

Isolated Roux-en-Y versus single loop pancreaticojejunal reconstruction after pancreaticoduodenectomy – a systematic review and meta-analysis of randomised controlled trials

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Background: Pancreaticoduodenectomy is a complex intra-abdominal operation used for the treatment of benign and malignant disease of the pancreatic head or periampullary region. Despite developments in surgical techniques, pancreaticoduodenectomy is still associated with high rate of postoperative complications. We performed this systematic review and meta-analysis to compare the surgical outcomes of isolated Roux-en-Y pancreaticojejunostomy (IRYPJ), and conventional pancreaticojejunostomy (CPJ).

Methods: We performed a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement. We searched the following electronic databases – PubMed, Embase, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and Clinical-Trials.gov. Published trials comparing the efficacy and safety of IRYPJ and CPJ after pancreaticoduodenectomy were evaluated. The search terms were “pancreaticoduodenectomy,” “Whipple,” “pylorus-preserving pancreaticoduodenectomy,” “pancreaticojejunostomy,” “Roux-en-Y,” and “isolated Roux loop pancreaticojejunostomy.” Only randomised controlled trials comparing outcome of IRYPJ and CPJ after pancreaticoduodenectomy were included.

The analysed outcome measures were postoperative pancreatic fistula (POPF), clinically relevant POPF (CR-POPF), bile leak and delayed gastric emptying (DGE).

Results: The initial search yielded 342 results but only four randomised control trials fulfilled the inclusion criteria and were included for data synthesis and meta-analysis. Meta-analysis of POPF revealed that IRYPJ is associated with less POPF compared to CPJ but the difference was not statistically significant (risk ratio = 0.58, $p = 0.56$). A similar finding was also observed with CR-POPF (risk ratio = 0.17, $p = 0.87$) and DGE (risk ratio = 0.74, $p = 0.46$).

Conclusion: Isolated Roux-en-Y pancreaticojejunostomy is not associated with a superior outcome when compared to CPJ.

Keywords: pancreaticoduodenectomy, isolated Roux-en-Y pancreaticojejunostomy, conventional pancreaticojejunostomy, pancreatic fistula

Introduction

Pancreaticoduodenectomy (PD) is the surgical procedure of choice for the treatment of periampullary neoplasms (cancers of the ampulla, distal common bile duct, head of the pancreas, and periampullary duodenum).^{1,2} The initial perioperative mortality after PD was reported at around 25–39% in the 1970s. However, with advances in operative and anaesthetic techniques, establishment of high-volume centres, implementation of standardised pathway for recovery and a better understanding and management of common complications, the perioperative mortality has reduced significantly to less than 5% especially in high volume centres. Despite the reduction in perioperative

mortality, perioperative morbidity remains high with most centres reporting complication rates of 30–50%.³⁻⁵

Most of the causes of morbidity after PD are related to the pancreaticojejunal (PJ) reconstruction. The most severe complication related to the PJ reconstruction is a postoperative pancreatic fistula (POPF) because it is considered a potential cause of mortality. The definition of POPF has been modified over the years but in 2016, it was defined as “any measurable volume of drain from third postoperative day with amylase level > 3 times the upper limit of normal”.⁶⁻⁸

There has been a continuous effort to reduce the risk and incidence of POPF after PD.⁹⁻¹¹ One of the proposed ways of reducing the risk of POPF was construction of the PJ anastomosis to an isolated intestinal loop as opposed

to conventional pancreaticojejunostomy in which all anastomoses are performed using a single loop of jejunum. This was first proposed by Machado et al.¹² in 1976. The aim of this reconstruction was to separate the pancreatic secretions from biliary and gastrointestinal secretions which in turn inhibits activation of pancreatic secretions. Results reported from this techniques have been conflicting.¹³⁻¹⁵ There were previous meta-analyses performed in which the authors included all types of study designs ranging from case controlled studies, randomised controlled trials and prospective studies, all of which may result in heterogeneity and bias. We updated this meta-analysis and minimised heterogeneity by including only randomised controlled trials in our meta-analysis.

We performed this systematic review and meta-analysis of randomised controlled trials to compare the surgical outcomes of isolated Roux-en-Y pancreaticojejunostomy (IRYPJ), and conventional pancreaticojejunostomy (CPJ).

Methods

This systematic review was performed in compliance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline. We prospectively registered the protocol for this systematic review in the International Prospective Register of Systematic Reviews, PROSPERO (CRD42023428390).

Search strategy

Two independent reviewers searched the following electronic databases: PubMed, Embase, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and Clinical- Trials.gov. The search terms were “pancreaticoduodenectomy,” “Whipple,” “pylorus-preserving pancreaticoduodenectomy,” “pancreaticojejunostomy,” “randomised controlled trials”, “RCTs”, “Roux-en-Y,” and “isolated Roux loop pancreaticojejunostomy.” The search terms were combined with the use of Boolean logic. Related articles and reference list were searched to completeness of the search. Conflict was resolved by involving a third researcher.

Study selection criteria

The inclusion criteria for a study to be included for the review were as follows – (i) studies published from 1990 to date, (ii) randomised controlled trials that compared the outcome of IRYPJ and CPJ after pancreaticoduodenectomy, and (iii) studies with full texts. Exclusion criteria were as follows – (i) conference presentations, editorials and commentaries, (ii) the absence of relevant data for comparison, and (iii) total study populations of less than 10.

Quality assessment and risk of bias assessment

The Jadad score which was developed by Jadad et al.¹⁶ was used to assess the quality and bias of the included RCTs. The score ranges from 0–5. A score of 3 and above was considered a good quality study.

Data extraction

Data extraction was performed by 2 independent researchers. The following information was extracted from each study – first author, year of manuscript publication, study design, number of patients in each group, gender of patients per group, mean age, indication for PD, texture of the pancreas, size of the pancreatic duct, method of reconstruction and outcome data. In the case of conflict between the two researchers, a third researcher was involved to resolve the conflict.

Outcome

The primary outcome of interest was the pancreatic fistula rate after PD. POPF was defined based on the 2005 definition of the International Study Group of Pancreatic Fistula (ISGPF).⁶ The secondary outcome of interest included clinically relevant pancreatic fistula, bile leak and delayed gastric emptying. Postoperative bile leak was defined according to the International Study Group of Liver Surgery (ISGLS) definition.¹⁷ Delayed gastric emptying was defined according to the International Study Group of Pancreatic Surgery (ISGPS) definition.¹⁸

Statistical analysis

Statistical analyses were done using RevMan software (version 5.4.1). If the variable was dichotomous, the pooled risk ratio (RR) was calculated with 95 per cent confidence interval. However, if the variable was continuous, the weighted mean difference (WMD) or standardised mean difference (SMD) with 95 per cent CI was calculated. Fixed-effects model was used to calculate the pooled effect sizes if the data were not significantly heterogeneous. Heterogeneity was assessed using the I² statistics. I² > 50% was considered as a statistically significant heterogeneity.

Results

Results were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

Study selection process and description of selected studies

We identified 342 references during the initial search. Out of these, 297 articles were excluded because of duplicate publications (Figure 1). The 45 remaining references were

Table I: Characteristics of included studies

S/N	Author	Year of publication	Sample size per group	Jadad score	Quality of the study
			IRYPJ*	CPJ [†]	
1	Ke et al.	2013	107	109	3 Good quality
2	Tani et al.	2014	75	76	3 Good quality
3	Elnakeeb et al.	2014	45	45	4 Good quality
4	Fawzy et al.	2022	26	26	3 Good quality

*IRYPJ – Isolated Roux-en-Y pancreaticojejunostomy, †CPJ – Conventional pancreaticojejunostomy

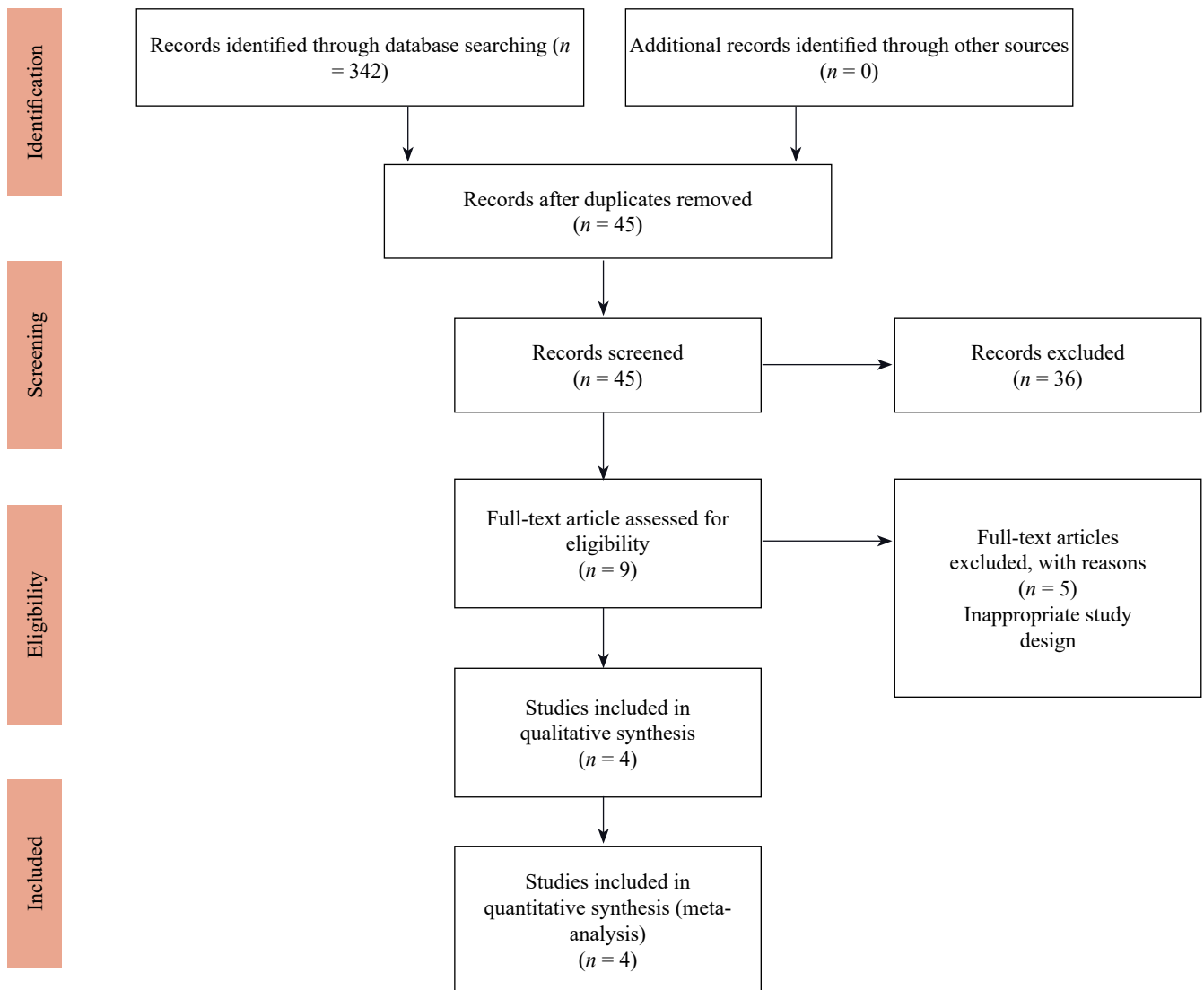


Figure 1: Studies selection process

further assessed in terms of title and abstracts. Thirty-six references were excluded for lack of relevant data. Nine full text articles were retrieved but 5 articles were excluded for inappropriate study design (the studies were all observational studies). Four studies were included for the data synthesis and meta-analysis. The studies included were all randomised control trials (RCTs). Details of selected studies are displayed in Table I.

The two groups did not show any statistical significance in age distribution (SMD = 0.33, 95% CI: -0.23–0.16), $p = 0.74$ and gender distribution (RR = 0.40, 95% CI: 0.87–1.22, $p = 0.69$).

Baseline pancreatic texture and duct diameter

Meta-analysis comparing the texture of the pancreas and the diameter of the pancreatic duct at the time of surgery was performed and revealed that there was no difference between the two groups with p -values of 0.24 and 1.00 respectively.

Primary outcome

The primary outcome considered was the occurrence of POPF after PD. All the four RCTs^{14,15,19,20} included in the study compared the incidence of POPF in the 2 groups. Our meta-analysis revealed that there was no difference between

patients that IRYPJ and CPJ regarding postoperative pancreatic fistula with risk ratio of 0.58, 95% CI: 0.66–1.25 and a p -value of 0.56. There was no heterogeneity among the studies with $I^2 = 0\%$ (Figure 2A).

Two of the RCTs^{15,19} compared the incidence of clinically relevant POPF (CR-POPF) between the two set of patients and meta-analysis of these studies revealed no difference in CRPOPF between the 2 groups with a p -value of 0.87, a risk ratio of 0.17 and 95% CI of 0.49–1.83. (Figure 2B).

Secondary outcome

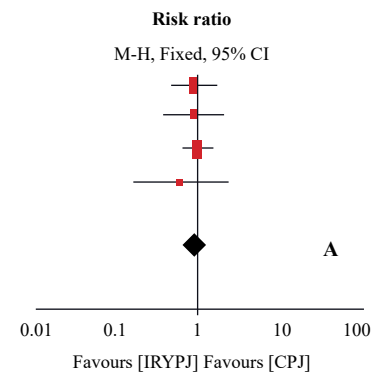
Postoperative bile leak

All the included RCTs^{14,15,19,20} compared the incidence of postoperative bile leak between patients that had IRYPJ and those that had CPJ. We found that there was no statistically significant difference between the 2 groups with RR of 1.39, 95% CI: 0.28–1.24 and a p -value of 0.17. There was no heterogeneity among the studies with $I^2 = 0\%$ (Figure 3).

Delayed gastric emptying

All the included RCTs^{14,15,19,20} compared the incidence of postoperative delayed gastric emptying between patients who had IRYPJ and those who had CPJ. We found that

Study or subgroup	IRYPJ		CPJ		Weight	Risk ratio		Year
	Events	Total	Events	Total		M-H, Fixed, 95% CI		
Ke 2013	17	107	19	109	31.6%	0.19	[0.50, 1.66]	2013
El Nakeeb 2014	9	45	10	45	16.8%	0.90	[0.40, 2.00]	2014
Tani 2014	25	75	26	76	43.3%	0.97	[0.62, 1.52]	2014
Fauzy 2022	3	26	5	26	8.4%	0.60	[0.16, 2.26]	2023
Total (95% CI)	253		256		100.0%	0.91	[0.66, 1.25]	
Total events	54	60						
Heterogeneity: Chi ² = 0.47, df = 3 (P = 0.93); I ² = 0%								
Test for overall effect Z = 0.58 (P = 0.56)								



Study or subgroup	IRYPJ		CPJ		Weight	Risk ratio		Year
	Events	Total	Events	Total		M-H, Fixed, 95% CI		
El Nakeeb 2014	4	45	7	45	43.9%	0.57	[0.18, 1.82]	2014
Tani 2014	11	75	9	76	56.1%	1.24	[0.54, 2.82]	2014
Total (95% CI)	120		121		100.0%	0.95	[0.49, 1.83]	
Total events	54	60						
Heterogeneity: Chi ² = 1.14, df = 1 (P = 0.29); I ² = 13%								
Test for overall effect Z = 0.17 (P = 0.87)								

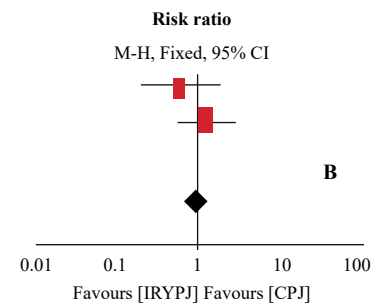


Figure 2: A – Meta-analysis comparing POPF after PD, B – Meta-analysis of CR-POPF after PD

Study or subgroup	IRYPJ		CPJ		Weight	Risk ratio		Year
	Events	Total	Events	Total		M-H, Fixed, 95% CI		
Ke 2013	2	107	3	109	17.5%	0.68	[0.12, 3.98]	2013
El Nakeeb 2014	4	45	6	45	35.4%	0.67	[0.20, 2.20]	2014
Tani 2014	1	75	2	76	11.7%	0.51	[0.05, 5.47]	2014
Fauzy 2022	3	26	6	26	35.4%	0.50	[0.14, 1.79]	2023
Total (95% CI)	253		256		100.0%	0.59	[0.28, 1.24]	
Total events	54	60						
Heterogeneity: Chi ² = 0.14, df = 3 (P = 0.99); I ² = 0%								
Test for overall effect Z = 1.39 (P = 0.17)								

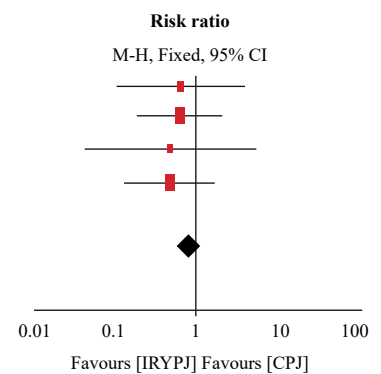


Figure 3: Meta-analysis comparing postoperative bile leak after PD

Study or subgroup	IRYPJ		CPJ		Weight	Risk ratio		Year
	Events	Total	Events	Total		M-H, Fixed, 95% CI		
Ke 2013	25	107	27	109	53.8%	0.94	[0.59, 1.52]	2013
Tani 2014	11	75	9	76	18.0%	1.24	[0.54, 2.82]	2014
El Nakeeb 2014	4	45	9	45	18.1%	0.44	[0.15, 1.34]	2014
Fauzy 2022	3	26	5	26	0.60%	0.60	[0.16, 2.26]	2023
Total (95% CI)	253		256		100.0%	0.87	[0.60, 1.26]	
Total events	54	60						
Heterogeneity: Chi ² = 2.55, df = 3 (P = 0.47); I ² = 0%								
Test for overall effect Z = 0.74 (P = 0.46)								

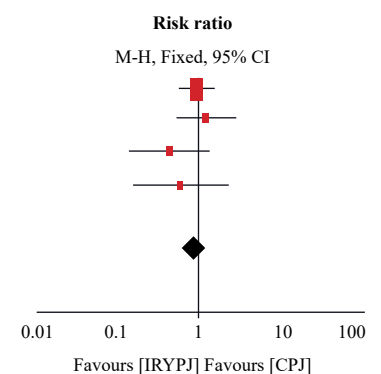


Figure 4: Meta-analysis comparing DGE bile leak after PD

Table II: Risk of bias summary

	Ke et al.	Fawzy et al.	El Nakeeb et al.	Tani et al.
Random sequence generation (selection bias)	Low Risk	Low Risk	Low Risk	Low Risk
Allocation concealment (selection bias)	Low Risk	Low Risk	Low Risk	Low Risk
Blinding of participants and personnel (performance bias)	Low Risk	Low Risk	Low Risk	Low Risk
Blinding of outcome assessment (detection bias)	Low Risk	Low Risk	Low Risk	Low Risk
Incomplete outcome data (attrition bias)	Low Risk	Low Risk	Low Risk	Low Risk
Selective reporting (reporting bias)	Low Risk	Low Risk	Low Risk	Low Risk
Other bias	Low Risk	Low Risk	Low Risk	Low Risk

there was no statistically significant difference between the 2 groups with RR of 0.74, 95% CI: 0.60–1.26 and a *p*-value of 0.46. There was no heterogeneity among the studies with $I^2 = 0\%$ (Figure 4).

Discussion

With advances in surgical and anaesthetic techniques, the postoperative mortality associated with PD has reduced significantly with reports from high-volume hospitals reporting mortality rate below 5%. This reduction has not been reflected in the postoperative morbidity which remains high and is currently reported at about 25–60%.^{5,21}

One of the most serious complications after PD is a POPF.^{5,21,22} The definition and diagnostic criteria of POPF have undergone modification over the last few years. In 2005, the ISGPF defined POPF as “an abnormal communication between the pancreatic ductal epithelium and another epithelial surface containing pancreas-derived, enzyme-rich fluid”. The diagnostic criterium was when the amylase content of the drain effluent was greater than 3 times the upper normal serum value starting from the third postoperative day. POPF was graded into 3 as part of the 2005 consensus.⁶⁻⁸ Grade A POPF indicates drainage of amylase rich fluid with no clinical complication and requires no treatment. In grade B fistulae, in addition to the drainage of fluid, there is the need for specific treatments to promote the healing of the fistula. Such treatment included parental nutrition, enteral nutrition and antibiotics therapy. The last grade of POPF is grade C fistula and it required invasive procedures including surgical reoperation as part of the management strategy. In 2016, the diagnostic criteria were reviewed and currently the amylase content of the drain alone is not enough to diagnose POPF if there is no impairment of clinical condition of the patient. Therefore grade A POPF has been replaced with the term ‘asymptomatic pancreatic leak called “biochemical leak” (BL)’.⁶⁻⁸

In this meta-analysis, all the included studies used the 2005 definition of POPF as their end points and we found that there was no statistically significant difference in POPF between patients who had conventional pancreaticojejunostomy and those who had isolated Roux-en-Y pancreaticojejunostomy. We did an additional analysis comparing only those with clinically relevant POPF and there was no difference between the two groups. This is similar to the meta-analysis of Mobarak et al.²³ and Lyu et al.²⁴ Their meta-analysis included RCTs, retrospective studies and prospective studies unlike ours that included only RCTs but the findings seem to be consistent.

DGE is also a frequent complication following PD, affecting 15–30% of patients postoperatively and has been associated with increased hospital stay and impaired quality

of life.²⁵⁻²⁷ The pathogenesis of DGE is not clear and multiple pathways have been implicated. These pathways include denervation of the antropyloric region, pyloric and antral ischaemia, and decreased levels of motilin.²⁵⁻²⁷ In our meta-analysis, we observed that DGE is not statistically different between the 2 types of reconstruction. This is similar to the findings from meta-analysis conducted by Mobarak et al.²³ and Lyu et al.²⁴

The ISGLS defined bile leakage as a measured bilirubin level in drain fluid about 3 times the bilirubin levels in form the third postoperative day. Bile leak can be classified as 3 grades depending on the severity.^{17,28-30} Grade A leaks are not associated with any changes in clinical condition of the patients. With grade B leaks, there may be need for additional radiological and pharmacological intervention while grade C leaks require surgical intervention.²⁸⁻³⁰ In our meta-analysis, we observed that postoperative bile leaks were not statistically different between the 2 types of reconstruction. This is similar to the findings from meta-analysis conducted by Mobarak et al.²³ and Lyu et al.²⁴

Conclusion

IRYPJ is not associated with a superior outcome when compared CPJ. The type of pancreaticojejunal reconstruction has no effect on POPF, DGE and bile leak after PD.

Conflict of interest


The authors declare no conflict of interest.


Funding source


We received no funding for this study.

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