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Preoperative Biliary Drainage is Associated with Increased Complications after Liver Resection for Proximal Cholangiocarcinoma

Rajesh Ramanathan, MD¹, Jeffrey Borrebach, MS², Samer Tohme, MD¹, and Allan Tsung, MD¹

¹University of Pittsburgh Medical Center, Department of Surgery, Pittsburgh, Pennsylvania

²University of Pittsburgh Medical Center, Wolff Center at UPMC, Pittsburgh, Pennsylvania

Abstract

Background: Preoperative biliary drainage (PBD) prior to liver resection for hilar and intrahepatic cholangiocarcinoma (CCA) is common. While PBD for those with distal obstructions has been studied extensively and is associated with increased infectious complications, the impact of PBD among patients undergoing hepatectomy for non-disseminated proximal CCA has yet to be clearly elucidated.

Methods: Patients undergoing liver resection between 2014 and 2016 for non-disseminated hilar and intrahepatic CCA were analyzed using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. Associations between PBD (percutaneous or endoscopic) and 30-day outcomes were evaluated.

Results: There were 905 liver resections performed, with 186 (20.6%) for hilar CCA and 719 (79.4%) for intrahepatic CCA. Of those, 251/897 (28.0%) patients underwent PBD. Independent preoperative predictors of PBD were hilar CCA, major hepatectomy, open surgery, lower BMI, and higher preoperative bilirubin. Adjusting for preoperative variables, extent of resection, and bilirubin, PBD was independently associated with increased wound infection (OR 2.93), organ space infection (OR 3.63), sepsis (OR 3.17), renal insufficiency (OR 4.25), transfusion (OR 2.40), bile leak (OR 3.23), invasive intervention (OR 2.72), liver failure (OR 3.20), readmission (OR 3.01), reoperation (OR 2.32), and mortality (OR 4.24, all $p < 0.05$).

Conclusions: Among patients undergoing hepatectomy for proximal CCA, PBD is associated with increased postoperative complications. These data suggest that avoidance of routine preoperative biliary drainage may decrease short-term complications.

Address Correspondence to: Allan Tsung MD FACS, 3459 Fifth Avenue, Pittsburgh, PA 15213-2582, tsunga@upmc.edu; Tel: 412-692-2001; Fax: 412-692-2002.

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Introduction

Cholangiocarcinoma (CCA) is a rare cancer that primarily affects patients in their fifties and sixties (1). The prognosis in these patients remain poor with a 5-year survival of 17.6% overall, and 45% of patients present with regional or distant disease. Systemic and non-surgical regional therapies in locally advanced and metastatic stages have limited effect on survival, with the best outcomes occurring in those with early stage tumors that are surgically resectable.

Obstructive jaundice occurs frequently in CCA at diagnosis and has been associated with increased morbidity and postoperative liver failure (2). As a result, most jaundiced patients with resectable hilar and intrahepatic CCA undergo preoperative biliary drainage (PBD) through endoscopic or percutaneous biliary stenting (3). The pancreaticoduodenectomy literature for distal biliary obstructions has consistently demonstrated that PBD increases the incidence of infectious complications (4). However, in patients with proximal biliary obstruction from CCA, the associations between complications and PBD are less well elucidated (5–11).

The current literature regarding PBD in CCA comprises several prospective single-institutional studies limited by small sample sizes, and a mix of proximal and distal lesions (5–8). Additional, larger, retrospective series are confounded by patient heterogeneity, including patients with pancreatic, ampullary and hepatocellular carcinoma lesions, and inclusion of large proportions of palliative biliary bypass procedures (2,8,10,11).

Thus, the objective of this study is to investigate the complications associated with PBD specifically in patients with non-disseminated, resectable hilar and intrahepatic CCA using a large patient sample from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).

Methods

Patient selection and characteristics

Adult patients over 18 years of age undergoing hepatectomy for hilar or intrahepatic CCA between 2014 and 2016 were identified in a merged dataset of the ACS-NSQIP participant user file (PUF) and the ACS-NSQIP hepatectomy procedure-targeted PUF. ACS-NSQIP is a national surgical quality improvement database that collects data from participating institution using trained data abstractors and administrative data (12). In addition to the general ACS- NSQIP PUF, the hepatectomy procedure-targeted PUF contain preoperative, intraoperative and postoperative variables tailored to hepatectomy (6). These data undergo the same rigorous data collection and validation as the general ACS-NSQIP PUF.

Patients undergoing hepatectomy were selecting using Current Procedural Terminology (CPT) codes for partial lobectomy (47120), trisegmentectomy (47122), total left lobectomy (47125), and total right lobectomy (47130). From this subset, those with hilar and intrahepatic CCA were selected from the hepatectomy procedure-targeted PUF based on data recorded in the histologic subtype section after resection and pathologic analysis. Those

undergoing surgery classified as emergency were excluded, and those with disease recorded as disseminated were excluded.

Baseline Variables and Outcomes

The PBD cohort included patients undergoing endoscopic and percutaneous drainage. Other preoperative patient variables assessed included age, gender, body mass index (BMI), and the presence of any of the following within 30 days prior to surgery: hypertension, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), diabetes (classified as no diabetes, non-insulin dependent diabetes, and insulin-dependent diabetes), current smoking status within the past year, and use of steroids for chronic conditions. The most recent preoperative bilirubin is recorded in the ACS-NSQIP data and were included in our analysis. Data on hilar location of CCA, use of minimally invasive surgery (MIS), preoperative portal vein embolization (PVE), preoperative systemic chemotherapy within 90 days, major liver resection, and pathologic tumor T stage were additionally recorded from the hepatectomy procedure-targeted dataset. Given that clinical T stage is not included in the dataset, pathologic T stage was considered a preoperative variable for the purposes of data analysis. Major resections were defined as those undergoing trisegmentectomy, total right lobectomy, or total left lobectomy.

All outcomes within the ACS-NSQIP database are 30-day outcomes. The post-operative outcomes analyzed in this study included wound infection (including both superficial and deep), organ space infection, wound dehiscence, sepsis and septic shock, pneumonia, reintubation, respiratory failure (ventilator dependence for > 48 hours), renal insufficiency or failure, cardiac arrest or myocardial infarction (MI), stroke, venous thromboembolism (VTE), urinary tract infection (UTI), need for blood product transfusion, need for postoperative invasive intervention, bile leak, liver failure, unplanned readmission within 30 days, unplanned reoperation within 30 days, discharge to a non-home facility, and death within 30 days. Abbreviated descriptions of the ACS-NSQIP defined outcomes are provided in Figure 1. If any of the outcomes were present on admission, they were excluded from analysis. Patients with post-surgical length of stay > 30 days, and patients who died during the hospitalization were excluded from the analysis of readmission.

Analysis

Univariate modeling with Mann-Whitney U tests and likelihood ratio chi-squared tests were used to examine associations between PBD, and baseline variables and outcomes. **Subset analysis was additionally performed for those with hilar CCA only.** A $p < 0.05$ was considered statistically significant.

A logistic regression model was performed using all available preoperative demographic, comorbidity, and tumor-specific variables to identify predictors of PBD. Of note, hilar location, MIS, PVE, preoperative systemic chemotherapy, major liver resection, and pathologic T-stage were included.

For outcomes with statistically significant associations with PBD, stepwise regressions including all baseline variables, including hilar location and preoperative bilirubin, were

performed to assess the independent contribution of PBD. For the stepwise regression models, a p-value threshold of $p < 0.20$ was used to identify variables with contribution to the model. Logistic odds ratios were calculated for variables with significant independent contribution at a statistical significance threshold of $p < 0.05$.

All analyses were performed using JMP 12 (SAS Institute, Cary, NC).

Results

Patient characteristics

Over the study period, 905 liver resections were performed for hilar and intrahepatic CCA. The mean age and BMI were 63.6 years and 28.3 kg/m^2 , respectively. Of the 905 resections, 314 (34.7%) were partial lobectomies, 231 (25.5%) were trisegmentectomies, 187 (20.7%) were total left lobectomies, and 173 (19.1%) were total right lobectomies. Major resections, defined as total lobectomies and trisegmentectomies, constituted 65.3% of the sample. 122 (13.5%) of the procedures were done using minimally invasive surgery (MIS) and 70 (7.8%) underwent preoperative PVE. The mean preoperative bilirubin was 1.2 mg/dL and the median preoperative bilirubin was 0.6 mg/dL. The pathologic T-stage distribution was 247 (29.5%) T1, 435 (52.0%) T2, 115 (13.7%) T3 and 39 (4.7%) T4 tumors, with the remained unknown or not available. (Table 1)

Preoperative biliary drainage

There were 897 patients with complete data on PBD, and 251 (28.0%) underwent PBD. The most frequent method being endoscopic (188/251, 74.9%), followed by percutaneous (50/251, 19.9%) and other type (13/251, 5.2%). Patients who received PBD were younger (62.5 vs. 64.1, $p = 0.04$), lower BMI ($26.4 \text{ vs. } 29.0 \text{ kg/m}^2$, $p < 0.01$), and lower incidences of hypertension and COPD. **The ACS-NSQIP dataset reports preoperative bilirubin. Patients who underwent PBD had higher preoperative bilirubin after PBD than patients who did not undergo PBD (2.3 vs. 1.2 mg/dL, $p < 0.01$), indicating that bilirubin levels did not universally normalize after PBD.** PBD was associated with a higher proportion of hilar CCA (53.4% vs. 7.9%, $p < 0.01$), major liver resection (85.7% vs. 57.4%, $p < 0.01$), and a lower rate of MIS (4.8% vs. 16.9%, $p < 0.01$). Those that had PBD also more frequently underwent PVE (14.5% vs. 5.1%, $p < 0.01$). The PBD cohort had a significantly higher proportion of T2, T3 and T4 tumors ($p < 0.01$). (Table 1)

On multivariate analysis including only preoperative variables and pathologic T stage, independent predictors of PBD were hilar CCA (odds ratio [OR]: 6.03, 95% confidence interval [CI]: 3.91–9.37), major resection (OR: 2.44, 95% CI: 1.53–3.94), open surgery (OR: 2.60, 95% CI: 1.21–6.07), lower BMI (OR: 2.16 per kg/m^2 decrease, 95% CI: 1.07–3.29), and higher preoperative bilirubin (OR: 1.03 per mg/dL, 95% CI: 0.78–1.29). (Table 2)

Post-operative complications and outcomes

Infectious complications were common after liver resection for proximal CCA with 71 of the 905 (8.1%) patients developing a wound infection, 154 (17.6%) developing an organ space infection, 49 (5.4%) developing a pneumonia, and 114 (13.3%) demonstrating sepsis

or septic shock. Two hundred and seventy-three (30.2%) required a product transfusion, 125 (13.8%) developed liver failure, 167 (18.6%) developed a bile leak, and 190 (21.2%) required an invasive intervention. (Figure 2) One hundred of the 166 patients (60.2%) with bile leak required an invasive intervention, although the dataset does not provide information on whether the indication for invasive intervention was bile leak. Other complications are listed in Table 3.

Multivariable stepwise regression models were used to assess the independent effect of PBD on the above complications after adjusting for all preoperative demographic and comorbidity variables, as well as hilar location, MIS, PVE, preoperative systemic chemotherapy, major liver resection, pathologic T-stage, and preoperative bilirubin. PBD continued to be independently associated with wound infection, organ space infection, sepsis and septic shock, unplanned reintubation, respiratory failure, renal insufficiency, VTE, product transfusion, bile leak, invasive intervention, liver failure, readmission, reoperation, facility discharge, and mortality. It was not independently associated with wound dehiscence and pneumonia. (Table 4)

Hilar CCA subset analysis—The associations between PBD and postoperative complications were additionally investigated in a subset of patients with hilar CCA (n=186). (Table 5) PBD was employed in 72.0% of patients with hilar CCA, and hilar CCA patients that underwent PBD had higher preoperative bilirubin levels than those that did not undergo PBD (2.4 vs. 1.8 mg/dL). Neoadjuvant chemotherapy within 30 days was used in 4.9% of patients, and 12.6% underwent PVE. MIS approaches were used in only 5.9% of patients, and 84.9% underwent a major resection. The most pathologic T stage was T2 (63.4%), followed by T3 (18.3%), T1 (7.0%), and T4 (5.9%).

Among those with hilar CCA, PBD was associated with increased need for blood transfusion (49.3% vs. 26.9%, $p<0.01$) on univariate analysis. PBD continued to be independently associated with blood transfusion on multivariable analysis (OR 2.41, 95% CI: 1.07–5.75), after adjusting for preoperative demographic and comorbidity variables, as well as MIS, PVE, preoperative systemic chemotherapy, major liver resection, pathologic T-stage, and preoperative bilirubin. There were no significant differences in bile leaks (31.3% vs. 20.0%, $p=0.12$), need for invasive interventions (36.4% vs. 28.9%, $p=0.33$), or liver failure (23.1% vs. 13.5%, $p=0.13$). In the hilar CCA subset, PBD was not associated with wound infection, organ space infection, wound dehiscence, sepsis/septic shock, pneumonia, reintubation, respiratory failure, renal insufficiency or failure, MI, stroke, VTE, UTI, readmission, reoperation, discharge destination, or mortality.

Discussion

Our results demonstrate that PBD is associated with increased infectious, renal, cardiopulmonary, and hepatectomy-specific complications, including blood transfusion, bile leak, invasive intervention, and liver failure after controlling for baseline patient and tumor variables. PBD was employed more frequently in those with hilar CCA, and PBD in hilar CCA was associated with increased blood transfusion after controlling for other variables.

The literature to date on PBD in proximal CCA is limited by small sample sizes, and heterogenous patient populations. Three prospective trials in the 1980s randomizing patients to hepatectomy alone or percutaneous PBD prior to hepatectomy reported no benefit (5–7). Notably, those trials were underpowered with sample sizes of less than 40 patients in each arm, and a mix of proximal and distal obstructions. A subsequent randomized trial of 87 patients investigating endoscopic PBD reported non-superiority with PBD, and increased infectious complications (8). In that study, however, over 50% of the patients had tumors of the pancreas and ampulla. In 2000, Cherqui et al. published a matched case-comparison study of jaundiced patients undergoing hepatectomy with or without PBD (2). They found higher infectious complications in jaundiced patients who did not undergo PBD, however only 15% of the control cohort and 70% of PBD cohort had CCA, with the remainder having gallbladder carcinomas, hepatocellular carcinomas, and metastatic liver lesions. Hochwald et al. retrospectively investigated the role of PBD in 71 patients with proximal CCA only, and reported higher rates of contaminated biliary trees and infections (11). The major limitation in this study was that over half the patients underwent palliative biliary bypasses.

Most hilar CCA have obstructive jaundice and the norm for hilar and intrahepatic CCA with jaundice is PBD through either percutaneous or endoscopic approaches (3,15). Obstructive jaundice has long been assumed to contribute to increase coagulopathy and post-hepatectomy liver failure by impairing the regenerative capacity of the liver (16). In canine animal models with obstructive jaundice, mortality after 70% hepatectomy was significantly higher among those with unrelieved jaundice as opposed to those with PBD (17). The mechanism is assumed to be mitochondrial dysfunction, thus affecting the regenerative capacity (16,18). Animal models have demonstrated that even after decompression, recovery of the affected mitochondria can take up to 6 weeks and may not reach normal levels (19,20). Additionally, restoration of biliary flow in the gastrointestinal tract may be beneficial in ameliorating the impaired intestinal barrier function noted in obstructive jaundice (21). From a surgical planning perspective, selective cholangiography via external biliary drainage is more accurate than endoscopic retrograde cholangiopancreatography (ERCP) in delineating tumor involvement of smaller biliary ductal systems, and thus may be useful in staging and hepatectomy planning for major resections (15,16). For these reasons, the Asian literature encourages the use of percutaneous PBD as the optimal approach (14-18). Our ACS-NSQIP data reflects a North American practice pattern with a predominance of endoscopic PBD over percutaneous PBD. **However, the ACS-NSQIP data does not provide granular detail on the proportion of ERCP versus nasobiliary endoscopic drainage, and the use of selective versus total percutaneous cholangiography.**

Despite theoretical and experimental evidence supporting PBD, prospective trials have failed to show superiority and have instead shown increased morbidity associated with biliary drainage (5,22). Specifically, they show significantly higher incidence of cholangitis, with intraoperative bile cultures after PBD demonstrating a positivity rate of 65% for bacterial contamination as opposed to 8% in those without PBD (19, 23). PBD, in a prospective randomized trial, has also been associated with longer hospital stay and higher costs (9). A systematic review and meta-analysis of five randomized controlled trials and 18 cohort

studies evaluating the benefits of PBD similarly reported increased complications and longer length of stay with PBD (10). In our study, we found that PBD was independently associated with increased wound infection, organ space infection, sepsis and septic shock, unplanned reintubation, respiratory failure, renal insufficiency, VTE, product transfusion, bile leak, invasive intervention, liver failure, readmission, reoperation, facility discharge, and mortality after controlling for baseline factors including pathologic tumor T stage. The increased infectious complications with PBD is in line with the existing literature and is likely attributed to bacterial colonization of the biliary tree. The increased transfusions need, bile leak, invasive intervention and liver failure rates are independent of the effect of preoperative bilirubin, major liver resection and PVE. **It has been suggested in the literature that PBD may increase tumor spread, however we are unable to analyze that using the ACS-NSQIP dataset.**

Hilar CCA has several differences when compared to intrahepatic CCA. Hilar CCA is associated more frequently with obstructive jaundice, likely reflecting the higher frequency of PBD utilization. Among the hilar CCA subset, the only significant association was between PBD and increased blood product transfusion requirements. This association persisted after adjusting for magnitude of resection, preoperative bilirubin, pathologic T stage, and use of PVE and preoperative therapy. PBD was not associated with other complications, although it must be noted that the small sample size of 186 patients increases the possibility of type II error. Further investigation of this association is warranted in larger datasets.

A primary strength of this study is the ability to analyze a large subset of patients with only hilar or intrahepatic CCA. Focusing on just proximal CCA has merit, in that the presentations, indications for operation, and expected outcomes vary as compared to hepatectomies for benign disease, distal CCA, and pancreatic and ampullary lesions. The addition of the hepatectomy procedure-targeted dataset improves the ability to analyze hepatectomy specific outcomes, and adjust for specific comorbid conditions. As a data source, the ACS-NSQIP has a unique data capture system consisting of administrative data and trained chart abstraction, enabling more accurate collection of data (24–26).

The limitations, however, are several and related primarily to those affecting retrospective analyses of large databases. Generalized limitations of the ACS-NSQIP PUF include that it only captures complications of up to 30 days, and thus may underreport complications. It also does not allow for stratification of surgeons and centers by volume and experience. The retrospective nature precludes an ability to control for all preoperative characteristics and confounders. By excluding those with disseminated disease, we attempted to cull those with palliative surgery from the dataset. The pathologic T stage was included as a preoperative baseline variable given that the dataset does not report clinical T stage. As a result, there could be discrepancies from stage migration that may explain the 4.7% of patients that received hepatectomy with pathologic T4 disease. **Specific limitations with regards to the analysis of PBD include an inability to glean data on the indications for PBD. Usual indications for PBD include symptomatic jaundice, hyperbilirubinemia precluding neoadjuvant treatment, cholangitis, and institutional hyperbilirubinemia thresholds for PBD. Unfortunately, indication for PBD is not a captured variable within ACS-NSQIP.**

The duration between PBD and surgery is also not obtainable from the present dataset. Furthermore, the bilirubin level available for analysis is the preoperative bilirubin with no available data on presenting bilirubin on diagnosis, or bilirubin prior to PBD. This precludes our ability to control for degree of obstructive jaundice on diagnosis, and assess adequacy of biliary drainage by PBD. Lastly, source and course of the bile leaks noted in the study cannot be further analyzed due to limitations in the dataset.

Overall, PBD was more widely used in those with hilar lesions, major liver resections, and open operations, and PBD was associated with increased postoperative complications after controlling for preoperative variables and pathologic T stage. These data indicate that routine PBD should be avoided. There are circumstances, however, in which PBD is required, and these circumstances are beyond the scope of this analysis. Such circumstances include nearly-obstructed patients with an anticipated need for neoadjuvant chemotherapy or PVE, for whom PBD may prevent progression to complete obstruction and cholangitis during an immunosuppressed period. Patients with active cholangitis or multiple bouts of previous cholangitis, such as those with primary sclerosing cholangitis, would also benefit from biliary drainage. Lastly, in asymptomatic or non-obstructing patients, cholangiography may be indicated if required for surgical planning.

Conclusion

PBD for intrahepatic and hilar CCA is independently associated with increased infectious, cardiopulmonary, renal, and hepatectomy-specific complications. Among those with hilar CCA, PBD is employed more frequently, and is independently associated with increased need for blood product transfusion. These data suggest that avoidance of routine PBD may decrease short-term complications.

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Variable	Definition
Wound infection	Infection involving skin or subcutaneous tissue with purulent drainage OR microbiologic confirmation OR opening of wound with suspicion
Organ space infection	Infection involved organs or spaces other than the incision, confirmed with purulence OR microbiologic confirmation OR physician diagnosis
Wound dehiscence	Loss of integrity of fascial closure or total breakdown of closure
Sepsis and septic shock	Two or more SIRS criteria AND positive culture or source, OR Operative confirmation of infarcted bowel, purulence, enteric contents AND/OR circulatory dysfunction
Pneumonia	Radiologic findings, AND Clinical signs with microbiological confirmation OR Respiratory symptoms
Reintubation	Unplanned endotracheal or other breathing tube with ventilator support intraoperatively or within 30 days
Respiratory failure	Ventilator requirement >48 hours after surgery
Renal insufficiency or failure	Creatinine increase >2 mg/dl from preoperative value, WITH/WITHOUT need for dialysis
Myocardial infarction and cardiac arrest	Indicative ECG changes OR new troponin elevation >3x upper limit of reference range OR physician diagnosis OR need for chest compressions or defibrillations
Stroke	Embolic, thrombotic or hemorrhagic vascular accident or stroke with dysfunction lasting >24 hours
VTE	New thrombus treated with anticoagulation or vena cava filter
UTI	One out of: Fever, urgency, frequency, dysuria, suprapubic tenderness AND urine culture with >10 ⁵ colonies/mL of no more than two organisms OR Two out of: Fever, urgency, frequency, dysuria, suprapubic tenderness AND dipstick positive for leukocyte esterase and/or nitrate, pyuria, gram stain positivity or positive urine culture OR physician documentation

Figure 1:
Abbreviated definitions of ACS-NSQIP outcomes.

Figure 2:
Comparison of postoperative complications based on PBD

Table 1:

Baseline characteristics and univariate analysis of PBD

	All Patients (N = 905)	No PBD (N = 646)	PBD (N = 251)	p-value
Mean age, years (SD)	63.6 (11.4)	64.1 (11.4)	62.5 (11.7)	0.041
Male gender, n (%)	454 (50.2%)	302 (46.7%)	148 (59.0%)	0.001
Mean BMI, kg/m ² (SD)	28.3 (5.8)	29.0 (6.1)	26.4 (4.3)	< 0.001
Hypertension, n (%)	482 (53.3%)	373 (57.7%)	103 (41.0%)	< 0.001
History of COPD, n (%)	47 (5.2%)	42 (6.5%)	4 (1.6%)	0.001
History of CHF, n (%)	4 (0.4%)	4 (0.6%)	0 (0.0%)	0.105
Diabetes: Non-Insulin, n (%)	121 (13.4%)	93 (14.4%)	26 (10.4%)	0.086
Diabetes: Insulin, n (%)	74 (8.2%)	58 (9.0%)	16 (6.4%)	
Smoker, n (%)	147 (16.2%)	103 (15.9%)	43 (17.1%)	0.667
Steroids, n (%)	23 (2.5%)	19 (2.9%)	4 (1.6%)	0.230
Mean bilirubin, mg/dL (SD)	1.2 (1.8)	0.8 (1.2)	2.3 (2.5)	< 0.001
Hilar CCA, n (%)	186 (20.6%)	51 (7.9%)	134 (53.4%)	< 0.001
MIS, n (%)	122 (13.5%)	109 (16.9%)	12 (4.8%)	< 0.001
Portal Vein Embolization, n (%)	70 (7.8%)	33 (5.1%)	36 (14.5%)	< 0.001
Preoperative chemotherapy, n (%)	90 (10.0%)	69 (10.7%)	20 (8.0%)	0.224
Major resection, n (%)	591 (65.3%)	371 (57.4%)	215 (85.7%)	< 0.001
PBD, n (%)	251 (28.0%)	N/A	N/A	N/A
T Stage: T0, n (%)	1 (0.1%)	1 (0.2%)	0 (0.0%)	< 0.001
T Stage: T1, n (%)	247 (29.5%)	213 (35.9%)	32 (13.6%)	
T Stage: T2, n (%)	435 (52.0%)	288 (48.6%)	144 (61.0%)	
T Stage: T3, n (%)	115 (13.7%)	70 (11.8%)	42 (17.8%)	
T Stage: T4, n (%)	39 (4.7%)	21 (3.5%)	18 (7.6%)	

Table 2:

Multivariate analysis of significant preoperative predictors of PBD

Variable	Odds Ratio	95% CI	p-value
Age (per year)	0.99	0.98, 1.01	<0.001
BMI (per kg/m2)	-2.16	-3.29, -1.07	<0.001
Bilirubin (per mg/dL)	1.03	0.78, 1.29	<0.001
Hilar	6.03	3.91, 9.37	<0.001
MIS	-2.60	-6.07, -1.21	0.013
Major resection	2.44	1.53, 3.94	<0.001

Table 3:

Postoperative complications with univariate analysis of patients undergoing PBD

	Total (N = 905)	PBD (N = 897)		
		No (N = 646)	Yes (N = 251)	p
Wound infection, n (%)	71 (8.1%)	30 (4.7%)	40 (17.5%)	< 0.001
Organ space infection, n (%)	154 (17.6%)	71 (11.1%)	83 (36.2%)	< 0.001
Wound dehiscence, n (%)	13 (1.4%)	5 (0.8%)	7 (2.8%)	0.027
Sepsis/Septic shock, n (%)	114 (13.3%)	53 (8.4%)	59 (27.1%)	< 0.001
Pneumonia, n (%)	49 (5.4%)	29 (4.5%)	20 (8.0%)	0.044
Reintubation, n (%)	59 (6.5%)	31 (4.8%)	28 (11.2%)	0.001
Respiratory failure, n (%)	46 (5.1%)	22 (3.4%)	24 (9.6%)	< 0.001
Renal Insufficiency/Failure, n (%)	44 (4.9%)	22 (3.4%)	22 (8.8%)	0.002
Myocardial infarction, n (%)	32 (3.5%)	22 (3.4%)	10 (4.0%)	0.678
Stroke, n (%)	4 (0.4%)	3 (0.5%)	1 (0.4%)	0.893
VTE, n (%)	59 (6.5%)	32 (5.0%)	26 (10.4%)	0.005
UTI, n (%)	22 (2.4%)	19 (2.9%)	3 (1.2%)	0.104
Transfusion, n (%)	273 (30.2%)	148 (22.9%)	121 (48.2%)	< 0.001
Invasive Intervention, n (%)	190 (21.2%)	95 (14.8%)	94 (37.8%)	< 0.001
Bile leak, n (%)	167 (18.6%)	81 (12.6%)	85 (34.4%)	< 0.001
Liver failure, n (%)	125 (13.8%)	60 (9.3%)	65 (25.9%)	< 0.001
Unplanned readmission, n (%)	147 (17.7%)	83 (13.7%)	64 (29.9%)	< 0.001
Unplanned reoperation, n (%)	56 (6.2%)	26 (4.0%)	29 (11.6%)	< 0.001
Discharge to facility, n (%)	105 (12.3%)	66 (10.6%)	38 (16.8%)	0.019
Mortality, n (%)	46 (5.1%)	22 (3.4%)	24 (9.6%)	< 0.001

Table 4:

Independent contribution of PBD to postoperative complications after adjusting for all preoperative demographic and comorbidity variables, hilar location, MIS, PVE, preoperative systemic chemotherapy, major liver resection, pathologic T-stage, and preoperative bilirubin.

	Adjusted PBD Odds Ratio	95% CI	p-value
Wound infection	2.93	1.62, 5.27	<0.001
Organ space infection	3.63	2.36, 5.61	<0.001
Wound dehiscence	1.39	0.36, 5.55	0.643
Sepsis	3.17	1.95, 5.16	<0.001
Pneumonia	1.40	0.67, 2.83	0.364
Reintubation	3.02	1.59, 5.68	<0.001
Respiratory failure	3.41	1.62, 7.14	<0.001
Renal insufficiency	4.25	1.98, 9.13	<0.001
VTE	1.96	0.99, 3.80	0.051
Transfusion	2.40	1.64, 3.52	<0.001
Invasive intervention	2.72	1.82, 4.06	<0.001
Bile leak	3.23	2.13, 4.93	<0.001
Liver failure	3.20	1.98, 5.18	<0.001
Readmission	3.01	1.92, 4.72	<0.001
Reoperation	2.32	1.18, 4.49	0.010
Mortality	4.24	2.01, 9.01	<0.001

Table 5:

Comparison of preoperative variables based on location of proximal CCA

	Hilar (n=186)	Intrahepatic (n=719)	p
Mean age, years (SD)	62.3 (11.9)	64.0 (11.3)	0.096
Male gender, n (%)	113 (60.8)	341 (47.4)	0.001
Mean BMI, kg/m² (SD)	26.7 (4.4)	28.7 (6.0)	<0.001
Hypertension, n (%)	76 (40.9)	406 (56.5)	<0.001
History of COPD, n (%)	6 (3.2)	41 (5.7)	0.153
Diabetes: Non-Insulin, n (%)	21 (11.3)	100 (13.9)	0.013
Diabetes: Insulin, n (%)	7 (3.8)	67 (9.3)	
Smoker, n (%)	37 (19.9)	110 (15.3)	0.138
Steroids, n (%)	3 (1.6)	20 (2.8)	0.341
Mean bilirubin, mg/dL (SD)	2.3 (2.4)	0.9 (1.5)	<0.001
MIS, n (%)	11 (5.9)	111 (15.4)	<0.001
Portal Vein Embolization, n (%)	12 (15.6)	41 (5.7)	<0.001
Preoperative chemotherapy, n (%)	9 (4.8)	81 (11.3)	0.005
Major resection, n (%)	158 (84.9)	433 (60.2)	<0.001
PBD, n (%)	134 (72.0)	117 (16.3)	<0.001
T Stage: T0, n (%)	10 (5.4)	59 (8.2)	<0.001
T Stage: T1, n (%)	13 (7.0)	234 (32.6)	
T Stage: T2, n (%)	118 (63.4)	317 (44.1)	
T Stage: T3, n (%)	34 (18.3)	81 (11.3)	
T Stage: T4, n (%)	11 (5.9)	28 (3.9)	