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Original article

Effect of antecolic or retrocolic route of gastroenteric anastomosis on delayed gastric emptying after pancreaticoduodenectomy: A meta-analysis of randomized controlled trials

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ABSTRACT

Background: Delayed gastric emptying (DGE) is one of the most troublesome complications after classical pancreaticoduodenectomy (PD) or pylorus-preserving PD. Whether the route of gastroenteric reconstruction has any influence on DGE remains controversial. The aim of this study was to investigate the influence of different types of gastroenteric anastomosis on DGE after PD/PPPD.

Methods: A systematic search of literature databases (Cochrane Library, PubMed, EMBASE, and Web of Science) was performed to identify eligible studies. Cochrane collaboration's tool for assessing risk of bias was utilized to evaluate the quality of included studies. The primary outcome was DGE incidence rate. Further outcomes included mortality, morbidity, and other operation related events. Random-effect or fix-effect models were used as appropriate.

Results: Five randomized controlled trials (RCTs) including a total of 530 patients were identified and included in the analysis. Based on these studies, no difference was found in DGE incidence between antecolic and retrocolic groups (relative risk [RR], 0.82; 95% confidence interval [CI], 0.51−1.32; $P = 0.41$). Mortality, morbidity, and operation related events were not significantly different between groups.

Conclusions: Results of the meta-analysis reveal that DGE occurrence is not affected by route of gastroenteric anastomosis. Anastomosis approach should be chosen according to the surgeons' preference.

Introduction

Pancreaticoduodenectomy (PD) or pylorus-preserving pancreaticoduodenectomy (PPPD) is the standard operation for lesions located in the periampullary area [1–3]. With advances in surgical techniques and better perioperative management, the mortality rate of the procedure has decreased to less than 5% in high-volume centers, but the morbidity rate still remains high [4,5]. One of the major postoperative complications following PD/PPPD is delayed gastric emptying (DGE), with a reported incidence rate varying between 14% and 61% [6]. DGE is detrimental to patient wellbeing due to a reduced level of comfort and prolonged length of hospital stay, which also incurs increased medical costs.

Various factors have been reported to effect the incidence of DGE. Among them, the method of gastroenteric anastomosis has been suggested as one of the major determinants for the incidence of DGE. Gastrojejunostomy anastomosis following a classic PD or duodenojejunostomy after pylorus-preserving PD can be done either via the antecolic or retrocolic routes. Some early trials [7,8] and an associated meta-analysis [9] show that antecolic reconstruction can significantly decrease DGE rate. However, these studies were either non-randomized [8] or had a small sample sizes [7]. Recently, several prospective randomized controlled trials

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[3,10–12] with more adequate case numbers were published and none of these demonstrated statistical superiority of either of the two reconstruction styles in terms of DGE incidence.

The aim of the meta-analysis presented herein is to analyze prospective, randomized controlled trials (RCTs) and to provide updated evidence to clarify whether the route of gastroenteric anastomosis has an impact on the prevalence of postoperative DGE.

Methods

Data sources and searches

Two authors (DQ and JLW) searched MEDLINE (PubMed), Web of Science, EMBASE, and Cochrane Library for RCTs that evaluated antecolic versus retrocolic reconstruction after PD/PPPD from January 1991 to January 2015. The search strategy in MEDLINE (PubMed) was based on the following search terms (Medical Subject Heading terms and text words) with the appropriate combinations:

(Retrocolic OR Antecolic)
AND
(Pancreaticojejunostomy[Mesh] OR Pancreatoduodenectomy OR Duodenopancreatectomy OR Whipple OR Pylorus preserv* OR Gastrojejunostomy OR Duodenojejunostomy OR Gastroenterostomy[Mesh] OR Delayed gastric emptying)
AND
((“1991/01/01”[PDat]: “2015/01/31”[PDat]) AND Humans [Mesh])

Citations were limited to those published on humans. We also searched the reference lists of articles retrieved. EndNote X7 citation management software (Thomson Corp., Stamford, CT, USA) was used for data collection. The results were verified and arbitrated by a third investigator (ZPL).

Inclusion and exclusion criteria

Only RCTs that include patients who underwent PD/PPPD for malignant or benign lesions and compared the antecolic route of gastrointestinal reconstruction to the retrocolic route were considered for inclusion. Papers lacking appropriate randomization of groups, including cases with total pancreatectomy (TP) or subtotal stomach-preserving PD (SSPPD) were excluded. Only RCTs reporting quantitative data for DGE and at least one of the following outcomes were selected: mortality, morbidity, length of stay, operating time, and intraoperative blood loss. Reviews, case reports, and studies that were not published as original papers, such as conference abstracts and letters to the editor, were excluded. When two or more studies were published by the same group of authors, only the most recent was included.

Eligibility assessment and data extraction

Two authors (DQ and XCL) screened the title and abstract of each article for potentially eligible studies independently. Next, full-text articles were assessed for eligibility. Three authors (DQ, JLW, and RJ) extracted data from the included trials independently to avoid bias. Details reviewed included sample size, randomization procedure, allocation concealment, consistency of the study population and extracted quantitative data on the incidence of DGE, postoperative mortality, morbidity, length of stay (LOS), operating time, and intraoperative blood loss. All disagreements during the process were resolved via a discussion with a fourth author (ZPL). We have neither academic nor private relationships with the authors or institutions of the included trials.

Quality assessment

Numerous tools are available for assessing methodological quality of clinical trials. The uses of scales for assessing quality or risk of bias were not recommended according to the Cochrane handbook. The Cochrane Collaboration tool for assessing risk of bias (version 5.1.0) [13], which evaluates bias of each study based on selection, performance, detection, attrition, reporting, and other biases, was used to assess the quality of included RCTs. The quality was described as at low/unclear/high risk of bias.

Statistical analysis

The primary outcome of interest was DGE. Secondary outcomes included DGE related outcomes (nasogastric tube removal time [NGT] and time to tolerating solid food following surgery [TSF]); operational outcomes (operating time, blood loss, blood transfusion units, hospital length of stay) and further clinical outcomes (mortality, morbidity, fistula, bile leak, postoperative bleed, abscess, and wound infection).

All statistical analyses were performed using RevMan 5.2 (http://ims.cochrane.org/revman/download) and R (version 3.0.2). For categorical data the efficacy parameter of interest was the risk ratio, for continuous data the mean difference is used. For each, associated 95% confidence intervals (CIs) are presented. For continuous outcomes, data are defined as means and associated standard errors using appropriate estimation from reported ranges or inter-quartile ranges where appropriate. Where there is evidence of a skewed distribution, for example given by a lower confidence interval with a value less than zero, log transformation was applied with standard errors obtained using the delta method. Heterogeneity between studies was assessed using χ^2 and I^2, and $I^2 > 50\%$ was considered as significant. When the results of the two statistics were substantially different or $I^2 > 50\%$, the random-effects model was utilized, otherwise the fixed-effects model was chosen [14]. Scaled results are presented via a forest plot with risk ratios presented on the log scale. A funnel plot was used to detect possible publication bias [15]. Results were considered statistically significant if a P-value <0.05 was observed.

Subgroup analysis and sensitivity analysis

To further verify the surgical route on DGE incidence in specific populations cohorts with relatively uniform characteristics, subgroup analyses stratified by type of surgical intervention (Classical PD versus PPPD) and definition of DGE were performed. Subgroup analyses by risk of bias were also conducted to further evaluate credibility and stability. Further sensitivity analysis for the main outcome (DGE) was carried out by removing one study at a time to examine its influence on the primary outcome.

Results

Eligible RCTs

The systematic literature search retrieved 189 potentially relevant studies. A further seven relevant papers were screened by hand searching from the reference lists. There were a total of 191 records after duplicates were removed. According to the criteria described above, 172 screened abstracts were excluded. Of the

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