



Laparoscopic *versus* open pylorus-preserving pancreaticoduodenectomy. The first meta-analyse of retrospective matched cases¹

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Abstract

Purpose: To compare the safety, feasibility, and short-term clinical benefits of laparoscopic pylorus-preserving pancreaticoduodenectomy (L-PPPD) to open pylorus-preserving pancreaticoduodenectomy (O-PPPD) through retrospective matched cases.

Methods: Web of Science, Cochrane, PubMed, CNKI were searched systematically identify studies published between January and December 2017 comparing L-PPPD to O-PPPD. The meta-analysis was performed by using Review Manager 5.3.

Results: Two studies matched the selection criteria, including 108 (50%) cases of laparoscopic pylorus-preserving pancreaticoduodenectomy and 108(50%) cases of open pylorus-preserving pancreaticoduodenectomy. None of the included studies were randomized, which were both retrospective matched cases. There was no difference in the incidence of postoperative pancreatic fistula, blood loss, diet start and lymph nodes. However, L-PPPD has a shorter hospital stay ($p=0.0003$) and O-PPPD has a shorter operative time ($p=0.02$) and tend to decrease the delayed gastric emptying.

Conclusions: The perioperative safety of laparoscopic surgery, which also has advantages of minimal invasion and shorter hospital stay, is comparable to that of open surgery. Laparoscopic surgery could be operated if the patients matched the indication and operation difficulty is not so great. However, blind pursuits of L-PPPD should be restrained because there is no essential difference between these two in terms of feasibility, safety and short-term complication.

Key words: Laparoscopy. Pylorus. Pancreaticoduodenectomy. Meta-Analysis.

■ Introduction

In 1935, Whipple¹ first reintroduced pancreatoduodenectomy (PD), which is the only potentially effective treatment for periampullary cancer so far². However, the PD is still associated with high postoperative morbidity rates and mortality rates because of clinical and biological characteristics of periampullary carcinoma despite the progress and proficiency³. With the development of surgical technology and many scholars had tried to improve PD in the hope of a better prognosis, the laparoscopic pylorus-preserving pancreatoduodenectomy (L-PPPD) was firstly reported by Gagner⁴ while there was still some controversy that the the safety, feasibility and short-term clinical benefits of the L-PPPD. To our knowledge, there is few articles involved L-PPPD and O-PPPD and no meta-analyse compared it. Based on a great deal of the published evidence and the conflicting conclusion, the purpose of the this study was to systematically review the literature that have compared L-PPPD with O-PPPD and to meta-analyze the best evidence available, to provide high-quality data for clinical practice the first time.

■ Methods

This study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines⁵. We searched medical databases in which articles involved L-PPPD versus O-PPPD. This search strategy was designed and executed by an experienced information specialist and reviewed by 2 writers (Liwei Pang and Jing Kong).

Literature strategy

A detailed literature search was performed in online databases including Web of Science (244), Cochrane (334),

PubMed (61), CNKI (43) (last search date: October 30, 2017), without restriction to regions, publication types, or languages. The following terms were included "laparoscopic/laparoscopy/minimally invasive, pylorus-preserving pancreatoduodenectomy". When similar reports describing the same population were published, the most recent or complete report was used. The research was conducted independently by Liwei Pang and Jing Kong, subsequently all the authors compared their results. References from the articles were investigated manually. Any differences were resolved by consensus. This review adhered to the guidelines outlined in the PRISMA statement.

Study selection

Included were studies comparing L-PPPD (either laparoscopic, or hybrid PD) with O-PPPD reporting on at least 10 patients in all age groups and that had at least one of the meaningful conclusions. The exclusion criteria were noncomparable studies, nonhuman studies, experimental trials, review articles, editorials, letters and case reports, and articles not reporting the outcomes of interest.

Data extraction

The following data were extracted: name of authors; study design; number of patients included in the laparoscopic or hybrid; age; body mass index (BMI); operative time; estimated blood loss; diet start time; postoperative complications; pancreatic fistula; delayed gastric emptying; number of lymph nodes harvested; postoperative hospital stay.

Quality assessment and statistical analysis

Studies were rated for the level of evidence provided according to criteria by the Centre for Evidence-Based Medicine in Oxford, UK. The methodological quality

was assessed by the modified Newcastle-Ottawa scale⁶, consisting of 3 factors: patient selection, comparability of the study groups, and assessment of outcome. A score of 0 to 9 (allocated as stars) was allocated to each study, and observational studies achieving Z6 stars were considered to be of high quality.

We used Review Manager 5.3 (Cochrane collaboration, Oxford, England) for all statistical analyses. Considering that patients were selected by different surgical teams and operated in different centers; we chose the random-effects model to assess this heterogeneity. I2 was used for heterogeneity assessment, and values of more than 50% were considered significant. Dichotomous variables were analyzed and assessed with an odds ratio (OR); a value of less than 1 favored the laparoscopic cohort, while values of $P < 0.05$ and 95% confidence intervals (CIs) without the value of 1 supported the statistical significance of odds ratio (OR). Continuous variables analyzed with the weighted mean difference (WMD). The Mantel-Haenszel method was used to combine the OR for the

outcomes of interest; Peto OR was used when necessary. This study was performed according to the Preferred Reporting Items for Systematic reviews (PRISMA)⁵ guidelines.

Results

The literature search referred to 682 studies initially. No other eligible studies were found from other sources. At first time, 10 potential meaningful articles were included for a full-text browsing after looking through their titles and abstracts. Of these, we excluded 1 article⁷ after look through the whole paper^{7,8} because they are from the same institution. U. F. Wellne *et al.*⁹ was excluded because the data was not impactful and the authors could not provide information in detail. We also excluded another study¹⁰ because there was no comparison in it. The rest 5 are case report. Finally, this left a total of 2 studies^{8,11} representing 216 patients for inclusion in the meta-analysis. The Figure 1 illustrates the PRISMA flow chart of literature search strategies.

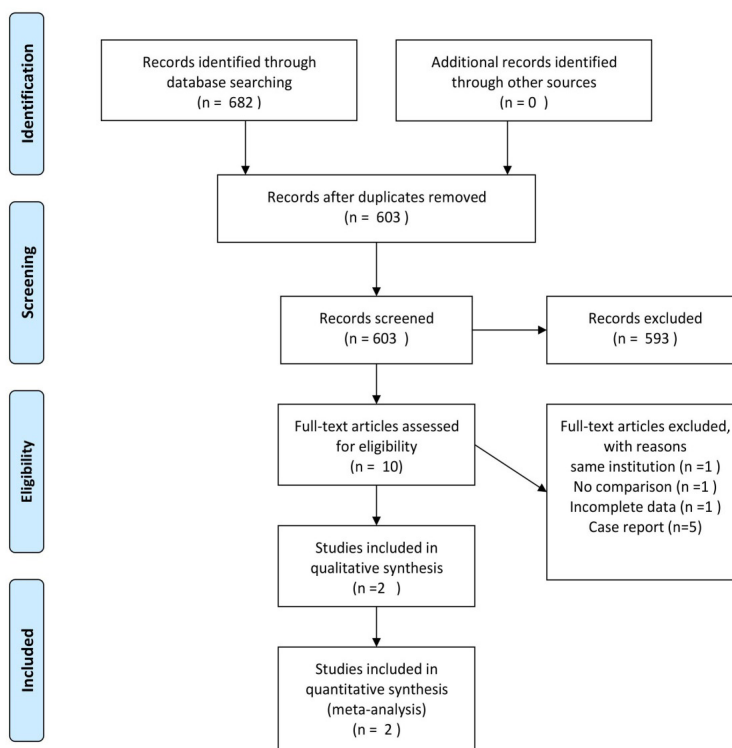


Figure 1 - Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram.

Meta-analysis

The meta-analysis determined that L-PPPD was associated with a longer operative time (MD: 119.74 min; 95% CI 92.76–146.72 min; I² = 81%; P<0.01) and hospital stay (MD: -1.53day; 95% CI -3.05 to 0; I² =92%; P = 0.05) (Figure 2). Among all studies, they all had tried to control variable such as age, BMI, ASA (Figure 3). The meta-analysis also showed the similar results in blood loss (MD: 13.52 ml; 95%

CI -94.36–121.4 min; I² = 1%; P=0.81), diet start (MD: -0.26 day; 95% CI -0.99–0.48 min; I² = 54%; P=0.49), lymph nodes (MD: -1.26; 95% CI -3.76–123 min; I² = 50%; P=0.32), respectively (Figure 4). In the meta-analysis, there were no significant differences between the two procedures about postoperative complication (OR: 0.95; 95% CI 0.52–1.74; I² = 0%; P=0.88), pancreatic fistula (OR: 1; 95% CI 0.36–2.78; I² = 0%; P=1.0). Delayed gastric emptying tended to be decreased in L-PPPD (OR:0.58; 95% CI 0.18–1.94; I² = 22%; P=0.38) (Figure 5).

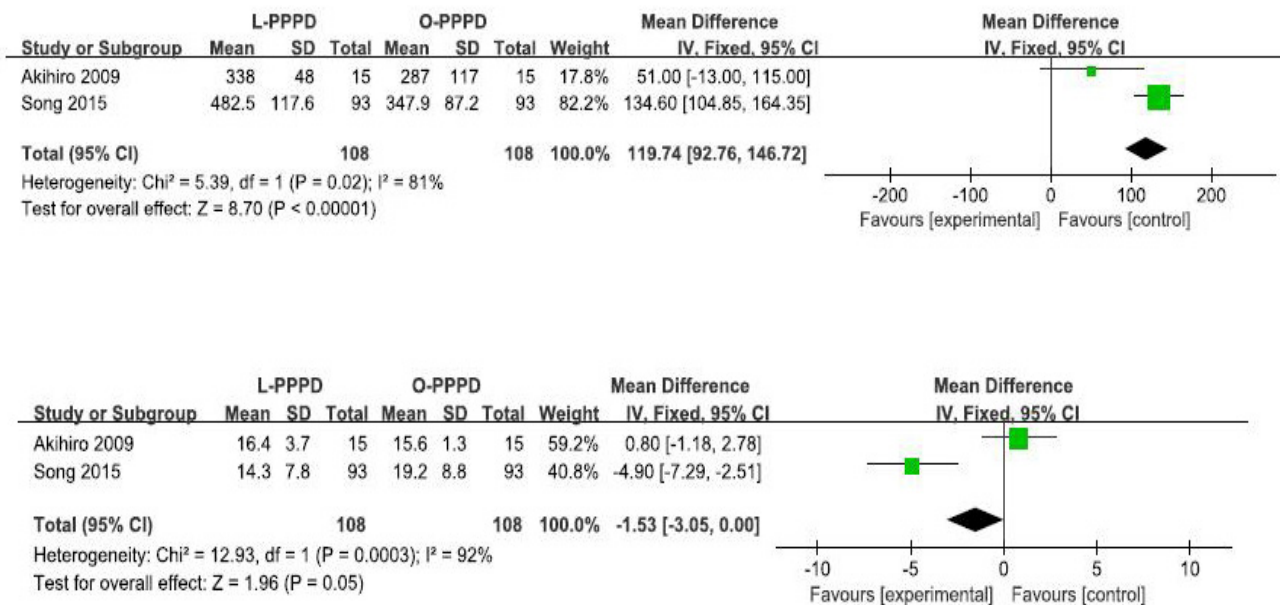


Figure 2 -Operative time and hospital stay L-PPPD versus O-PPPD. 95% CI and df.

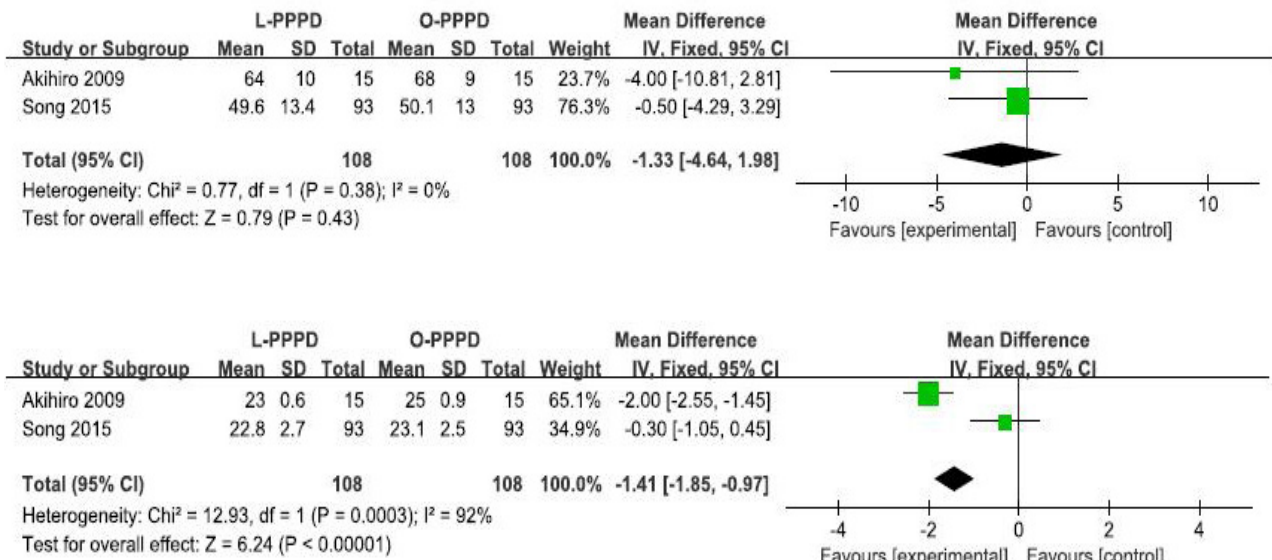


Figure 3 - Age and BMI controlled comparing L-PPPD versus O-PPPD. 95% CI and df.

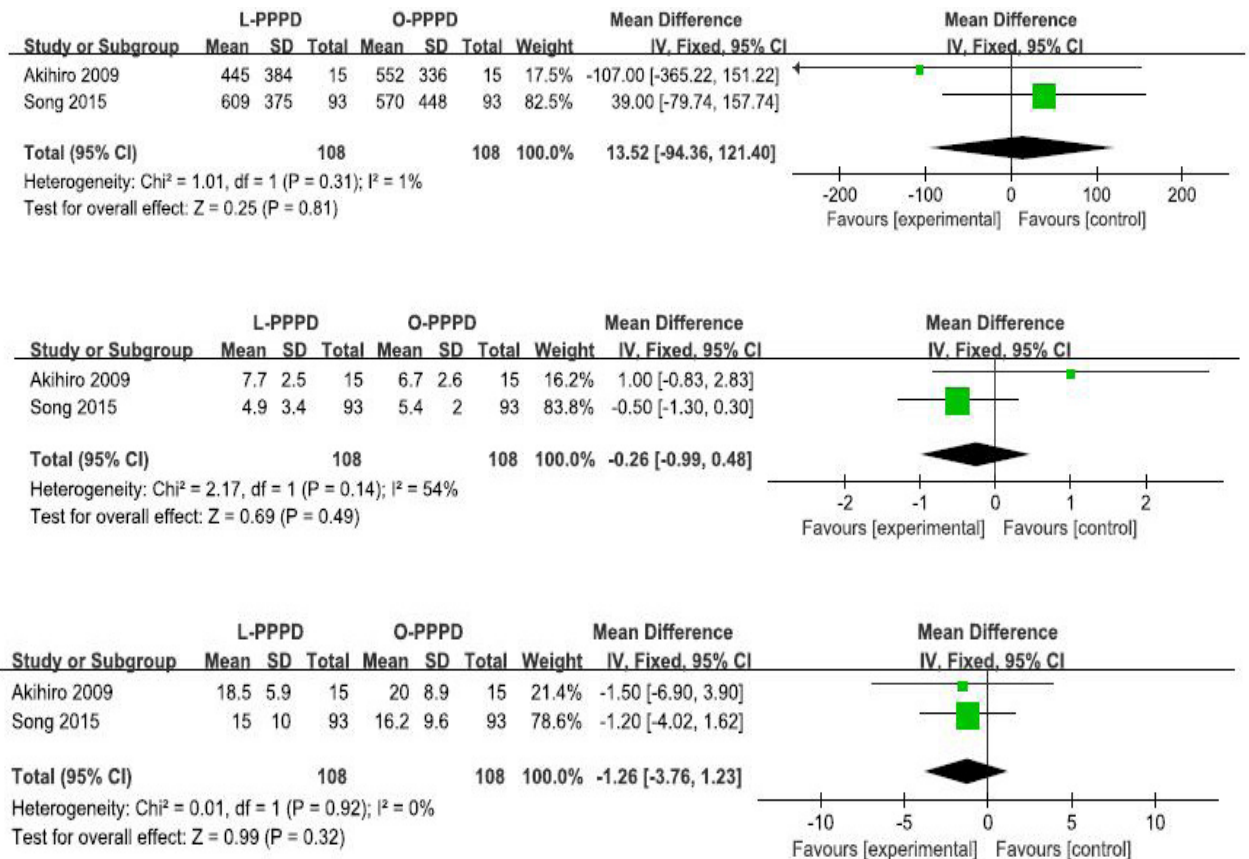


Figure 4 - Blood loss and diet start and lymph nodes comparing L-PPPD versus O-PPPD. 95% CI and df.

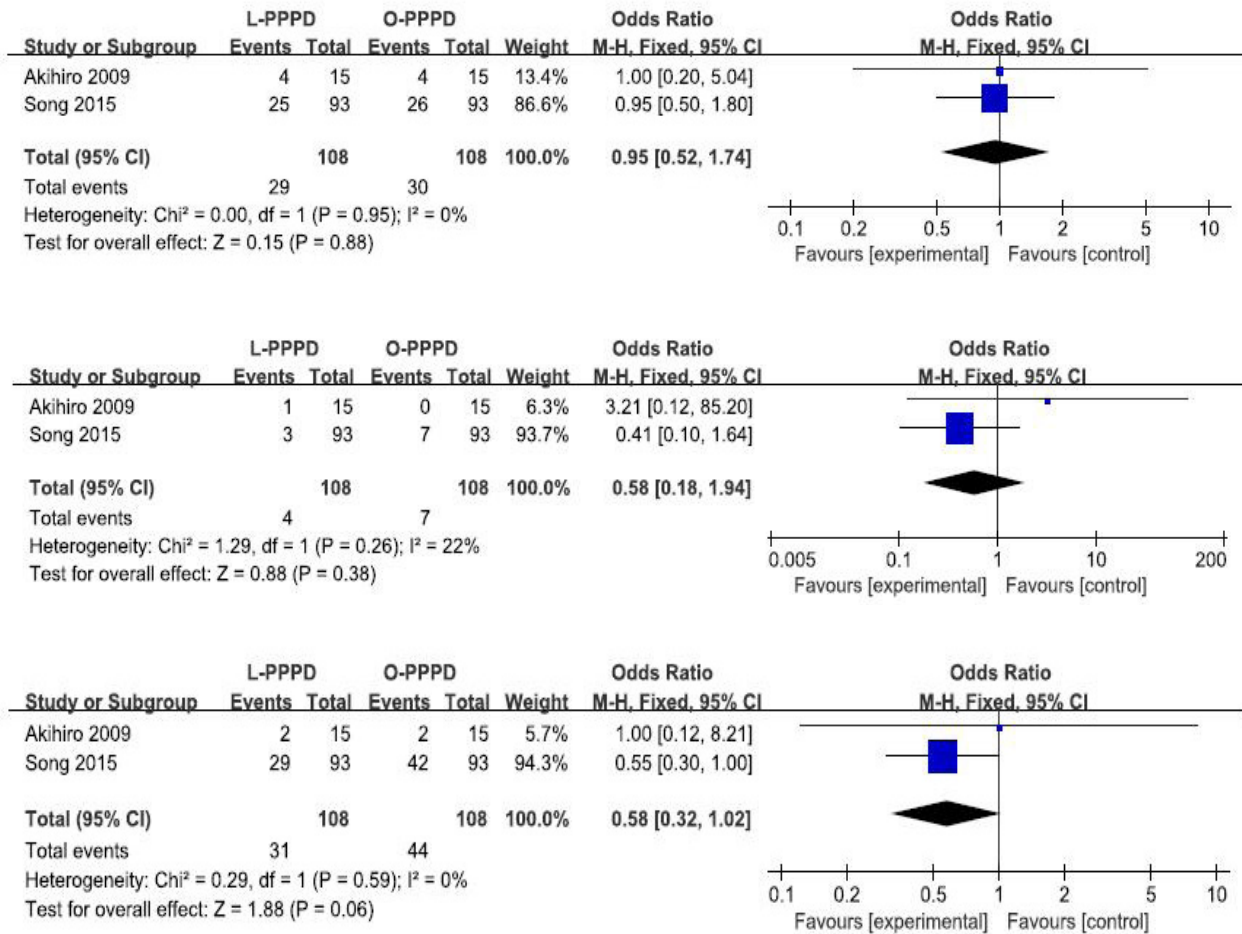


Figure 5 - Postoperative complication and pancreatic fistula and DGE comparing L-PPPD versus O-PPPD. 95% CI and df.

Discussion

Technological progress in recent decades has brought about great development of laparoscopic techniques. However, PD still remains a arduous challenge and since when Gagner performed the first laparoscopic PD. Although laparoscopy has the visual advantage of a magnified view, it is still a time-consuming surgery because of the procedural complexities, such as difficulties in exposing the retroperitoneal spaces, control blood loss or the major vasculature, and complex suture techniques¹². In addition, some meta-analysis studies¹²⁻¹⁵ that laparoscopic

PD compared to open surgery had shown extremely long operating time in the absence of significant benefits and a similar safety, feasibility. Meanwhile, pylorus-preserving pancreatoduodenectomy could improve the quality of life and reduce the incidence of anastomotic complications in postoperative patients compared to traditional PD. However, the outcomes of literature discussed L-PPPD and O-PPPD are not in complete accord, even in opposite, such as blood loss^{8,11}. To the best of our knowledge, this is the first meta-analysis that compares these two. It included 216 patients, 108 (50%) of which underwent L-PPPD and 108 (50%) of which underwent O-PPPD.

In sum, our meta-analysis did not detect any statistically significant differences in incidence of postoperative pancreatic fistula, time of diet start, lymph nodes major morbidity, blood loss. L-PPPD showed a statistically significant reduced hospital length of stay.

The main disadvantage of L-PPPD was the duration of operation caused to inefficiency. The longer operative time was related to multiple reasons, including the longer learning curve, difficulty in accessing and exposure of the pancreas, a technically demanding reconstruction of the biliary and pancreatic remnants, hemorrhage control from major vasculature¹³. Some articles hold that intraoperative blood loss was lower during laparoscopic than open. This is often attributed to the magnified view supplied by laparoscopy which opens the surgeon's eyes of the structures surrounding the specimen, allowing precise resection along appropriate levels^{2,13,16}. But those with expected bleeding or difficulty in surgery were directly decided to receive an open PD during preoperative assessment, which obviously led to selection bias. Our meta-analysis doesn't show an optimistic point on blood loss maybe due to the long learning curve and early-period group of L-PPPD may be more easy to blood loss as a result of inexperience. Despite the advances in surgical technique, pancreatic resection is still associated with a high level of morbidity because of pancreatic fistula and delayed gastric emptying. No clinically significant advantages in the L-PPPD had showed either in the early or late period. DGE tended to be decreased in L-PPPD because laparoscopic surgery reduced the frequency of surgical-site infections and occurrence of postoperative adhesion¹⁷. Although long-term oncologic outcomes are not addressed in these studies, lymph node retrieval are used as indicators of the oncologic adequacy of laparoscopic surgery. Lymph node staging is a very relevant prognostic factor for pancreatic

cancer patients. However, it is depressed that there was no obvious difference in these two. Our meta-analysis showed L-PPPD has a shorter length of stay. A short hospital stay theoretically can reduce the pain of the patients and expense of the whole treatment but minimally invasive surgery is known to be associated with higher intraoperative costs. The cost-effectiveness of L-PPPD is worth considering.

The advantage of this review is that it provides a comprehensive comparison of L-PPPD with O-PPPD. To our knowledge, this meta-analysis is the first to explore these two using matched case controlling the age, BMI, ASA, et al. Of course, this meta-analysis has some limitations, which must be worth to note. First, there were no RCT and selection bias could be a big problem because of the retrospective matched cases such as the choice of patients, the assessment of complication such as pancreatic fistula, delayed gastric emptying. Second, the small number of patients and studies decreased the reliability although we had searched several databases. The quantity of this study was not large enough, and the results need more effective evidence in further high-quality trials. Moreover, high statistical heterogeneity was found among included studies, which even reached 90% for some parameters limiting the quality of results. Furthermore, we did not analyze the surgical technique such as types of pancreatic and biliary anastomoses, which must influence the complication. And we didn't discuss the prognosis and long-term complications about L-PPPD and O-PPPD.

■ Conclusions

This meta-analysis reveals the laparoscopic pylorus-preserving pancreaticoduodenectomy (L-PPPD) has minimal invasion and shorter hospital stay while the operative time may prolong.

The time of diet start, postoperative complications, lymph nodes have no significant difference. Laparoscopic pylorus-preserving pancreaticoduodenectomy can be a reasonable alternative to open pylorus-preserving pancreaticoduodenectomy with potential advantages once the operators grasp the points of laparoscopic skills. However, blind pursuits of L-PPPD should be restrained because of the long learning curve and cost-effectiveness.

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