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REVIEW ARTICLE

Meta-analysis of antecolic versus retrocolic gastric reconstruction after a pylorus-preserving pancreatoduodenectomy

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Abstract

Introduction: Delayed gastric emptying (DGE) is a common complication after a pylorus-preserving pancreatoduodenectomy (PPPD) and is associated with significant morbidity. This study determines whether DGE is affected by antecolic (AC) or retrocolic (RC) reconstruction after a PPPD.

Method: An electronic search was performed of the MEDLINE, EMBASE and PubMed databases to identify all articles related to this topic. Pooled risk ratios (RR) were calculated for categorical outcomes, and mean differences (MD) for secondary continuous outcomes using the fixed-effects and random-effects models for meta-analysis.

Results: Nine studies including 878 patients met the inclusion criteria. DGE was lower with an AC reconstruction RR 0.31 [0.12, 0.78] Z = 2.47 ($P = 0.010$). Length of stay (LOS) MD –4 days [–7.63, –1.14] Z = 2.65 ($P = 0.008$) and days to commence a solid diet MD –5 days [–6.63, –3.15] Z = 5.50 ($P \leq 0.000$) were also significantly in favour of the AC group. There was no difference in the incidence of pancreatic fistula, intra-abdominal collection/bile leak or mortality between the two groups.

Conclusion: AC reconstruction after PPPD is associated with a lower incidence of DGE. Time to oral intake was significantly shorter with AC reconstruction, with a reduced hospital stay.

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Introduction

A pancreatoduodenectomy (PD) is an established operation offering a potential chance of a cure to patients with peri-ampullary malignancies as well as other benign and malignant conditions.[1] Morbidity associated with this procedure is high with delayed gastric emptying (DGE) being a common complication with an incidence of between 5% and 80%.[2–5]

The most widely accepted and validated definition of DGE is that by the International Study Group on Pancreatic Surgery (ISGPS).[6] Although DGE is not usually a life-threatening complication it leads to patient symptoms, prolonged hospital stay and increased cost.[7] There are a number of factors which might influence the return of normal stomach emptying after a pylorus-preserving pancreatoduodenectomy (PPPD), including pancreatic leak, diabetic gastroparesis, roux limb versus loop and anterior or posterior anastamosis.[8]

Another factor that has been suggested is the route of reconstruction, either antecolic (AC) or retrocolic (RC). The incidence of DGE ranges from 5% to 80% between studies[2–4,9,10] and generally favours AC over RC reconstruction. But there have been other studies that have failed to demonstrate any advantage.[7,11] The aim of this systematic review and meta-analysis was to compare AC and RC reconstruction after PPPD for the relative risk of DGE and other secondary measures.

Method

Randomized and case-controlled studies, irrespective of language, country of origin, hospital, blinding, sample size or publication status, that compared AC and RC gastroenteric reconstruction for PPPD were included in this review. The Cochrane Colorectal Cancer Group Controlled Trials Register, the Cochrane Central Register of Controlled Trials in the Cochrane Library, MEDLINE,

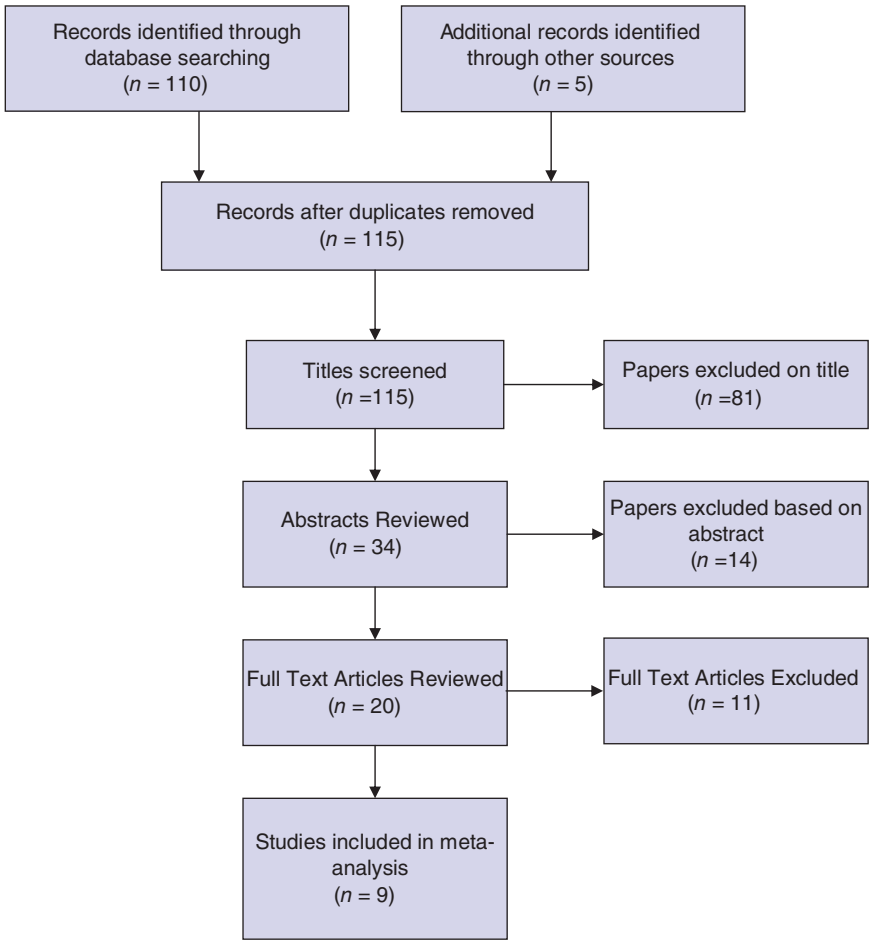

Figure 1 PRISMA flow diagram

Embase and Science Citation Index Expanded were searched for articles published up to January 2014 using the medical subject headings (MeSH) terms 'AC, RC, gastroenteric reconstruction and pylorus-preserving pancreatoduodenectomy'. Equivalent free-text search terms, such as 'AC and RC' were used in combination with 'pylorus-preserving pancreatoduodenectomy'. The references from the included studies were searched to identify additional studies comparing the two techniques.

All patients who underwent PPPD for both benign and malignant conditions were included. Inclusion criteria for searching were: randomized and non-randomized studies evaluating the use of AC gastroenteric reconstruction and RC gastroenteric reconstruction for PPPD. The search strategy is illustrated in Fig. 1.

Outcome measures

The primary outcome measure was the incidence of DGE. Secondary outcome measures were pancreatic fistula, intra-abdominal collection and bile leak, days to start liquid food, days to start solid food, length of stay (LOS) and 90-day mortality.

Definitions

DGE was defined on the basis of the requirement for prolonged gastric drainage and delayed return to a solid diet as per the ISGPS[6] definition.

The definition of intra-abdominal collection and bile leak was any fluid collection requiring drainage.

A pancreatic fistula was defined as drainage of fluid with an amylase concentration three times the upper limit of normal serum as per the ISGPF definition.[12]

Data extraction and quality assessment

Studies were identified and data were extracted by two authors independently (R.B. and S.P.). The accuracy of the extracted data was further adjudicated by a third author.

Statistical analysis

Statistical analysis was performed using Review Manager Version 5.2 software (Cochrane Collaboration). The risk ratio (RR) with 95% confidence interval (CI) was calculated for categorical data,

and the mean difference with 95% CI for continuous variables. When median and range were reported instead of mean and variance, the latter was calculated using the methods described by Hozo *et al.*[13] Random and fixed-effects models were used to calculate the combined outcomes of both binary and continuous data.[14,15] In cases of heterogeneity, only the results of the random-effects model were reported. Heterogeneity was explored using the χ^2 test, with significance set at $P < 0.050$. Low heterogeneity was defined as an I^2 value of 33% or less.[16] If the standard deviation was not available, it was calculated according to the guidelines of the Cochrane Collaboration.[17] This process involved assumptions that both groups had the same variance, which may not have been true, and variance was estimated either from the range or from the *P*-value. Forest plots were used for graphical display of the results. The quality of included studies was assessed using the Jadad score[18] for randomized controlled trials and the Newcastle–Ottawa score[19] for case–control studies.

Results

Nine studies met the inclusion criteria and formed the basis of this meta-analysis.[2–4,7,9–11,20,21] Five studies were randomized controlled trials, one was a prospective observational study and there were three retrospective studies. There were a total of 878 patients, including 451 in the AC group and 427 in the RC group. The characteristics and quality of the studies are given in Table 1. Pooled data were analysed by combining the results of the nine studies.

Primary outcome measure

Delayed gastric emptying

Eight studies were included in this analysis. There was marked heterogeneity amongst the included studies [$\tau^2 = 1.41$, $\chi^2 = 68.38$, d.f. = 7 ($P \leq 0.000$); $I^2 = 90\%$]. In a random effects model, there was a significant difference in the incidence of DGE between AC and RC reconstruction in favour of AC reconstruction RR 0.31 [0.12, 0.78] Z = 2.47 ($P = 0.010$) (see Fig. 2). No difference was seen in grade A DGE ($P = 0.790$) or grade B and C DGE ($P = 0.500$) between AC and RC reconstruction.

A subset analysis was performed using only the five randomized controlled trials (RCTs). There was some heterogeneity amongst the included studies [$\tau^2 = 0.43$, $\chi^2 = 9.00$, d.f. = 4 ($P = 0.060$); $I^2 = 56\%$]. There was no significant difference in DGE amongst the included RCTs (OR 0.5 [0.23, 1.17] Z = 1.59 ($P = 0.110$) (see Fig. 3).

Table 1 Characteristics of included studies

Study	Year	Country	*n* per Group		Design	Reconstruction			% DGE		Quality Score (Jadad – RCT/ Newcastle Ottawa – Non RCT)
			AC	RC		AC	RC	PD	AC (%)	RC (%)	
Chijiiwa *et al.*	2005–2007	Japan	17	18	RCT	Antecolic duodenojejunostomy	Vertical end to side duodenojejunostomy. Caudal side.	PJ	6	22	2
Eshuis *et al.*	2009–2011	The Netherlands	121	125	RCT	Antecolic duodenojejunostomy	End to side duodenojejunostomy. Stomach fixed to transverse mesocolon	PJ	61	60	3
Hartel *et al.*	1996–2001	Germany	100	100	Retro	Antecolic duodenojejunostomy. On same limb as HJ and PJ	Retrocolic duodenojejunostomy. On same limb as HJ and PJ.	PJ	5	24	9
Imamura *et al.*	2005–2011	Japan	58	58	RCT	End to side antecolic duodenojejunostomy	Vertical end to side duodenojejunostomy. Caudal side.	PJ	12.1	20.7	3
Murakami *et al.*	1994–2006	Japan	78	54	Retro	Antecolic roux-en-y reconstruction	Retrocolic Bilroth I reconstruction	PG	10	81	9
Sugiyama *et al.*	NS	Japan	12	18	Retro	Jejunal loop with antecolic duodenojejunostomy on same limb as HJ and PJ	Retrocolic duodenojejunostomy Same limb as HJ and PJ.	PJ	8	72	9
Tamandl *et al.*	2007–2009	Austria	34	26	RCT	Antecolic duodenojejunostomy on same limb as HJ and PJ	Retrocolic Duodenojejunostomy on same limb as HJ and PJ	PJ	18	23	1
Tanabe *et al.*	2001–2006	Japan	11	8	Prosp	Antecolic duodenojejunostomy	Retrolic duodenojejunostomy	PJ	NS	NS	8
Tani *et al.*	2002–2004	Japan	20	20	RCT	Antecolic duodenjejunostomy on same proximal jejunal loop as HJ and PJ	Retrocolic duodenojejunostomy on same proximal jejunal loop as HJ and PJ	PJ	5	50	3

AC, antecolic; RC, retrocolic; PD, pancreatoduodenectomy; DGE, delayed gastric emptying; RCT, randomized controlled trial; NS, not significant.

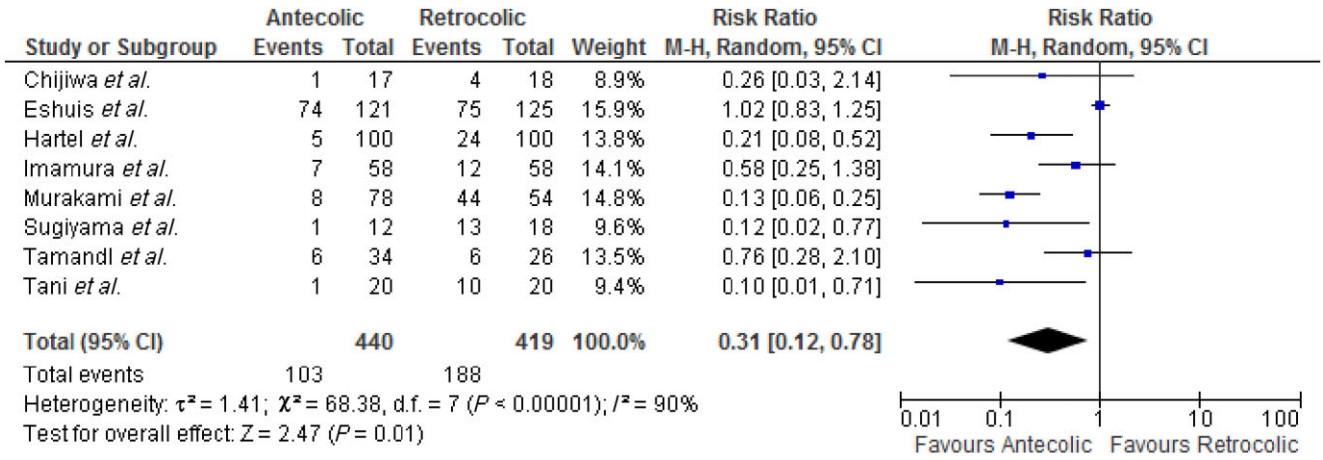

Figure 2 Delayed gastric emptying (DGE) – all studies

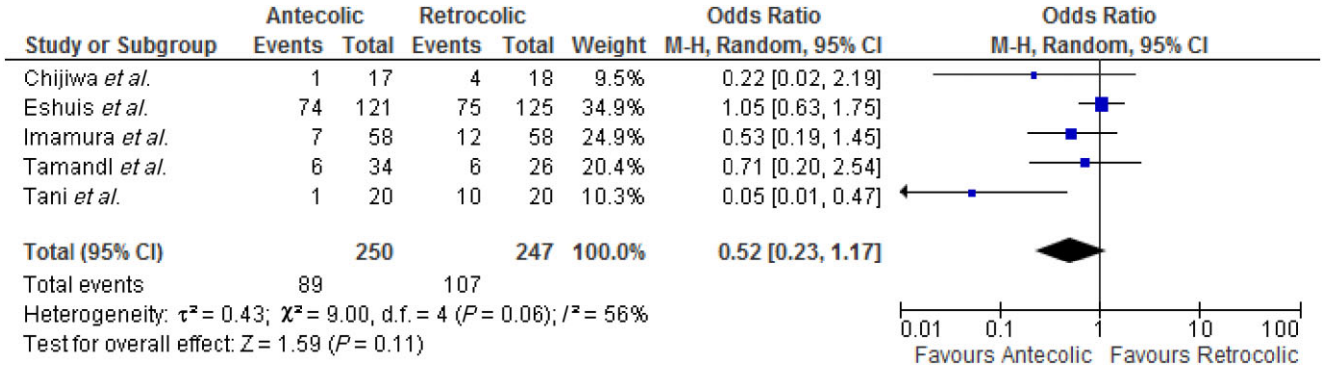

Figure 3 Delayed gastric emptying (DGE) – randomized controlled trails (RCTs)

Secondary outcome measures

Pancreatic leak

Nine studies were included in the analysis. There was no heterogeneity amongst the included studies [χ^2 = 3.33, d.f. = 8 (P = 0.910); I^2 = 0%]. In a fixed effects model there was no significant difference in the frequency of pancreatic leak between the AC and RC groups OR 1.06 [0.71, 1.58] Z = 0.29 (P = 0.770) (see Fig. 4).

Intra-abdominal collection and bile leak

Eight studies were included in the analysis. There was no heterogeneity amongst the included studies [χ^2 = 4.64, d.f. = 7 (P = 0.700); I^2 = 0%]. In a fixed effects model there was no significant difference in the frequency of intra-abdominal collection/abscess between the AC and RC groups OR 0.91 [0.57, 1.45] Z = 0.42 (P = 0.680).

Time to start liquid diet

Five studies were included in the analysis. There was marked heterogeneity amongst the included studies [τ^2 = 42.97, χ^2 = 178.63, d.f. = 4 ($P \leq 0.000$); I^2 = 98%]. In a random effects model there was a significant difference in the days taken to restart a liquid diet in favour of the AC group MD −7 days [−13.23, −1.33] Z = 2.40 (P = 0.020).

Time to start solid food

Eight studies were included in the analysis. There was marked heterogeneity amongst the included studies [τ^2 = 4.14, χ^2 = 288.70, d.f. = 7 ($P \leq 0.000$); I^2 = 98%]. In a random effects model there was a significant difference in the days taken to restart a solid diet in favour of AC reconstruction MD −5 days [−6.63, −3.15] Z = 5.5 ($P \leq 0.000$). See Fig. 5.

LOS

Nine studies were included in the analysis. There was marked heterogeneity amongst the included studies [τ^2 = 16.68, χ^2 = 490.02, d.f. = 8 ($P \leq 0.000$); I^2 = 98%]. In a random effects model there was a significant difference in the LOS after surgery in favour of the AC group MD −4 days [−7.63, −1.14] Z = 2.65 (P = 0.008). See Fig. 6.

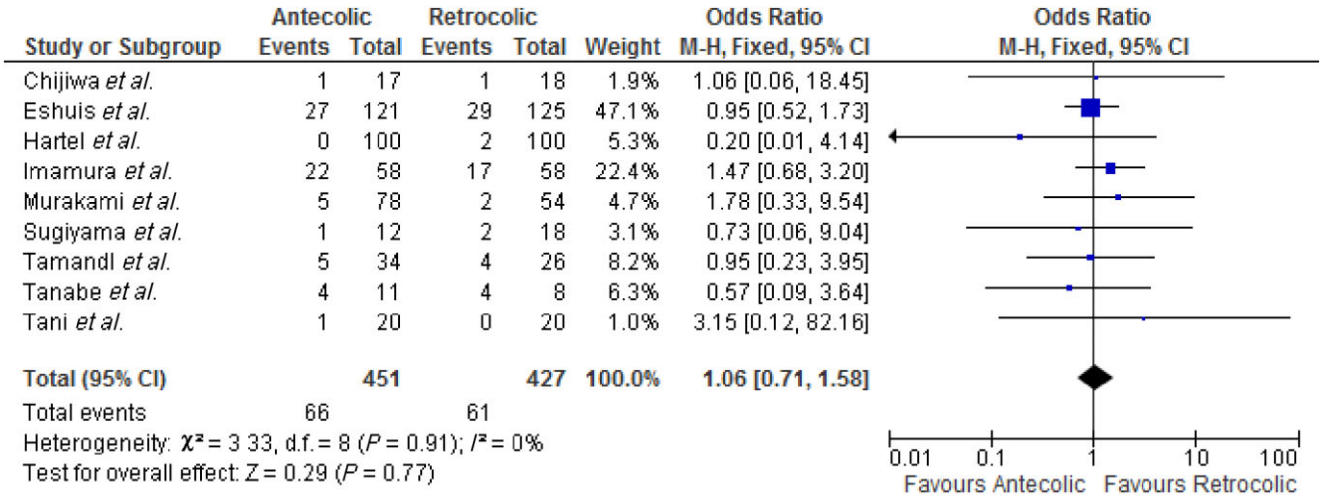

Figure 4 Pancreatic leak

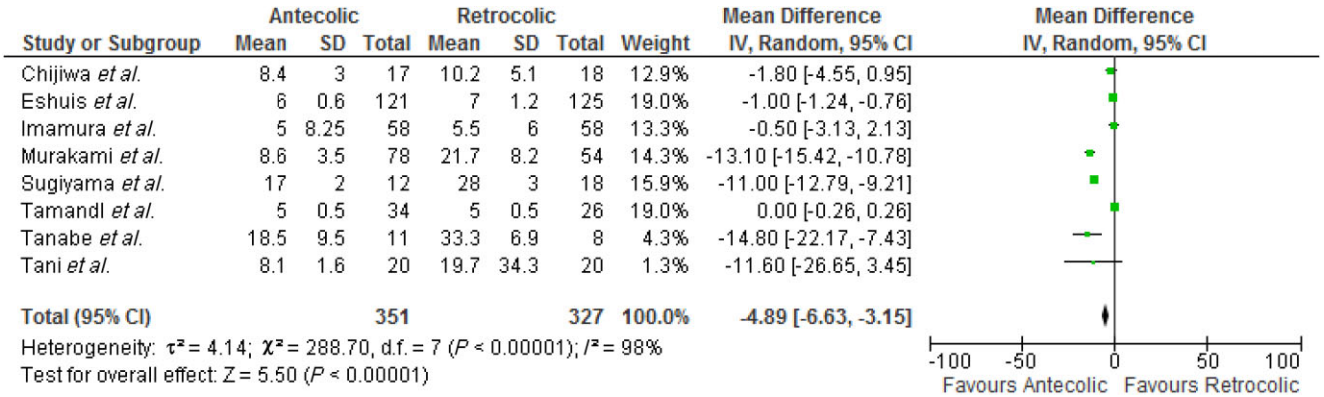

Figure 5 Days to commence solid diet

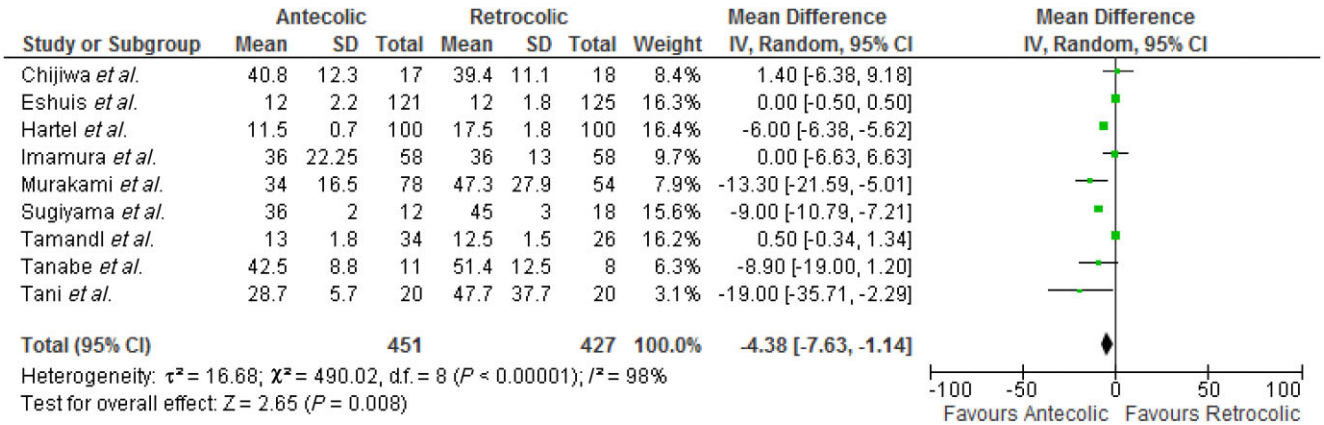

Figure 6 Length of stay

Mortality

Five studies were included in the analysis. There was no heterogeneity amongst the included studies [$\chi^2 = 0.18$, d.f. = 2 ($P = 0.910$); $I^2 = 0\%$]. In a fixed effects model there was no significant difference between mortality with AC or RC reconstruction RR 0.61 [0.24, 1.60] Z = 1.00 ($P = 0.300$).

Discussion

This meta-analysis shows that AC reconstruction after PPPD is associated with a lower incidence of DGE, reduced LOS and a more rapid resumption of normal oral intake, and this occurred without any increase in pancreatic leak or intra-abdominal collection or mortality. The overall incidence of DGE using the ISGPS definitions in this meta-analysis was 23% with AC reconstruction and 45% with RC reconstruction. The absolute risk reduction with AC reconstruction was 0.21 and the number needed to treat in this way to avoid one case of DGE is 5.

Although well described, the aetiology of DGE after PPPD in the absence of other post-operative complications remains unclear. There are a number of potential causes for 'primary' DGE including local ischaemia of the pylorus and antrum,[22] reduced levels of motilin leading to gastric atony,[23] gastric atony as a result of vagotomy[23] and torsion or angulation of the gastroenteric reconstruction.[24] This last point may help explain the superiority of the AC reconstruction and it has been hypothesized that one reason that no difference has been identified in some studies is the use of the vertical RC duodenojejunostomy. It was suggested that the vertical nature of the RC reconstruction avoided flexion and angulation of the stomach which in turn contributed to flow of gastric contents.[11] The authors felt this may be a reason why no difference was seen between the two groups.

The subgroup analysis of the five RCTs that compared AC and RC reconstructions gave variable results with one trial favouring an AC anastomosis and four showing no difference. The pooled data of just these RCT's seemed to favour AC reconstruction but did not show a statistically significant difference ($P = 0.110$). Interestingly, no difference was noted in the grade of DGE amongst the included studies. Eshuis *et al.* noted in a RCT that one possible explanation for the difference between their study and previous studies was that their RC reconstruction was performed by bringing the duodenal stump through a separate opening in the transverse mesocolon so that the gastroenteric anastamosis is in a different abdominal compartment to the other two anastamoses. It has been speculated that this may help to reduce inflammation around the gastroenteric anastamosis in the event of small pancreatic or biliary leaks. In addition the duodenal stump is sutured to the transverse mesocolon to prevent angulation.[7] Indeed Tani *et al.* had to suspend their RCT at the first interim analysis owing to the disparity between rates of DGE between the AC and RC group with this trial strongly favouring AC reconstruction.[3]

The quality of the studies was variable and is demonstrated in Table 1. Retrospective studies were of generally good quality and RCTs were generally of intermediate quality. There are several limitations to this review. The definitions of DGE varied between most of the studies. The ISGPS definition was used in two of the nine studies[7,21] although variations of the criteria used in this definition were used in the other studies.[2–4,9,11,12,20] Another limitation of the meta-analysis was inclusion of both randomized and non-randomized studies. This was considered necessary because of the small number of potential studies.

In conclusion, this meta-analysis supports the use of AC as opposed to RC gastroenterostomy and is associated with shorter LOS and early oral intake and is routinely recommended during PPPD.

Conflicts of interest

None declared.

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