The effect of preoperative biliary stents on outcomes after pancreaticoduodenectomy

A meta-analysis

Lei Gong, MD, Xin Huang, MD, Liang Wang, MD, Canhong Xiang, MD∗

Abstract

Background: Whether biliary drainage should be performed before surgery in jaundiced patients is a topic of debate. Published studies on the effect of preoperative biliary drainage show great discrepancies in their conclusions, and the use of different drainage methods is an important factor. The aim of the present study was to investigate the effect of preoperative biliary stents (PBS) on postoperative outcomes in patients following pancreaticoduodenectomy (PD).

Methods: MEDLINE, EMBASE, Science Citation Index Expanded, and the Cochrane database were searched up to October 2019 to identify all published articles related to the topic. A meta-analysis was performed to compare postoperative outcomes in patients with and without PBS. Quality assessment and data extraction from included studies were performed by 2 independent authors. Statistical analysis was performed using RevMan 5.2 software.

Results: Twenty-seven studies involving 10,445 patients were included in the analysis. Biliary drainage was performed in 5769 patients (PBS group), and the remaining 4676 patients underwent PD directly (direct surgery [DS] group). Overall mortality, severe complications, abdominal hemorrhage, bile leakage, intra-abdominal abscess, and pancreatic fistula were not significantly different between the PBS and DS groups. However, overall morbidity, delayed gastric emptying, and wound infection were significantly higher in the PBS group compared to the DS group. Subgroup analysis indicated that the adverse effect of PBS on postoperative complications was more evident with increased stent proportion.

Conclusions: Preoperative biliary stenting increases overall morbidity, delayed gastric emptying, and wound infection rates in patients following PD. Thus, preoperative biliary drainage via stent placement should be avoided in patients waiting for PD.

Abbreviations: CI = confidence interval, DGE = delayed gastric emptying, DS = direct surgery, ENBD = endoscopic nasobiliary drainage, ERCP = endoscopic retrograde cholangiopancreatography, IAA = intra-abdominal abscess, OR = odds ratio, PBD = percutaneous biliary drainage, PBS = preoperative biliary stents, PD = pancreaticoduodenectomy, PTBD = percutaneous transhepatic biliary drainage, PTC = percutaneous transhepatic cholangiography, RCT = randomized controlled trial.

Keywords: complications, meta-analysis, pancreaticoduodenectomy, preoperative biliary drainage, stent

1. Introduction

Pancreaticoduodenectomy (PD) is a common procedure for the treatment of pancreatic head cancer, distal cholangiocarcinoma, and periampullary tumors. The postoperative morbidity and mortality rates of PD are still high with current techniques, and obstructive jaundice has been considered as an important risk factor influencing outcomes.1–2 Biliary obstruction alters the physiological circulation of bile acid and affects multiple tissues and organs, leading to bacterial translocation and a systemic inflammatory response.3–5 The use of preoperative biliary drainage (PBD) has been shown to reverse these pathological changes and improve postoperative outcomes in experimental and clinical studies.6–8 However, performing biliary drainage before surgery with curative intent in jaundiced patients is still a controversial topic in clinical practice. Some studies support the application of PBD for the decreased incidence of postoperative complications.7–9 On the other hand, some studies have reported that the incidence of postoperative complications does not decrease with the reduction of serum bilirubin by PBD, especially in patients undergoing PD.10–12 Iacono et al13 concluded that middle-distal obstruction in patients who are candidates for PD does not usually require routine biliary drainage.

The reason why some studies support the use of PBD, whereas others do not may be due to the use of different drainage
methods. Currently, PBD can be accomplished either internally or externally, including biliary stents, percutaneous transhepatic biliary drainage (PTBD), and endoscopic nasobiliary drainage (ENBD). Recent studies have shown that the drainage-related perioperative complications vary among different PBD methods. Therefore, analysis of a single PBD method is recommended in further investigations. Although conclusions about the effect of PBD on surgical outcome after PD have been made by many meta-analyses, none of them have clearly determined the effect of biliary stents. In this meta-analysis, we attempted to clarify the effect of preoperative biliary stents (PBS) on surgical outcome and included studies that made use of PBS in patients undergoing PD to come to a reliable conclusion.

2. Materials and methods

2.1. Search strategy and study selection

A search was conducted in MEDLINE, EMBASE, Science Citation Index Expanded, and the Cochrane database until October 2019 using the terms “preoperative biliary drainage,” “stent,” “pancreaticoduodenectomy,” “complication,” “outcome,” and combinations of these words. English language studies comparing complications after PD between patients with biliary stents and those without drainage were included in this study. The exclusion criteria were: surgery other than PD and percentage of stent placement in the drainage group < 90%. If data were duplicated from the same research group, the most recent publication was selected. The included studies were reviewed independently by 2 reviewers and group discussion held to settle disagreements. Ethical approval was not applicable for this meta-analysis.

2.2. Data extraction

Relevant data concerned with outcomes were collected by 2 reviewers, using a standardized form designed for data abstraction. Data included study group, year, country, study design, number of cases, type of biliary drainage, overall postoperative mortality and morbidity, incidence of postoperative severe complications (Clavien-Dindo classification grade III or more), abdominal hemorrhage, bile leakage, delayed gastric emptying (DGE), intra-abdominal abscess (IAA), pancreatic fistula, and wound infection.

2.3. Quality assessment

The quality of each study was evaluated according to the Newcastle-Ottawa Scale designed for non-randomized studies. Each study was analyzed in accordance with the following standards: selection and comparability of study groups and ascertainment of the outcomes. Complications were defined according to the International Study Group of Pancreatic Surgery. The assessment of each study was accomplished independently by two authors.

2.4. Statistical analysis

RevMan 5.2 was used for the meta-analysis. All measured data were categorical variables. Heterogeneity was calculated by the $\chi^2$ test. The $I^2$ value was also used to evaluate the heterogeneity ($I^2 = 0\%–50\%, \text{no or moderate heterogeneity} ; I^2 > 50\%, \text{significant heterogeneity}$). The fixed-effect model was used if there was no significant heterogeneity; otherwise the random-effect model was used. Results were expressed as forest plots and summarized with odds ratios (ORs) and 95% confidence intervals (CIs). A 2-sided $P$ value < 0.05 was considered to indicate significance.

3. Results

3.1. Search results

The present study followed the guidelines for systematic review and meta-analysis (PRISMA). As shown in Figure 1, we...
retrieved a total of 298 records from the electronic search. After screening titles and abstracts, 266 articles were excluded because of review articles, irrelevant publications, and overlapping studies. Thirty-two publications that met the inclusion criteria were fully reviewed with the full article, including five articles subsequently excluded because of <90% stent placement in the drainage group. Finally, 27 studies were selected for the present meta-analysis.

### 3.2. Description of included studies

The eligible studies were published between 1998 and 2019. One article was a randomized controlled trial (RCT) and 26 articles were retrospective studies. All the included articles were eligible for synthesized meta-analysis after quality assessment. The percentage of patients with stent placement in the drainage group was ≥90% in each included study. A total of 10,445 patients were included, PBD was applied in 5769 patients (PBS group), and the remaining 4676 patients underwent PD directly (direct surgery [DS] group). All patients successfully underwent standard Whipple’s operation or pylorus-preserving PD. Subgroup analysis was performed based on the proportion of stent placement in the PBS group (Stent-100: all patients received biliary stents; Stent-90: the proportion was ≥90% but <100%). Table 1 summarizes the characteristics of the included clinical studies. Table 2 shows the results of pooled ORs and heterogeneity in the meta-analysis. Publication bias was observed in terms of overall morbidity, severe complications, IAA, pancreatic fistula, and wound infection.

### 3.3. Overall mortality

Twenty-five studies reported the difference in overall mortality between patients with and without biliary drainage. Meta-analysis of these studies did not show any significant difference in overall mortality between the two groups (OR 0.95, 95% CI 0.73–1.24; P = .72). The results of the subgroup analysis were similar in accordance with the total effect. (See supplemental Figure 1, http://links.lww.com/MD/F16. Forest plot of overall mortality).

### 3.4. Overall morbidity

Twenty-three studies reported the difference in overall morbidity between patients with and without biliary drainage (Fig. 2). The postoperative morbidity rate ranged from 19.5% to 63.3% in the DS group and 27.1% to 73.0% in the PBS group. The overall morbidity rate was significantly higher in the PBS group than the DS group (OR 1.22, 95% CI 1.05–1.42; P = .01). The Stent-100 subgroup analysis also showed a significant difference between the two groups (OR 1.29, 95% CI 1.08–1.53; P = .005), but no significant difference was observed in the Stent-90 subgroup analysis. However, there was significant heterogeneity among the included studies (Total: P = .001, I² = 54%; Stent-100: P = .004, I² = 53%).

### 3.5. Severe complications

Only 6 studies reported a difference in severe postoperative complications. Unlike overall morbidity, no significant difference was observed in severe complications between patients with and without biliary drainage (OR 1.00, 95% CI 0.74–1.35; P = 1.00).

Subgroup analysis was not performed due to an insufficient number of included studies. Nevertheless, heterogeneity was still significant among the 6 studies (P = .06, I² = 53%). (See supplemental Figure 2, http://links.lww.com/MD/F16. Forest plot of severe complications).

### 3.6. Abdominal hemorrhage

Fifteen studies reported the difference in terms of abdominal hemorrhage between patients with and without biliary drainage. No significant difference was observed between the 2 groups (OR 0.95, 95% CI 0.76–1.19; P = .66). The results of the subgroup analysis were similar to those for the total effect. (See supplemental Figure 3, http://links.lww.com/MD/F16. Forest plot of abdominal hemorrhage).

### 3.7. Bile leakage

Seventeen studies reported the difference in terms of bile leakage between patients with and without biliary drainage. No significant difference was observed between the 2 groups (OR 0.88, 95% CI 0.67–1.15; P = .36). The results of the subgroup analysis were similar to those for the total effect. (See supplemental Figure 4, http://links.lww.com/MD/F16. Forest plot of bile leakage).

### 3.8. Delayed gastric emptying

The incidence of postoperative DGE was reported in 18 studies (Fig. 3). The meta-analysis showed that the incidence of DGE was significantly higher in the PBS group than the DS group (OR 1.21, 95% CI 1.03–1.42; P = .02). The Stent-100 subgroup analysis also showed a significant difference between the 2 groups (OR 1.29, 95% CI 1.06–1.58; P = .01). No significant difference was observed in the Stent-90 subgroup analysis.

### 3.9. Intra-abdominal abscess

Nineteen studies were included in the IAA analysis. The meta-analysis showed no significant difference in postoperative IAA between patients with and without biliary drainage (OR 1.06, 95% CI 0.67–1.66; P = .81). The results of the subgroup analysis were similar to those for the total effect. The heterogeneity test for subgroup differences was significant (P = .05, I² = 73.1%). (See supplemental Figure 5, http://links.lww.com/MD/F16. Forest plot of intra-abdominal abscess).

### 3.10. Pancreatic fistula

The incidence of postoperative pancreatic fistula was compared between patients with and without biliary drainage in 21 studies. No significant difference was found between the 2 groups (OR 1.05, 95% CI 0.83–1.33; P = .66). The results of the subgroup analysis were similar to those for the total effect. The heterogeneity test for subgroup differences was significant (P = .03, I² = 78.7%). (See supplemental Figure 6, http://links.lww.com/MD/F16. Forest plot of pancreatic fistula).

### 3.11. Wound infection

The incidence of postoperative wound infection was reported in 23 studies (Fig. 4). The overall wound infection rate in
| No. | Study                          | Year | Country       | Study type | No. of outcomes | Group | Sample size | Age | Male | PBD methods                      |
|-----|-------------------------------|------|---------------|------------|----------------|-------|-------------|-----|------|----------------------------------|
| 1   | Abdullah et al [22]           | 2009 | Singapore     | Retro.     | 7              | DS    | 47          | 62 (38–84) | 55%  | PBS: ERCP 94%; PBD without stents: 6% |
| 2   | Agalianos et al [23]          | 2016 | Greece        | Retro.     | 6              | DS    | 70          | NA            | NA   | PBS: ERCP 100%                     |
| 3   | Arkadopoulos et al [24]       | 2014 | Greece        | Retro.     | 8              | DS    | 76          | 56 ± 11        | 59%  | PBS: ERCP 100%                     |
| 4   | Barnett and Collier [24]      | 2006 | Australia     | Retro.     | 3              | DS    | 52          | NA            | NA   | PBS: ERCP 100%                     |
| 5   | Bhati et al [25]              | 2007 | India         | Retro.     | 5              | DS    | 27          | 48 (30–72)     | 56%  | PBS: ERCP 100%                     |
| 6   | Cavell et al [26]             | 2013 | USA           | Retro.     | 6              | DS    | 289         | 65 (19–88)     | 52%  | PBS: ERCP 100%                     |
| 7   | De Pastena et al [27]         | 2018 | Italy         | Retro.     | 8              | DS    | 786         | 66 (58–72)     | 59%  | PBS: ERCP 100%                     |
| 8   | El Nakeeb et al [28]          | 2018 | Egypt         | Retro.     | 9              | DS    | 274         | NA            | NA   | PBS: ERCP 100%                     |
| 9   | Gavazzi et al [29]            | 2016 | Italy         | Retro.     | 8              | DS    | 90          | NA            | 56%  | PBS: ERCP 91%; PBD without stents: 9% |
| 10  | Heslin et al [30]             | 1998 | USA           | Retro.     | 5              | DS    | 35          | 62 ± 2         | 69%  | PBS: ERCP 87%, PTC 13%             |
| 11  | Hodul et al [31]              | 2003 | USA           | Retro.     | 7              | DS    | 58          | 64 ± 10        | 57%  | PBS: ERCP 91%, PTC 9%              |
| 12  | Huang et al [32]              | 2015 | China         | Retro.     | 9              | DS    | 170         | 57.8 ± 8.6     | 67%  | PBS: ERCP 100%                     |
| 13  | Japannath et al [33]          | 2005 | India         | Retro.     | 7              | DS    | 70          | 50             | 69%  | PBS: ERCP 100%                     |
| 14  | Lermite et al [34]            | 2008 | France        | Retro.     | 8              | DS    | 28          | 64.4 ± 9.5     | 61%  | PBS: ERCP 100%                     |
| 15  | Marcus et al [35]             | 1998 | USA           | Retro.     | 7              | DS    | 30          | 71.5 ± (45–89) | 63%  | PBS: ERCP 100%                     |
| 16  | Martignoni et al [36]         | 2001 | Switzerland   | Retro.     | 6              | DS    | 158         | 64 ± 18–87     | 54%  | PBS: ERCP and PTC 90%; PBD without stents: 10% |
| 17  | Mezhir et al [37]             | 2009 | USA           | Retro.     | 5              | DS    | 94          | 69 ± 10        | 50%  | PBS: ERCP 89%, PTC 11%             |
| 18  | Mullen et al [38]             | 2005 | USA           | Retro.     | 7              | DS    | 92          | 68 ± 10        | 51%  | PBS: ERCP 100%                     |
| 19  | Ng et al [39]                 | 2017 | Australia     | Retro.     | 2              | DS    | 21          | 64             | 45%  | PBS: ERCP 100%                     |
| 20  | Peliková et al [40]           | 2005 | Czech Republic| Retro.     | 2              | DS    | 160         | 53.2           | NA   | PBS: ERCP 100%                     |
| 21  | Sahora et al [41]             | 2016 | USA           | Retro.     | 9              | DS    | 500         | 61 ± 13        | 47%  | PBS: ERCP 97%; PBD without stents: 3% |
| 22  | Shaib et al [42]              | 2017 | Northern America| Retro. | 3              | DS    | 503         | 66.4 ± 10.1    | 54%  | PBS: ERCP 100%                     |
| 23  | Sohn et al [43]               | 2000 | USA           | Retro.     | 7              | DS    | 159         | 61.4 ± 1.2     | 49%  | PBS: ERCP 36%, PTC 64%             |
| 24  | van der Gaag et al [44]       | 2010 | Netherlands   | RCT        | 8              | DS    | 94          | 64.7 ± 9.5     | 70%  | PBS: ERCP and PTC 94%; PBD without stents: 6% |
| 25  | Velanovich et al [45]         | 2009 | USA           | Retro.     | 4              | DS    | 58          | NA            | NA   | PBS: ERCP 93%, PTC 7%              |
| 26  | Wu et al [46]                 | 2019 | Taiwan        | Retro.     | 3              | DS    | 662         | 60.4 ± 13.5    | 52%  | PBS: ERCP 70%, PTC 30%             |
| 27  | Yanagimoto et al [47]         | 2014 | Japan         | Retro.     | 8              | DS    | 73          | 67 (33–90)     | 57%  | PBS: ERCP 95%; PBD without stents: 5% |

**Legend:** DS = direct surgery, ERCP = endoscopic retrograde cholangiopancreatography, NA = not available, PBD = preoperative biliary drainage, PBS = preoperative biliary stenting, PTC = percutaneous transhepatic cholangiography, RCT = randomized controlled trial, Retro. = retrospective.
patients with and without biliary drainage was 14.9% and 8.1%, respectively. The meta-analysis showed a significantly higher wound infection rate in the PBS group than the DS group (OR 2.06, 95% CI 1.69–2.52; P < .00001). The same effect was observed in the subgroup analysis (Stent-100: OR 2.08, 95% CI 1.68–2.58, P < .00001; Stent-90: OR 1.77, 95% CI 1.05–2.97, P = .03). Significant heterogeneity was found in the Stent-90 subgroup analysis (P = .05, I² = 54%).

### 4. Discussion

The results of this meta-analysis showed that PBD performed with biliary stents significantly increased the incidence of postoperative morbidity, DGE, and wound infection in patients undergoing PD. However, the overall mortality, severe complications, abdominal hemorrhage, bile leakage, IAA, and pancreatic fistula rates were not significantly different between patients with and without PBS. Subgroup analyses provided some interesting results. Great discrepancies were found between subgroup and total effects in the analysis of overall morbidity and DGE. The overall morbidity and DGE rates were significantly higher in the PBS group than the DS group according to the Stent-100 subgroup analysis. However, the rates were not significantly different in the Stent-90 subgroup analysis. Heterogeneity was also significant for subgroup differences in the analysis of IAA and pancreatic fistula. The adverse effect of PBS on postoperative complications seemed to be more remarkable with an increased proportion of stent placement. Therefore, the application of PBS did not result in clear benefits to patients, but it increased postoperative complications in patients undergoing PD. PBS should not be used conventionally in patients waiting for PD unless there is a definite indication for stent placement.

PBD currently includes internal and external drainage methods. Biliary stents, an internal drainage method, can be placed by either endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC). External drainage methods include PTBD and ENDB. Different approaches result in varied outcomes. Kitahata et al.\(^{[14]}\) compared perioperative complications between patients with internal drainage and external drainage methods and concluded that the incidence of preoperative cholangitis and severe postoperative complications were significantly higher in the internal drainage group than the external drainage group. There was also an investigation comparing PTBD with biliary stenting.

### Table 2

Summary of pooled odds ratios and heterogeneity in the meta-analysis.

| Outcome                  | No. of studies | PBS | DS | Pooled odds ratio | Z   | P   | I²  | P   |
|--------------------------|----------------|-----|----|-------------------|-----|-----|-----|-----|
| Mortality                | 19             | 17  | 86 | 0.71              | .48 | .33 | 11% |
| Morbidity                | 18             | 86  | 107| 1.23              | 2.28| .06 | .52 | .0% |
| Abdominal hemorrhage     |                |     |    |                   |     |     |     |     |
| Stent-100                | 9              | 155 | 130| 0.96              | 0.73| .36 | .41 | .0% |
| Stent-90                 | 6              | 44  | 37 | 0.93              | 1.24| .32 | .75 | .0% |
| Severe complications     |                |     |    |                   |     |     |     |     |
| Stent-100                | 12             | 15  | 121| 0.90              | 0.67| .36 | .45 | .0% |
| Stent-90                 | 6              | 37  | 38 | 0.93              | 1.24| .32 | .75 | .0% |
| Bile leakage             |                |     |    |                   |     |     |     |     |
| Stent-100                | 12             | 15  | 121| 0.90              | 0.67| .36 | .45 | .0% |
| Stent-90                 | 6              | 37  | 38 | 0.93              | 1.24| .32 | .75 | .0% |
| Severe complications     |                |     |    |                   |     |     |     |     |
| Stent-100                | 12             | 15  | 121| 0.90              | 0.67| .36 | .45 | .0% |
| Stent-90                 | 6              | 37  | 38 | 0.93              | 1.24| .32 | .75 | .0% |
| DGE                      |                |     |    |                   |     |     |     |     |
| Stent-100                | 12             | 15  | 121| 0.90              | 0.67| .36 | .45 | .0% |
| Stent-90                 | 6              | 37  | 38 | 0.93              | 1.24| .32 | .75 | .0% |
| IAA                      |                |     |    |                   |     |     |     |     |
| Stent-100                | 14             | 183 | 229| 1.32              | 2.22| .05 | .001| 72% |
| Stent-90                 | 5              | 76  | 55 | 0.70              | 1.02| .86 | .65 | .0% |
| Pancreatic fistula       |                |     |    |                   |     |     |     |     |
| Stent-100                | 15             | 424 | 394| 1.24              | 1.60| .11 | .66 | 40% |
| Stent-90                 | 6              | 149 | 132| 0.72              | 1.09| .56 | .12 | 39% |
| Wound infection          |                |     |    |                   |     |     |     |     |
| Stent-100                | 17             | 233 | 664| 2.08              | 2.58| .06 | .0001| 25% |
| Stent-90                 | 6              | 91  | 161| 1.77              | 2.09| .03 | .05 | 54% |
| Total                    | 23             | 324 | 825| 2.06              | 2.52| 7.13| .0001| 27% |

DGE = delayed gastric emptying, DS = direct surgery, IAA = intra-abdominal abscess, PBS = preoperative biliary stenting.
stents that found that PTBD could rapidly decompress biliary obstruction with a lower frequency of drainage-related complications.\cite{44} Different results were also obtained between plastic and metal stents, even if using the same approach. For example, Wasan et al\cite{45} showed that metal stents could reduce the occurrence of cholangitis and postoperative complications compared to plastic stents in patients with surgically resectable pancreatic cancer. Therefore, combined analysis of different PBD methods can increase the uncertainty of conclusions in related studies. This kind of conclusion conceals the real effect of each PBD method on outcomes and misleads on the clinical use of biliary drainage. Another reason why the reported results are distinct is that the surgical approaches are different in the same study or meta-analysis. Thus, the analysis of a single PBD method with similar types of operations is recommended. However, many published studies on the issue have ignored these points. Some meta-analyses included both internal and external drainage methods.\cite{1,46} Some meta-analyses analyzed the effect of PBS on patients with obstructive jaundice, but the proportion of stent placement or surgical procedures varied, resulting in discrepancies in the conclusions.\cite{47,48} In the studies included in the present meta-analysis, biliary stenting by ERCP or PTC was the major PBD method. There was no significant difference in complications between ERCP and PTC ways.\cite{40,43} The exclusion criterion regarding the proportion of stented patients in the drainage group was intended to reduce selection bias. Similarly, only patients undergoing PD were included in this meta-analysis. Subgroup analysis was also introduced for the potential discrepancy among included studies. The threshold percentage of stented patients was set to 90% and 100% to ensure a sufficient number of studies and low heterogeneity in the subgroup analysis. Under these circumstances, the conclusions of the present meta-analysis were more convincing.

Although the postoperative overall morbidity rate was high in patients with stent placement, the incidence of severe complications did not increase in the PBS group. The overall morbidity rate was significantly different in the Stent-100 subgroup analysis but was not significantly different in the Stent-90 subgroup analysis. Subgroup analysis was not performed in terms of severe complications.

Figure 2. Forest plot of overall morbidity.
complications due to the low number of included studies. Heterogeneity was significant in the analysis of overall morbidity and severe complications. However, the test for subgroup differences showed moderate heterogeneity. The possible reasons for the high level of heterogeneity in terms of overall morbidity and severe complications were the long time span and different definitions of complications in the included studies. These factors increased selection bias, which could not be solved by the meta-analysis. Among the included studies, the only RCT was published in 2010 and the percentage of stent placement in the drainage group was 94%.[21] This clinical trial reported that the rate of surgery-related complications was 37% in the early surgery group and 47% in the biliary drainage group, but the difference was not significant. Thus, the real effect of PBS on postoperative overall morbidity is still unclear. More RCTs with high-quality designs are needed.

DGE is a common complication following PD, with a reported incidence of up to 44%. [49] The occurrence of DGE prolongs the duration of hospital stays and increases hospital costs. Many studies have investigated the risk factors for the occurrence of postoperative DGE. Independent risk factors for the development of DGE include retrocolic gastro-jejunostomy, diabetes, the presence of complications, pancreatic reconstruction type, and severity of pancreatic fistula. [49] Eisenberg et al analyzed a total of 721 patients undergoing PD and found that DGE was a frequent secondary complication to abdominal infection. They suggested that reducing abdominal infectious complications is probably an effective strategy for avoiding the occurrence of DGE.[30] Most studies investigating how to reduce the incidence of DGE have focused on surgical planning or styles, such as subtotal stomach-preserving PD or resection of the antrum.[51,52] Although PBS has not been recognized as a risk factor for postoperative DGE, the use of PBS did significantly increase the incidence of DGE in patients undergoing PD in the present meta-analysis. A possible explanation is that the occurrence of DGE is secondary to the increased complications resulting from preoperative stent placement.

Most relevant studies support biliary stents increasing the incidence of postoperative infectious complications, such as wound infection and IAA. There is conclusive evidence supporting the association between wound infection and biliary stents. Studies have shown that the microorganisms found in intraoperative bile cultures strongly correlate with the bacteria in infected wounds.[31,38,53] For example, Sahora et al retrospectively analyzed a large series of patients and reported that the presence of Citrobacter spp. and Enterobacter spp. in bile culture significantly increased the incidence of wound infection in stented patients.[38] Gavazzi et al analyzed a total of 180 patients to
investigate the risk factors for wound infection after PD; multivariate analysis revealed that biliary stents significantly increased the incidence of wound infection, and Enterococcus spp., Escherichia coli, and Klebsiella spp. were the most frequent bacteria in bile culture.[29] In the present study, we found almost twice as many wound infections in the PBS group than the DS group, which is similar to other studies.[38,54] Besides wound infection, the occurrence of IAA was also reported to be related to PBS. Three studies concluded that postoperative IAA and the total infectious complication rates were significantly higher in patients with biliary stents.[10,12,43] However, most published articles did not confirm the association between IAA and PBS. For example, the included RCT reported that the incidence of preoperative cholangitis in the drainage group was 13-times as high as that of the DS group. In contrast, the incidence of postoperative IAA did not show any differences between the 2 groups.[21] Meanwhile, a review concluded that the use of PBS increased the wound infection rate but not the IAA rate.[35] In the present study, the incidence of postoperative IAA was not significantly different between the 2 groups.

Pancreatic fistula is an important complication after PD. The development of pancreatic fistula may cause subsequent complications, and even death. Some studies have observed that patients with PBS experience higher pancreatic fistula rates than patients undergoing DS.[40,53] However, the incidence of pancreatic fistula after PD was not significantly influenced by PBS in the present meta-analysis, and PBS has not been recognized as a risk factor for pancreatic fistula after PD. The risk factors for pancreatic fistula include being male, body mass index >25 kg/m², pancreatic duct-jejunum double-layer mucosa-to-mucosa pancreaticojejunal anastomosis, pancreatic duct diameter ≤3 mm, and soft pancreas.[56] In another article, univariate and multivariate analyses showed that preoperative cholangitis after PBS and a small pancreatic duct are closely associated with the development of pancreatic fistula.[42]

Although the use of PBS could increase preoperative cholangitis in patients waiting for surgery, there is no clear evidence to support the direct association between PBS and pancreatic fistula. Therefore, the effect of PBS on the occurrence of postoperative pancreatic fistula remains unclear.
An advantage of the present work is the analysis of a single PBD method and surgical style to reduce selection bias. The subgroup analysis based on the proportion of stent placement and analysis of severe complications are also strong points. The present analysis also has limitations that should be taken into consideration. First, this analysis included both RCTs and retrospective studies. The quality of most included studies was not high. Not every outcome was reported in the included studies. Second, heterogeneity was high among the included studies, possibly due to different definitions of complications, ways of stent placement, stent types and materials. Third, some relevant data, such as stent-related complications, drainage interval and postoperative hospital stay, were not included in this study. Therefore, RCTs using standardized assessments, a single preoperative drainage method, and limited surgical procedures are needed.

In conclusion, the use of PBS can increase postoperative complications, and it is not routinely recommended for use in patients waiting for PD. None of the biliary drainage method is widely accepted, and the optimal approach and drainage duration need to be investigated in future clinical trials.

**Author contributions**

Conceptualization: Canhong Xiang.

Data curation: Lei Gong, Liang Wang.

Formal analysis: Lei Gong, Xin Huang.

Methodology: Liang Wang, Canhong Xiang.

Software: Lei Gong, Liang Wang.

Validation: Xin Huang.

Visualization: Xin Huang.

Writing – original draft: Lei Gong, Xin Huang.

Writing – review & editing: Canhong Xiang.

**References**

[1] Moole H, Bechtold M, Puli SR. Efficacy of preoperative biliary drainage in malignant obstructive jaundice: a meta-analysis and systematic review. World J Surg Oncol 2016;14:182.

[2] Dixon JM, Armstrong CP, Duffy SW, et al. Factors affecting mortality and morbidity after surgery for obstructive jaundice. Gut 1994;25:104.

[3] Nehez L, Anderson R. Compromise of immune function in obstructive jaundice. Eur J Surg 2002;168:315–28.

[4] Greve JW, Gouma DJ, Buurman WA. Complications in obstructive jaundice: role of endotoxins. Scand J Gastroenterol Suppl 1992;156:19.

[5] Kimmings AN, van Deventer SJ, Obertop H, et al. Inflammatory and immunologic effects of obstructive jaundice: pathogenesis and treatment. J Am Coll Surg 1995;115:12–8.

[6] Gouma DJ, Coelho JC, Fisher JD, et al. Endotoxemia after relief of biliary obstruction by internal and external drainage in rats. Am J Surg 1996;174:57–81.

[7] Arakura N, Takayama M, Ozaki Y, et al. Efficacy of preoperative endoscopic nasobiliary drainage for hilar cholangiocarcinoma. J Hepatobiliary Pancreat Surg 2009;16:473–7.

[8] Lygidakis NJ, van der Heyde MN, Lubbers MJ. Evaluation of preoperative biliary drainage in the surgical management of pancreatic head carcinoma. Acta Chir Scand 1987;133:665–9.

[9] Huang X, Liang B, Zhao XQ, et al. The effects of different preoperative biliary drainage methods on complications following pancreatoduodenectomy. Medicine (Baltimore) 2015;94:e273.

[10] Arkadopoulos N, Kyriazi MA, Papanikolaou IS, et al. Preoperative biliary drainage of severely jaundiced patients increases morbidity of pancreatoduodenectomy: results of a case-control study. World J Surg 2014;38:2967–72.

[11] Hodul P, Creech S, Pickleman J, et al. The effect of preoperative biliary stenting on postoperative complications after pancreaticoduodenectomy. Am J Surg 2003;186:420–5.
[36] Ng ZQ, Suthananthan AE, Rao S. Effect of preoperative biliary stenting on post-operative infectious complications in pancreaticoduodenectomy. Ann Hepatobiliary Pancreat Surg 2017;21:212–6.

[37] Pesiková M, Gürlich R. Preoperative biliary drainage before pancreaticoduodenectomy in patients with obstructive jaundice. Eur Surg 2005; 37:331–5.

[38] Sahora K, Morales-Oyarvide V, Ferrone C, et al. Preoperative biliary drainage does not increase major complications in pancreaticoduodenectomy: a large single center experience from the Massachusetts General Hospital. J Hepatobiliary Pancreat Sci 2016;23:181–7.

[39] Shaib Y, Rahal MA, Rammal MO, et al. Preoperative biliary drainage for malignant biliary obstruction: results from a national database. J Hepatobiliary Pancreat Sci 2017;24:637–42.

[40] Sohn TA, Yeo CJ, Cameron JL, et al. Do preoperative biliary stents increase postpancreaticoduodenectomy complications? J Gastrointest Surg 2000;4:258–67. discussion 67–68.

[41] Velanovich V, Kheibek T, Khan M. Relationship of postoperative complications from preoperative biliary stents after pancreaticoduodenectomy. A new cohort analysis and meta-analysis of modern studies. JOP 2009;10:24–9.

[42] Yanagimoto H, Satos S, Yamamoto T, et al. Clinical impact of preoperative choledangiography after biliary drainage in patients who undergo pancreaticoduodenectomy on postoperative pancreatic fistula. Am Surg 2014;80:36–42.

[43] Wu JM, Ho TW, Yen HH, et al. Endoscopic retrograde biliary drainage causes intra-abdominal abscess in pancreaticoduodenectomy patients: an important but neglected risk factor. Ann Surg Oncol 2019;26:1086–92.

[44] Zhao XQ, Dong JH, Jiang K, et al. Comparison of percutaneous transhepatic biliary drainage and endoscopic biliary drainage in the management of malignant biliary tract obstruction: a meta-analysis. Dig Endosc 2015;27:137–45.

[45] Wasan SM, Ross WA, Stærkel GA, et al. Use of expandable metallic biliary stents in resectable pancreatic cancer. Am J Gastroenterol 2005;100:2036–61.

[46] Fang Y, Gurusamy KS, Wang Q, et al. Meta-analysis of randomized clinical trials on safety and efficacy of biliary drainage before surgery for obstructive jaundice. Br J Surg 2013;100:1589–96.

[47] Sun C, Yan G, Li Z, et al. A meta-analysis of the effect of preoperative biliary stenting on patients with obstructive jaundice. Medicine (Baltimore) 2014;93:e189.

[48] Scheufele F, Schorn S, Demir IE, et al. Preoperative biliary stenting versus operation first in jaundiced patients due to malignant lesions in the pancreatic head: a meta-analysis of current literature. Surgery 2017;161:939–50.

[49] El Nakeeb A, Askr W, Mahdy Y, et al. Delayed gastric emptying after pancreaticoduodenectomy. Risk factors, predictors of severity and outcome. A single center experience of 388 ases. J Gastrointest Surg 2015;19:1093–100.

[50] Eisenberg JD, Rosato EL, Lavu H, et al. Delayed gastric emptying after pancreaticoduodenectomy: an analysis of risk factors and cost. J Gastrointest Surg 2015;19:1572–80.

[51] Yamamoto Y, Ashida R, Ohgi K, et al. Combined antrectomy reduces the incidence of delayed gastric emptying after pancreaticoduodenectomy. Dig Surg 2018;35:121–30.

[52] Hanna MM, Galdle R, Tamariz L, et al. Delayed Gastric Emptying After Pancreatectoduodenectomy: Is Subtotal Stomach Preserving Better or Pylorus Preserving? J Gastrointest Surg 2015;19:1542–52.

[53] Morris-Stiff G, Tamijmarane A, Tan YM, et al. Pre-operative stenting is associated with a higher prevalence of post-operative complications following pancreatectoduodenectomy. Int J Surg 2011;9:145–9.

[54] Smith RA, Dajani K, Dodd S, et al. Preoperative resolution of jaundice following biliary stenting predicts more favourable early survival in resected pancreatic ductal adenocarcinoma. Ann Surg Oncol 2008; 15:3138–46.

[55] Schulick RD. Complications after pancreatectoduodenectomy: intra-abdominal abscess. J Hepatobiliary Pancreat Surg 2008;15:252–6.

[56] Hu BY, Wan T, Zhang WZ, et al. Risk factors for postoperative pancreatic fistula: analysis of 539 successive cases of pancreatectoduodenectomy. World J Gastroenterol 2016;22:7797–803.