Original research

Pancreaticogastrostomy or pancreaticojejunostomy? Methods of digestive continuity reconstruction after pancreaticodudenectomy: A meta-analysis of randomized controlled trials

Purun Lei 1, Jiafeng Fang 1, Yong Huang, Zongheng Zheng, Bo Wei, Hongbo Wei *

Department of Gastrointestinal Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou 0086-510000, China

Highlights

- Pancreatogastrostomy reduces pancreatic fistula following pancreaticoduodenectomy.
- Pancreatogastrostomy also reduces the bile leakage incidence.
- No difference in operative time and blood loss between PG and PJ anastomosis.
- No difference in other complications between PG and PJ anastomosis.

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Abstract

Background and aims: Reconstruction of digestive tract after pancreaticoduodenectomy now has been proved associated with pancreatic fistula and complication incidence. The meta-analysis was conducted at the appropriate time enough randomized controlled trials were reported. Methods: Systematically literature search was performed through PubMed, EMBASE and Cochrane Library database without restriction to regions, or languages, only randomized controlled trials was included. 7 studies compared pancreatogastrostomy with pancreaticojejunostomy were included for meta-analysis. Fixed and random-effects models were used to measure the pooled estimates. Results: Patient underwent pancreatogastrostomy after pancreatoduodenectomy suffered less pancreatic fistula (p = 0.001) and bile leakage (p = 0.02), while the operative time, hospital stay, delayed gastric emptying and overall morbidity were comparable. Conclusion: Pancreatogastrostomy is a recommended anastomosis technique according to the meta-analysis due to minimize incidence of pancreatic fistula and bile leakage.

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1. Introduction

Mortality after pancreaticoduodenectomy (PD) has fallen below 5% [1–3], but morbidity rates remain 30–65% [3]. The most common complications after PD are delayed gastric emptying, pancreatic fistula, and wound infection, which affects mortality rate, length of hospital stay, and costs [4]. Pancreatic fistula has a central role in the development of other intra-abdominal complications, with a frequency of 6%–14% [5–7]. Therefore to avoid leakage of pancreatic juice from anastomosis site manifests an important role in clinic.

Until now, various preventive measures have been proposed [8,9], including methods to decrease pancreatic secretion or variations in anastomotic techniques: such as pancreaticojejunostomy technique (PJ), reconstruction with pancreaticogastrostomy (PG) and placement of pancreatic duct stents. Nevertheless, the best method to restore pancreatic digestive continuity is still debated. Thus, it is important to discuss the proper method of GI tract reconstruction after PD with pooled results from high quality studies, to help find a better approach for the management of patients underwent PD.

2. Methods

2.1. Literature strategy

Comprehensive literature search was performed through PubMed, EMBASE and the Cochrane Library (last search date: December 16, 2013), without restriction to regions, publication types, or languages. We used the following MeSH terms and/or text words: ‘pancreatic neoplasm’, ‘pancreatic cancer’, ‘pancreatic

2.2. Study selection

Only randomized controlled trials compared the perioperative outcomes between PG and PJ were included. The exclusion criteria were observational studies, no-randomized studies, non-comparable studies, non-human studies, experimental trials, review articles, editorials, letters and case reports, and articles not reporting the outcomes of interest.

2.3. Data extraction and outcomes of interest

Two reviewers (PR Lei and JF Fang) independently considered the eligibility of potential titles and abstracts. When there was a disagreement, the full-text evaluation was taken. Data were extracted independently and in duplicate by another two reviewers (ZH Zheng and Y Huang); discrepancies were resolved by mutual agreement, the full-text evaluation was taken. Data were extracted independently and in duplicate by another two reviewers (ZH Zheng and Y Huang); discrepancies were resolved by mutual agreement, the full-text evaluation was taken.

3. Results

3.1. Study characteristics

Through electronic searches, 733 articles were retrieved; finally seven randomized controlled trials were included [13–19], involving 1121 patients (562 for PG and 559 for PJ after pancreaticoduodenectomy). Table 1 displays the characteristics of each study and Fig. 3 illustrates the study screening and selection process.

Table 1

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Cases PG/PJ</th>
<th>Age PG/PJ</th>
<th>Gender male of PG</th>
<th>PF definition</th>
<th>Texture</th>
<th>Diameter</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bassi [13]</td>
<td>2005</td>
<td>69/82</td>
<td>59/56</td>
<td>44/51</td>
<td>Any clinical significant output of fluid, rich in amylase, confirmed by fistulography</td>
<td>soft</td>
<td>≤5 mm</td>
<td>PD</td>
</tr>
<tr>
<td>Duffas [14]</td>
<td>2005</td>
<td>81/68</td>
<td>58/59</td>
<td>51/35</td>
<td>Fluid obtained through drains containing at least 4 times normal serum values of amylase for 3 days, or radiologically</td>
<td>soft/hard</td>
<td>≥3 mm</td>
<td>PPPD/PD</td>
</tr>
<tr>
<td>Topai [16]</td>
<td>2013</td>
<td>162/167</td>
<td>67/66</td>
<td>91/100</td>
<td>ISGPF</td>
<td>NA</td>
<td>≤3 mm</td>
<td>PPPD/PD</td>
</tr>
<tr>
<td>Yeo [18]</td>
<td>1995</td>
<td>73/72</td>
<td>62/62</td>
<td>33/38</td>
<td>Radiographically documented leak or &gt;50 mL drainage of amylase rich fluid on or after postoperative day 10</td>
<td>soft/hard</td>
<td>≥4 mm</td>
<td>PPPD/PD</td>
</tr>
<tr>
<td>Figueras [19]</td>
<td>2013</td>
<td>65/58</td>
<td>67/66</td>
<td>44/37</td>
<td>ISGPF</td>
<td>soft/hard</td>
<td>≥3 mm</td>
<td>PPPD/PD</td>
</tr>
</tbody>
</table>

NA – not available.
Age, gender, texture of pancreas, diameter of pancreatic duct and surgical approach of patients underwent PG and PJ after pancreaticoduodenectomy were comparable in all studies. Surgical indications were complicated, including the pancreatic adenocarcinoma, ampullary adenocarcinoma, ductal cancer et al. Standard PD or pylorus preserved PD was taken in majority of studies, one study perform standard PD [13], another PP-PD only [15].

Three of the studies [15–17] described pancreatic fistula defined by ISGPF [20] as: a drain output of any measurable volume of fluid on or after postoperative day 3 with amylase content greater than 3 times the serum amylase activity. One study [14] described PF similar to ISGPF definition. Others [13,14,18] adopted the self-defined concepts of pancreatic fistula.

The risks of bias were respectively evaluated by the Jadad Scale for all studies. Almost all RCTs described the random sequence production and withdraw situation adequately, performed single-blind or double-blind method, only one study [15] scored 1 point and considered as low quality.

### 3.2. Perioperative complications

Pooling data from all RCTs assessed overall perioperative complication (both intra-operative and postoperative complications), such as pancreatic fistula, delayed gastric emptying, biliary leak and hemorrhage, showed no significant difference between both groups (OR: 0.91 [0.70, 1.17]; p = 0.46). Showed in Table 2.

#### 3.2.1. Pancreatic fistula and bile leakage

All studies reported the incidence of pancreatic fistula (PF), manifested an encouraging result that patients underwent PG suffered significantly less incidence of PF (14.77% vs 22.18% OR: 0.60 CI, 0.44–0.82; p = 0.001). Moreover, the bile leakage also decreased obviously in PG group (1.47% vs 5.07% OR: 0.33, CI, 0.13–0.82; p = 0.02). Showed in Figs. 1 and 2.

#### 3.2.2. Post-operative hemorrhage, ascites and delayed gastric emptying

Post-operative hemorrhage incidence was available in 6 studies [13–17,19], no significant differences were found (11.66% vs 9.03%, OR: 1.29, CI, 0.85–1.96; p = 0.24). The occurrence of ascites or delayed gastric emptying [13,15–19] also showed comparable

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### Table 3

Jadad score of the included studies of meta-analysis.

<table>
<thead>
<tr>
<th>Author</th>
<th>Randomize generation</th>
<th>Blinding</th>
<th>Description of withdraws and drop-outs</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bassi [13]</td>
<td>Adequate</td>
<td>Improper Numbers and reasons described</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Duffas [14]</td>
<td>Adequate</td>
<td>Double blinding Numbers and reasons described</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Fernandez [15]</td>
<td>Inadequate</td>
<td>Improper Numbers and reasons undescribed</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Topai [16]</td>
<td>Adequate</td>
<td>Improper Numbers and reasons described</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Ulrich [17]</td>
<td>Adequate</td>
<td>Improper Numbers and reasons described</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Yeo [18]</td>
<td>Adequate</td>
<td>Improper Numbers and reasons described</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Figueras [19]</td>
<td>Adequate</td>
<td>Improper Numbers and reasons described</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Studies scored more than 2 points are considered as high quality.

---

**Table 3**

Jadad score of the included studies of meta-analysis.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>PG Events</th>
<th>PG Total</th>
<th>PJ Events</th>
<th>PJ Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bassi 2005</td>
<td>9 9</td>
<td>13 82</td>
<td>14 82</td>
<td>19 99</td>
<td>9.9%</td>
<td>0.80 [0.32, 1.99]</td>
<td></td>
</tr>
<tr>
<td>Duffas 2005</td>
<td>13 81</td>
<td>14 68</td>
<td>17 68</td>
<td>20 96</td>
<td>12.2%</td>
<td>0.74 [0.32, 1.70]</td>
<td></td>
</tr>
<tr>
<td>Fernandez 2008</td>
<td>3 53</td>
<td>10 55</td>
<td>13 60</td>
<td>17 75</td>
<td>8.9%</td>
<td>0.27 [0.07, 1.04]</td>
<td></td>
</tr>
<tr>
<td>Figueras 2013</td>
<td>10 65</td>
<td>20 58</td>
<td>23 73</td>
<td>25 98</td>
<td>17.1%</td>
<td>0.35 [0.15, 0.82]</td>
<td></td>
</tr>
<tr>
<td>Topai 2013</td>
<td>33 162</td>
<td>52 167</td>
<td>46 179</td>
<td>55 194</td>
<td>39.0%</td>
<td>0.57 [0.34, 0.94]</td>
<td></td>
</tr>
<tr>
<td>Ulrich 2012</td>
<td>6 59</td>
<td>7 57</td>
<td>8 66</td>
<td>10 72</td>
<td>6.1%</td>
<td>0.81 [0.26, 2.57]</td>
<td></td>
</tr>
<tr>
<td>Yeo 1995</td>
<td>9 73</td>
<td>8 72</td>
<td>10 77</td>
<td>12 90</td>
<td>6.8%</td>
<td>1.13 [0.41, 3.10]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>562</td>
<td>559</td>
<td>100.0%</td>
<td>1121</td>
<td>0.60</td>
<td>[0.44, 0.82]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>83</td>
<td>124</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Ch² = 5.29, df = 6 (p = 0.51); I² = 0%

Test for overall effect: Z = 3.25 (p = 0.001)

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**Fig. 1.** Forest plot and meta-analysis of pancreatic fistula.

**Fig. 2.** Forest plot and meta-analysis of bile leakage.
between both groups (OR: 0.58, CI, 0.29–1.13; \( p = 0.11 \)) and (OR: 0.98, CI, 0.53–1.82; \( p = 0.95 \)).

3.2.3. Reoperation and mortality

5 studies [13–17] reported incidence of reoperation, main reason was severe pancreatic fistula and intra-abdominal hemorrhage. Overall no significant differences was found (8.45% vs 8.38%, OR: 0.96; 95% CI, 0.61–1.52; \( p = 0.87 \)). Mortality of 5 studies [13,14,16,17,19] turned out a comparable result (4.13% vs 4.63%, OR:0.82; CI, 0.43–1.58; \( p = 0.56 \)). Majority deaths were caused by pancreatic fistula, intra-abdominal hemorrhage, pancreatitis after surgery, intra-abdominal or respiratory infection, thrombus or myocardial ischemia, the accurate percentage was unavailable as deficiency in some studies.

3.3. Operative outcomes

6 studies [14–19] reported operative time and hospital stay of the 970 included patients, the random-effects model was considered as appropriate, as test for heterogeneity of both outcomes being statistically significant. The mean operative time was comparable in both groups (WMD: 0.04, CI, –0.13–0.22; \( p = 0.63 \)).

Meanwhile despite different anastomosis was taken, the length of hospitalization showed outcome without differences (WMD: –1.45, CI:–3.41–0.52; \( p = 0.15 \)).

4. Discussion

Consequences of PF include morbidity, mortality, increasing hospital stay and cost. Incidence of PF after PD ranged from 6% to 14%, the reported mortality from 1.4% to 3.7% [21–24]. Moreover, other complications such as delayed gastric emptying, ileus, wound infection, intra-abdominal abscess, pancreatitis, hemorrhage, and sepsis are correlated with pancreatic fistula. Eventually result in increase in length of hospital stay and cost.

Risk factors for pancreatic fistula include patient-related (age, gender, jaundice, and malnutrition), disease-related risk factors (pancreatic pathology, pancreatic texture, pancreatic duct size, pancreatic juice output), and procedure-related factors (operative time, resection type, anastomotic technique, intraoperative blood loss) [9]. In addition, surgeons experience has been shown to correlate with PF incidence.

Different PJ techniques have been reported, including the site of jejunum used (end vs. side), the type of anastomosis (binding or...
invagination or duct-to-mucosa), and the use of pancreatic ductal stenting. Recently some observational studies and RCTs have reported lower pancreatic fistula rate with PG instead of PJ [13–19,25–28] Thus this meta-analysis was at an appropriate time because enough randomized clinical trials have been accumulated for clinical practice.

Four RCTs [13,14,17,18] included in this meta-analysis did not show any advantages to PG; three RCTs [15,16,19] manifested there is lower PF incidence in the PG group. Either pancreaticoduodenectomy or pylorus preserved pancreatic-odudenectomy was performed in majority of the study [14,16–19]. In the specific details, texture and duct diameter was comparable in all studies. Patients’ age and gender were also similar after pooling the results. Therefore the meta-analysis was conducted at the circumstance that patient, disease and procedure-related risk factors resembled, except the anastomotic technique. An inspiring result was arisen after data analysis, manifesting that pancreatic fistula and bile leakage incidence was minimized significantly.

Waugh and Claggett reported the first pancreaticogastrostomy anastomosis in 1946 [29], and it has gained favors in recent years. PG has several potential physiological advantages [18]. First, the PG anastomosis can be easier to perform, because the posterior wall of the stomach lies immediately anterior to the mobilized pancreatic remnant and is always wider than the transected pancreatic neck. Second, with PG, the pancreatic exocrine secretions enter the potentially acidic gastric environment, where the low pH prevents their activation. In contrast with PJ, the activation of pancreatic exocrine secretions in PG can theoretically occur more easily in the presence of intestinal enterokinase and a neutral pH. Third, the performance of PG reduces the number of anastomoses in a single loop of retained jejunum, thereby potentially decreasing the likelihood of loop kinking [18]. Fourthly, once anastomosis hemorrhage or leakage occurs, it is easy to perform gastroscopy treatment rather than reoperation. Just as it is, results of this study confirmed the physiological hypothesis and may provide a possible guidance for clinical practice.

However, some potential disadvantages of PG have been identified, including an increased incidence of delayed gastric emptying, pancreatic duct obstruction due to overgrowth by the gastric mucosa and remnant hemorrhage due to acid erosion [8].

The funnel plot (Fig. 4) indicated this meta-analysis is of none obvious publication bias. Between-study heterogeneity was significant for operative time and LOS. To confirm reliability of the pooled estimates, we performed a sensitivity analysis including only studies scored more than 2 points [13,14,16–19] and no changes occurred, manifesting the stability of the meta-analysis.

5. Limitations

Although the meta-analysis possibly provides the best methodology, it is usually limited by clinical heterogeneity. The lack of a uniform surgical approach, PF definition and other instrument application may hampered the data analysis and result in clinical heterogeneity fluctuation. For example, majority of the studies performed PD or PPPD; but two of them [13,15] individually adopt PD/PPPD only, one study adopt gastric partition surgery after PPPD, in another study [15], a pancreatic duct stent was placed across anastomoses. Moreover, the different definition of pancreatic fistula also may lead to observational bias. Therefore, one must make interpretations with caution.

6. Conclusions

Current evidence demonstrates that there was a trend to reduce the pancreatic fistula and bile leakage through pancreaticogastrostomy without compromising surgical safety and efficiency. However, future large-volume, well-designed RCTs with extensive follow-up are awaited to confirm and update the findings of the analysis.

Ethical approval

No.

Funding source

No.

Author contribution

The contribution of each author to the paper, e.g. study design, data collections, data analysis and writing.

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<tr>
<th>Concepts</th>
<th>Design</th>
<th>Definition of intellectual content</th>
<th>Literature search</th>
<th>Data acquisition</th>
<th>Data analysis</th>
<th>Statistical analysis</th>
<th>Manuscript preparation</th>
<th>Manuscript editing</th>
<th>Manuscript review</th>
<th>Guarantor</th>
</tr>
</thead>
</table>

Conflict of interest

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

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