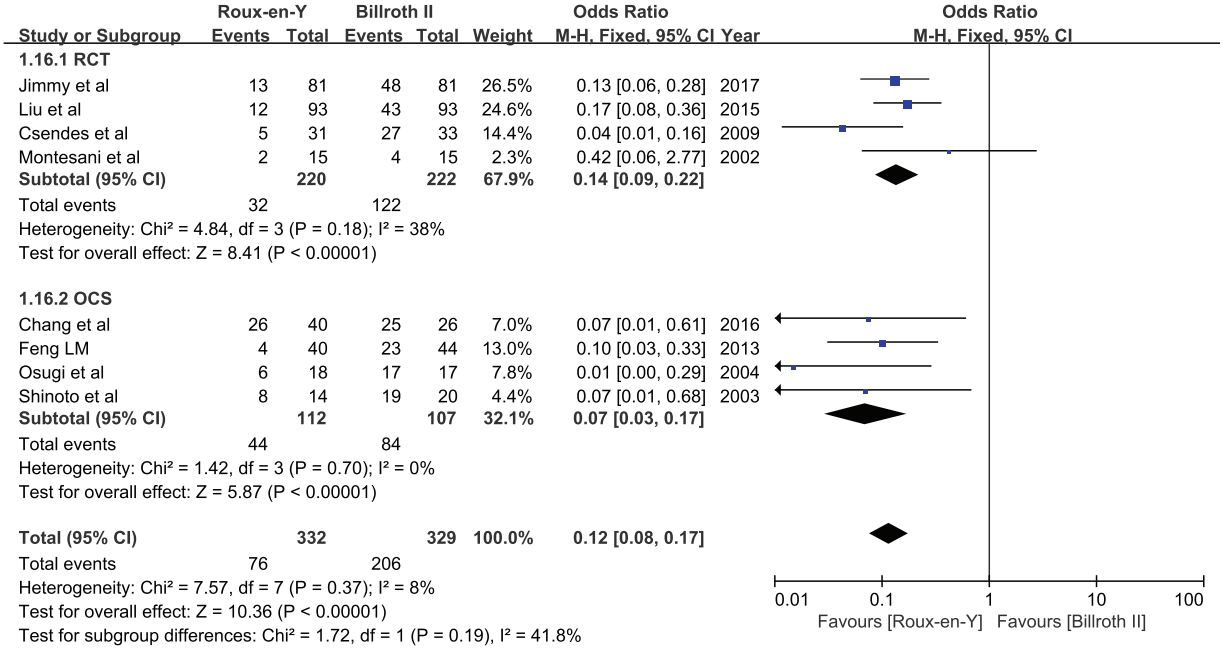


Figure 10. Meta-analysis of incidence of remnant gastritis.

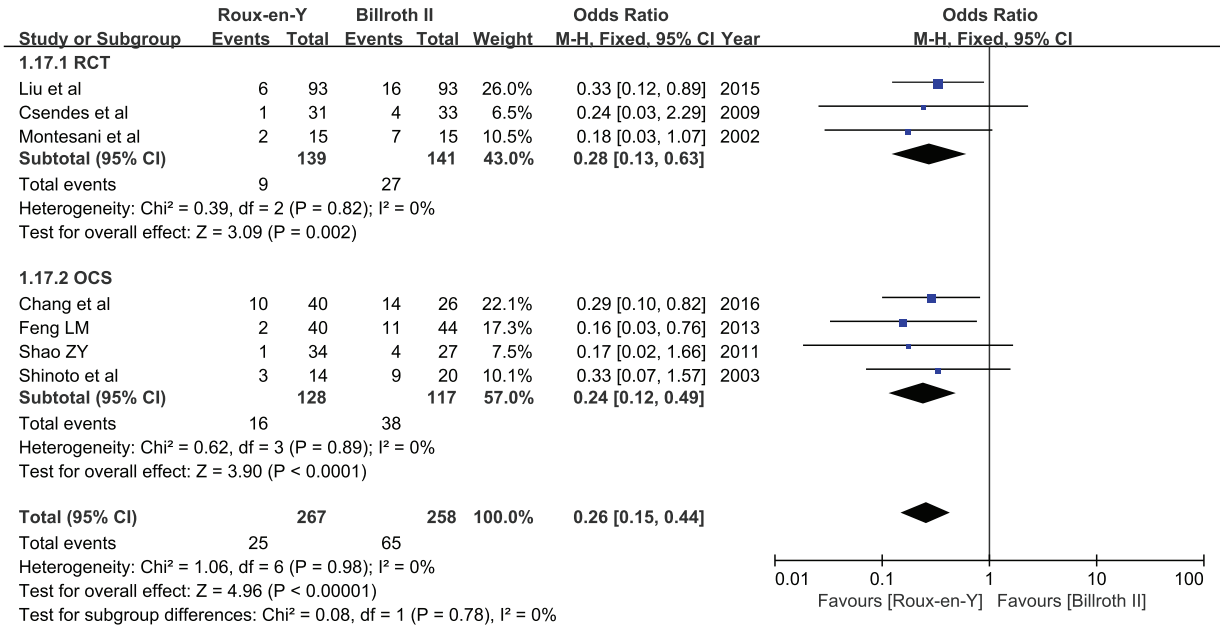


Figure 11. Meta-analysis of incidence of reflux esophagitis.

4. Sensitivity analysis

Sensitivity analysis was conducted by excluding studies that were of relatively low quality (Feng et al and Shao et al). The study data did not change with respect to the outcomes of overall postoperative morbidity, dumping symptoms, remnant gastritis, and reflux esophagitis following exclusion (Table 6). The results suggest that the excluded studies had low publication bias on the outcomes. Besides, our results were robust to the sensitivity analysis for Feng et al and Shao et al, and the results reported in this study are acceptable.

4.1. Publication bias

The deviation of shape in a funnel plot can indicate publication bias. There was no obvious asymmetry in the funnel plot (Fig. 12), which indicated a low publication bias.

4.2. Discussion

Billroth-I gastroduodenostomy is usually performed in Japan and Korea. This kind of anastomosis can be carried out with minimal tension. Billroth-I is also more physiological because it maintains the normal passage of food into the duodenum. Billroth II and Roux-en-Y reconstructions are the 2 most commonly used techniques when Billroth I reconstruction is not applicable after distal gastrectomy. As far as we know, Billroth II reconstruction is often used because of its simplicity. However, the disadvantage of Billroth II anastomosis is remnant gastritis and reflux esophagitis; moreover, the reflux of intestinal contents into the esophagus and remnant stomach is also observed, which is closely related to the high risk of Barrett's esophageal or esophageal cancer and remnant gastric cancer after gastrectomy.[23] The Roux-en-Y technique, on the contrary, significantly reduces the risk of bile reflux. However, it is more complicated to perform with more anastomoses. It also increases the difficulty to assess the bile duct during endoscopic retrograde cholangiopancreatography (ERCP). In addition, some patients may develop delayed gastric emptying known as Roux stasis syndrome with functional obstruction of the Roux limb. Zong et al.[24] retrieved 15 studies involving Billroth I vs. Billroth II vs. Roux-en-Y following distal gastrectomy in 2011. This meta-analysis was an updated one and included more RCT and OCS studies to compare the clinical advantages between Billroth II and Roux-en-Y procedures regarding complications in the perioperative period and long-term outcome.

4.3. Perioperative outcome

The duration of surgery and the amount of intraoperative blood loss are important indicators to evaluate the safety of the

Table 6

Sensitivity analysis.

	All included studies				Studies of high quality			
Outcomes	**Cases**	**I^2**	**OR (95% CI)**	***P***	**Cases**	**I^2**	**OR (95% CI)**	***P***
Overall postoperative morbidity	555	0%	0.92 (0.6–1.42)	.72	410	0%	1.12 (0.67–1.88)	.66
Dumping symptoms	305	0%	0.31 (0.13–0.73)	.008	160	0%	0.19 (0.04–0.86)	.03
Remnant gastritis	661	8%	0.12 (0.08–0.17)	<.00001	577	20%	0.12 (0.08–0.18)	<.00001
Reflux esophagitis	525	0%	0.26 (0.15–0.44)	<.00001	380	0%	0.29 (0.16–0.52)	<.0001

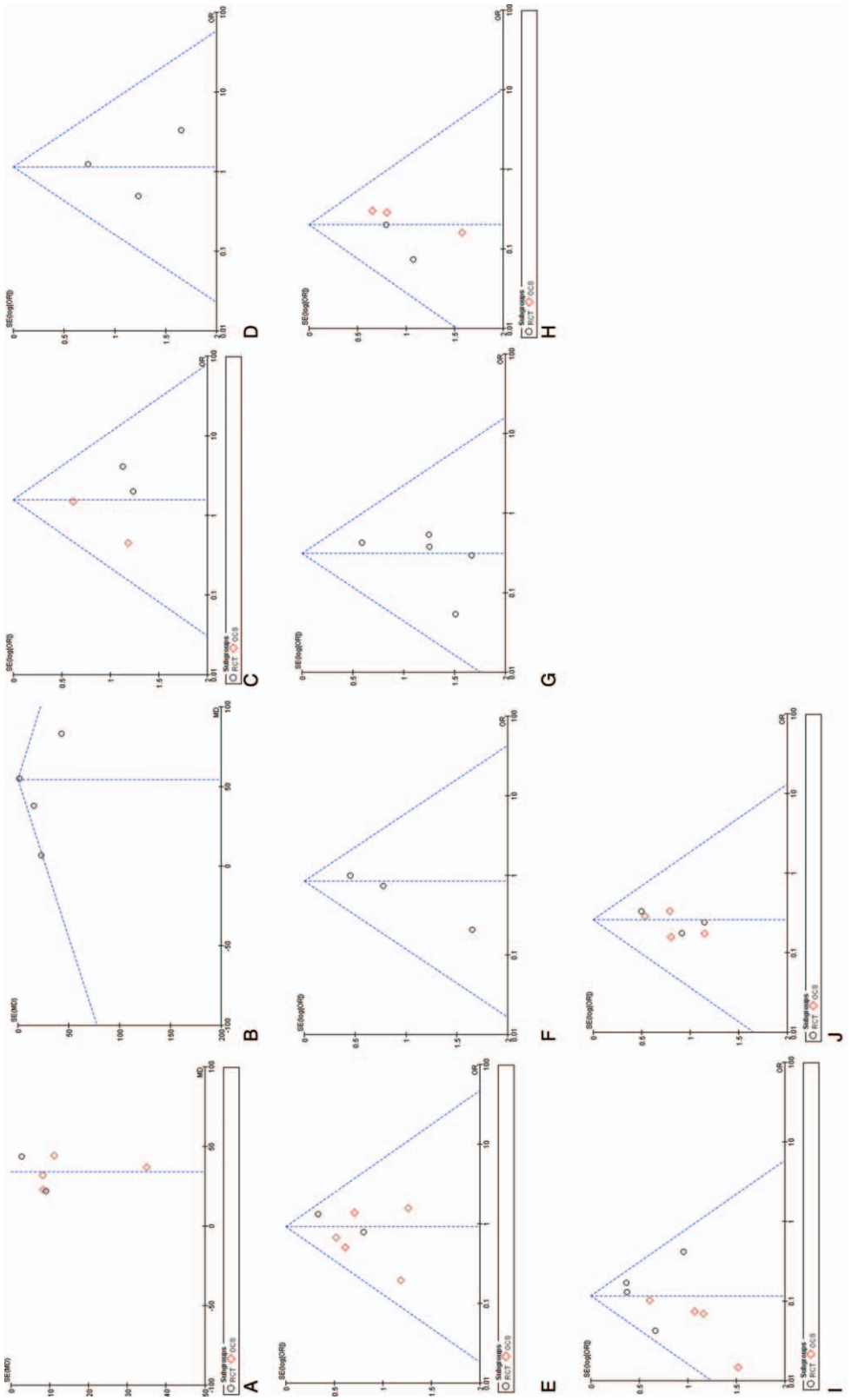


Figure 12. Funnel plots: Funnel plots were created to assess the publication bias in our meta-analysis of included studies. In the absence of publication bias, it assumes that studies with high precision will be plotted near the average, and studies with low precision will be spread evenly on both sides of the average, creating a roughly funnel-shaped distribution. A: Operation time B: Intraoperative blood loss C: Anastomotic leakage D: Postoperative mortality E: Overall postoperative morbidity F: Delayed gastric emptying G: Dumping symptoms H: Reflux symptoms I: Remnant gastritis J: Reflux esophagitis.

intraoperative period. The results of this meta-analysis showed that the intraoperative blood loss was significantly lower and the operating time was significantly shorter in the Billroth II group, which can be explained by the additional anastomosis in Roux-en-Y reconstruction. Regarding the incidence of anastomotic leakage, no significant difference in the rate of anastomotic leak between the 2 reconstruction methods. This may be largely attributed to the refinement of technique and use of gastrointestinal stapling devices. Further, the results of this meta-analysis support that Roux-en-Y reconstruction does not carry greater postoperative mortality and overall postoperative morbidity than the Billroth-II reconstruction.

Some studies have shown that the Roux-en-Y anastomosis is associated with high incidence of delayed gastric emptying (Roux stasis syndrome) after Roux-en-Y, which is characterized by abdominal pain, vomiting, and nausea after oral intake of food. Some studies showed that the Roux stasis syndrome has been known to be prevalent in over 30% of patients after Roux-en-Y. Gustavsson et al[25] suggested that Roux-Y stasis seems to be main caused by a functional obstruction of the Roux-Y limb rather than by a mechanical obstruction, he emphasized the importance of the length of the Roux-Y limb and the limb length longer than 40 cm was a higher risk of Roux stasis syndrome after surgery. What is more, some experts stated that the Roux-Y limb itself contributes to the development of the Roux stasis syndrome. This is perhaps because the Roux-en-Y anastomosis is known to damage the intestinal continuity and integrity of the intestinal nerve. The intestinal loops in Roux lack electrical activity from the duodenum after cutting off the jejunum. Morrison et al[26] found that the direction of propagation of the jejunal pacesetter through Roux-Y limbs can sometimes be retrograde. This finding means Roux-Y limb have a retrograde moving sequence, which could result in stasis in the limb. Mathias et al[27] determined that contractions of the Roux-Y limb were abnormal or even absent after surgery, and did not propel contents distally. Besides, Gustavsson et al[25] found a lower incidence of Roux-Y stasis in patients with total gastrectomy, he speculated that the gastric acid produced by remnant stomach could pass into the Roux-Y limb and affect its motility. Although these factors result in delayed gastric emptying, the exact incidence and reason of Roux stasis syndrome is also debatable. The results of this meta-analysis showed that Roux-en-Y and Billroth-II anastomosis had no significant difference.

4.4. Medium and long-term outcome after operation

This meta-analysis showed that Roux-en-Y anastomosis was superior to the Billroth-II anastomosis in reducing reflux esophagitis and remnant gastritis. Billroth II is associated with deficiencies in reflux control, and duodenal juice reflux into the stomach can increase the value of gastric pH and destroy the normal gastric acid environment. The Roux-en-Y anastomosis was superior to the Billroth-II anastomosis in reducing bile and pancreatic juice reflux mainly because of the active function of the interposed jejunal "Y" limb, which can prevent the esophagus and stomach from being damaged by alkaline intestinal secretions. Prassana et al[28] found that the structure of Roux-en-Y loop could decrease the incidence of duodenal reflux from 26% to 2%.

The refluxed bile and pancreatic juice not only cause reflux symptoms, but also is harmful to the mucosa of the gastric remnant. Lawson et al[29] demonstrated that extensive gastritis was seen in remnant stomach after Billroth II, whereas after Roux-en-Y, no significant changes in gastric mucosa were seen. Vanheenden et al[30] described that all patients after Billroth II gastrectomy had chronic atrophic gastritis, in addition to the appearance of intestinal metaplasia as early as 2 years after surgery. Moreover, the bile and pancreatic juice reflux into the stomach are the causative factors of remnant gastric carcinoma. Tersnette et al [31] demonstrated a significant increased incidence of gastric remnant carcinoma 15 to 20 years after Billroth II (OR = 1.48) in a meta-analysis. Ochiai et al[32] reported that a mutant form of p53 protein was detected in 10% of patients who had duodenal juice reflux after distal gastrectomy. Werscher et al[33] reported that duodenal juice reflux into the stomach caused adenocarcinoma in rats. Therefore, preventing duodenal juice reflux not only improves the quality of postoperative life but also reduces the risk of remnant gastric carcinoma. We can conclude that Roux-en-Y reconstruction following resection of the distal stomach is likely superior to Billroth II reconstruction in preventing remnant gastritis and reflux esophagitis, as it reduces gastroesophageal and duodenogastric reflux. However, gastroesophageal and duodenogastric reflux in some patients with Roux-en-Y reconstruction was likely attributed to pressure from the afferent loop to the remnant gastric cavity being lower than that to the efferent loop.[17]

The results of this meta-analysis regarding dumping syndrome show that Roux-en-Y reconstruction reduces the incidence of dumping symptoms in comparison with Billroth-II reconstruction after surgery. However, the clear mechanisms of Roux-en-Y reconstruction in preventing dumping syndrome are not well known. It is supposed that the interruption of the migration motor complex and diminished jejunal contractions may play an important role in slowing down the transit of chyme through the Roux limb.[34,35]

4.5. Limitations

The main limitations of this meta-analysis include reporting bias and clinical heterogeneity in the study. In this meta-analysis, almost all included OSCs had not performed an unbiased evaluation of endpoints, likely resulting in potential and degree of reporting bias. To reduce reporting bias, we tried to retrieve and include all reports that met the inclusion criteria and contacted the authors of the study to retrieve unpublished data. Although we were able to get unpublished results from authors and perform subgroup analyses according to study type (RCT/OSC), we cannot exclude all publication bias.

The clinical heterogeneity between studies cannot be ignored, which is related to the patient's characteristics, treatment methods, and monitoring. Operative experience and treatment of complications in different hospitals may produce different outcomes and increase heterogeneity between the included studies. Besides, narcotic drugs, especially opioids, may reduce gastrointestinal function. In addition, acid base and electrolyte imbalance may also affect gastrointestinal function. Although we try to control some covariates, we cannot adjust our analysis of all confounding factors.

To accurately compare the perioperative safety and long-term complications of Billroth-II and Roux-en-Y reconstruction after surgery, we suggest that researchers planning observational studies should carefully select appropriate databases, apply correct statistical methods, stringently collect information about

potential interferences, and report on the details of the subjects. Besides, future studies should have clear and agreed definitions of complications and details regarding the therapeutic methods. Further well-designed, large multicenter RCTs are needed to investigate the long-term outcome and complications between these two reconstruction methods.

4.6. Conclusion

Roux-en-Y reconstruction does not carry greater postoperative complications than the Billroth II reconstruction. Furthermore, Roux-en-Y reconstruction can improve the postoperative quality of life owing to less remnant gastritis, reflux esophagitis, dumping symptoms, and reflux symptoms. Considering the long-term postoperative outcomes, Roux-en-Y reconstruction should be a better choice following resection of distal stomach.

Author contributions

Writing – original draft: Lirong He.
Writing – review, and editing: Yajie Zhao.

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