The Impact of Preoperative Biliary Drainage on Postoperative Outcomes after Pancreaticoduodenectomy: A Single Center Retrospective Study

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Research

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Abstract

Background The effect of preoperative biliary drainage (PBD) on the short-term outcomes after pancreaticoduodenectomy (PD) remains controversial.

Methods 164 consecutive patients with obstructive jaundice who underwent PD in our center from 2016 to 2017 were retrospectively analyzed. The 120 patients who underwent PBD prior to PD (PBD group) were compared with 44 patients who did not (DS group). The short-term outcomes include overall morbidity, severe complications, postoperative pancreatic fistula(POPF), postpancreatectomy hemorrhage(PPH), intra-abdominal abscess (IAA), sepsis, delayed gastric emptying (DGE), postoperative hospital stay and 90-day death were assessed.

Results There were no significant statistical differences in overall morbidity, severe complications, POPF, PPH, IAA, LOS and ninety-day mortality between two groups. The incidence of DGE in PBD group was significantly lower than that in DS group (4.5% vs. 19.2%, $P = 0.021$). Multivariate regression analysis showed that age over 66 years (OR: 3.094, 95% CI: 1.268-7.55) and direct surgery (OR: 5.298, 95% CI: 1.176-23.865) were independent risk factors for DGE.

Conclusion For patients with obstructive jaundice, preoperative biliary drainage is independently associated with delayed gastric emptying, but does not affect the overall morbidity and mortality of patients undergoing PD.

Introduction

Periampullary carcinoma includes pancreatic head cancer, ampullary carcinoma, lower common bile duct cancer and duodenal papillary carcinoma. The most symptom is obstructive jaundice, with an incidence of 64–77% [1]. For periampullary carcinoma, the current standard operation is PD. PBD can relieve biliary obstruction, reverse the pathophysiological changes caused by hyperbilirubinemia, such as liver and kidney dysfunction, coagulation abnormality, immune system damage, and so on, thereby affecting the postoperative rehabilitation and long-term survival of patients. Early in 1935, Whipple first used the method of two-stage operation to treat patients with obstructive jaundice, that is, PD was performed in the second stage after the obstruction was relieved by Cholangiojejunostomy to reduce the postoperative complications and mortality. Henceforth, the concept of PBD has been widely accepted. A study based on SEER database in USA showed that the utilization of preoperative biliary stent placement doubled from 1992 to 2007 [2]. However, since the 21st century, with the continuous progress of surgical technology and perioperative management, more and more studies have shown that PBD could not benefit the patients, on the contrary, it can increase the postoperative complications [3–9]. But in clinical practice, there are still many situations that patients need PBD due to different reasons. Therefore, it is still controversial whether PBD should be recommended in patients with obstructive jaundice.

Methods

Patients

164 consecutive cases of PD in our center from 2016 to 2017 were retrospectively collected. The patients were divided into PBD group (n = 44) and direct DS group (n = 120) according to whether PBD was performed or not. The demographic characteristic perioperative parameters were extracted, including age, gender, comorbidity, operation time, blood loss, pathology, complications, length of hospital stay and ninety-day mortality.

PBD and surgical technique

Preoperative biliary drainage includes percutaneous transhepatic biliary drainage (PTBD) and endoscopic retrograde biliary drainage (ERBD) and endoscopic nasobiliary drainage (ENBD). PD was performed according to the standard procedure, including classic pancreaticoduodenectomy (PD) and pylorus preserving pancreaticoduodenectomy (PPPD). Retroperitoneal Lymphadenectomy was performed in all malignant tumors. In our center, Child method is performed for digestive tract reconstruction and the drainage was placed on the basis of the surgeon's habits.

Definition

Postoperative morbidity mainly include pancreatic fistula (POPF), postpancreatectomy hemorrhage (PPH), intra-abdominal abscess (IAA), sepsis, delayed gastric emptying (DGE). POPF, PPH and DGE were assessed according to International Study Group on Pancreatic Surgery (ISGPS) [10–12]. According to the Clavien-Dindo classification system [13], Clavien-Dindo grade III or higher were defined as major complication. Perioperative death was described as death during hospitalization or within 90 days after surgery.

Statistical analysis

Categorical variables were expressed as the number and percentage and compared using the chi-squared test or the Fisher's exact test as appropriate. Continuous variables were expressed as the mean and standard deviation and compared using the T-test. Univariate and multivariate analyses were performed to find the risk factors for major morbidity, by using the forward stepwise regression method of maximum likelihood estimation (forward: LR). The parameters which had a statistical significance of < 0.1 (indicating a tendency toward significance) in univariate analysis were included in a multiple logistic regression model. A two-tailed P-value less than 0.05 was considered statistically significant. All statistical analyses were performed by SPSS (version 25.0).

Results

Demographic and Clinical characteristics

A total of 164 consecutive patients were included in the study. The demographic data and clinical characteristics of the two groups are shown in Table 1. There was no statistical difference in average age

(PBD 61.8 ± 10.6 , DS 61.9 ± 8.8 , $P = 0.94$), gender (108 males, 58 females, $P = 0.56$), comorbidity (hypertension 22.7% in PBD group, 24.2% in DS group, $P = 0.848$; diabetes 18.2% in PBD group, 16.7% in DS group, $P = 0.819$). The total bilirubin (TB) before surgery in PBD group was significantly lower than that in DS group (PBD $125.9 \pm 109.5 \mu\text{mol/L}$, DS $250.6 \pm 124.1 \mu\text{mol/L}$, $P = 0.001$)

Table 1
Demographic and clinical characteristics

		PBD (n = 44)	DS (n = 120)	P
Age, years		61.8 ± 10.6	61.9 ± 8.8	0.94
Gender	male	30(68.2)	76(63.3)	0.56
	female	14(31.8)	44(36.7)	
BMI		22.4 ± 2.7	22.4 ± 3.5	0.9
Smoking history	yes	29(65.9)	87(72.5)	0.41
	no	15(34.1)	33(27.5)	
Drinking history	yes	28(63.6)	77(64.2)	0.95
	no	16(36.4)	43(35.8)	
ASA score	≤ 2	35(79.5)	103(85.8)	0.32
	3	9(20.5)	17(14.2)	
hypertension	yes	10(22.7)	29(24.2)	0.848
	no	34(77.3)	91(75.8)	
diabetes	yes	8(18.2)	20(16.7)	0.819
	no	36(71.8)	100(83.3)	
TB, $\mu\text{mol} / \text{L}$		125.9 ± 109.5	250.6 ± 124.1	0.001
ALB, U/L		39.4 ± 4.5	38.4 ± 3.6	0.128
ALT, U/L		77.8 ± 53.1	197.8 ± 124.7	0.001
AST, U/L		53.5 ± 27.5	129.9 ± 113.6	0.001
BMI, body mass index; ASA, American Society of Anesthesiologists; TB, total bilirubin; ALB, albumin; ALT, alanine Aminotransferase; AST, aspartate aminotransferase				

Surgical outcomes

The operation-related data are shown in Table 2. The operation methods were divided into standard PD and PPPD. PD was performed in 84.1% of PBD group, and that of DS group was 85.8%. There was no

significant difference between the two groups ($P = 0.9087$). The softness of pancreatic texture is an important factor causing postoperative pancreatic fistula. The ratio of soft pancreatic texture of the two groups were 86.4% and 85.8%, respectively, without significant difference ($P = 0.931$). There was no significant difference in vascular resection rate between the two groups (PBD 13.6%, DS 26.7%, $P = 0.08$). In addition, there was no significant difference in operation time (PBD 187 ± 68.8 min, DS 187 ± 68.8 min, $P = 0.309$) and intraoperative blood loss (PBD 485 ± 443 ml, DS 485 ± 443 ml, $P = 0.858$) between this two groups.

Table 2
Intraoperative data

		PBD (n = 44)	DS (n = 120)	P
Operation type	PPPD	7(15.9)	20(16.7)	0.908
	PD	37(84.1)	100(83.3)	
Pancreatic texture	soft	38(86.4)	103(85.8)	0.931
	hard	6(13.6)	17(14.2)	
Diameter of pancreatic duct, mm	≤ 2	3.75 ± 1.2	3.87 ± 1.3	0.599
	> 2			
Vascular invasion	yes	10(22.7)	44(36.7)	0.092
	no	34(77.3)	76(63.3)	
Vascular resection	yes	6(13.6)	32(26.7)	0.08
	no	38(86.4)	88(73.3)	
Operation time		$187. \pm 68.8$	177.9 ± 47.7	0.309
Intraoperative blood loss, ml		485 ± 443	501 ± 528	0.858

Postoperative outcomes

The comparison of postoperative complications is shown in Table 3. The incidence of overall morbidity in PBD group was 54.5%, and major complications 20.5%. DS group was 61.7% and 11.7% respectively, in the meanwhile. There was no significant difference in the overall morbidity and severe complications between the two groups ($P = 0.41$, 0.151 , respectively). The incidence of POPF was 31.8% in PBD group and 26.7% in DS group, with no significant difference ($P = 0.515$). There was no significant difference in PPH (PBD 25%, DS 17.5%, $P = 0.283$), IAA (PBD 36.4, DS 34.2%, $P = 0.793$), sepsis (PBD 11.4%, DS 6.7%, $P = 0.509$), postoperative hospital stay (PBD 19.5 days, DS 18.2 days, $P = 0.534$) and 90-day death (PBD

6.8%, DS 3.3%, $P = 0.588$). The incidence of DGE in PBD group was significantly lower than that in DS group PBD 4.5%, DS 19.2% ($P = 0.021$).

Table 3
Postoperative outcomes

		PBD (n = 44)	DS (n = 120)	P
Overall morbidity	yes	24(54.5)	74(61.7)	0.41
	no	20(45.5)	46(38.3)	
CD score	grade I-II	35(79.5)	106(88.3)	0.151
	≥ Grade III	9(20.5)	14(11.7)	
POPF	yes	14(31.8)	32(26.7)	0.515
	no	30(68.2)	88(73.3)	
PPH	yes	11(25)	21(17.5)	0.283
	no	33(75)	99(82.5)	
IAA	yes	16(36.4)	41(34.2)	0.793
	no	28(63.6)	79(65.8)	
Sepsis	yes	5(11.4)	8(6.7)	0.509
	no	39(88.6)	112(93.3)	
DGE	yes	2(4.5)	23(19.2)	0.021
	no	42(95.5)	97(80.8)	
Postoperative hospital stay, days		19.5 ± 14.5	18.2 ± 9.8	0.534
90-day death	yes	3(6.8)	4(3.3)	0.588
	no	41(93.2)	116(96.7)	
POPF, postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage; IAA, intra-abdominal abscess; DGE, delayed gastric emptying				

Multivariate regression analysis

Univariate analysis showed that age over 66 years ($P = 0.013$) and direct surgery ($P = 0.021$) were associated with postoperative DGE. In the multivariate logistic regression analysis, age over 66 years (OR: 3.094, 95% CI: 1.268–7.55) and direct surgery (OR: 5.298, 95% CI: 1.176–23.865) were independent risk factors of DGE (Table 4).

Table 4
Multivariate regression analysis of risk factors for DGE

Variable	group	univariate	multivariate		
		N	P	OR(95%CI)	P
age, years	< 66	10(9.8)	0.013	3.094(1.268–7.55)	0.013
	≥ 66	15(24.2)			
Sex	male	16(15.1)	0.943		
	female	9(15.5)			
BMI	< 18.5	2(18.2)	0.418		
	18.5–24.9	16(12.8)			
	25–29.9	6(26.1)			
	≥ 30	1(20)			
Smoking	Yes	8(16.7)	0.744		
	no	17(14.7)			
ECOG score	≤ 1	14(13.7)	0.488		
	> 1	11(17.7)			
ASA score	≤ 2	21(15.2)	1		
	3	4(15.4)			
Hypertension	yes	8(20.5)	0.294		
	no	17(13.6)			
Diabetes	Yes	6(21.4)	0.477		
	no	19(14)			
PBD status	no	23(19.2)		5.298(1.176–23.865)	0.03
	Yes	2(4.5)			
Operation type	PPPD	1(3.7)	0.125		
	PD	24(17.5)			
Operation time, min	< 180	12(14.5)	0.777		
	≥ 180	13(16)			

Variable	group	univariate	multivariate
Intraoperative blood loss, ml	< 400	13(16)	0.777
	≥ 400	12(14.5)	

Discussion

For patients of resectable periampullary carcinoma with obstructive jaundice, whether to perform biliary drainage prior to PD is still controversial. The previous researches and meta-analysis approached various conclusions. With the development and progress of technology, the drainage technology, operation technology and perioperative management being constantly improved, the necessity of PBD is gradually questioned. In a multicenter retrospective study, 1200 resectable pancreatic cancer patients with obstructive jaundice were included to explore the impact of severe obstructive jaundice on postoperative outcomes, drew a conclusion that serum total bilirubin (TB) > 300 $\mu\text{mol} / \text{L}$ was an independent risk factor for major morbidity, and was associated with worse prognosis [14]. An RCT study by van der Gaag et al. [3] involved patients with serum total bilirubin between 40–250 $\mu\text{mol} / \text{L}$, and it showed that preoperative biliary drainage increased the incidence of complications, suggesting that PBD should not be routinely performed in patients with TB $\leq 250 \mu\text{mol} / \text{L}$. In the study of De Pastena et al. [5], TB > 7.5 mg / dl (128 $\mu\text{mol} / \text{L}$) without PBD indicated poor postoperative outcomes, and this kind of patients may benefit from PBD. Henceforth, many studies have focused on the necessity of preoperative jaundice. Most studies have shown that PBD is not really beneficial to patients. Therefore, in the latest *guidelines for the diagnosis and treatment of pancreatic cancer (2020 V1.0)*, which is published by National Comprehensive Cancer Network (NCCN), it is no longer recommended to perform PBD in patients with obstructive jaundice. According to the guidelines, PBD treatment can be considered for patients with following situations: a. cholangitis or fever; b. severe symptomatic jaundice, such as severe pruritus; c. being delayed for any reason, such as neoadjuvant therapy.

In this study, there was no significant difference in the incidence of postoperative overall morbidity and severe complications in the PBD group. Among the various complications, only DGE was related to PBD. As result shows, PBD can significantly reduce the incidence of postoperative DGE. At present, DGE is still a common complication after PD. In patients with obstructive jaundice, the incidence of DGE after PD ranges from 9.4–17.9% [4–6, 15]. The causes and mechanism of DGE are still unclear. It is still difficult to deal with DGE, without enough effective methods. Based on our results, compared with direct surgery, PBD can reduce the risk of DGEs by 81%, which has a positive effect on promoting the early recovery from the surgery. Through preoperative biliary drainage, preoperative liver function and nutritional status of patients were restored to a certain extent, which may promote the recovery of postoperative gastrointestinal function, thereby reducing the risk of DGE.

There are several limitations in this study. First, this study is a retrospective analysis, confounding factors are unavoidable. Secondly, the sample size of PBD group is small, and the results should be treated with caution. In addition, many patients accepted PBD outside the hospital, and the liver function data before

biliary drainage are incomplete, so that the indications of preoperative biliary drainage could not be analyzed in this study. The indication of preoperative biliary drainage is still urgent problem, which needs to be solved in the future.

Owing to the lack of high-quality RCT studies, the necessity of PBD still needs to be explored by prospective study of large sample size.

Abbreviations

PBD: preoperative biliary drainage; PD: Pancreaticoduodenectomy; POPF: Postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage; IAA, intra-abdominal abscess; DGE, delayed gastric emptying; BMI: Body mass index; ASA, American Society of Anesthesiologists; TB, total bilirubin; ALB, albumin; ALT, alanine Aminotransferase; AST, aspartate aminotransferase

Declarations

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None

Authors' contributions

All authors helped to perform the research. Concept and clinical design were conducted by Gang Li. Acquisition of data was done by Daihai Mo and Hongyun Ma. Zhen Wang actively involved in this study especially in statistical design. Interpretation of article were done by Daihai Mo and Jiayang Hu. Finally, this article was revised and approved by Hongyun Ma and Gang Li.

Authors' information

Daihai Mo and Hongyun Ma contributed equally to this work.

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Availability of data and materials

The data of the current study are available from the corresponding author on reasonable request. Ethics approval and consent to participate. This study was approved by the Human Research Ethics Committee of The First Affiliated Hospital of Naval Medical University.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

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