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# Comparison of Billroth I, Billroth II, and Roux-en-Y reconstructions after distal gastrectomy according to functional recovery: a meta-analysis

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**Abstract. – OBJECTIVE: Gastric cancer is common, with a high mortality rate. Billroth I (B-I), Billroth II (B-II), and Roux-en-Y (R-Y) are the major reconstruction procedures after distal gastrectomy. In our study, we aimed to evaluate the functional recovery following the B-I, B-II, and R-Y reconstructions through a network meta-analysis.**

**MATERIALS AND METHODS: PubMed, Embase, and Cochrane Library databases were searched until April 2018. From the included studies, first oral-intake time, early complications, endoscopic finding, quality of life (QoL), and body weight changes were extracted as the short- and long-term outcomes of reconstructions. The network meta-analysis was performed with R 3.4.2 software as well as "gemtc" and "forestplot" packages.**

**RESULTS: Our work included a total of 26 articles involving 6212 patients with gastric cancer. Network meta-analysis revealed that R-Y reconstruction has a lower risk and degree of residual gastritis and bile reflex than B-I and B-II reconstructions. However, no differences in first oral-intake time, complications, risk of reflux esophagitis, and residual food, QoL, and body weight changes existed among the three reconstructions.**

**CONCLUSIONS: R-Y may be the appropriate reconstruction procedure after distal gastrectomy based on postoperative functional recovery. However, more reports with a large sample size are warranted to investigate its long-term outcomes.**

*Key Words:*
Gastric cancer, Distal gastrectomy, Reconstruction, Functional recovery.

## Introduction

Gastric cancer is the fourth most common malignancy and the second leading cause of cancer-related death worldwide, with about 951,600 new cases and 723,100 deaths every year[1,2]. Up to now, surgical resection is still the most effective measure for gastric cancer, especially for the early stage. Distal gastrectomy is recommended for the mid-lower gastric tumors, which account for approximately 70% of gastric tumors and always have a better prognosis than the upper tumors.

Billroth I (B-I), Billroth II (B-II), and Roux-en-Y (R-Y) are the major reconstruction procedures after distal gastrectomy. Also, some of their modified procedures have been introduced in the last decade. However, the most appropriate reconstruction procedure among the three still remains unclear for surgeons. For early gastric cancer, B-I is a common reconstruction technology, especially in Japan and Korea. However, B-II and R-Y are mostly performed in advanced western countries. Indeed, efforts to compare these three reconstructions have been made in some systematic reviews[3,4]. However, due to the lack of reasonable methods, their effective evaluation was insufficient. Thus, this work aimed to evaluate the functional recovery following the B-I, B-II, and R-Y reconstructions through a Bayesian network meta-analysis with relatively comprehensive data.

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## Material and Methods

### Literature Searches and Study Selection

A systematic search of PubMed, Embase, and Cochrane Library was performed until April 2018. The search terms included "(Stomach Neoplasms) OR gastric cancer) OR gastric carcinoma", "(Distal) OR Subtotal", "Gastrectomy", and "(Reconstructive Surgical Procedures) OR Reconstructive Surgery) OR reconstruction". Only English articles were included in our analysis. Two reviewers screened the search results independently. The procedures of this meta-analysis followed the PRISMA guidelines.

### Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) gastric cancer diagnosed clearly according to pathological findings; (2) distal gastrectomy, regardless of open or laparoscopy, performed for each patient; (3) B-I, B-II, or R-Y, including the modified procedures, chosen as the digestive reconstruction procedure after distal gastrectomy; (4) no prior chemotherapy or radiation therapy before gastrectomy. However, studies with duplicated data, letters, comments, reviews, abstracts, or editorial articles were excluded.

### Data Extraction and Quality Assessment

The following data were extracted from each study by two reviewers: first author, year of publication, study design, age, proportion of male, TNM stage, reconstruction techniques, first oral-intake time, early complications (including Clavien-Dindo Classification), RGB Classification of residual stomach, Los Angeles Classification of lower esophagus, quality of life (QoL) of EORTC QLQ-C30, and study population sizes. For analysis of bias risks, two reviewers assessed the quality of literature. The modified Jadad scale and Newcastle-Ottawa Quality Assessment Scale (NOS) were used for randomized controlled trial (RCT) and cohort or case-control studies, respectively.

### Evaluation of Short- and Long-term Outcomes

Given that no significant difference in prognosis existed between B-I, B-II, and R-Y, we mainly compared the postoperative functional recovery, which is being strongly considered by surgeons nowadays. We regarded the first oral-intake time and postoperative complications, which could reflect the early recovery of gastrointestinal tract, as the short-term outcomes. Moreover, the endoscopic finding, QoL, and body weight changes were evaluated as the long-term outcomes.

### Statistical Analysis

We performed the network meta-analysis with R software and "gemtc" and "forest plot" packages. We established the random-effects network models, fitting a generalized linear model under the Bayesian framework, by linking to JAGS. Odds ratios (ORs) and mean difference (MD) with corresponding 95% confidential intervals (CIs) were calculated for binary and continuous outcomes, respectively. We also estimated the consistency between direct and indirect evidence using a node-splitting method. Moreover, if the results of node-splitting were $p>0.05$, the consistency model was selected for the meta-analysis. All analyses were performed with R 3.4.2 software (R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Baseline Characteristics of Studies

A total of 964 potential researches without duplication were searched through PubMed, Embase, and Cochrane Library databases. According to the criteria, 26 studies with 6212 patients were finally included in our work[5-30], of which 9 and 17 were RCTs and case-control studies, respectively. The literature screening process is shown in Figure 1, the characteristics of the included studies are listed in Table I, and the quality of literature is presented in **S1 Table.**

## Short-term Outcomes

### First Oral-Intake Time

To compare the postoperative recovery of gastrointestinal function, 11 studies[6,9-12,14,18,20,25,27,30] reporting the first oral-intake time were included. As shown in Figure 2a, there was no difference in short-term gastrointestinal function restoration between B-I, B-II, and R-Y reconstructions.

### Complications

A total of 16 studies[7,10-12,14,17-19,22-29] were included to compare the overall complications. The overall complication rates of B-I, B-II, and R-Y were 11.6%, 20.2%, and 19.8%, respectively. However, according to our network meta-analysis results, no

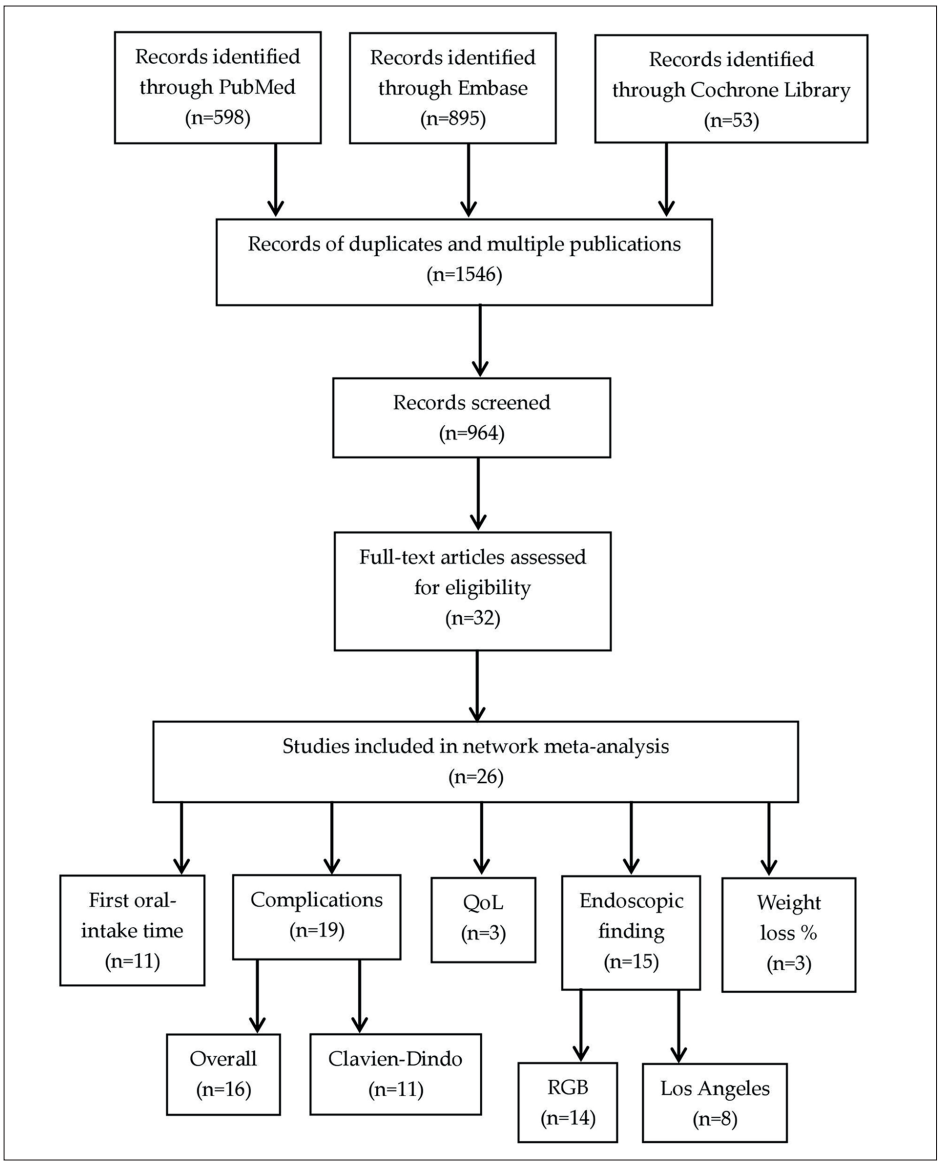


**Figure 1.** Flowchart of the study search and selection process.

difference existed between B-I, B-II, and R-Y (Figure 2b). In addition, another 10 studies[9,14,18,20,23-27,30], which adopted the Clavien-Dindo Classification, were analyzed for the severity of complications. Similar to the overall result, there was no difference in the incidence rates of grade III-IV complications between these three reconstructions (Figure 2b).

## Long-term Outcomes

### *Endoscopic Finding*

A total of 17 reports[7,15,16,20,22,23,30] that compared the difference in endoscopic findings were included. Of these, 8 studies assessed reflux esophagitis according to the Los Angeles Classification and 14 researches[5,7,8,12,16,18-20,22,23,25,27,28,30] assessed gastric residue, gastritis, and bile reflux according to the RGB classification. No difference existed between B-I, B-II, and R-Y in terms of risk of reflux esophagitis and residual food. However, the gastritis and bile reflex were relatively more unusual for R-Y group than for B-I and B-II groups [R-Y *vs.* B-II: OR (95% CIs)=0.08 (0.03, 0.20); R-Y *vs.* B-I: OR (95% CIs)=0.17 (0.075, 0.38)] (Figure 3a). Moreover, as shown in Figure 3b, we evaluated the severity of endoscopic findings using the RGB classifi-

**Table I.** Original characteristics of included studies.

| ID | Study | Design | Open/ Laparoscopy | Reconstruction | No. | Gender Male/Female | Age | TNM stage | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 2002 Kubo et al[5] | Retrospective case-control | Open | B-I<br>R-Y | 175<br>93 | None | None | None | EF |
| 2 | 2005 Ishikawa et al[6] | RCT | Open | B-I<br>R-Y | 26<br>24 | 19/7<br>17/7 | 61<br>64 | I-IV | EF; FOIT |
| 5 | 2008 Kojima et al[7] | Retrospective case-control | Laparoscopy | B-I<br>R-Y | 65<br>68 | 48/17<br>43/25 | 62.0 ± 8.9<br>62.8 ± 12.2 | I-IIIA | EF; Com; BWC |
| 7 | 2010 Namikawa et al[8] | Retrospective case-control | Open | B-I<br>R-Y | 47<br>38 | 25/22<br>22/16 | 70.5 ± 10.9<br>66.2 ± 11.4 | I-IV | EF; |
| 8 | 2011 Kumagai et al[9] | Retrospective case-control | Laparoscopy | B-I<br>R-Y | 329<br>95 | 197/132<br>74/21 | 63.5<br>62.7 | IA | FOIT; Com |
| 9 | 2011 Kang et al[10] | Retrospective case-control | Laparoscopy | B-I<br>B-II | 875<br>384 | 540/252<br>335/132 | 58.0 ± 12.1<br>57.5 ± 12.1 | I-IV | FOIT; Com |
| 10 | 2012 Imamura et al[11] | RCT | Open/ Laparoscopy | B-I<br>R-Y | 163<br>169 | 105/58<br>115/54 | 64.4 ± 9.3<br>63.9 ± 10.5 | I-IV | FOIT; Com |
| 11 | 2012 Lee et al[12] | RCT | Open/ Laparoscopy | B-I<br>B-II<br>R-Y | 49<br>52<br>47 | 31/18<br>42/10<br>28/19 | 60.0 ± 11.6<br>58.5 ± 10.7<br>59.7 ± 10.9 | None | EF; FOIT; Com |
| 12 | 2012 Takiguchi et al[13] | RCT | Open/ Laparoscopy | B-I<br>R-Y | 132<br>136 | 105/58<br>113/53 | 64.5 ± 9.8<br>64.1 ± 10.5 | I-IV | QoL |
| 13 | 2013 An et al[14] | Retrospective case-control | Laparoscopy | B-I<br>R-Y | 50<br>50 | 28/22<br>30/20 | 58.2 ± 13.2<br>59.0 ± 11.9 | None | FOIT; Com |
| 14 | 2013 Hirao et al[15] | RCT | Laparoscopy | B-I<br>R-Y | 163<br>169 | 105/58<br>115/54 | 65<br>65 | I-IV | EF |
| 15 | 2013 Inokuchi et al[16] | Retrospective case-control | Laparoscopy | B-I<br>R-Y | 89<br>83 | 62/27<br>51/32 | 62.0 ± 8.2<br>61.5 ± 12.2 | I-III | EF; BWC |
| 18 | 2014 Komatsu et al[17] | Retrospective case-control | Laparoscopy | B-I<br>R-Y | 74<br>48 | 37/37<br>27/16 | 61.9<br>65.2 | I-III | Com |
| 19 | 2014 Shim et al[18] | Retrospective case-control | Laparoscopy | B-II<br>R-Y | 43<br>38 | 34/9<br>25/13 | 58.0<br>60.9 | I-III | EF; FOIT; Com |
| 22 | 2014 Park et al[19] | Retrospective case-control | Laparoscopy | B-I<br>B-II<br>R-Y | 39<br>76<br>96 | None | None | I-IIIA | EF; Com; BWC |
| 23 | 2015 Kim et al[20] | Retrospective case-control | Laparoscopy | B-I<br>B-II<br>R-Y | 165<br>371<br>161 | 105/60<br>239/132<br>105/56 | 60.7 ± 10.2<br>57.5 ± 12.0<br>55.9 ± 10.9 | I-III | EF; FOIT; Com |

*Table continued*

**Table I *(Continued)*.** Original characteristics of included studies.

| ID | Study | Design | Open/ Laparoscopy | Reconstruction | No. | Gender Male/Female | Age | TNM stage | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| 24 | 2015 Smolskas et al[21] | Retrospective case-control | Open | B-I<br>B-II<br>R-Y | 37<br>101<br>15 | 17/20<br>51/50<br>7/8 | 67.0 ± 12.0<br>67.0 ± 13.0<br>62.0 ± 13.0 | I-III | QoL |
| 25 | 2016 Choi et al[22] | Retrospective case-control | Laparoscopy | B-II<br>R-Y | 26<br>40 | 18/8<br>28/12 | 59.7 ± 9.1<br>57.2 ± 10.7 | I-IIIA | EF; Com |
| 26 | 2016 Nakamura et al[23] | RCT | Open/ Laparoscopy | B-I<br>R-Y | 60<br>62 | 40/20<br>45/17 | 66<br>67 | I-III | EF; Com |
| 27 | 2016 Tran et al[24] | Retrospective case-control | Open/ Laparoscopy | B-II<br>R-Y | 190<br>257 | 102/88<br>147/110 | 67.0 ± 12.0<br>65.0±13.0 | I-III | Com |
| 28 | 2017 Cui et al[25] | Retrospective case-control | Laparoscopy | B-II<br>R-Y | 26<br>30 | 15/11<br>22/8 | 60.1 ± 13.3<br>57.6 ± 12.6 | I-III | EF; FOIT; Com |
| 29 | 2017 Virgilio et al[26] | Retrospective case-control | Open/ Laparoscopy | B-II<br>R-Y | 36<br>96 | 19/17<br>57/39 | 67.0 ± 10.0<br>68.0 ± 13.0 | I-IV | Com |
| 30 | 2017 Yang et al[27] | RCT | Open/ Laparoscopy | B-I<br>R-Y | 70<br>70 | 40/30<br>30/23 | 56.3 ± 10.7<br>54.9 ± 11.5 | I-IV | EF; FOIT; Com; QoL |
| 31 | 2017 Yang et al[28] | RCT | Laparoscopy | B-II<br>R-Y | 79<br>79 | 54/25<br>60/19 | 61.8 ± 11.4<br>58.0 ± 11.4 | I-III | EF; Com |
| 32 | 2018 So et al[29] | RCT | Open/ Laparoscopy | B-II<br>R-Y | 81<br>81 | 46/35<br>45/36 | 62.0 ± 10.9<br>64.5 ± 10.9 | I-IV | EF; Com |
| 33 | 2018 Okuno et al[30] | Retrospective case-control | Laparoscopy | B-I<br>R-Y | 47<br>47 | 35/12<br>36/11 | 62.0 ± 8.0<br>62.0 ± 12.0 | I-III | EF; FOIT; Com |

*Note:* RCT: randomized controlled trials; EF: endoscopic finding; FOIT: first oral-intake time; BWC: body weight change; Com: complications; QoL: quality of life.

cation. Similarly, R-Y had a milder degree of gastritis and bile reflux than B-I and B-II [R-Y *vs.* B-II: MD (95% CIs) = -0.75 (-1.0, -0.40); R-Y *vs.* B-I: MD (95% CIs) = -0.47 (-0.66, -0.27)], but the degree of residue was similar in these three reconstructions.

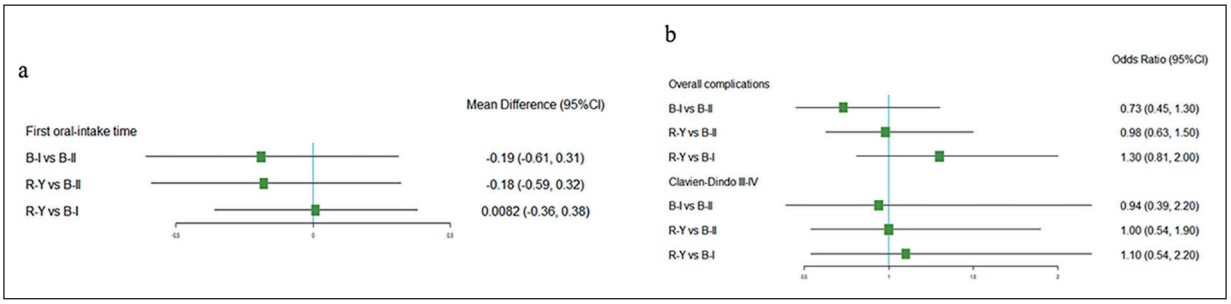


**Figure 2.** Comparison of short-term outcomes between B-I, B-II, and R-Y. **a,** First oral-intake time; **b,** Postoperative complications (overall and Clavien-Dindo III-IV Classification).

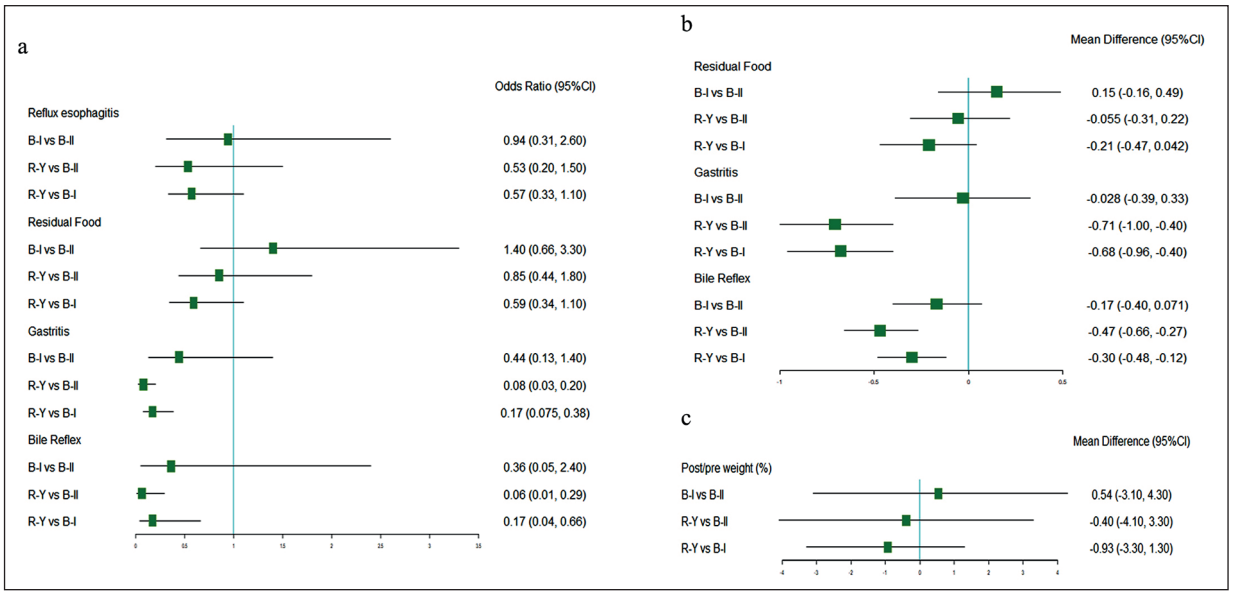


**Figure 3.** Comparison of long-term outcomes, such as endoscopic finding and body weight changes, between B-I, B-II, and R-Y. **a,** RGB Classification; **b,** RGB Classification; **c,** Postoperative/preoperative body weight ratio.

### *Body Weight Changes*

A total of 3 studies[7,16,19], which reported postoperative/preoperative weight ratio (%), were included in our comparison of body weight changes. As shown in Figure 3c, there was no significant difference between B-I, B-II, and R-Y reconstructions in terms of postoperative long-term nutrition status.

### *QoL*

In our work, 3 reports[13,21,27] were included to compare the QoL between the three reconstructions using EORTC QLQ-C30. Using the network meta-analysis, no significant differences existed between the three reconstructions in QoL, such as global health status, functional scales, or symptom scales (Figure 4).

### *Node-Spitting Results*

The node-spitting analysis was performed to confirm the consistency between direct and indirect comparisons. No significant difference existed in the comparison of B-I, B-II, and R-Y ($p$>0.05) in terms of consistency, and the consistency model was finally adopted.

## Discussion

In recent years, with the advancement of surgical techniques, postoperative short- and long-term outcomes, such as complications, QoL, and nutritional status, have become the major criteria in selecting the reconstruction procedure[31,32]. Indeed, if no difference exists in terms of prognosis, minimizing postoperative morbidity and improving QoL should be the ideal goals of gastrointestinal reconstruction. Thus, in this meta-analysis, we compared the difference in the first oral-intake time, early complications, endoscopic findings, QoL, and body weight changes between B-I, B-II, and R-Y reconstructions, to identify the best reconstruction approach for distal gastrectomy.

Clinically, the first oral-intake time was always regarded as the indicator of early postoperative gastrointestinal recovery. Compared with B-I, the B-II and R-Y are the non-physiological reconstructions, which might result in weaker gastrointestinal peristalsis. However, in our analysis, there was no difference in the first oral-intake time between the three reconstructions.

Early postoperative complications are also important indicators of early postoperative gastrointestinal recovery, since they could result in increases in postoperative hospital stay and treatment cost. In this study, there was no significant difference in early postoperative complications between the reconstructions according to the meta-analysis. Also, we evaluated the severity of postoperative complications according to the Clavien-Dindo classification[33]. For distal gastrectomy, the grade III-IV complications, including A-loop

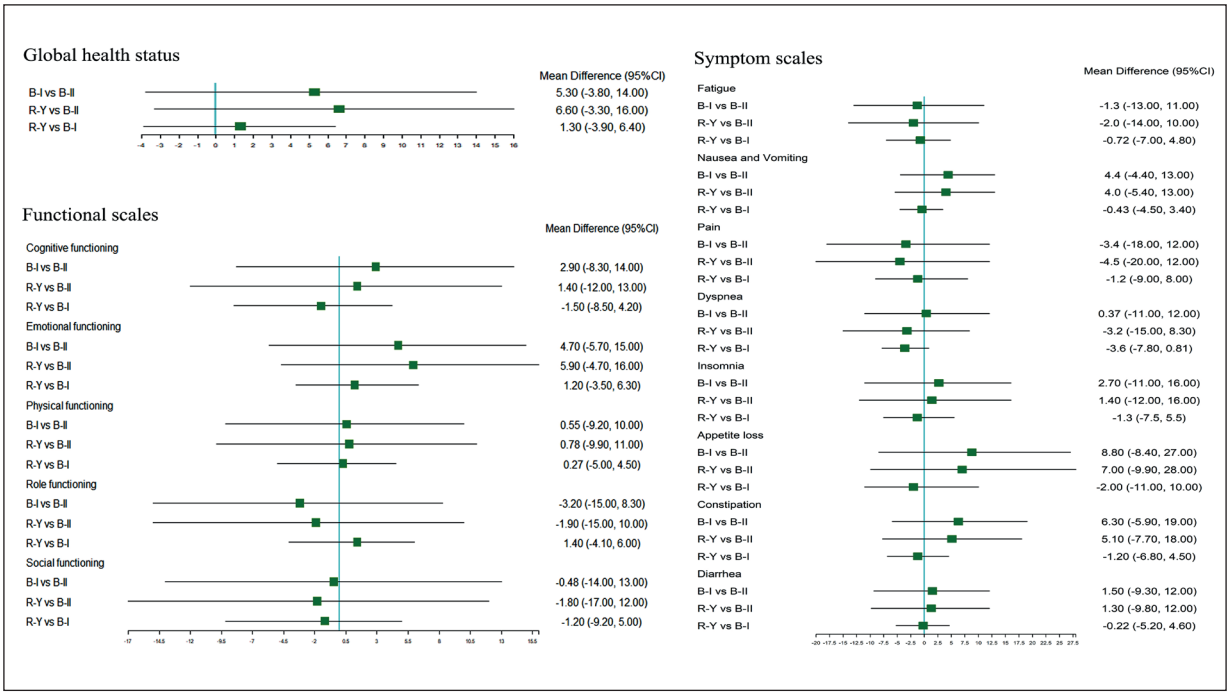


**Figure 4.** Comparison of long-term outcomes, such as QoL, between B-I, B-II and R-Y in terms of global health status, functional scales, and symptom scales.

syndrome, pancreatic fistula, anastomotic leakage, anastomotic stricture, and so on, were regarded as serious complications and could influence patients' early postoperative QoL. After the analysis, we did not find any significant difference in the severity of complications between B-I, B-II, and R-Y. Notably, although the R-Y reconstruction is a more complex procedure requiring additional anastomosis, the risk of anastomotic-site leakage did not increase. Chen and Li et al[34] found that non-physiological reconstruction might be a risk factor of gallstone formation, with a morbidity rate of approximately 6.1%. However, in our included reports, we did not find any difference in terms of morbidity between the reconstructions.

Endoscopic follow-up was necessary for patients with distal gastrectomy to evaluate the esophageal and gastric status, which has been recommended by the NCCN Guideline. Studies suggested that patients with biliary reflux always had a disturbance of the gastrointestinal motility, which could influence their long-term QoL. In addition, the alkaline environment caused by biliary reflux is the major risk factor of residual gastritis and gastric cancer[35]. In our included researches, endoscopy was performed at least 3 months after surgery. Results of the meta-analysis revealed that there were no differences in the incidence rates of reflux esophagitis and gastric residue between the three reconstructions; however, R-Y had a lesser risk of gastritis and bile reflux. In addition, we further evaluated the severity of endoscopic results according to the RGB Classification. Similar to previous results, the degree of gastritis and bile reflux was significantly milder for R-Y reconstruction. However, the degree of residue was similar in B-I, B-II, and R-Y. Therefore, we considered that R-Y reconstruction was a more appropriate procedure after distal gastrectomy since it reduces the risk of residual gastric cancer occurrence and improves the patients' long-term QoL. Notably, no difference in terms of endoscopic findings existed between B-I and B-II, but residual gastric cancer was common at the anastomotic stoma of B-II, which requires the surgeons' attention[36].

Gastrectomy has been proved as an effective choice for controlling body weight and diabetes, and the degree of control between B-I, B-II, and R-Y might be different. Terashima et al[37] found that B-I could result in lower 1-year a postoperative weight loss than R-Y. However, a 1-year RCT study[38] showed that B-I had a significant advantage of maintaining visceral fat change than R-Y. In our analysis, there was no difference in a postoperative/preoperative body weight ratio between

B-I, B-II, and R-Y. Similarly, some works[12,15,39] also reported that there was no difference in the postoperative body mass index changes between B-I, B-II, and R-Y. In addition, a study[40] reported that hyperglycemia might be associated with *Helicobacter pylori* infection. Thus, diabetes was a risk factor for gastric cancer[40]. In the literature review[41-43], we found that distal gastrectomy combined with R-Y could lead to the development of type 2 diabetes in patients with gastric cancer, with a remission rate of approximately 50%.

Postoperative QoL has become an important evaluating outcome measure of surgery in recent decades. As a key assessment tool of QoL, several survey questionnaires were developed and validated, such as EORTC QLQ-C30, EORTC QLQ-STO22, GSRS, and PGSAS-45. In our meta-analysis, we adopted the QLQ-C30, which was composed of 30 items, including global health status, functional scales (physical, role, emotional, cognitive, and social), and symptom scales (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties), to compare postoperative QoL of patients with gastric cancer. According to our results, no significant difference in QoL scores existed among the three reconstructions. However, in the other questionnaires, patients who have undergone the R-Y procedure might have a lower likelihood of experiencing gastrointestinal symptoms, such as dumping syndrome-related symptoms, since R-Y has a stronger anti-reflux capability.

Based on our network meta-analysis findings, we consider R-Y as the appropriate procedure of reconstruction after distal gastrectomy. Indeed, in recent years, surgeons have modified the R-Y reconstruction, such as uncut R-Y, jejunal pouch, and the application of laparoscopy, which significantly improved the outcomes of patients with gastric cancer. Shibata et al[44,45] suggested that adding transmural silk stitches around the staples in the "uncut" portion prevents dehiscence of the staples. Also, they reported that R-Y reconstruction with a jejunal pouch had advantages of earlier food-intake time, as well as nutrition and weight maintenance compared to the conventional R-Y. Kawahira et al[46] referred that the residual stomach of 1/3 or 1/4 and the shorter route of the Roux limb could significantly improve the patient's QoL. In addition, laparoscopic gastrectomy has been proved to have a lower risk of infection, earlier recovery, and better QoL than open distal gastrectomy, which should be widely popularized[12,47-49]. Therefore, the abovementioned modified R-Y reconstructions are recommended for patients after distal gastrectomy. Although Kumagai et al[9] observed that R-Y is one of the risk factors of severe postoperative complications for older patients with gastric cancer, the choice of reconstruction procedure should also consider the specific health conditions of each patient.

Even if this was the first network meta-analysis based on the Bayesian model that compared three reconstructions after distal gastrectomy, our paper also had some limitations. First, the size of the included studies was relatively small, and the insufficiency of direct evidence might lead to inconsistency in some comparison items. For example, only 3 reports of QoL and body weight were included, which reduced the reliability of the results. Second, due to a limited number of included RCTs, we did not perform subgroup analysis according to the study design, which reduced the persuasiveness of the conclusions. Thus, more pairwise RCT researches with large cohorts should be included in the future.

## Conclusions

The R-Y is the appropriate reconstruction procedure for distal gastrectomy, due to its lower risk of gastritis and bile reflux compared to B-I and B-II. Moreover, no significant differences in postoperative functional recovery existed between B-I and B-II. However, more studies with a large sample size are needed to evaluate their long-term outcomes.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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