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ORIGINAL ARTICLE

Preoperative biliary drainage for malignant biliary obstruction: results from a national database

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Abstract
Background The impact of preoperative biliary drainage (PBD) on postoperative morbidity and mortality in patients with malignant biliary obstruction is still unclear. We examined short-term surgical outcomes among drained and non-drained patients.
Methods Patients who underwent surgical resection for their malignancies with biliary obstruction were identified using the American College of Surgeons National Surgical Quality Improvement Program Participant Use Files from 2014 to 2015. Mortality and morbidity were compared among patients who had PBD to those who did not undergo biliary drainage prior to surgery.
Results A total of 2,306 patients were included; of these 1,803 (77.8%) had PBD. The postoperative mortality was 3.0% and 2.2% among direct surgery (DS) group and PBD group, respectively (P = 0.3). Postoperative complications were higher in the PBD group compared to the DS group (27.1% vs. 19.5%; P = 0.0005). Patients in the PBD group had higher risk of sepsis (13.5% vs. 7.2%; P = 0.0001), wound infections (16.5% vs. 10.9%; P = 0.002) and pancreatic fistula (17.5% vs. 12.4%; P = 0.006) compared to the DS group.
Conclusion Preoperative biliary drainage is associated with increased risk of sepsis and wound infections, but does not impact the postoperative mortality of patients undergoing PBD.

Keywords Biliary drainage · Biliary obstruction · Morbidity · Mortality · Pancreas · Surgery

Introduction

Biliary obstruction with associated jaundice is a common presentation of malignancies involving the distal biliary tract and head of pancreas. This obstruction could lead to hepatic dysfunction, coagulopathy, infection and contribute to patients' symptoms [1].

While biliary drainage, mainly endoscopic, is the established intervention of choice for patients with un-resectable malignancies, the role of biliary drainage among patients being considered for surgical resection remains controversial.

A recent single center study reported no increase in mortality or morbidity among patients undergoing preoperative drainage [2]. Previously other studies have shown mixed results regarding the risk of complications in this patient population. Many of these studies were included in a meta-analysis that concluded biliary drainage is harmful and is associated with increased risk of complications [3]. A more recent meta-analysis reached a different conclusion suggesting that drainage is associated with better outcomes [4].

The argument to drain is based on the assumption that drainage leads to an improvement of liver function and decreases hepatic inflammation, which would result in fewer complications and improve surgical outcomes. On the other hand, the argument against drainage is based on studies that showed higher rates of complications associated with drainage, mostly infectious in nature. These studies were criticized for design issues. For example, many studies included both percutaneously and endoscopically drained patients and the larger ones were mostly retrospective [4]. In addition, some of the better designed studies reported a

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higher rate of procedure-related complications, which were blamed for the poorer outcomes in the drainage group [5].

In this study we used the National Surgical Quality Improvement Program (NSQIP) dataset to examine short-term outcomes and surgical complications in this patient population. We compared surgical outcomes between drained and non-drained patients with malignant biliary obstruction.

Methods

Study population

The American College of Surgeons (ACS)-NSQIP is a large prospective surgical database representing a national validated program that provides risk-adjusted information on short-term surgical outcomes (30-day) and their predictors for the purpose of improving hospital surgical quality. ACS-NSQIP collects data from around 570 institutions across the USA and Canada and cases are collected based on current procedural terminology (CPT) codes using a random sampling of procedures per institution.

Inclusion and exclusion criteria

All patients who underwent surgery for malignant biliary obstruction for the years 2014–2015 were identified. Patients were included if they had pancreatic resection based on the following codes: Whipple-type procedures (CPT codes 48150, 48152, 48153, 48154).

Patients were excluded if they had preoperative percutaneous drainage, disseminated cancer, preoperative chemo or radiotherapy or if the final pathology did not show a malignancy.

Predictor variables

The primary predictor variable was preoperative biliary drainage using an endoscopic stent. The secondary predictor variables included sex, race, age, body mass index (BMI), diabetes mellitus, smoking status, severe chronic obstructive pulmonary disease (COPD), hypertension, >10% body weight loss (BWL) in last 6 months, transfusion of >4 units packed red blood cells in the 72 h before surgery, wound classification (clean, clean/contaminated, contaminated, dirty/infected), ASA classification (American Society of Anesthesiologists physical status examination). Collected data also included preoperative total bilirubin and white count, operative approach, pancreatic duct size, vascular resection during surgery, and the histologic subtype of the malignant disease with tumor staging.

Outcome variables

The primary outcome of the study was 30-day mortality after surgery. The secondary postoperative outcomes included the following: wound infections; cardiac complications, including cardiac arrest and myocardial infarction; respiratory complications; sepsis; venous thromboembolism, including deep venous thrombosis and pulmonary embolism; bleeding requiring transfusion; and return to operative room within 30 days after surgery. We also compared surgery related variables including length of total hospital stay, operation time, and the development of pancreatic fistula between both groups.

Statistical analysis

Statistical analyses were conducted using the Statistical Analyses Software (SAS), version 9.4. Descriptive statistics were reported using mean and standard deviation (SD) for continuous variables and frequency distributions for categorical variables. Comparisons of categorical variables were performed using the χ^2 or the Fisher's exact test. Similar comparisons of continuous variables used the independent Student's *t*-test. Multiple logistic regression was used to identify individual predictors of postoperative outcomes while controlling for potential confounders. Results were reported using the odds ratio (OR) and the 95% confidence interval (CI). A *P*-value of <0.05 was considered statistically significant.

Results

Patient characteristics

We identified 2,985 patients who underwent Whipple type pancreatic resection for presumed malignant biliary obstruction. We excluded a total of 679 patients: 170 had a percutaneous stent, 533 received pre-op chemo radiotherapy, 111 were identified with disseminated disease and 164 had pathology reports showing benign disease (some excluded patients had more than one of the exclusion criteria). A total of 2,306 patients were included in the final analysis. Of these 1,803 patients (78.2%) had preoperative biliary drainage (PBD group) prior to surgery, while 503 (21.8%) patients were referred for direct surgery (DS group). Table 1 outlines the demographic and clinical characteristics of the study population. At baseline, most of the patient characteristics were similar. Mean age of our population was 66.5 ± 10.2 years with no significant difference between both groups. The prevalence of diabetics was 27.0% in the DS group and 25.2% in the PBD

Table 1 Descriptive statistics

	All n = 2,306	DS group n = 503 (21.8)	PBD group n = 1,803 (78.2)	P-value
Female	979 (42.5)	231 (45.9)	748 (41.5)	0.07
White	1,764 (87.5)	387 (86.6)	1,377 (87.8)	0.48
Age, mean ± SD	66.50 ± 10.23	66.43 ± 10.14	66.52 ± 10.26	0.86
Body mass index, mean ± SD	27.44 ± 5.86	26.82 ± 5.58	27.61 ± 5.92	0.007
Social/medical history				
Diabetes mellitus	590 (25.6)	136 (27.0)	454 (25.2)	0.40
Current smoker within 1 year	409 (17.7)	79 (15.7)	330 (18.3)	0.18
Severe COPD	99 (4.3)	16 (3.2)	83 (4.6)	0.16
Hypertension	1,250 (54.2)	258 (51.3)	992 (55.0)	0.14
>10% BWL in last 6 months	522 (22.6)	120 (23.9)	402 (22.3)	0.46
Surgery				
Transfusion >4 units PRBCs in 72 h before surgery	22 (1.0)	9 (1.8)	13 (0.7)	0.04
ASA classification >II	1,785 (77.4)	402 (79.9)	1,383 (76.8)	0.13
Preoperative total bilirubin, mean ± SD	3.47 ± 3.52	6.29 ± 4.53	2.81 ± 2.87	<0.0001
Preoperative WBC × 1,000, mean ± SD	7.64 ± 2.52	7.32 ± 2.48	7.73 ± 2.53	0.001
Operative approach				
Laparoscopic	40 (1.7)	11 (2.2)	29 (1.6)	0.64
Open (planned)	2,149 (93.2)	467 (92.8)	1,682 (93.3)	
Robotic	52 (2.3)	9 (1.8)	43 (2.4)	
Others	65 (2.8)	16 (3.2)	49 (2.7)	
Pancreatic duct size (>6 mm)	362 (20.0)	93 (24.4)	269 (18.8)	0.02
Vascular resection performed	376 (16.5)	88 (17.7)	288 (16.2)	0.40

ASA American Society of Anesthesiologists, *BWL* body weight loss, *COPD* chronic obstructive pulmonary disease, *DS* direct surgery, *PBD* preoperative biliary drainage, *PRBC* packed red blood cell, *SD* standard deviation, *WBC* white blood cell count

group (P = 0.40). Of note, preoperative total bilirubin levels were significantly different between DS and PBD groups (6.29 ± 4.53 vs. 2.81 ± 2.87 mg/dl, P < 0.0001). Also, a higher percentage of DS group patients had pancreatic duct size dilation >6 mm compared to PBD group patients (24.4% vs. 18.8%, P = 0.02) (Table 1).

Postoperative pathology results showed that the absolute majority of the patients were diagnosed with either pancreatic adenocarcinoma (74.5%), ampullary carcinoma (12.9%) or distal cholangiocarcinoma (5.3%). Most patients had a locally advanced disease according to the tumor staging following surgery: 82.0% of the patients had beyond T2 tumor and 72.9% of them had positive lymph nodes on postoperative pathology. There were no significant TNM staging discrepancies between the two groups under study.

Surgery related variables

The examined operative outcomes are detailed in Table 2. The average operative time was significantly shorter for the DS group compared to the PBD group (341 ± 128 min vs. 370 ± 126 min, P < 0.0001). Length of hospital stay was similar between both groups averaging 11.4 ± 8.0 days. The rate of postoperative pancreatic fistula was significantly higher in the PBD group (17.5%) relatively to the DS group (12.4%), P = 0.006 (Table 2).

Major complications

The overall 30-day postoperative mortality was 2.3% in the whole study population. There was no significant difference in mortality between DS and PBD groups (3% and 2.2%, respectively; OR = 0.7, 95% CI: 0.4–1.3, P = 0.28). Similarly, there were no significant differences in postoperative bleeding and reoperation rates between the two groups. As far as post-op morbidity, composite morbidity was higher in the PBD group when compared to the DS group (27.1% vs. 19.5%), an increase that was statistically significant (OR = 1.5, 95% CI: 1.2–2, P = 0.0005). Examining morbidity details, we found that only two of the studied outcomes varied significantly between the groups, namely sepsis and wound infection. The percentage of patients who developed sepsis in the PBD group was 13.5%, significantly higher than that of DS group at 7.2% (OR = 2.0, 95% CI: 1.4–2.9, P < 0.0001). The second significant difference was seen

Table 2 Operative and pathology findings

	All (%) (n = 2,306)	DS group (n = 503)	PBD group (n = 1,803)	P-value
Drain still present at POD#30	175 (7.6)	39 (7.8)	136 (7.5)	0.87
Pancreatic fistula	376 (16.4)	61 (12.4)	315 (17.5)	0.006
Total operation time, mean ± SD	363.71 ± 127.30	341.04 ± 127.81	370.03 ± 126.47	<0.0001
Length of total hospital stay, mean ± SD	11.41 ± 8.04	11.97 ± 7.78	11.26 ± 8.10	0.08
Wound classification				
Clean/contaminated	1,890 (82.0)	451 (89.7)	1,439 (79.8)	<0.0001
Contaminated	307 (13.3)	42 (8.4)	265 (14.7)	
Dirty/infected	109 (4.7)	10 (2.0)	99 (5.5)	
Pathologic diagnosis				
Pancreatic adenocarcinoma	1,715 (74.5)	380 (76.0)	1,335 (74.1)	<0.0001
Ampullary carcinoma	297 (12.9)	55 (11.0)	242 (13.4)	
Distal cholangiocarcinoma	123 (5.3)	12 (2.4)	111 (6.2)	
Duodenal carcinoma	31 (1.3)	14 (2.8)	17 (0.9)	
IPMN-invasive	27 (1.2)	6 (1.2)	21 (1.2)	
Neuroendocrine-functioning	8 (0.3)	1 (0.2)	7 (0.4)	
Neuroendocrine-nonfunctioning	30 (1.3)	5 (1.0)	25 (1.4)	
Other type	71 (3.0)	27 (5.4)	44 (2.4)	
Tumor staging				
>T2	1,864 (82.0)	414 (83.8)	1,450 (81.5)	0.23
Positive nodes	1,655 (72.9)	363 (73.8)	1,292 (72.6)	0.61
Metastatic (M1)	22 (1.3)	5 (1.5)	17 (1.3)	0.79

DS direct surgery, *IPMN* intraductal papillary mucinous neoplasm, *PBD* preoperative biliary drainage, *POD* postoperative day, *SD* standard deviation

with wound infection, the rates were significantly higher in the PBD group at 16.5% compared to DS group at 10.9% (OR = 1.6, 95% CI: 1.2–2.2, P = 0.0002).

Multivariate analysis

In a multivariate analysis we compared the postoperative outcomes between both groups after adjusting for: gender, race, preoperative blood transfusion, ASA classification, pancreatic duct size, and BMI. There were no significant changes in the results and the rates of postsurgical morbidity, sepsis and wound infection remained higher in the PBD group as illustrated in Table 3.

Discussion

Our study showed that more than three quarters of patients presenting with potentially resectable malignant

Table 3 Major outcomes

	DS group	PBD group	Unadjusted		Adjusted	
	(n = 503)	(n = 1,803)	OR (95% CI)	P-value	OR (95% CI)	P-value
Mortality	15 (3.0)	39 (2.2)	0.72 (0.39–1.32)	0.28	0.71 (0.39–1.31)	0.27
Composite morbidity[a]	98 (19.5)	489 (27.1)	1.54 (1.20–1.96)	0.0005	1.48 (1.16–1.89)	0.002
Wound	55 (10.9)	297 (16.5)	1.61 (1.18–2.18)	0.002	1.48 (1.09–2.02)	0.01
Cardiac	10 (2.0)	37 (2.1)	1.03 (0.51–2.09)	0.93	0.96 (0.47–1.95)	0.91
Respiratory	36 (7.2)	118 (6.5)	0.91 (0.62–1.34)	0.63	0.91 (0.62–1.34)	0.62
Sepsis	36 (7.2)	243 (13.5)	2.02 (1.40–2.91)	0.0001	1.97 (1.37–2.85)	0.0003
Thromboembolism	13 (2.6)	66 (3.7)	1.43 (0.78–2.62)	0.24	1.39 (0.76–2.56)	0.28
Bleeding	109 (21.7)	367 (20.4)	0.92 (0.73–1.18)	0.52	0.94 (0.73–1.20)	0.62
Return to operating room	27 (5.4)	109 (6.1)	1.13 (0.73–1.75)	0.57	1.05 (0.68–1.63)	0.81

CI confidence interval, *DS* direct surgery, *OR* odds ratio, *PBD* preoperative biliary drainage

[a]Composite morbidity considered positive if any of wound, cardiac, respiratory, central nervous system, sepsis or thromboembolism is positive

biliary obstruction underwent PBD using an endoscopic stent. This finding is consistent with recent studies where PBD was performed in more than 50% of the patients [6, 7]. There is an increase in PBD use over the last two decades rising from around 30% in the mid 1990s to over 50% in recent years despite the fact that there was no evidence of benefits from the use of PBD in addition to increasing reports of high morbidity associated with percutaneous stenting [3, 4, 6].

The concept of PBD was advocated as a method to restore the normal physiology of biliary-obstructed patients, hence reducing the risks associated with hyperbilirubinemia, which have been linked to poor surgical outcomes [8, 9]. In this study, preoperative bilirubin levels were significantly lower in patients who underwent PBD compared to those who went straight for surgery, which suggests that the goal of lowering bilirubin level has been achieved. Previous studies advocate that lowering bilirubin levels should boost the immune function, improve the nutritional conditions and reduce the chance of infections [10–12]. However, our analysis revealed that the rates of wound infection as well as sepsis were significantly higher in patients in the PBD group compared to DS group. These results contradict previous conclusions and question the importance of bilirubin as an agent that affects the immune system and the microbiological profile in the biliary tree.

Overall, PBD did not decrease the composite postoperative morbidity. Patients who underwent preoperative drainage had a 50% greater chance of developing postsurgical complications compared to patients in DS group. This falls in line with findings from previous studies that showed similar rates of postoperative complications in patients undergoing PBD before surgery [2, 5, 13–15]. Among these complications, only wound infection and sepsis were significantly higher in the PBD group compared to the DS group which is consistent with findings by Sahora et al., Morris et al. as well as in a recent meta-analysis by Scheufele et al. [2, 14, 15]. The increased incidence of complications was not limited to the immediate postoperative period, patients undergoing PBD were still at increased risk even several weeks after the surgery as shown in a recent trial by Van der Gaag et al. revealing that the rate of postoperative complications and infections was significantly higher in the PBD group 4 months after the surgery [5].

There was no significant difference in mortality between both groups which is consistent with findings from previous studies. A large meta-analysis performed by Moole et al. including mostly retrospective studies and a few randomized controlled trials, showed that mortality rates were comparable between PBD and DS groups [4]. Similarly, mortality rates were not different between both groups in a Cochrane review including six trials out of which only one trial by Van der Gaag et al. was recent [5, 16]. A longer follow-up performed by Morris et al. looked at 30 days and 1 year mortality differences in both groups and reported that there were no discrepancies between the groups [15].

Another significant operative outcome was the risk of developing a pancreatic fistula or leak which was higher in the PBD group despite the fact that PBD was shown not to increase the risk of pancreatic fistula in a recent study [14]. This undesired postoperative outcome could explain the increased risk of infections and sepsis in those patients [2].

Our analysis has several notable strengths. First it is based on a large database prospectively collected to examine quality indicators in surgical care. Data from the NSQIP were established from a group of representative hospitals in different regions with a strong emphasis on ensuring high-quality data collection through rigorous training and auditing of chart abstractors. Second the large sample size in this study, which is more than two-fold higher than any of the previously published studies, allowed us to study actual practice patterns and outcomes and to detect the differences between both groups in the common and less-frequent postoperative complications. Third, our analysis included only patients who were endoscopically drained in the PBD group making the population more homogenous and eliminating biases that could be introduced if percutaneous drainage was included as was the case in many previous studies. Fourth our results reflect outcomes that are more representative of real life practice combining different practice settings and eliminating biases seen in reports from high volume referral centers.

It is important to recognize that our study is not a randomized clinical trial, comparisons between treatments options need to be made with caution.

One of the limitations of the NSQIP database is that it only measures outcomes 30 days after surgery, so further large-scale studies should be performed to study the long-term outcomes between both groups of patients. Another limitation is that the type of endoscopic stent whether plastic or metal was not specified as the outcome of both stents was shown to be different in previous studies [17]. The period between stenting and surgery was not specified as well in the NSQIP data.

Conclusion

In conclusion, our study showed that PBD is associated with significantly higher risk of postoperative complications, sepsis, wound infections and pancreatic fistula in patients presenting with malignant biliary obstruction. PBD did not alter mortality or length of stay in this group of patients.

Conflict of interest None declared.

Author contributions Yasser Shaib: conception and design; analysis and interpretation of the data; drafting of the article; critical revision of the article for important intellectual content; final approval of the article. Mahmoud A. Rahal: analysis and interpretation of the data; drafting of the article; critical revision of the article for important intellectual content. Mohammad O. Rammal: analysis and interpretation of the data; drafting of the article; critical revision of the article for important intellectual content. Aurelie Mailhac: analysis and interpretation of the data; drafting of the article. Hani Tamim: conception and design; analysis and interpretation of the data; drafting of the article; critical revision of the article for important intellectual content; final approval of the article.

References

1. Van der Gaag NA, Kloek JJ, de Castro SM, van Busch OR, Gulik TM, Gouma DJ. Preoperative biliary drainage in patients with obstructive jaundice: history and current status. J Gastrointest Surg. 2009;13:814–20.
2. Sahora K, Morales-Oyarvide V, Ferrone C, Fong ZV, Warshaw AL, Lillemoe KD, 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.
3. Sewnath ME, Karsten TM, Prins MH, Rauws EJ, Obertop H, Gouma DJ. A meta-analysis on the efficacy of preoperative biliary drainage for tumors causing obstructive jaundice. Ann Surg. 2002;236:17–27.
4. 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.
5. van der Gaag NA, Rauws EA, van Eijck CH, Bruno MJ, van der Harst E, Kubben FJ, et al. Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med. 2010;362:129–37.
6. Jinkins LJ, Parmar AD, Han Y, Duncan CB, Sheffield KM, Brown KM, et al. Current trends in preoperative biliary stenting in patients with pancreatic cancer. Surgery. 2013;154:179–89.
7. Sargent M, Boeck S, Heinemann V, Jauch KW, Seufferlein T, Bruns CJ. Surgical treatment concepts for patients with pancreatic cancer in Germany–results from a national survey conducted among members of the "Chirurgische Arbeitsgemeinschaft Onkologie" (CAO) and the "Arbeitsgemeinschaft Internistische Onkologie" (AIO) of the Germany Cancer Society (DKG). Langenbecks Arch Surg. 2011;396:223–9.
8. Kawarada Y, Higashiguchi T, Yokoi H, Vaidya P, Mizumoto R. Preoperative biliary drainage in obstructive jaundice. Hepatogastroenterology. 1995;42:300–7.
9. Blamey SL, Fearon KC, Gilmour WH, Osborne DH, Carter DC. Prediction of risk in biliary surgery. Br J Surg. 1983;70:535–8.
10. Gouma DJ, Coelho JC, Fisher JD, Schlegel JF, Li YF, Moody FG. Endotoxemia after relief of biliary obstruction by internal and external drainage in rats. Am J Surg. 1986;151:476–9.
11. Gouma DJ, Roughneen PT, Kumar S, Moody FG, Rowlands BJ. Changes in nutritional status associated with obstructive jaundice and biliary drainage in rats. Am J Clin Nutr. 1986;44:362–9.
12. Roughneen PT, Gouma DJ, Kulkarni AD, Fanslow WF, Rowlands BJ. Impaired specific cell-mediated immunity in experimental biliary obstruction and its reversibility by internal biliary drainage. J Surg Res. 1986;41:113–25.
13. Fang Y, Gurusamy KS, Wang Q, Davidson BR, Lin H, Xie X, 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.
14. Scheufele F, Schorn S, Demir IE, Sargut M, Tieftrunk E, Calavrezos L, 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.
15. Morris-Stiff G, Tamijmarane A, Tan YM, Shapey I, Bhati C, Mayer AD, et al. Pre-operative stenting is associated with a higher prevalence of post-operative complications following pancreatoduodenectomy. Int J Surg. 2011;9:145–9.
16. Fang Y, Gurusamy KS, Wang Q, Davidson BR, Lin H, Xie X, et al. Pre-operative biliary drainage for obstructive jaundice. Cochrane Database Syst Rev. 2012;CD005444.
17. Crippa S, Cirocchi R, Partelli S, Petrone MC, Muffatti F, Renzi C, et al. Systematic review and meta-analysis of metal versus plastic stents for preoperative biliary drainage in resectable periampullary or pancreatic head tumors. Eur J Surg Oncol. 2016;42:1278–85.