REVIEW ARTICLE

The impact of pancreaticojejunostomy versus pancreaticogastrostomy reconstruction on pancreatic fistula after pancreaticoduodenectomy: meta-analysis of randomized controlled trials

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Abstract

Background: Pancreatic fistula (PF) remains a common source of morbidity following pancreaticoduodenectomy (PD). Despite numerous studies, the optimal method of pancreatic remnant reconstruction is controversial. This study examines the hypothesis that pancreaticogastrostomy (PG) is associated with a lower risk for PF after PD compared with pancreaticojejunostomy (PJ).

Methods: Five electronic databases and the grey literature were searched for randomized controlled trials (RCTs) comparing PJ and PG after PD. Two reviewers independently selected studies, extracted data and assessed methodology. The primary outcome was the occurrence of PF of International Study Group on Pancreatic Fistula (ISGPF) Grade B or C.

Results: Four RCTs including 676 patients were included. Pancreaticogastrostomy reduced the risk for PF [relative risk (RR) 0.41, 95% confidence interval (CI) 0.21–0.62] without any difference between high- and low-risk patients. Absolute risk reduction for PF was 4% (95% CI 2.4–5.6) in low-risk patients compared with 10% (95% CI 6.5–14.8) in high-risk patients undergoing PG rather than PJ. The strength of evidence for PF outcome was moderate according to the GRADE classification.

Conclusions: Reconstruction by PG decreases the rate of PF in comparison with PJ. Surgeons should consider reconstructing the pancreatic remnant following PD with PG, particularly in patients at high risk for PF.

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Introduction

Advances in pancreatic surgery techniques and perioperative care have led to reduced mortality rates for pancreaticoduodenectomy (PD) in high-volume expert centres.[1,2] However, morbidity after pancreatic resection remains high, with 30–60% of patients

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experiencing complications following surgery, mainly as a result of leak and subsequent fistula from the pancreatic anastomosis.[2,3]

Pancreatic reconstruction is particularly demanding; a variety of methods and techniques have been proposed to maintain the continuity of the anastomosis and diminish rates of leak.[4–7] The abundance of literature on this issue reflects the ongoing controversy regarding the optimal method of pancreatic anastomosis. The conventional anastomosis described for this operation is pancreaticojejunostomy (PJ).[8] Pancreaticogastrostomy (PG) has

been described and studied as an alternative to jejunal anastomosis in both observational studies and randomized controlled trials (RCTs) with inconsistent results.[9–11]

Given the ongoing frequency of pancreatic leak or fistula and the major morbidity associated with this complication, robust evidence is needed to determine which reconstruction technique yields better outcomes. Five systematic reviews and meta-analyses have attempted to summarize the impact of PG compared with PJ on the occurrence of pancreatic fistula (PF); however, most included small numbers of RCTs among large numbers of observational studies, suffered from important methodological limitations, lacked a consensus definition of PF and sensitivity analyses, and failed to identify a significant benefit of either technique.[10,12–14] More recently, two larger RCTs examining this important question have been published.[9,15] The present systematic review and meta-analysis of RCTs was undertaken to examine the impact of PG compared with that of PJ on PF in patients undergoing PD, and to address methodological issues arising from previous meta-analyses.

Materials and methods

This review was registered in PROSPERO (2013: CRD42013005288).[16]

Search strategy

MEDLINE (1966 to August 2013), EMBASE (1974 to August 2013), the Cochrane Central Register for Controlled Trials, Web of Knowledge, and the Scopus database (1966 to August 2013) were systematically searched, with the help of an information specialist, to identify potential RCTs, without language or other limitations. The following search terms were used: (i) pancreatic dis$, pancreatic neo$, pancreas cancer, chronic pancreatitis, and (ii) pancreatectomy, pancreatic resection, pancreaticojej$, pancreaticogas$, pancreas reconstruction, and pancreas anast$. A standardized filter was applied for RCTs. The grey literature (informally published material not indexed in formal search engines) was searched for unpublished results using the OpenSIGLE database, Trip database, Google Scholar, and the database of registered trials (http://www.clinicaltrials.gov). Bibliographies of all included studies and previous narrative or systematic reviews were also reviewed for relevant publications.

Two authors (FSWZ and RGD) independently selected studies, extracted data and assessed the risk for bias. Disagreements were resolved by consensus or by a third party (JH). A single reviewer (JH) assessed the references from the grey literature.

Study selection

Explicit eligibility criteria allowed the inclusion of RCTs reporting the effects on PF of PG compared with PJ PD. Studies including at least 10 adults (aged ≥18 years) submitted to PD for benign or malignant disease, and defining PF according to the International Study Group on Pancreatic Fistula (ISGPF) definitions were eligible.[17] Studies that examined PD for trauma or acute pancreatitis were excluded. Studies that included patients who did not meet the present inclusion criteria were excluded if it was not possible to distinguish those patients from the larger population. In the event of duplicate publications, the most relevant and most informative study was included.

Data abstraction

A standardized data extraction form was developed and pilot-tested following the recommendations of the Cochrane Effective Practice and Organization of Care Review Group.[18] The following patient characteristics were collected: age; gender, and indication for surgery. The corresponding author for each study was contacted to obtain additional details about missing or incomplete data when this was deemed necessary. Pancreas-associated risk was categorized based on baseline risk for PF when possible, as reported by the authors in the original manuscript as: (i) high risk for PF (soft gland or small pancreatic duct), or (ii) low risk for PF (hard gland or large pancreatic duct).

Outcome measures

The primary outcome was the occurrence of clinically significant PF defined as Grade B or C fistula based on the ISGPF classification.[17] Secondary outcomes included operating time (min), estimated blood loss (ml), bile leak, delayed gastric emptying (DGE), postoperative bleeding (divided into intraluminal and extraluminal bleeding), 30-day postoperative major morbidity (Clavien–Dindo Grades III and IV) and mortality, and length of stay (LoS) (days).[19–21]

Risk for bias assessment

The methodological quality of included studies was evaluated using a checklist of key methodological components derived from the CONSORT (*con*solidated *s*tandards *o*f *r*eporting *t*rials) statement rather than by using a summary score.[22–25] The GRADE (*g*rading of *r*ecommendations *a*ssessment, *d*evelopment and *e*valuation) system was used to present a summary of findings and rate the overall strength of evidence.[26] The robustness of included RCTs that reported a significant difference in PF favouring PG was assessed by computing the Fragility Index (FI). This index assesses the minimum number of patients that are required to switch from non-event (no PF) to event (PF) in the group with fewer events (PG) in order to reverse statistical significance.[27] Thus, it evaluates how many patients in the PG group would have needed to experience a PF for the difference between PG and PJ to become non-significant.

Statistical analysis

Descriptive statistics were presented as means and standard deviations (SDs) for continuous variables, and as proportions with 95% confidence intervals (95% CIs) for dichotomous variables. When studies presented medians and ranges, the mean and SD were estimated using the method of Hozo *et al.*[28] Meta-analysis was

conducted using Review Manager (RevMan) Version 5.2.5 (Cochrane Collaboration, Copenhagen, Denmark) for each outcome with data in two or more studies. The data were pooled for each outcome using random-effects models. The relative risk (RR) with 95% CI was calculated for dichotomous outcomes. Absolute risk reduction (ARR) in PF with PG was computed using the pooled RR for risk reduction and PF rate with PJ for baseline risk. The standard mean difference (95% CI) was used for continuous variables.[18] The I^2 statistic was used to assess the extent of heterogeneity.[29] The following *a priori* hypotheses were generated to explain heterogeneity in results: (i) study design (single-centre versus multicentre studies); (ii) population (high- versus low-risk pancreas, and malignant versus benign indications for surgery); (iii) intervention (duct-to-mucosa PJ versus a 'fish-mouth' PJ technique), and (iv) intervention (pancreatic stent versus no stent). Publication bias was assessed visually by creating a funnel plot for each outcome for which data were available from five or more trials.[18]

The review was conducted and results reported in accordance with the PRISMA (*preferred reporting items for systematic reviews and meta-analyses*) statement.[30]

Results

Systematic search

Four RCTs enrolling a total of 676 patients were included (Fig. 1).[9,15,31,32]

Searches of the grey literature and of the references of included studies did not identify additional citations. One additional reference was identified after the initial electronic search in the table of contents of a surgical journal, and included in the analysis.[15]

Description of included studies

All studies were published in English between 2008 and 2013 and included between 108 and 329 patients (Table 1). Study techniques and postoperative management protocols are presented in Table 2.

Key methodological elements are summarized in Table 3. The FIs of the studies reporting a significant benefit were 2 ($n = 108$),[31] 6 ($n = 329$),[9] and 5 ($n = 123$).[15]

Primary outcome: pancreatic fistula

Rates of PF varied from 18% ($n = 10/55$) to 33% ($n = 19/58$) in the PJ control groups, and from 11% ($n = 12/108$) to 21% ($n = 26/123$) in entire cohorts. Patients undergoing PG had a significantly lower risk for PF than patients who underwent PJ (RR 0.41, 95% CI 0.27–0.62) (Fig. 2). The funnel plot did not show convincing asymmetry. The strength of evidence supporting risk reduction in PF with PG was moderate (Table 4).

In studies that did not report the use of pancreatic stents, the summary estimate was similar (RR 0.46, 95% CI 0.12–1.79) but non-significant and was associated with greater heterogeneity ($I^2 = 58\%$). Finally, an analysis of only multicentre trials revealed a significant reduction in PF with PG (RR 0.38, 95% CI 0.23–0.61;
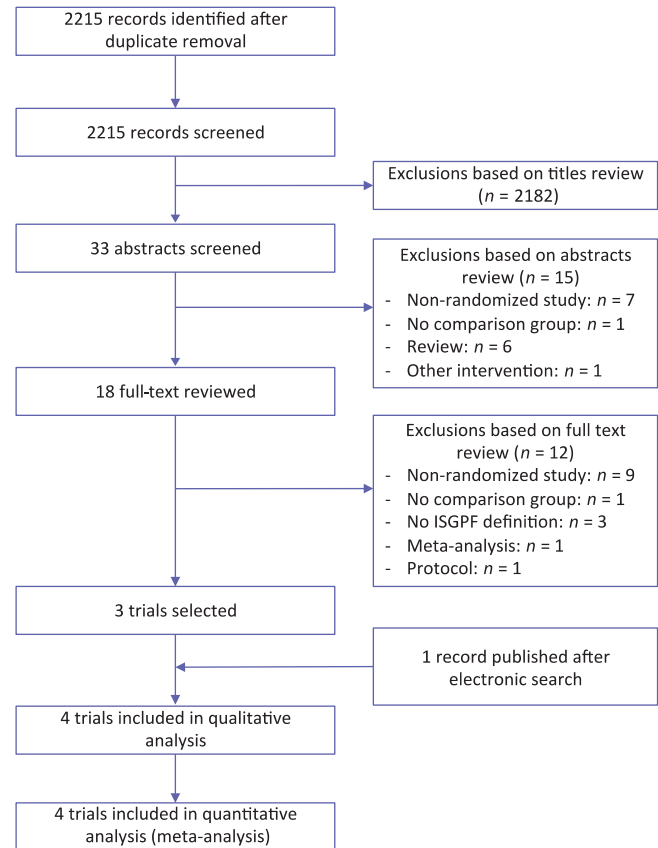

Figure 1 Study selection conducted in line with PRISMA (*preferred reporting items for systematic reviews and meta-analyses*) guidelines

$I^2 = 0\%$), compared with a non-significant result for single-centre trials (RR 0.46, 95% CI 0.12–1.76; $I^2 = 56\%$).

Secondary outcomes

One study used a consensus definition for DGE and one used Clavien–Dindo classifications to report morbidity. No significant difference was observed in secondary outcomes between PG and PJ (Figs 3 and 4). None of the funnel plots for secondary outcomes showed convincing asymmetry. The quality of evidence was low for all secondary outcomes (Table 4).

Discussion

This study systematically reviewed and pooled data from four RCTs investigating the impacts of PG compared with PJ on PF. Based on evidence of moderate quality, PG is associated with a lower occurrence of PF (RR 0.41, 95% CI 0.27–0.62), but no significant differences emerged in biliary leak, DGE, postoperative bleeding, major morbidity, mortality or LoS. When only high- or low-risk pancreas groups were considered, there was no difference in RR. However, when baseline risks for PF were

Table 1 Populations and clinical characteristics of the included studies

Study	Study period	Population characteristics			High-risk pancreas *n* (%)
		Sample, *n*	Pancreatic cancer *n* (%)	Age, years old, mean (SE or range)	
Fernández-Cruz et al.[31] **2008** Spain	2005–2007	108	PG: 26 (49%) PJ: 28 (51%)	PG: 63 (13) PJ: 63 (14)	PG: 24 (45%) PJ: 25 (45%)
Wellner et al.[32] **2012** Germany	2006–2011	116	PG: 26 (44%) PJ: 30 (53%)	PG: 67 (34–84) PJ: 64 (23–81)	PG: 35 (59%) PJ: 29 (51%)
Topal et al.[9] **2013** Belgium	2009–2012	329	PG: 98 (61%) PJ: 107 (64%)	PG: 67 (61–73) PJ: 66 (59–75)	PG: 98 (60%) PJ: 102 (61%)
Figueras et al.[15] **2013** Spain	2008–2012	123	PG: 55 (85%) PJ: 49 (84%)	PG: 67 (35–80) PJ: 66 (42–80)	PG: 34 (52%) PJ: 33 (57%)

PG, pancreatogastrostomy; PJ, pancreatojejunostomy; SE, standard error.

Table 2 Surgical management in the included studies

Study	Surgical technique					Postoperative management	
	Surgeons, *n*	PJ technique	PG technique	Pylorus-preserving *n* (%)	Use of stent	Use of drain	Prophylactic octreotide
Fernández-Cruz et al.[31] **2008**	NR	2 layers Duct-to-mucosa End-to-side	2 layers Duct-to-mucosa To bottom of gastric partition	PG: 53 (100%) PJ: 55 (100%)	Yes, internal	Yes	No
Wellner et al.[32] **2012**	3	2 layers Duct-to-mucosa	2 layers Dunking To posterior gastric wall	PG: 52 (88%) PJ: 55 (96%)	Yes, external (only for PJ)	Yes	Yes, selective[a]
Topal et al.[9] **2013**	NR	Layers based on surgeon decision Dunking End-to-side	Layers based on surgeon decision Dunking To posterior gastric wall	PG: 98 (60%) PJ: 102 (61%)	No	Yes	Yes, all
Figueras et al.[15] **2013**	3	2 layers Duct-to-mucosa	2 layers Dunking To posterior gastric wall	PG: 30 (46%) PJ: 28 (48%)	NR	Yes	No

[a]Information from referenced publication.[33]
PG, pancreatogastrostomy; PJ, pancreatojejunostomy; NR, not reported.

considered, ARR was greater in patients with a high-risk pancreas (10%) compared with those with a low-risk pancreas (4%), which indicates that PG offers more critical benefits in high-risk patients.

The proposed technical and physiological advantages of PG over PJ have been discussed in several studies reporting the technique.[34–38] The anastomosis may be facilitated by a thick gastric wall, can rely on an excellent gastric blood supply, and is subject to less tension as a result of the anatomic proximity of the pancreatic remnant to the posterior gastric wall. Lack of enterokinase in the gastric remnant may prevent the activation of pancreatic enzymes, thereby avoiding both damage to the anasto-

mosis itself and the repercussions associated with potential PF. A nasogastric tube may be used to decompress the stomach and relieve tension on the anastomosis immediately after surgery, and can eventually be reinserted to deal with ileus or manage a leak without percutaneous intervention. Finally, PG can be accessed endoscopically for instrumentation if needed, and is located away from major vessels skeletonized during resection, which may theoretically mitigate the risk for vascular damage by proteolytic pancreatic enzymes in the event of PF. Retrospective studies have raised concerns regarding increased intraluminal bleeding and compromised longterm pancreas exocrine function with PG.[12] Although this analysis revealed no difference in the overall risk for

Table 3 Assessment of methodology

Study	Setting	Timing of randomization	Stratification of randomization	Allocation concealment	Blinding	Standardization of technique	Pancreatic fistula measure
Fernández-Cruz et al.[31] 2008	Single centre	Before surgery	No	No	NR	Yes	ISGPF
Wellner et al.[32] 2012	Single centre	During surgery, before reconstruction	No	No	NR	Yes	ISGPF
Topal et al.[9] 2013	Multiple centres	During surgery, before reconstruction	Yes (pancreas duct size)	Yes	No	No	ISGPF
Figueras et al.[15] 2013	Multiple centres	During surgery, before reconstruction	Yes (diagnosis and centre)	Yes	NR	Yes	ISGPF

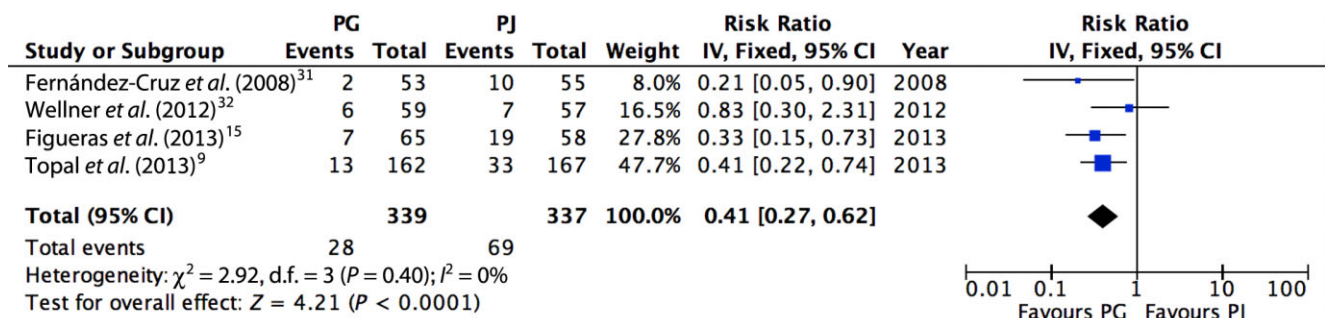NR, not reported; ISGPF, International Study Group on Pancreatic Fistula.

Figure 2 Comparison of the occurrence of pancreatic fistula after pancreaticogastrostomy (PG) with that after pancreaticojejunostomy (PJ). IV, inverse variance; 95% CI, 95% confidence interval

postoperative bleeding, patterns appeared to differ among those experiencing it, with more intraluminal events with PG and more extraluminal events with PJ. The former occurs early in the postoperative course and is theoretically more easily managed than the latter, which can potentially represent a devastating delayed result of PF. Because of the very small number of patients experiencing bleeding overall, no significant difference could be detected. Additional concerns regarding the longterm outcomes and durability of PG have also been voiced. Although it was not a specific outcome of this review, one RCT assessed exocrine pancreatic function and identified poorer function with PJ.[15] Interestingly, some have suggested that PJ anastomotic stricture resulting from PF is associated with pancreatic insufficiency, which may explain this finding.[39]

A soft pancreas and small pancreatic ducts have been associated repeatedly with significantly higher rates of PF. The trials included in this meta-analysis included pancreases of both low and high risk, resulting in a heterogeneous population in terms of baseline risk. Although the RR did not change when high- or low-risk pancreas subgroups were considered, the ARR was larger for patients with a high-risk pancreas (10% versus 4%) submitted to PG rather than PJ as a result of the considerable differences in baseline risk for PF. This highlights the more pronounced benefits of PG on PF in the context of a high-risk pancreas.

Some potential differences between PG and PJ may not be obvious in the current analysis as a result of the heterogeneous nature of the studied population. Firstly, there are potential negative impacts of PG compared with PJ on postoperative management, mainly arising from the need for nasogastric tube decompression if the stomach fills with pancreatic secretions and the subsequent delay in oral intake, and the routine use of surgical drains. As a result, PG may potentially be associated with a longer LoS. No difference in LoS was observed in this meta-analysis. Mean lengths of stay were quite long (range: 12–16 days), indicating that the studies included were probably conducted before the adoption of 'fast-track' protocols, when postoperative nasogastric tubes, surgical drains and delayed oral intake were routine for all patients.[40,41] It is possible that with contemporary clinical pathways and enhanced recovery after surgery protocols, patients submitted to PG and not experiencing a leak would have a longer LoS than those with PJ who are fast-tracked through the postoperative course. Nevertheless, the reduction of PF obviously takes priority over a potentially longer LoS. Secondly, despite the reduction in PF, DGE, morbidity and mortality did not differ between patients submitted to PG and PJ, respectively. With regard to DGE, this may also be explained by the heterogeneity of the population, whereby the lower rate of PF in PG balances out a potentially higher occurrence of DGE in this group. Given the smaller ARR in

Table 4 GRADE summary of findings for the effect of pancreaticogastrostomy versus pancreaticojejunostomy for reconstruction after pancreaticoduodenectomy

Outcome	Participants, n (studies, n)	Illustrative comparative risk		Summary measure (95% CI)[a]	Absolute risk reduction (95% CI)[b]	Quality of evidence (GRADE)[c]
		PG	PJ			
Clinically significant pancreatic fistula	1133 (4)	8% (28/339)	20% (69/337)	RR 0.41 (0.27–0.62)		+++ Moderate
Among high-risk pancreas	69 (2)	11% (15/133)	24% (32/131)		10% (6.5–14.8)	+++ Moderate
Among low-risk pancreas	180 (2)	5% (4/87)	9% (8/93)		4% (2.4–5.6)	++ Low
Operative time (min)	676 (4)	–	–	SMD 0.01 (–0.22 to 0.25)	–	++ Low
Estimated blood loss (ml)	560 (3)	–	–	SMD 0.20 (–0.12 to 0.53)		++ Low
Biliary leak	231 (2)	0.8% (1/118)	6% (7/113)	RR 0.18 (0.03–1.07)		++ Low
Delayed gastric emptying	676 (4)	18% (60/339)	13% (45/337)	RR 1.23 (0.70–2.16)		++ Low
Postoperative bleeding	676 (4)	12% (41/339)	9% (29/337)	RR 1.39 (0.89–2.17)		++ Low
Extraluminal bleeding[d]	32 (3)	50% (10/20)	92% (11/12)	RR 0.65 (0.41–1.04)		++ Low
Intraluminal bleeding[d]	30 (2)	58% (11/19)	9% (1/11)	RR 3.79 (0.87–16.91)		++ Low
Major postoperative morbidity	437 (2)	52% (112/215)	55% (123/222)	RR 0.78 (0.40–1.53)		++ Low
Postoperative mortality	676 (4)	2% (8/339)	4% (12/337)	RR 0.66 (0.27 –1.6)		++ Low
Length of stay (days)	676 (4)	–	–	SMD –0.31 (–1.03 to 0.42)		++ Low

[a]Values of <1 favour PG.
[b]Values are the expected difference in absolute risk if patients undergo PG instead of PJ.
[c]Quality rated from + (very low) to ++++ (very high).
[d]Data reported among the subgroup of patients with postoperative bleeding.
PG, pancreaticogastrostomy; PJ, pancreaticojejunostomy; 95% CI, 95% confidence interval; RR, relative risk; SMD, standard mean difference.

PF associated with the use of PG in a low-risk pancreas, PG may not appear to be best suited to use in this context. However, because of the larger ARR associated with PG in patients with a high-risk pancreas, the benefits of reducing PF outweigh the potential drawbacks of the technique. Hence, a selective approach to the use of PG after PD based on the baseline risk for PF may be advisable in order to maximize the benefits of the technique. New tools that enable the surgeon to appreciate a patient's risk for PF, such as the fistula risk score, are now available and may help in implementing this selective use of PG.[42]
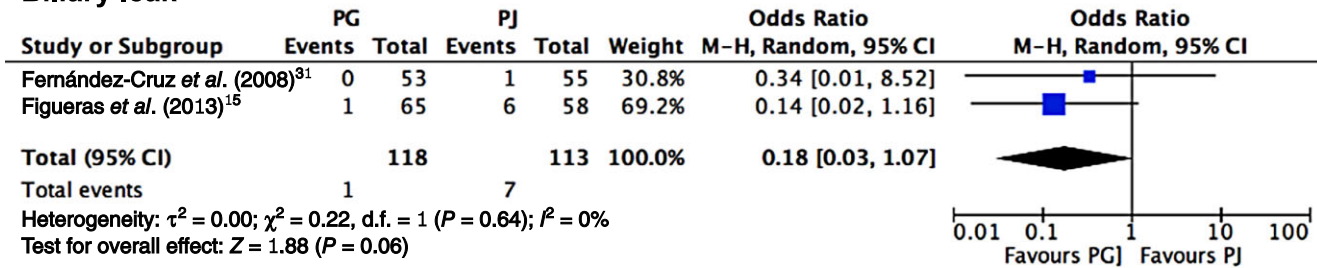
Among previous meta-analyses, two observed a significant benefit of PG on the occurrence of PF[10,12] and three did not.[13,14,43] However, with one exception, these previous studies suffered from important methodological limitations, including a search strategy limited to one or a few electronic databases of material published only in English, the absence of systematic methodological assessment, the lack of sensitivity analyses to explore the heterogeneity of results, and the inclusion of a large number of observational studies, along with a few RCTs.[12–14,31] A meta-analysis by McKay *et al.* used sound methodology, but included only one RCT.[10] Therefore, the pooling of previous data to examine the impacts of PG versus PJ on PF was limited by the inclusion of data from inherently biased observational studies. The present meta-analysis is the first to include only RCTs and to observe a significant reduction in PF with PG. It also offers insights into the differences in results through an exploration of heterogeneity and subgroup analyses, leading to a detailed practical proposal for the transfer of results into practice in order to maximize the benefits of selecting the use of PG in patients with a high-risk pancreas.
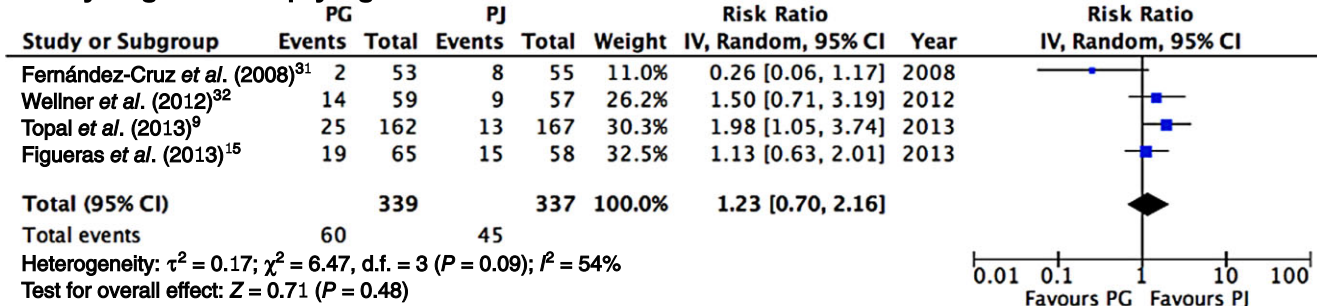
Although meta-analyses offer increased power to detect treatment effects by synthesizing the results of individual studies, they remain limited by the quality of the studies included and the heterogeneity of results. The weaknesses of this study refer to the methodological limitations of the studies included, most of which are related to allocation concealment and blinding, which are known limitations of surgical RCTs.[44,45] Nevertheless, the summary of the findings of this study indicates that conclusions on the primary outcome of PF are based on evidence of moderate quality. The FI analysis shows that at least two of the three trials reporting a benefit for PG are robust, with indices of 5 and 6.[9,15,31] This index indicates that the results are unlikely to be changed by the transforming of only a few events (of PF) into non-events (of no PF) and thus can be relied upon. Such a finding is closely related to sample size: studies with larger sample sizes are less prone to fragile results in which the significance of the measure of effect can be modified by the transformation of only one or two events into non-events.

The strengths of this systematic review and meta-analysis include a comprehensive, systematic and highly selective search conducted without restriction for language or types of publication, which also considered the grey literature and was performed in duplicate. The studies included were rigorously evaluated using a
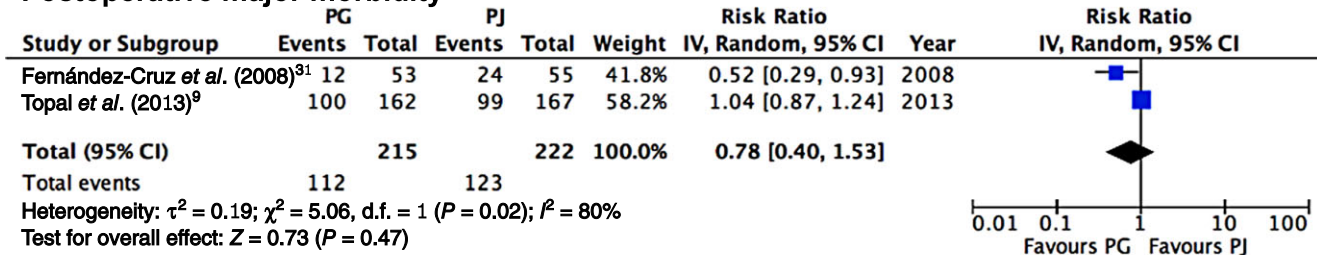
Biliary leak

Study or Subgroup	PG Events	Total	PJ Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Fernández-Cruz et al. (2008)[31]	0	53	1	55	30.8%	0.34 [0.01, 8.52]
Figueras et al. (2013)[15]	1	65	6	58	69.2%	0.14 [0.02, 1.16]
Total (95% CI)		**118**		**113**	**100.0%**	**0.18 [0.03, 1.07]**
Total events	1		7			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.22$, d.f. = 1 ($P = 0.64$); $I^2 = 0\%$
Test for overall effect: $Z = 1.88$ ($P = 0.06$)

Delayed gastric emptying

Study or Subgroup	PG Events	Total	PJ Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Year
Fernández-Cruz et al. (2008)[31]	2	53	8	55	11.0%	0.26 [0.06, 1.17]	2008
Wellner et al. (2012)[32]	14	59	9	57	26.2%	1.50 [0.71, 3.19]	2012
Topal et al. (2013)[9]	25	162	13	167	30.3%	1.98 [1.05, 3.74]	2013
Figueras et al. (2013)[15]	19	65	15	58	32.5%	1.13 [0.63, 2.01]	2013
Total (95% CI)		**339**		**337**	**100.0%**	**1.23 [0.70, 2.16]**	
Total events	60		45				

Heterogeneity: $\tau^2 = 0.17$; $\chi^2 = 6.47$, d.f. = 3 ($P = 0.09$); $I^2 = 54\%$
Test for overall effect: $Z = 0.71$ ($P = 0.48$)

Postoperative major morbidity

Study or Subgroup	PG Events	Total	PJ Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Year
Fernández-Cruz et al. (2008)[31]	12	53	24	55	41.8%	0.52 [0.29, 0.93]	2008
Topal et al. (2013)[9]	100	162	99	167	58.2%	1.04 [0.87, 1.24]	2013
Total (95% CI)		**215**		**222**	**100.0%**	**0.78 [0.40, 1.53]**	
Total events	112		123				

Heterogeneity: $\tau^2 = 0.19$; $\chi^2 = 5.06$, d.f. = 1 ($P = 0.02$); $I^2 = 80\%$
Test for overall effect: $Z = 0.73$ ($P = 0.47$)

Postoperative mortality

Study or Subgroup	PG Events	Total	PJ Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Year
Fernández-Cruz et al. (2008)[31]	0	53	0	55		Not estimable	2008
Wellner et al. (2012)[32]	1	59	1	57	10.5%	0.97 [0.06, 15.08]	2012
Figueras et al. (2013)[15]	3	65	3	58	32.6%	0.89 [0.19, 4.25]	2013
Topal et al. (2013)[9]	4	162	8	167	56.9%	0.52 [0.16, 1.68]	2013
Total (95% CI)		**339**		**337**	**100.0%**	**0.66 [0.27, 1.60]**	
Total events	8		12				

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.39$, d.f. = 2 ($P = 0.82$); $I^2 = 0\%$
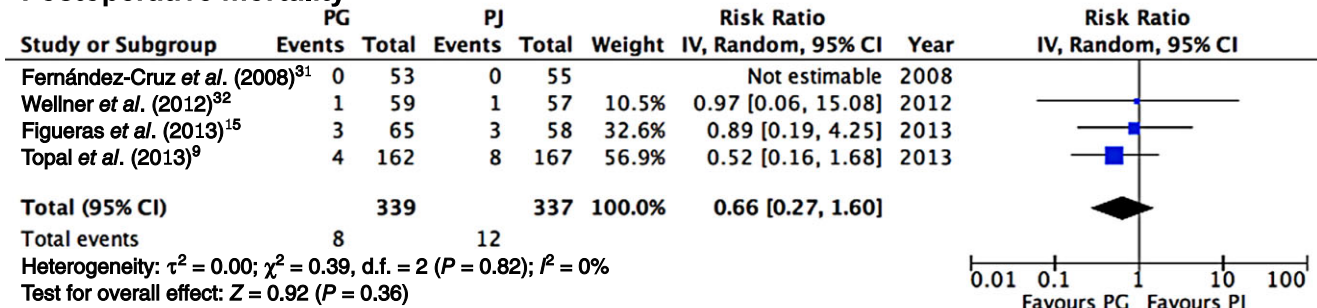Test for overall effect: $Z = 0.92$ ($P = 0.36$)

Figure 3 Comparisons of the occurrences of biliary leak, delayed gastric emptying, postoperative morbidity (Clavien–Dindo Grades III and IV) and postoperative mortality after pancreaticogastrostomy (PG) with occurrences after pancreaticojejunostomy (PJ). M–H, Mantel–Haenszel method; IV, inverse variance; 95% CI, 95% confidence interval

checklist of key methodological elements drawn from a consensus statement on RCTs, GRADE quality of evidence classification, and the FI to assess the robustness of positive results. The primary outcome chosen was based on a consensus definition, was common, was significant in terms of clinical repercussions, and was important to patients. Results of *a priori* sensitivity analyses were provided in order to give insight into the heterogeneity of results.

Conclusions

This study observed that PG is associated with a lower risk for PF compared with PJ. This benefit appeared to be greater in high-risk patients. Surgeons should consider reconstructing the pancreatic remnant following PD with PG, particularly in patients at high risk for PF.

Operating time, min

Study or Subgroup	PG Mean	SD	Total	PJ Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year	Std. Mean Difference IV, Random, 95% CI
Fernández-Cruz et al. (2008)[31]	300	50	53	310	60	55	21.3%	−0.18 [−0.56, 0.20]	2008	
Wellner et al. (2012)[32]	431.5	98.2	59	452	128.2	57	22.2%	−0.18 [−0.54, 0.19]	2012	
Figueras et al. (2013)[15]	378.5	111.2	65	340	78	58	22.6%	0.39 [0.04, 0.75]	2013	
Topal et al. (2013)[9]	269.9	82.7	162	269.7	86.4	167	33.9%	0.00 [−0.21, 0.22]	2013	
Total (95% CI)			**339**			**337**	**100.0%**	**0.01 [−0.22, 0.25]**		

Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 6.44$, d.f. = 3 ($P = 0.09$); $I^2 = 53\%$
Test for overall effect: $Z = 0.10$ ($P = 0.92$)

Favours PG Favours PJ

Estimated blood loss, ml

Study or Subgroup	PG Mean	SD	Total	PJ Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Fernández-Cruz et al. (2008)[31]	965	786	53	972	725	55	29.4%	−0.01 [−0.39, 0.37]	
Figueras et al. (2013)[15]	1,406.5	1,154.4	65	875.5	548.5	58	30.4%	0.57 [0.21, 0.93]	
Topal et al. (2013)[9]	592.2	514.9	162	550.2	495.7	167	40.3%	0.08 [−0.13, 0.30]	
Total (95% CI)			**280**			**280**	**100.0%**	**0.20 [−0.12, 0.53]**	

Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 6.28$, d.f. = 2 ($P = 0.04$); $I^2 = 68\%$
Test for overall effect: $Z = 1.25$ ($P = 0.21$)

Favours PG Favours PJ

Length of stay, days

Study or Subgroup	PG Mean	SD	Total	PJ Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year	Std. Mean Difference IV, Random, 95% CI
Fernández-Cruz et al. (2008)[31]	12	2	53	16	3	55	24.3%	−1.55 [−1.98, −1.12]	2008	
Wellner et al. (2012)[32]	43	37	59	26	14.5	57	24.8%	0.60 [0.22, 0.97]	2012	
Figueras et al. (2013)[15]	19.2	14.7	65	23	14.1	58	25.0%	−0.26 [−0.62, 0.09]	2013	
Topal et al. (2013)[9]	21.5	13.1	162	22.2	14.9	167	26.0%	−0.05 [−0.27, 0.17]	2013	
Total (95% CI)			**339**			**337**	**100.0%**	**−0.31 [−1.03, 0.42]**		

Heterogeneity: $\tau^2 = 0.51$; $\chi^2 = 57.04$, d.f. = 3 ($P < 0.00001$); $I^2 = 95\%$
Test for overall effect: $Z = 0.83$ ($P = 0.41$)

Favours PG Favours PJ

Figure 4 Comparisons of operating time, estimated blood loss, and length of stay after pancreaticogastrostomy (PG) with those after pancreaticojejunostomy (PJ). IV, inverse variance; 95% CI, 95% confidence interval

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