

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2019 July 27; 11(7): 303-332



EDITORIAL

- 303 Optimizing neoadjuvant radiotherapy for resectable and borderline resectable pancreatic cancer using protons
Nichols RC, Rutenberg M

ORIGINAL ARTICLE**Retrospective Cohort Study**

- 308 Vascular calcification does not predict anastomotic leak or conduit necrosis following oesophagectomy
Jefferies BJ, Evans E, Bundred J, Hodson J, Whiting JL, Forde C, Griffiths EA

META-ANALYSIS

- 322 Pancreatogastrostomy vs pancreatojejunostomy after pancreaticoduodenectomy: An updated meta-analysis of RCTs and our experience
Jin Y, Feng YY, Qi XG, Hao G, Yu YQ, Li JT, Peng SY

ABOUT COVER

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The *WJGS* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Yan-Xia Xing*

Proofing Production Department Director: *Yun-Xiaojuan Wu*

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Varut Lohsirawat, Shu-You Peng

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

EDITORIAL OFFICE

Jin-Lei Wang, Director

PUBLICATION DATE

July 27, 2019

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<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

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Pancreatogastrostomy vs pancreatojejunostomy after pancreaticoduodenectomy: An updated meta-analysis of RCTs and our experience

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Supported by Training Project of Health High Level Talents in Zhejiang Province (2014).

Conflict-of-interest statement: We declare that we have no conflict of interest to this work.

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Abstract

BACKGROUND

Pancreatoduodenectomy (PD) is one of the most important operations in hepatobiliary and pancreatic surgery.

AIM

To evaluate the advantages and disadvantages of pancreatojejunostomy (PJ) and pancreatogastrostomy (PG).

METHODS

This meta-analysis was performed using Review Manager 5.3. All clinical randomized controlled trials, in which patients underwent PD with pancreatico-digestive tract reconstruction *via* PJ or PG, were included.

RESULTS

The search of PubMed, Wanfang Data, EMBASE, and the Cochrane Library provided 125 citations. After further analysis, 11 trials were included from nine countries. In all, 909 patients underwent PG and 856 underwent PJ. Meta-analysis showed that pancreatic fistula (PF) was a significantly lower morbidity in the PG group than in the PJ group (odds ratio [OR] = 0.67, 95% confidence interval [CI]: 0.53-0.86, $P = 0.002$); however, grades B and C PF was not significantly different between the two groups (OR = 0.61, 95%CI: 0.34-1.09, $P = 0.09$). Postoperative hemorrhage showed a significantly lower morbidity in the PJ group than in the PG group (OR = 1.47, 95%CI: 1.05-2.06, $P = 0.03$). Delayed gastric emptying was not significantly different between the two groups (OR = 1.09, 95%CI: 0.83-1.41, $P = 0.54$).

CONCLUSION

There is no difference in the incidence of grades B and C PF between the two

Manuscript source: Invited Manuscript

Received: April 16, 2019

Peer-review started: April 19, 2019

First decision: June 3, 2019

Revised: June 11, 2019

Accepted: June 20, 2019

Article in press: June 21, 2019

Published online: July 27, 2019

P-Reviewer: Aoki H, Bandyopadhyay SK, Uhlmann D

S-Editor: Cui LJ

L-Editor: Wang TQ

E-Editor: Wang J



groups. However, postoperative bleeding is significantly higher in PG than in PJ. Binding PJ or binding PG is a safe and secure technique according to our decades of experience.

Key words: Pancreaticojejunostomy; Pancreaticogastrostomy; Systematic review; Meta-analysis

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Core tip: Pancreatico-digestive tract anastomosis after pancreaticoduodenectomy is still controversial. This systematic review and meta-analysis aimed to further evaluate the role and importance of pancreaticojejunostomy and pancreaticogastrostomy. We compared the complications of these two surgical procedures, including pancreatic fistula, delayed gastric emptying, and hemorrhage.

Citation: Jin Y, Feng YY, Qi XG, Hao G, Yu YQ, Li JT, Peng SY. Pancreatogastrostomy vs pancreaticojejunostomy after pancreaticoduodenectomy: An updated meta-analysis of RCTs and our experience. *World J Gastrointest Surg* 2019; 11(7): 322-332

URL: <https://www.wjgnet.com/1948-9366/full/v11/i7/322.htm>

DOI: <https://dx.doi.org/10.4240/wjgs.v11.i7.322>

INTRODUCTION

Pancreatoduodenectomy (PD) is the main treatment procedure for benign and malignant tumors of the pancreatic head, lower common bile duct, and ampulla^[1]. The incidence of complications after PD is still high, with some large pancreatic centers reporting an incidence of approximately 10-45%^[2-7]. The incidence of pancreatic fistula (PF), delayed gastric emptying (DGE), and gastrointestinal or abdominal hemorrhage has been reported to be 3-45%^[8], 5%-61%^[9,10], and 1%-8%^[11], respectively. Other complications include abdominal empyema, incision infection, and pulmonary infection^[12].

Since the establishment of PD, pancreatico-digestive tract reconstruction has been a highly valued research area, which is considered to be closely related to the success/failure of the surgery^[13]. In general, pancreatico-digestive tract reconstruction includes pancreaticojejunostomy (PJ) and pancreaticogastrostomy (PG). Unlike gastrointestinal anastomosis, these two types of reconstruction after pancreatic surgery are diverse, with different results and evaluations. Therefore, there is still room for improvement in PJ and PG, and these procedures are still the focus of future research in PD.

This systematic review and meta-analysis aimed to further evaluate the role and importance of pancreatico-digestive tract anastomosis. Further, the advantages and disadvantages of PJ and PG were compared to provide a valuable reference for a more reasonable and safe choice of pancreatico-digestive tract reconstruction in the future.

MATERIALS AND METHODS

Eligibility criteria

All clinical randomized controlled trials, in which patients underwent PD with pancreatico-digestive tract reconstruction *via* PJ or PG, were included.

Information sources

Studies were identified by searching electronic databases and scanning reference lists of articles. No limits were applied for languages and foreign papers were translated to English. The search was applied to Medline, Wanfang Data, EMBASE, Science Citation Index Expanded, and the Cochrane Library. The last search was run on March 15, 2019.

Search

We used the following search terms to search all trial registers and databases: Pancreatoduodenectomy or Pancreatoduodenectomies or Duodenopancreatotomy or

Duodenopancreatectomies or Pancreaticoduodenectomy or Whipple or PD or Whipple procedure or Pancreatoduodenal resection or Pancreaticoduodenal resection, Pancreaticojejunostomy or Pancreaticojejunostomies or Pancreatojejunostomy or Pancreatojejunostomies or Pancreaticoenteric anastomosis or Pancreatoenteric anastomosis or Pancreaticojejunal anastomosis or Pancreatojejunal anastomosis or PJ, or Pancreaticogastrostomy or PG.

Study selection

Eligibility assessment was performed independently in an unblinded standardized manner by two reviewers. Disagreements between reviewers were resolved by discussion.

Data collection process

One review author extracted the following data from the included studies and the second author checked the extracted data. Disagreements were resolved by discussion between the two review authors; if no agreement could be reached, a third author would take the decision.

Data items

Data were extracted from each included trial on: (1) Characteristics of trial participants including age, disease, and number of patients; (2) Intervention with PG *vs* PJ; (3) Type of outcome measures including the definition and occurrence of PF, DGE, and other postoperative complications.

Risk of bias in individual studies

To ascertain the validity of eligible randomized trials, two independent reviewers with adequate reliability determined the adequacy of randomization, concealment of allocation, blinding of patients, healthcare providers, data collectors, and outcome assessors.

Statistical analysis

The meta-analysis was performed using Review Manager 5.3. The Chi-square test was used to test heterogeneity among studies. The heterogeneity level was judged according to I^2 . Relative risk (RR), weighted mean difference (WMD), standardized mean difference (SMD), and 95% CI (confidence interval) were used.

For data with clinical heterogeneity, it is not easy to merge effect quantities. First, we tested heterogeneity among studies. Then subgroup analysis or meta-regression analysis was conducted according to heterogeneity. If data were insufficient or heterogeneity cannot be found, a random-effects model was used. The homogeneity of data was tested by the χ^2 test, and the homogeneity was quantitatively analyzed by the I^2 test. If there was no statistical heterogeneity, a fixed-effects model was used. When statistical analysis showed heterogeneity, a random-effects model was used. The significance level of the hypothesis test was set at $P < 0.05$.

To assess the risk of bias across studies, we plotted the effect by the inverse of its standard error for each trial. The symmetry was assessed both visually, and formally by the Egger's test.

RESULTS

A total of 11 studies involving 11 trials were identified for inclusion in the review^[14-24]. The search of PubMed, Wanfang Data, Embase, and the Cochrane Library provided 125 citations. Of the total 125 citations, 29 studies were discarded because they did not meet the inclusion criteria. Nine additional studies were discarded because full texts for these were not available. The full texts of the remaining 65 citations were examined in further detail. Following this, 51 studies were found not to meet the inclusion criteria as described, and three were repeat studies from the same institute at different time points (we chose the latest study in this case). Finally, 11 studies met the inclusion criteria and were included in the systematic review. Figure 1 shows the flow diagram of study selection (Figure 1).

From 1995 to 2016, 11 trials were included from nine countries. In all, 909 patients underwent PG and 856 underwent PJ. PF was defined and classified following the International Study Group on Pancreatic Fistula (ISGPF) consensus guidelines in seven trials^[15,17-22] (Table 1). The quality of these 11 trials is presented in Figure 2.

PF data were available for all 11 trials randomizing 1765 patients and reporting data for them. In the meta-analysis, there was no significant heterogeneity between these studies ($I^2 = 20\%$); therefore, a fixed-effects model was applied. PF showed a significantly lower morbidity in the PG group than in the PJ group (odds ratio [OR] =

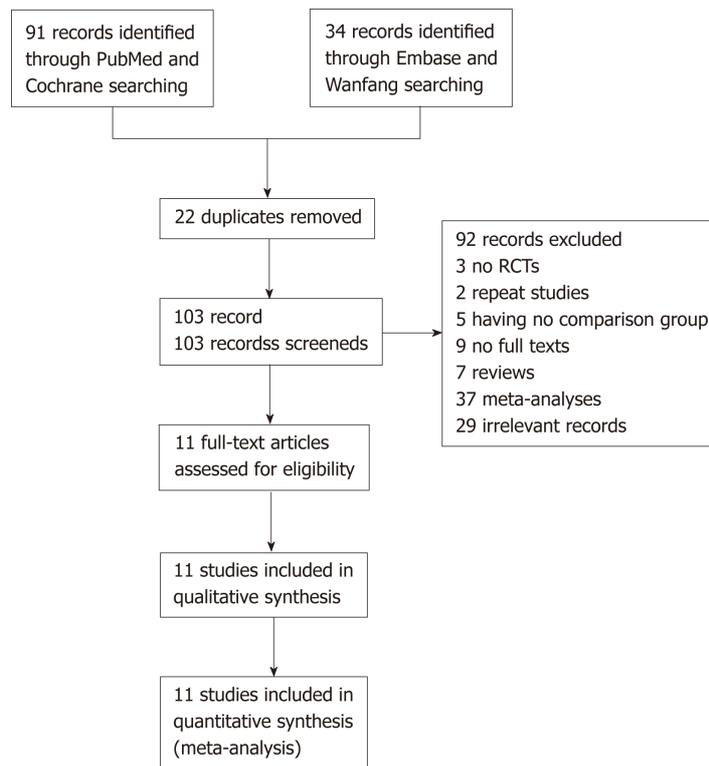


Figure 1 Study flow diagram.

0.67, 95%CI: 0.53-0.86, $P = 0.002$) (Figure 3). Grade A PF did not affect the disease outcome; therefore, we further analyzed the incidence of grades B and C PF. Seven trials with 603 PG and 581 PJ patients were included. In the meta-analysis, there was a significant difference in heterogeneity between these studies ($I^2 = 61\%$); accordingly, a random-effects model was applied. Grades B and C PF was not significantly different between the two groups (OR = 0.61, 95%CI: 0.34-1.09, $P = 0.09$) (Figure 4).

Nine trials with 788 PG and 734 PJ patients were included for analyzing postoperative hemorrhage. In the meta-analysis, there was no significant heterogeneity between these studies ($I^2 = 0\%$); accordingly, a fixed-effects model was applied. Postoperative hemorrhage showed a significantly lower morbidity in the PJ group than in the PG group (OR = 1.47, 95%CI: 1.05-2.06, $P = 0.03$) (Figure 5).

Nine trials including 780 PG and 738 PJ patients were included for the analysis of DGE. In the meta-analysis, there was no significant heterogeneity between these studies ($I^2 = 47\%$), and therefore a fixed-effects model was applied. DGE was not significantly different between the two groups (OR = 1.09, 95%CI: 0.83-1.41, $P = 0.54$) (Figure 6).

DISCUSSION

PF is one of the most common complications after PD. PF not only causes serious complications such as abdominal bleeding but also increases the length of hospital stay and cost for patients. Our study showed that PG anastomosis can reduce the incidence of all grades of PF than PJ anastomosis. In 2005, the ISGPF defined PF and divided it into three levels^[25]. In 2016, the group adjusted the classification of PF and defined grade A PF as a biochemical fistula^[6]. Therefore, in this study, we considered the incidence of grades B/C PF in subgroup analysis. We believe that this statistical analysis has more clinical value and significance. We found no statistical difference in grades B/C PF between the two groups (PJ and PG). However, our result showed that PG anastomosis may increase the incidence of bleeding compared with PJ anastomosis.

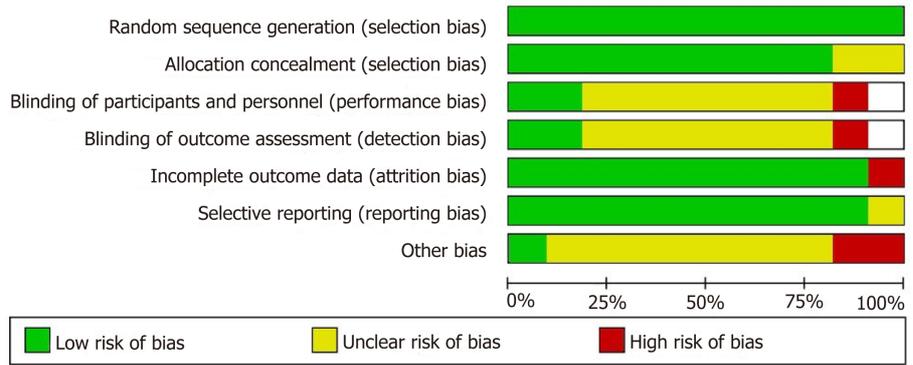
Our group has studied the anastomosis of the pancreas and digestive tract for more than 20 years, and has accumulated some experiences^[7,26,27]. In 1996, we established the binding pancreaticojejunostomy (BPJ). The main feature of this surgery is that the anastomosis between the jejunum and pancreas is mainly made with a binding line. It avoids the needle hole penetrating the intestinal cavity on the surface of the

Table 1 Characteristic of included trials

Author	Year	Country	Study type	Number of PG	Number of PJ	Definition of PF
Yeo <i>et al</i> ^[14]	1995	United States	Single blind, controlled randomized, single center trial	73	72	PF was defined as drainage of greater than 50 mL of amylase-rich fluid on or after postoperative day 10
Duffas <i>et al</i> ^[23]	2005	France	Single blind, controlled randomized, multicenter trial	81	68	Fluid obtained through drains or percutaneous aspiration, containing at least 4 times normal serum values of amylase for 3 day
Bassi <i>et al</i> ^[25]	2005	Italy	Single blind, controlled randomized, single center trial	69	82	Any clinically significant output of fluid, rich in amylase, confirmed by fistulography
Bassi <i>et al</i> ^[6]	2008	Spain	Single blind, controlled randomized, single center trial	53	55	ISGPF definition
Wellner <i>et al</i> ^[15]	2012	Germany	Single blind, controlled randomized, single center trial	59	57	ISGPF definition
Wang <i>et al</i> ^[30]	2012	China	Single blind, controlled randomized, multicenter trial	83	53	ISGPF definition
El Nakeeb <i>et al</i> ^[20]	2013	Egypt	Single blind, controlled randomized, single center trial	45	45	ISGPF definition
Topal <i>et al</i> ^[18]	2013	Belgium	Single blind, controlled randomized, multicenter trial	162	167	ISGPF definition
Figueras <i>et al</i> ^[22]	2013	Spain	Single blind, controlled randomized, multicenter trial	65	58	ISGPF definition
Grendar <i>et al</i> ^[24]	2015	Canada	Single blind, controlled randomized, single center trial	48	50	Either radiologically proven anastomotic leak or continued drainage (via drain, enterocutaneous fistula, or wound) of lipase-rich fluid on postoperative day 10
Keck <i>et al</i> ^[19]	2016	Germany	Single blind, controlled randomized, multicenter trial	171	149	ISGPF definition

PG: Pancreaticogastrostomy; PJ: Pancreaticojejunostomy; PF: Postoperative pancreatic fistula.

anastomotic site, thus preventing the leakage of pancreatic juice from the pinholes, to fundamentally eliminate the possibility of PF. At present, BPJ has been applied in more than a thousand of cases, which has a significant effect on the prevention of PF after surgery^[7]. In 2010, Buc, a French scholar, named BPJ procedure as Peng's PJ and reported that BPJ was a safe and secure technique^[28]. In 2008, Peng created the binding pancreaticogastrostomy (BPG), which simplified the operation steps of the previous pancreas-stomach anastomosis^[29]. After continuous improvement, only the bundled method was used in the posterior wall of the stomach, avoiding the suture of pancreas parenchyma and thus greatly shortening the surgical time and preventing anasto-



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bassi C 2015	+	+	?	?	+	+	?
Cheng 2012	+	?	?	?	+	+	?
Duffas JP 2005	+	+	+	+	+	+	?
EI Nakeeb A 2013	+	+	?	?	+	+	+
Fernandez-Cruz L 2008	+	+	?	?	+	+	?
Figueras J 2013	+	+	?	?	+	+	?
Grendar J 2015	+	+	+	+	+	+	+
Keck T 2016	+	+	+	+	+	+	?
Topal B 2013	+	+	?	?	+	+	+
Wellner UF 2012	+	+	?	?	+	+	?
Yeo CJ 1995	+	?	?	?	+	+	?

Figure 2 Quality of the included trials.

motric leakage. BPG not only solves the problem of excessive pancreatic stump but also reduces the harm of bile leakage because the biliary-enteric anastomosis is not in the same channel as PG anastomosis^[27]. The mid-term results of the randomized controlled study showed that the incidence of PF in BPG and BPJ was acceptable^[17].

In recent years, with the continuous development of laparoscopic technology, laparoscopic PD has gradually become an alternative method, used as a routine treatment in some pancreatic surgeries^[30-32]. Thus, laparoscopic pancreatico-gastrointestinal anastomosis has become a new focus for research. Owing to the limitation of the laparoscopic visual field, pancreatic duct to mucosa anastomosis is the first choice of procedure under laparoscopy^[30].

The attempt of various methods makes the technique of PJ dazzling. However, the basic content cannot be separated from pancreas-jejunum (stomach) anastomosis or pancreatic duct-jejunum (stomach) anastomosis. The objective of evaluation should be as simple as possible. Moreover, the lower the incidence of pancreatic leakage compared with classical anastomosis, the better. As long as these principles are followed, sample enlargement and randomized controlled trials should be conducted

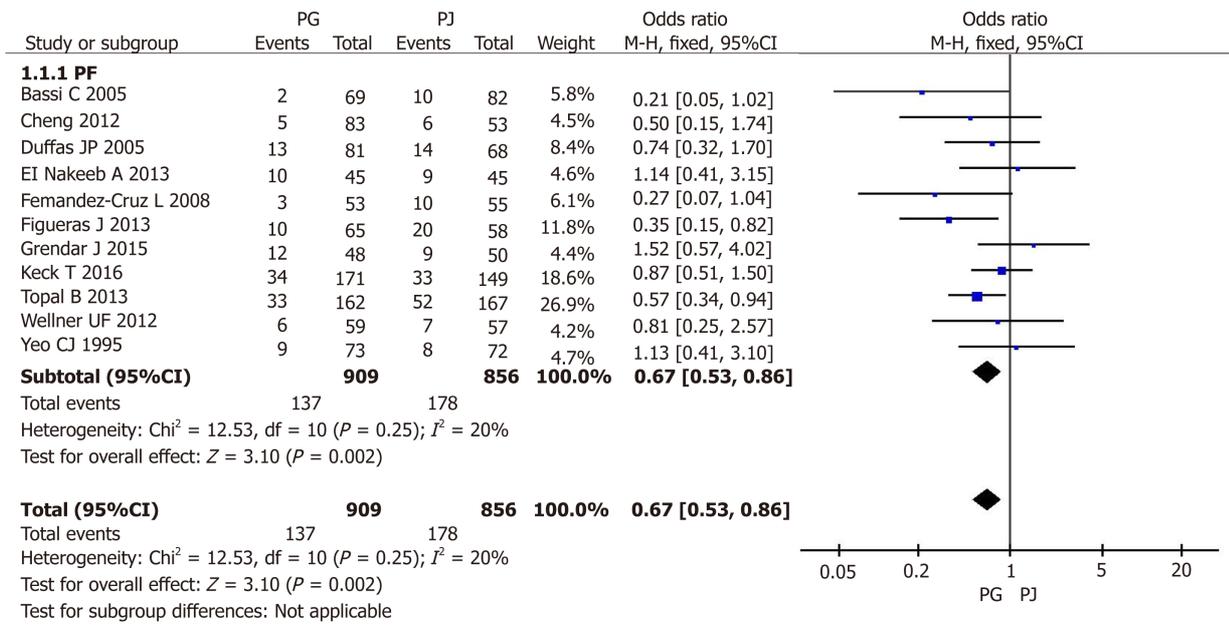


Figure 3 Forest plot of the incidence of all grades of postoperative pancreatic fistula. PG: Pancreaticogastrostomy; PJ: Pancreaticojejunostomy; PF: Postoperative pancreatic fistula.

to find the best method.

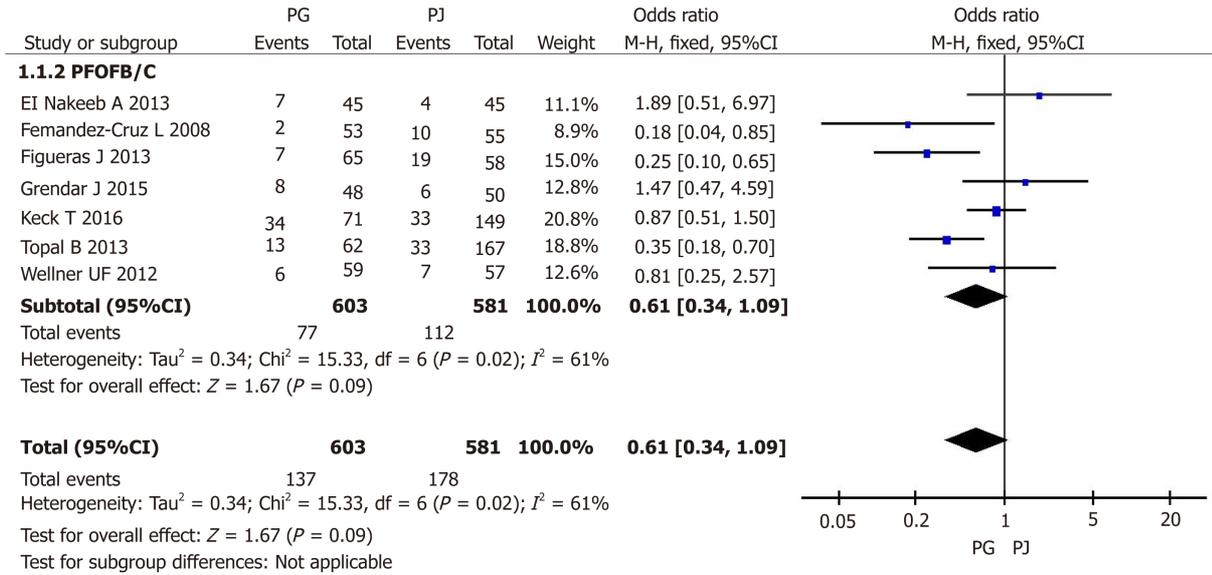


Figure 4 Forest plot of the incidence of grade B/C postoperative pancreatic fistula. PG: Pancreaticogastrostomy; PJ: Pancreaticojejunostomy; PF: Postoperative pancreatic fistula.

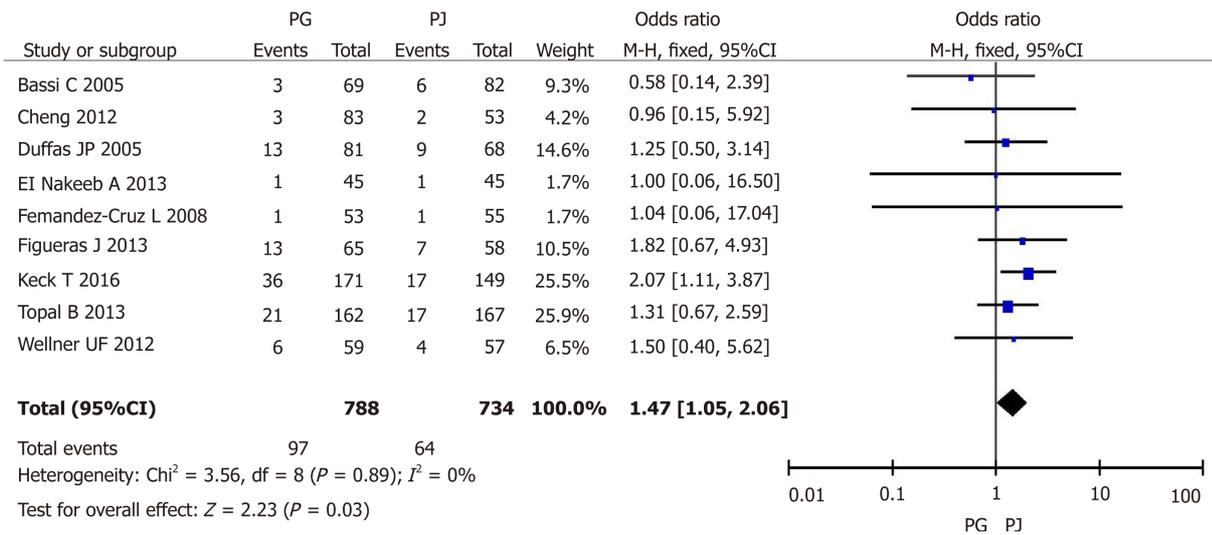


Figure 5 Forest plot of the incidence of postoperative hemorrhage. PG: Pancreaticogastrostomy; PJ: Pancreaticojejunostomy.

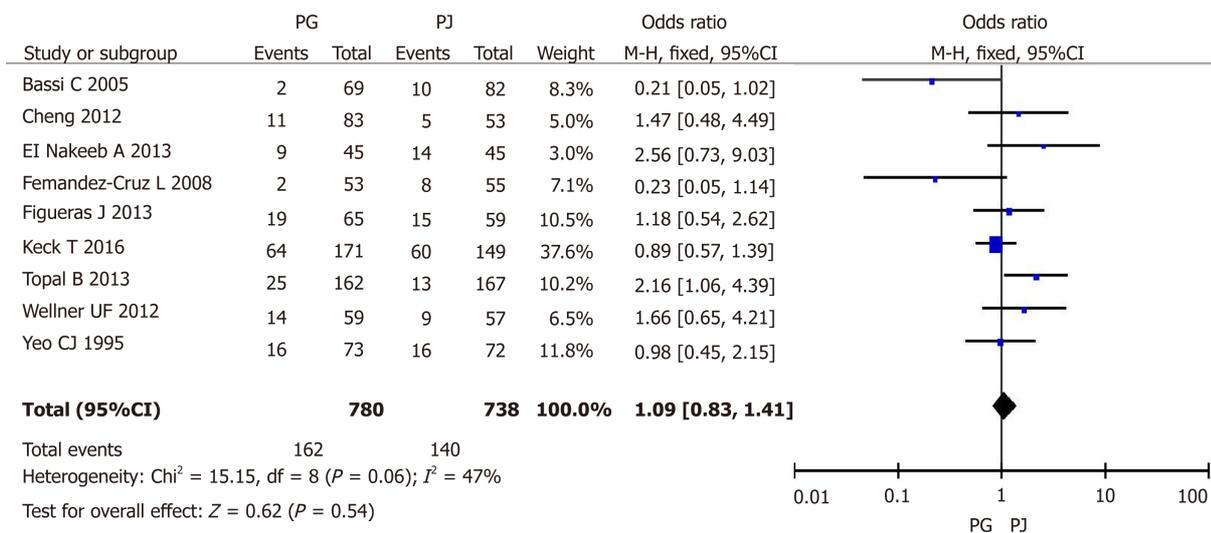


Figure 6 Forest plot of the incidence of delayed gastric emptying. PG: Pancreaticogastrostomy; PJ: Pancreaticojejunostomy; PF: Postoperative pancreatic fistula.

ARTICLE HIGHLIGHTS

Research background

Pancreatoduodenectomy (PD) is one of the most important operations in hepatobiliary and pancreatic surgery. Pancreatico-digestive tract reconstruction includes pancreaticojejunostomy (PJ) and pancreaticogastrostomy (PG). Unlike gastrointestinal anastomosis, these two types of reconstruction after pancreatic surgery are diverse, with different results and evaluations. Therefore, there is still room for improvement in PJ and PG, and these procedures are still the focus of future research in PD.

Research motivation and objectives

This systematic and meta-analysis aimed to evaluate the role and importance of pancreatico-digestive tract anastomosis. Advantages and disadvantages of PJ and PG were compared to provide a valuable reference and safe choice in the future.

Research methods

This search was applied to Medline, Wanfang Data, Embase, Science Citation Index Expanded, and the Cochrane Library. The last search was run on March 15, 2019. All clinical randomized controlled trials, in which patients underwent PD with pancreatico-digestive tract reconstruction via PJ or PG, were included. The Chi-square test was used to test heterogeneity among studies. The heterogeneity level was judged according to *I*². Relative risk (RR), weighted mean difference (WMD), standardized mean difference (SMD), and 95% CI were used.

Research results

In the meta-analysis of postoperative hemorrhage, there was no significant heterogeneity between these studies ($I^2 = 0\%$); accordingly, a fixed-effect model was applied. Postoperative hemorrhage showed a significantly lower morbidity in the PJ group than in the PG group (OR = 1.47, 95%CI: 1.05-2.06, $P = 0.03$). In the meta-analysis of DGE, there was no significant heterogeneity between these studies ($I^2 = 47\%$), and therefore a fixed-effects model was applied. DGE was not significantly different between the two groups (OR = 1.09, 95%CI: 0.83-1.41, $P = 0.54$).

Research conclusions

Our group has studied the anastomosis of the pancreas and digestive tract for more than 20 years, and has accumulated some experiences. We established the binding pancreaticojejunostomy (BPJ) and binding pancreaticogastrostomy (BPG). The mid-term results of the randomized controlled study showed that the incidence of PF in BPG and BPJ was acceptable.

Research perspectives

Laparoscopic pancreaticogastrointestinal anastomosis has become a new focus for research. The objective of evaluation should be as simple as possible. Moreover, the lower the incidence of pancreatic leakage compared with classical anastomosis, the better. As long as these principles are followed, sample enlargement and randomized controlled trials should be conducted to find the best method.

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