Effect of Billroth II or Roux-en-Y Reconstruction for the Gastrojejunostomy After Pancreaticoduodenectomy: Meta-analysis of Randomized Controlled Trials

Ji Yang · Chao Wang · Qiang Huang

Abstract

Background and Objectives This study aimed to compare Billroth II with Roux-en-Y reconstruction after pancreaticoduodenectomy (PD).

Methods A literature search was carried out to identify all randomized controlled trials (RCTs) comparing postoperative complications of Billroth II versus Roux-en-Y reconstruction following PD published from 1 January 1990 to 31 August 2014. Pooled risk ratios (RRs) with 95 % confidence intervals (CIs) were calculated using fixed effects or random effects models.

Results In total, three RCTs with 470 patients were included. Using International Study Group of Pancreatic Surgery (ISGPS) definitions, incidences of delayed gastric emptying (DGE) [grades B and C (3.9 versus 12.9 %; RR 0.30, 95 % CI 0.11–0.79; P= 0.01), DGE grade C (0.7 versus 9.6 %; RR 0.11, 95 % CI 0.02–0.61; P=0.01)] were significantly lower in the Billroth II group than in the Roux-en-Y group, as was the length of hospital stay (weighted mean difference −4.72, 95 % CI −8.91, −0.53; P=0.03).

Conclusions Meta-analysis revealed that the incidence of DGE (grades B and C) after PD can be decreased by using Billroth II rather than Roux-en-Y reconstruction.

Keywords Billroth II reconstruction · Delayed gastric emptying · Gastrojejunostomy · Pancreatic fistula · Pancreaticoduodenectomy · Roux-en-Y reconstruction

Introduction

Pancreaticoduodenectomy (PD) represents the only and adequate surgical option for many malignant and benign diseases of the pancreaticoduodenal area. Although mortality after PD has decreased to fewer than 5 % in high-volume centers, it is still accompanied by a high postoperative complication rate (30–50 %).1–8 In most series, the three leading causes of morbidity after PD are postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and wound infection.6–9 The leakage of activated pancreatic enzymes with autolytic activity as well as the pancreatic fistula can cause injury to the surrounding intra-abdominal tissues, giving rise to abscesses, sepsis, and life-threatening hemorrhage. So the POPF can be a source of considerable morbidity and may contribute to mortality. The reported POPF rate after PD ranges from 5 to 25 % in most high-volume centers.1,4–5

Since the PD was first described by Allen Whipple et al.10 back in the 1930s, many efforts have been made to reduce the main postoperative complication pancreatic anastomotic leakage after PD, such as the creation of pancreaticogastrostomy (PG) and pancreaticojunostomy (PJ),11,12 duct ligation, duct occlusion by synthetic polymers as Ethiblock or Neoprene,13,14 and the placement of pancreatic duct stents.15 DGE is also a major postoperative complication after PD and is seen in a significant proportion of patients, contributing to prolong hospital stay and increase in hospital costs.
Although DGE is not a life-threatening morbidity after PD, this condition often results in delaying the oral intake, prolonging the hospital stay, decreasing the life quality of patients after operation, and increasing the cost of hospitalization. DGE is induced by postoperative intra-abdominal complications such as bleeding, ileus, and infection. Due to the disadvantage and influence of DGE, various technical and therapeutic methods have been advocated to decrease the incidence of DGE after PD. These include pyloric dilation, preoperative use of erythromycin, the preservation of the left gastric vein, and the construction of duodenojejunostomy (DJ) or gastrojejunostomy (GJ).

There has been long-standing interest in the development of techniques to reduce the rate of POPF, DGE, and its associated morbidity. Studies have reported that the route of DJ or GJ might have a role in decreasing the incidence of POPF and DGE. Also the debate between the Roux-en-Y reconstruction and the Billroth II (B-II) reconstruction still remains controversial. The use of Roux-en-Y or isolated Roux loop reconstruction is a technique which reduces the activation of pancreatic juice by biliary secretion will reduce the incidence of POPF-related morbidity and mortality in patients undergoing PD compared to that of B-II reconstruction. However, in the B-II reconstruction, the gastric passage can more easily and smoothly pass down to the jejunum because of two direct routes to the afferent and efferent jejunum compared with the Roux-en-Y (R-Y) reconstruction. At almost high-volume centers, this type of reconstruction is selected because of the low DGE incidence of Billroth II reconstruction. Currently, studies comparing the Billroth II or Roux-en-Y are small sizes or retroprospective. Therefore, it is still controversial as to which is the best reconstruction for reducing the POPF, DGE, and its associated morbidity after PD. Due to the relatively small sample sizes of previous randomized controlled trials (RCTs), it is difficult to draw a definitive conclusion. The present paper is a meta-analysis of all published RCTs performed since 1990. It is an effort to determine the best method of reconstruction after PD.

Material and Methods

Search Strategy

A computerized literature search of the Medline, Embase, Web of Science, Cochrane Library, and Cochrane Clinical Trials Registry databases was performed to identify articles published in English until 31 August 2014. The following MeSH terms combined with free-text search terms were used: pancreatic resection, pancreaticoduodenal resection, Whipple’s operation, pancreaticoduodenectomy, Roux-en-Y, isolated Roux loop, and Billroth II. The function of “related articles” was used to broaden the search, and all abstracts, studies, and citations scanned were reviewed. Two researchers (J.Y. and C.W.) searched for articles independently.

Inclusion and Exclusion Criteria

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Inclusion Criteria

Inclusion criteria include the following: (1) only prospective randomized controlled trials were included in this study; PD procedures performed for any reason (malignant or benign pancreatic tumor, chronic pancreatitis, etc.) were included; (2) all the studies were published in English and compared the Billroth II and Roux-en-Y or isolated Roux loop using the quantitative data on POPF, DGE, and other overall complications; and (3) the study publication of the included studies was from 1 January 1990 to 31 August 2014.

Exclusion Criteria

Exclusion criteria include the following: (1) studies that did not report adequately postoperative complications, reoperations, and mortality were excluded; (2) any studies were excluded if the participants were younger than 18 years; (3) PD without immediate pancreatic anastomosis or duodenum-preserving pancreatoduodenectomy was excluded; and (4) observational studies, case reports, and prospective studies were excluded.

Data Extraction and Quality Assessments

Data regarding study description, population characteristics, intraoperative conditions, and outcome parameters were extracted independently by two authors (J.Y. and C.W.). Inconsistencies were resolved by consensus, and when this could not be reached, the third author adjudicated. The quality of all studies was evaluated using the scoring systems of Jadad et al. The Jadad scales were used to evaluate the included articles according to appropriate randomization, double blinding, and adequate description of withdrawals and dropouts.

Statistical Analysis

The statistical analyses were performed using the Review Manager (RevMan) version 5.2.10 software. We analyzed dichotomous variables using estimation of risk ratio (RR) with 95% confidence interval (CI) and continuous variables using weighted mean difference (WMD) with 95% CI. P<0.05 indicated statistically significant difference. Before performing meta-analyses, homogeneity of effect sizes was assessed using chi-square test to determine the I² value. We
considered heterogeneity to be present if the $I^2$ statistic was >50%. A fixed effects (Mantel-Haenszel) statistical model was used in the absence of significant heterogeneity. On the other hand, a random effects (DerSimonian and Laird) model was used. If the heterogeneity was high or extracted data were less than three sets, we performed subgroup analysis. Publication bias was examined in a funnel plot of log RR against its standard error using Begg’s test, and the degree of asymmetry was tested statistically using Egger’s unweighted regression asymmetry test.

Results

Systematic Search

A total of 257 studies were searched in the databases; after reading the full text and the qualitative synthesis of the 257 articles, finally, three RCTs enrolling a total of 470 patients were included.\textsuperscript{31–33} The flow of PRISMA statement of literature selection process is shown in Fig. 1. The two reviewers had 100% agreement in the reviews of the data extraction.

Description of Included Studies

Baseline patient, study characteristics, and surgical procedures are shown in Tables 1, 2, and 3. A total of 470 patients were included in the study, 237 in the Billroth II group and 233 in the Roux-en-Y group. Two\textsuperscript{31,32} of the three studies were single-center study and the other one was multicenter study.\textsuperscript{33} There were no differences between groups in the patient’s age and sex or the pathology that motivated PD in all included studies. Pancreatic cancer was the most frequent diagnosis, followed by other tumors of the pancreaticoduodenal area.

Quality Assessment of the Included Studies

According to the Jadad et al., two of the studies\textsuperscript{31,33} included were of low quality as a result of their use of inadequate randomization methods (randomized during the operation) and the absence of blinding, power calculations, and intention-to-treat analysis. The other trial\textsuperscript{32} was scored as being of high strength as a result of their use of relatively good randomization techniques and the presence of blinding, power calculations, and intention-to-treat analysis. The score of the included studies were 4 points of Tani et al.\textsuperscript{31} and Ke et al.\textsuperscript{33} and 5 points of Shimoda et al.\textsuperscript{32} (Table 4).

Outcomes of Interests

The primary outcomes of the present meta-analysis was the incidence of DGE which includes grades A, B, and C. The definition of DGE was proposed by the International Study Group of Pancreatic Surgery (ISGSP).\textsuperscript{35} DGE was classified into three grades based on its clinical impact: grade A, need for nasogastric tube (NGT) intubation for 4 days or NGT reinsertion after postoperative day (POD) 3 or inability to tolerate a solid diet by POD 7; grade B, need for NGT intubation for 8 days or NGT reinsertion after POD 7 or inability to tolerate a solid diet by POD 14; and grade C, need for NGT

Table 1 Populations and clinical characteristics of the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Patients</th>
<th>Age (years)</th>
<th>Gender (M/F)</th>
<th>Study period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tani M et al.\textsuperscript{31}</td>
<td>2014</td>
<td>Billroth II 76</td>
<td>68.0±8.9</td>
<td>42/34</td>
<td>June 2009–September 2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Roux-en-Y 77</td>
<td>69.6±7.9</td>
<td>39/36</td>
<td></td>
</tr>
<tr>
<td>Shimoda et al.\textsuperscript{32}</td>
<td>2013</td>
<td>Billroth II 52</td>
<td>66.5±9.8</td>
<td>20/32</td>
<td>April 2008–August 2011</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Roux-en-Y 49</td>
<td>65.7±11.1</td>
<td>21/28</td>
<td></td>
</tr>
<tr>
<td>Ke et al.\textsuperscript{33}</td>
<td>2013</td>
<td>Billroth II 109</td>
<td>59.3±6.6</td>
<td>50/59</td>
<td>January 2006–April 2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Roux-en-Y 107</td>
<td>58.3±5.9</td>
<td>51/56</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{30} Springer
intubation for 15 days or NGT reinsertion after POD 14 or inability to tolerate a solid diet by POD 21, based on the ISGPS definition. DGE grade B/C was clinically important because it prolonged the hospital stay after PD and increased the hospital cost. The secondary outcome of the present study was POPF. Definitions of pancreatic fistula and its severity were extracted from the International Study Group on Pancreatic Fistula (ISGPF)\(^34\) in the three included RCTs. In the ISGPF definition, POPF was classified as grade A, B, or C and grade B fistulas. Grade C POPF is a severe, clinically significant fistula that requires major deviations in clinical management. The other outcome measures included intra-abdominal abscess, bile leak, postoperative length of stay (LOS), peptic ulcer, wound infection, postoperative pneumonia, reoperation, morbidity, and mortality.

**Primary Outcome: DGE**

The meta-analysis of the primary outcome investigated the occurrence of DGE (grades A, B, and C) in all of the included RCTs (18.1%). Meta-analysis indicated that there was no significant difference in DGE (grades A, B, and C) between the Billroth II and Roux-en-Y groups (fixed effects model, 16.4 versus 19.9%; RR 0.83, 95% CI 0.56–1.21; \(P=0.34\)) (Fig. 2). In the subgroup analysis of the occurrence of DGE (grades B and C), the meta-analysis indicated that the Roux-en-Y reconstruction group had a significantly higher rate of DGE (grades B and C) compared to Billroth II (3.9 versus 12.9%; relative risk 0.30, 95% CI 0.11–0.79; \(P=0.01\)) (Fig. 3). The subgroup analysis also indicated that DGE grade C was less likely to occur in Billroth II group (0.7 versus 9.6%; RR 0.11, 95% CI 0.02–0.61; \(P=0.01\)).

**Secondary Outcomes**

**POPF**

All trials included provided specific information about total POPF rate in the two groups, but not classified into the three grades (A, B, and C). There was no significant heterogeneity

### Table 2  Pathologies and surgical procedures of the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Groups</th>
<th>Pathologies</th>
<th>Operation type</th>
<th>Surgical techniques</th>
<th>Stenting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tani et al.(^31)</td>
<td>2014</td>
<td>Billroth II</td>
<td>37 11 2 6 18 2</td>
<td>Pylorus-resecting PD</td>
<td>End-to-side hepaticojejunostomy and GJ</td>
<td>Yes</td>
</tr>
<tr>
<td>Shimoda et al.(^32)</td>
<td>2013</td>
<td>Billroth II</td>
<td>46</td>
<td>Pylorus-resecting PD</td>
<td>End-to-side GJ</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Roux-en-Y</td>
<td>38 11 2 7 14 3</td>
<td>SSPPD</td>
<td>End-to-side GJ; Duct-to-mucosa PJ; 2 layers</td>
<td>Yes</td>
</tr>
<tr>
<td>Ke et al.(^33)</td>
<td>2013</td>
<td>Billroth II</td>
<td>39 32 6 18 12 0</td>
<td>Standard PD</td>
<td>End to side</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Roux-en-Y</td>
<td>37 35 8 16 13 0</td>
<td>Standard PD</td>
<td>Duct to mucosa; 2 layers</td>
<td>Yes</td>
</tr>
</tbody>
</table>

PC pancreatic cancer, BC biliary cancer, DC duodenal cancer, AC ampullary cancer, OT other tumors, CP chronic pancreatitis, SSPPD subtotal stomach-preserving pancreaticoduodenectomy, PJ pancreaticojejunostomy, GJ gastrojejunostomy

### Table 3  Definition of the postoperative complications in the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Primary objective</th>
<th>Secondary objective</th>
<th>Inclusion criteria</th>
<th>Definition of pancreatic fistula</th>
<th>Definition of DGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tani et al.(^31)</td>
<td>2014</td>
<td>Pancreatic fistula within 30 days of operation</td>
<td>Mortality and complications within 30 days of operation</td>
<td>Benign or malignant tumor in the pancreatic periampullary region</td>
<td>According to the ISGPF(^34) definition</td>
<td>According to the ISGPS(^35) definition</td>
</tr>
<tr>
<td>Shimoda et al.(^32)</td>
<td>2013</td>
<td>Delayed gastric emptying (DGE)</td>
<td>Pancreatic fistula Mortality Postoperative length of stay</td>
<td>Benign or malignant tumor in the pancreatic periampullary region</td>
<td>According to the ISGPF(^34) definition</td>
<td>According to the ISGPS(^35) definition</td>
</tr>
<tr>
<td>Ke et al.(^33)</td>
<td>2013</td>
<td>POPF</td>
<td>Postoperative complications Postoperative hospital stay</td>
<td>Benign or malignant tumor in the pancreatic periampullary region</td>
<td>According to the ISGPF(^34) definition</td>
<td>According to the ISGPS(^35) definition</td>
</tr>
</tbody>
</table>

\(ISGPF\) International Study Group on Pancreatic Fistula, \(ISGPS\) International Study Group of Pancreatic Surgery, \(POPF\) postoperative pancreatic fistula
among these trials ($I^2=1\%$; $P=0.37$). Meta-analysis showed that the occurrence of POPF was statistically similar in both groups (24.4 versus 20.7 %; RR 1.25, 95 % CI 0.80–1.96; $P=0.32$) (Fig. 4).

**Postoperative LOS**

Two trials\(^{31,32}\) that included 252 patients reported the data of postoperative length of stay. Meta-analysis showed that the postoperative LOS was significantly shorter in the Billroth II group than in the Roux-en-Y group (fixed effects model, WMD $-4.72$, 95 % CI $-8.91$, $-0.53$; $P=0.03$). However, significant heterogeneity was apparent among the two trial studies ($I^2=64\%$; $P=0.10$) (Table 5).

**Operation Time**

All trials included provided the data of operation time between the groups. Meta-analysis showed that the operation time was significantly shorter in the Billroth II group than in the Roux-en-Y group (fixed effects model, WMD $-6.60$, 95 % CI $-12.72$, $-0.49$; $P=0.03$). There was no significant heterogeneity among these trials ($I^2=19\%$; $P=0.29$).

**Bile Leak**

Two trials\(^{31,33}\) compared Billroth II with Roux-en-Y for the occurrence of bile leak. Using a fixed effects model, the pooled data showed that there was no significant difference in postoperative bile leak between the two groups (2.7 versus 1.6 %; RR 1.64, 95 % CI 0.40, 6.76; $P=0.49$) and no significant heterogeneity ($I^2=0\%$; $P=0.85$) (Table 5).

**Intra-abdominal Abscess**

Intra-abdominal abscess was analyzed in the two studies\(^{31,33}\) Rates of intra-abdominal abscess in the Billroth II and Roux-en-Y groups were 7.6 and 5.9 %, respectively, and thus showed no significant difference (RR 1.27, 95 % CI 0.60, 2.70; $P=0.54$). No heterogeneity was found ($I^2=0\%$; $P=0.70$).

**Peptic Ulcer**

Postoperative peptic ulcer occurrence was similar between groups from the pooled analysis (fixed effects model, RR 0.33, 95 % CI 0.04, 3.18; $P=0.34$) from two RCTs\(^{31,33}\) Also no heterogeneity was found ($I^2=0\%$; $P=0.99$).

**Wound Infection**

The rate of postoperative wound infection was similar between the two groups. The data from two RCTs\(^{31,33}\) was amenable for pooling showing a RR of 1.31 (95 % CI 0.78, 2.19; $P=0.30$). No statistical heterogeneity was found ($I^2=0\%$; $P=0.40$).

**Pneumonia**

At last, the occurrence of postoperative pneumonia was similar between the two groups. The pooled data from two RCTs\(^{31,33}\) showed a RR of 0.98 (95 % CI 0.35, 2.74; $P=0.97$) with the fixed effects model. No statistical heterogeneity was found ($I^2=0\%$; $P=0.51$).

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**Table 4** Quality assessment of the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Centers</th>
<th>Randomized</th>
<th>Double blinding</th>
<th>Description of withdraws and dropouts</th>
<th>Total scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tani et al.(^{31})</td>
<td>2014</td>
<td>Single center</td>
<td>During the operation</td>
<td>Yes</td>
<td>Yes</td>
<td>4 points</td>
</tr>
<tr>
<td>Shimoda et al.(^{32})</td>
<td>2013</td>
<td>Single center</td>
<td>Before the operation</td>
<td>Yes</td>
<td>Yes</td>
<td>5 points</td>
</tr>
<tr>
<td>Ke et al.(^{33})</td>
<td>2013</td>
<td>Multicenter</td>
<td>During the operation</td>
<td>Yes</td>
<td>Yes</td>
<td>4 points</td>
</tr>
</tbody>
</table>

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Fig. 2 Comparison of Billroth II versus Roux-en-Y in terms of DGE (grades A, B, and C)
Publication Bias

To explore the publication bias in the present meta-analysis, a funnel plot analysis (Fig. 5) was applied to assess the possibility of publication bias; findings showed a nonsignificant likelihood.

Discussion

Since the PD was first described by Allen Whipple et al. in the 1930s, the best technique for pancreatic anastomosis has remained controversial. The present meta-analysis and systemic reviews of three RCTs allowed for an analysis of pooled data for Roux-en-Y and Billroth II reconstruction, respectively, after PD. Also, the present study was the first meta-analysis which compared the Roux-en-Y and Billroth II reconstruction after the PD. The pooled results showed that the Billroth II reconstruction represents a better option than Roux-en-Y reconstruction by comparing the occurrences of DGE (grades B and C), DGE grade C, and postoperative length of hospital stay. However, no differences between the groups emerged in terms of pancreatic fistula, bile leak, intra-abdominal abscess, peptic ulcer, wound infection, and pneumonia.

Many studies have reported the incidence and the risks of DGE when it was first reported by Warshaw after PPPD. Up to now, the precise mechanism of DGE has not yet been clarified. DGE is thought to be caused by various risk factors, such as the age of patient, pylorospasm caused by disruption of the vagal nerve system and vascular supply to the antrpyloric region, angulation or torsion of the DJ, and other postoperative morbidities such as PF and intra-abdominal abscess. Various studies including resection and reconstruction methods and postoperative medication with erythromycin have been performed to decrease the occurrence of DGE. In this study, we compared the incidence of DGE, POPF, and other complications after PD in Billroth II versus Roux-en-Y reconstruction through the systemic review and meta-analysis, and we found that Billroth II reconstruction was associated with a decrease incidence of DGE (grades B and C) after PD (3.9 versus 12.9%; relative risk 0.30, 95% CI 0.11–0.79, P=0.01). According to the ISGPS classification of DGE, DGE (grades B and C) was clinically important because it prolonged the hospital stays after PD and can increased the hospital cost. The decrease of DGE in Billroth II mainly because of the gastric passage can more easily and smoothly pass down to the jejunum because of two direct routes to the afferent and efferent jejunum compared with the Roux-en-Y (R-Y) reconstruction. The present meta-analysis concluded that the Billroth II had a shorter operation time than that of Roux-en-Y reconstruction (fixed effects model, WMD −6.60, 95% CI −12.72, −0.49; P=0.03). Also the present meta-analysis revealed a result that the Billroth II reconstruction was associated with shorter hospital stays after the PD than that of Roux-en-Y procedures (fixed effects model, WMD −4.72, 95% CI −8.91, −0.53; P=0.03).

Fig. 3  Comparison of Billroth II versus Roux-en-Y in terms of DGE (grades B and C)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Billroth II</th>
<th>Roux-en-Y</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (95% CI)</td>
<td>128</td>
<td>124</td>
<td>100.00%</td>
<td>0.30 [0.11, 0.79]</td>
</tr>
<tr>
<td>Event</td>
<td>5</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 2.01, df = 1 (P = 0.16); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.44 (P = 0.01)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 4  Comparison of Billroth II versus Roux-en-Y in terms of POPF
Numbers of studies have been demonstrated the pros and cons of the Billroth II versus the Roux-en-Y procedures of PD, of which the most primary endpoints were the incidence of pancreatic fistula. The present meta-analysis showed that the occurrence of POPF was statistically similar in both groups (24.4 versus 20.7 %; relative risk 1.25, 95 % CI 0.80–1.96, \(P=0.32\)), which indicates that the Roux-en-Y procedure or the isolated Roux loop does not decrease the incidence of pancreatic anastomotic leakage after PD compared to the Billroth II or conventional reconstruction. As it is known to all, pancreatic fistula is the most important postoperative complication and is at times fatal; it may also play a central role in the development of other intra-abdominal complications, such as hemorrhage and leak. Pancreatic surgeons generally agreed that pancreatic fistula represents the “Achilles heel” of PD.\(^{38,39}\) Several factors can lead to pancreatic fistula, including disease factors (pancreatic texture, pancreatic pathology, pancreatic duct size, and pancreatic juice output), patient-related factors (age, sex, jaundice, comorbid illness, and previous gastric surgery), surgeon-related factors (familiarity), and operative factors (operation time, type of anastomosis, and stenting of pancreatic duct).\(^{39-42}\) In the discussion of Billroth II versus the Roux-en-Y procedures in the present meta-analysis, the occurrence of pancreatic fistula was statistically similar. However, based on previous studies,\(^{43-44}\) we concluded that the Roux-en-Y procedure had several advantages: firstly, isolation of the pancreatic anastomosis from the biliary and gastric anastomoses prevents activation of the secreted inactive precursor pancreatic enzymes by low gastric pH or duodenal enterokinase, and secondly, suction drains placed within the lesser sac adjacent to the pancreatic stump isolate any drainage from around the pancreaticojejunal anastomosis from the rest of the operative field. However, the disadvantages of the Roux-en-Y procedure were the longer operation time, the need for an additional anastomosis, and so on. The Roux-en-Y reconstruction has several advantages which may decrease the pancreatic fistula than that of the Billroth II reconstruction, but in the present meta-analysis,

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Included studies</th>
<th>Heterogeneity</th>
<th>RR/WMD</th>
<th>95 % CI</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGE (all grades)</td>
<td>30–32</td>
<td>50</td>
<td>0.14</td>
<td>0.83 (0.56, 1.21)</td>
<td>0.34</td>
</tr>
<tr>
<td>DGE (grade B)</td>
<td>30–31</td>
<td>0</td>
<td>0.97</td>
<td>0.96 (0.25, 3.77)</td>
<td>0.96</td>
</tr>
<tr>
<td>DGE (grade C)</td>
<td>30–31</td>
<td>0</td>
<td>0.97</td>
<td>0.11 (0.02, 0.61)</td>
<td>0.01</td>
</tr>
<tr>
<td>DGE (grades B and C)</td>
<td>30–31</td>
<td>0</td>
<td>0.88</td>
<td>0.30 (0.11, 0.79)</td>
<td>0.01</td>
</tr>
<tr>
<td>POPF</td>
<td>30–32</td>
<td>1</td>
<td>0.37</td>
<td>1.25 (0.80, 1.96)</td>
<td>0.32</td>
</tr>
<tr>
<td>LOS</td>
<td>30–31</td>
<td>64</td>
<td>0.10</td>
<td>−4.72 (−8.91, −0.53)</td>
<td>0.03</td>
</tr>
<tr>
<td>Operation time</td>
<td>30–32</td>
<td>19</td>
<td>0.29</td>
<td>−6.60 (−12.72, −0.49)</td>
<td>0.03</td>
</tr>
<tr>
<td>Bile leak</td>
<td>30, 32</td>
<td>0</td>
<td>0.85</td>
<td>1.64 (0.40, 6.76)</td>
<td>0.49</td>
</tr>
<tr>
<td>Intra-abdominal abscess</td>
<td>30, 32</td>
<td>0</td>
<td>0.70</td>
<td>1.27 (0.60, 2.70)</td>
<td>0.54</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>30, 32</td>
<td>0</td>
<td>0.99</td>
<td>0.33 (0.04, 3.18)</td>
<td>0.34</td>
</tr>
<tr>
<td>Wound infection</td>
<td>30, 32</td>
<td>0</td>
<td>0.40</td>
<td>1.31 (0.78, 2.19)</td>
<td>0.30</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>30, 32</td>
<td>0</td>
<td>0.51</td>
<td>0.98 (0.35, 2.74)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Fig. 5 Funnel plot analysis showing no publication bias for the occurrence of delayed gastric empty. \(SE\) standard error, \(OR\) odds ratio
we concluded that the difference of pancreatic fistula was not significant; this was mainly because both Billroth II and Roux-en-Y had the same pancreaticojejunostomy anastomosis in the included studies. On the other hand, the Roux-en-Y procedure was more complicated (an additional anastomosis) and need more time, so that in the clinical practice, the Billroth II procedure is widely used. Hence, in the future, randomized controlled trials are required to further clarify its efficacy.

We also evaluated the incidence of bile leak (biliary fistula), intra-abdominal abscess, peptic ulcer, wound infection, and pneumonia between the two groups. Pooled analysis showed that there exist no statistically differences in terms of bile leak, intra-abdominal abscess, peptic ulcer, wound infection, and pneumonia in the Billroth II and Roux-en-Y reconstruction.

However, as an observational study, the limitations of the present meta-analysis should be recognized. At first, the small number of included studies may not provide the comprehensive and precise results, but the present study was the first meta-analysis of randomized controlled trials, the results of the meta-analysis depends on large numbers of the patients in the three included RCTs, and the results were convincing. Secondly, there was clinical heterogeneity in some outcomes, such as the length of hospital stay and the presence of DGE (grades A, B, and C). The heterogeneity was due to the differences in operative technique, the experience of the surgeons, the postoperative management, and so on. For example, the differences of surgical techniques (duct-to-mucosa, invagination, and single-layer, and two-layer methods) may lead to different operation time periods and blood loss, and these factors were risks of the postoperative morbidities and mortality. Thirdly, there were insufficient data for a pooled analysis of the POPF (grade B or C), which cannot provide the sufficient data for comparing the POPF (grades B and C) (clinically, pancreatic fistula). Finally, none of the studies described long-term follow-ups of postoperative mortality and morbidity of the patients after PD, which are crucial to any assessment of the curative effects of Billroth II and Roux-en-Y reconstruction.

In summary, the present study is the first meta-analysis of randomized prospective clinical trials to have demonstrated the superiority of Billroth II over Roux-en-Y in terms of the development of DGE after PD. The incidence of DGE (grades B and C) in the Billroth II group was obviously lower than that in the Roux-en-Y group. Billroth II reconstruction thus seems to have certain benefits in terms of reducing the incidence of severe DGE. Further, adequately powered and well-designed RCTs are required to verify the result and to confirm whether this result can be applied to an equal extent in all patient subgroups.

References

17. Fischer CP, Hong JC. Method of pyloric reconstruction and impact upon delayed gastric emptying and hospital stay after pylorus-