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BRIEF ARTICLE

Preoperative biliary drainage in patients with hilar cholangiocarcinoma undergoing major hepatectomy

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Abstract

AIM: To investigate the effect of preoperative biliary drainage (PBD) in jaundiced patients with hilar cholangiocarcinoma (HCCA) undergoing major liver resections.

METHODS: An observational study was carried out by reviewing a prospectively maintained database of HCCA patients who underwent major liver resection for curative therapy from January 2002 to December 2012. Patients were divided into two groups based on whether PBD was performed: a drained group and an undrained group. Patient baseline characteristics, preoperative factors, perioperative and short-term postoperative outcomes were compared between the two groups. Risk factors for postoperative complications were also analyzed by logistic regression test with calculating OR and 95%CI.

RESULTS: In total, 78 jaundiced patients with HCCA underwent major liver resection: 32 had PBD prior to operation while 46 did not have PBD. The two groups were comparable with respect to age, sex, body mass index and co-morbidities. Furthermore, there was no significant difference in the total bilirubin (TBIL) levels between the drained group and the undrained group at admission (294.2 ± 135.7 *vs* 254.0 ± 63.5, $P = 0.126$). PBD significantly improved liver function, reducing not only the bilirubin levels but also other liver enzymes. The preoperative TBIL level was significantly lower in the drained group as compared to the undrained group (108.1 ± 60.6 *vs* 265.7 ± 69.1, $P = 0.000$). The rate of overall postoperative complications (53.1% *vs* 58.7%, $P = 0.626$), reoperation rate (6.3% *vs* 6.5%, $P = 1.000$), postoperative hospital stay (16.5 *vs* 15.0, $P = 0.221$) and mortality (9.4% *vs* 4.3%, $P = 0.673$) were similar between the two groups. In addition, there was no significant difference in infectious complications (40.6% *vs* 23.9%, $P = 0.116$) and noninfectious complications (31.3% *vs* 47.8%, $P = 0.143$) between the two groups. Univariate and multivariate analyses revealed that preoperative TBIL > 170 μmol/L (OR = 13.690, 95%CI: 1.275-147.028, $P = 0.031$), Bismuth-Corlette classification (OR = 0.013, 95%CI: 0.001-0.166, $P = 0.001$) and extended liver resection (OR = 14.010, 95%CI: 1.130-173.646, $P = 0.040$) were independent risk factors for postoperative complications.

CONCLUSION: Overall postoperative morbidity and mortality rates after major liver resection are not improved by PBD in HCCA patients with jaundice. Preoperative TBIL > 170 μmol/L, Bismuth-Corlette classification and extended liver resection are independent risk factors linked to postoperative complications.

Key words: Obstructive jaundice; Hilar cholangiocarcinoma; Preoperative biliary drainage; Major hepatectomy; Surgical outcome

Core tip: There is currently no consensus on the use of preoperative biliary drainage (PBD) in jaundiced patients with hilar cholangiocarcinoma undergoing major liver resection. We retrospectively analyzed prospectively maintained database of these patients who underwent PBD or not. The baseline characteristics, perioperative and short-term postoperative outcomes between these two groups were compared and no significant differences were identified. We found that a preoperative total bilirubin level > 170 μmol/L, Bismuth-Corlette classification and extended liver resection are three independent risk factors for postoperative complications. There is a need to undertake well-designed, prospective multicenter studies to inform future practice.

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INTRODUCTION

Hilar cholangiocarcinoma (HCCA), which was first defined by Klatskin[1] as an adenocarcinoma of the hepatic duct at its bifurcation within the porta hepatis, is associated with a poor prognosis[1,2]. Currently, the only curative treatment is radical surgical resection[3]. However, a R0 resection margin is difficult to achieve because the tumor often infiltrates the portal vein, the hepatic artery and liver parenchyma[4,5]. In order to obtain negative histological margins and improve survival, many surgeons have adopted a more aggressive surgical approach, namely, extended hepatectomy combined with portal vein or hepatic artery resection and reconstruction, and hepato pancreaticoduodenectomy for the treatment of this malignancy[6-8]. However, the majority of patients with HCCA have obstructive jaundice at presentation, which increases the risk of complications, such as sepsis, bleeding and liver failure, especially in patients undergoing major hepatectomy[9,10]. Therefore, preoperative biliary drainage (PBD) was introduced with the aim to abrogate these potential complications in patients with jaundice secondary to HCCA, despite that a consensus on an appropriate cut-off level of total bilirubin (TBIL)[11-14] and duration of drainage[8,15,16] has not been reached yet.

There is still controversy with regard to whether PBD is essentially needed for jaundiced patients with HCCA undergoing major liver resection. It was shown that PBD reverses cholestasis-associated hepatic and systemic toxicity, and improves liver function, nutritional status and cell-mediated immune function[17]. However, concerns were also raised as PBD may associate with an increased incidence of postoperative morbidity and mortality[18-20], although this was not the case for other studies[21,22]. Recently, one multicenter European study including patients undergoing major liver resection for HCCA suggested that overall morbidity was not affected by PBD procedure[14]. Furthermore, preoperative portal vein embolization (PVE), which is restricted to the treatment of postoperative inadequate residual liver volume and induces hypertrophy of the future remnant liver, has led to a change to PBD strategy[23]. PBD followed by PVE prior to major hepatectomy is considered a safe management strategy for HCCA, particularly in patients with remnant liver volume less than 40%[24-26].

The aim of this study was to inform the debate by comparing the perioperative and short-term postoperative outcomes of jaundiced patients with HCCA undergoing curative major liver resection with or without PBD, at a large specialist center in China.

MATERIALS AND METHODS

Study population and preoperative management

The prospectively maintained database for a cohort of consecutive HCCA patients treated at the West China Hospital of Sichuan University between January 2002 and December 2012 was retrospectively reviewed. From the database, only patients with HCCA who had jaundice and underwent major hepatectomy for curative resection were included in this study. Jaundice was defined as a serum TBIL level > 85.5 μmol/L (5 mg/dL). HCCA was defined as lesions arising from the common hepatic duct, left, right, or both hepatic duct and intrahepatic bile duct cancer invading the hepatic hilus[11]. The tumors were classified according to Bismuth-Corlette classification[27].

In our series, blood sampling for serum biochemistry was completed 2-3 d before drainage or surgery. Color Doppler ultrasound and contrast enhanced computed tomography (CT) were used routinely before surgery. Furthermore, magnetic resonance imaging (MRI) was used in most of patients. If distant metastases were suspected, further investigations with positron emission tomography-CT scan were performed. PVE was carried out at our hospital if the remnant liver volume post surgical resection was expected to be less than 50% of the whole liver volume. PBD was performed if patients fulfilled one of the following criteria: duration of jaundice of more than 4 wk; poor nutritional status (serum albumin < 3 g/dL); signs of cholangitis. PBD procedures in our center were percutaneous transhepatic cholangio-drainage (PTCD), endoscopic biliary stenting (EBS), endoscopic nasobiliary drainage (ENBD) and/or surgical drainage. For patients who had inadequate PBD before admission to our hospital, a further drainage by a percutaneous approach was adapted. Adequate PBD was evident by a relief of cholangitis, and an improvement in the liver function and/or the nutritional status of the patient.

Surgical procedures

At our center, curative excision was defined as histologically negative surgical margins with a minimum tumor-free margin of 5 mm at the hepatic stump of the bile duct, the duodenal stump of the bile duct, and the excision surface. It included resection of the gallbladder and extrahepatic bile duct; skeletonization of the vasculature of the hepatoduodenal ligament; and partial hepatectomy, or even removal of the caudate lobe or portal vein or hepatic artery as required. The postoperative biliary drainage was established by a Roux-en-Y hepaticojejunostomy. Major hepatectomy was defined as resection of three or more Couinaud segments. Caudate lobectomy was performed in patients in whom it was considered necessary to achieve complete tumor clearance.

Postoperative complications

While patients were followed routinely after discharge from hospital, as part of this study, we endeavored to investigate the effect of PBD on in-hospital postoperative outcomes. Hence, postoperative mortality was defined as death prior to hospital discharge. All postoperative complications were defined as events that lengthened hospital stay. Infectious complications were defined according to the study by Hochwald *et al*[19]; these were intraabdominal abscess, wound infection, cholangitis, sepsis and lung infection. Noninfectious complications included liver failure, bile leak, anastomotic leak, abdominal collection, gastrointestinal bleeding, abdominal bleeding, respiratory failure and renal failure. Liver failure was defined as an increased international normalized ratio and concomitant hyperbilirubinemia on or after postoperative day five[28]. Bile leak was defined as the drainage of 50 mL or more of bile from the surgical drain or from drainage of an abdominal collection, over a period of three days or more[29]. In addition, the complications were graded according to the Clavien-Dindo classification of surgical complications[30].

Literature search

Existing literature was also reviewed by performing a systematic search in PubMed, Medline and Embase from January 1990 to May 2013. The following search terms were used: "preoperative biliary drainage" or "percutaneous transhepatic biliary drainage" or "endoscopic biliary drainage" or "endoscopic nasobiliary drainage" or "endoscopic biliary stenting" and "hilar cholangiocarcinoma" or "hilar bile duct cancer" or "proximal bile duct cancer" or "Klatskin tumor" or "carcinoma of the hepatic duct confluence" along with their synonyms or abbreviations. The search was restricted to studies conducted on human subjects and in the English language only.

Statistical analysis

Data are presented as mean ± SD or median and interquartile range. The χ^2 test or Fisher's exact test or RxC table analysis was used to compare categorical variables, and the Student's *t* test or Mann-Whitney *U* test was used to compare continuous variables. A statistically significant difference was defined as a *P* value < 0.05. The variables of statistical significance during univariate analysis were included in a follow-up multivariate analysis, by using the logistic regression test. The OR and 95%CI were also calculated for individual factors in the multivariate analysis. All statistical analyses were performed with SPSS software (SPSS version 17.0, Chicago, Illinois).

Table 1 Baseline characteristics *n* (%)

	Drained (*n* = 32)	Undrained (*n* = 46)	*P* value
Age (yr)	59.6 ± 11.0	58.2 ± 11.3	0.568
Sex (M/F)	21/11	28/18	0.669
Body mass index (kg/m^2)	20.3 ± 1.9	21.0 ± 2.5	0.190
Concomitant diseases			
Diabetes	2 (6.3)	3 (6.5)	1.000
Hypertension	3 (9.4)	7 (15.2)	0.678
Cardiovascular	2 (6.3)	5 (10.9)	0.765
Previous history of abdominal surgery	9 (28.1)	12 (26.1)	0.842
Serum total bilirubin (μmol/L)			
At admission	294.2 ± 135.7	254.0 ± 63.5	0.126
Before surgery	108.1 ± 60.6	265.7 ± 69.1	0.000
Time of PBD (d)	15.3 ± 3.4	-	-
Time between admission and surgery (d)	20.7 ± 2.1	3.8 ± 1.6	0.000
Portal vein embolization	5 (15.6)	3 (6.5)	0.355
Bismuth-Corlette classification			
Ⅰ	1 (3.1)	1 (2.2)	1.000
Ⅱ	8 (25)	14 (30.4)	0.600
Ⅲa	6 (18.8)	7 (15.2)	0.680
Ⅲb	9 (28.1)	15 (32.6)	0.673
Ⅳ	8 (25)	9 (19.6)	0.567
Perioperative details			
Hilar bile duct resection	32 (100)	46 (100)	-
Left hepatectomy	17 (53.1)	31 (67.4)	0.203
Extended left hepatectomy	2 (6.3)	1 (2.2)	0.747
Right hepatectomy	8 (25)	10 (21.7)	0.737
Extended right Hepatectomy	5 (15.6)	4 (8.7)	0.561
Caudate lobectomy	8 (25)	12 (26.1)	0.914
Pedicle clamping	17 (53.1)	26 (56.5)	0.767
Portal vein resection	6 (18.8)	8 (17.4)	0.878
Hepatic artery resection	2 (6.3)	3 (6.5)	1.000
Number of blood Transfusions	11 (34.4)	24 (52.2)	0.120
Intraoperative blood transfusion (mL)	900 (800-900)	800 (600-1100)	0.513

PBD: Preoperative biliary drainage.

RESULTS

Baseline characteristics

During the study period, 78 patients with jaundice underwent major hepatic resection for HCCA at our hospital. There were 32 patients in the drained (PBD) group and 46 patients in the undrained (no PBD) group. The baseline characteristics of patients are outlined in Table 1. The drained group was comparable with the undrained

Table 2 Postoperative outcomes of patients undergoing major hepatectomy *n* (%)

	Drained (n = 32)	Undrained (n = 46)	P value
Morbidity	17 (53.1)	27 (58.7)	0.626
Infectious morbidity	13 (40.6)	11 (23.9)	0.116
Intra-abdominal abscess (Ⅱ-Ⅲa)	3 (9.4)	2 (4.3)	0.673
Wound infection (Ⅰ-Ⅲb)	4 (12.5)	4 (8.7)	0.869
Cholangitis (Ⅱ)	1 (3.1)	2 (4.3)	1.000
Sepsis (Ⅳa-Ⅴ)	2 (6.3)	1 (2.2)	0.747
Lung infection (Ⅱ)	6 (18.8)	5 (10.9)	0.325
Noninfectious morbidity	10 (31.3)	22 (47.8)	0.143
Liver failure (Ⅱ-Ⅴ)	3 (9.4)	6 (13)	0.890
Bile leak			
Remnant liver[1] (Ⅱ-Ⅲa)	2 (6.3)	4 (8.7)	1.000
Anastomotic leak[2] (Ⅱ-Ⅲb)	1 (3.1)	2 (4.3)	1.000
Abdominal collection (Ⅰ-Ⅲa)	6 (18.8)	9 (19.6)	0.928
Gastrointestinal bleeding (Ⅲa-Ⅴ)	0	2 (4.3)	0.510
Abdominal bleeding (Ⅱ-Ⅲb)	1 (3.1)	2 (4.3)	1.000
Respiratory failure (Ⅳa)	0	3 (6.5)	0.265
Renal failure (Ⅳa-Ⅴ)	3 (9.4)	4 (8.7)	1.000
Mortality (Ⅴ)	3 (9.4)	2 (4.3)	0.673
Reoperation	2 (6.3)	3 (6.5)	1.000
Postoperative hospital stay (d)	16.5 (13.5-20.5)	15 (12-18)	0.221

Clavien-Dindo grades of surgical complications are within parentheses. [1]From remnant liver; [2]From hepaticojejunostomy.

group with regards to age, sex, body mass index, comorbidity and previous history of abdominal surgery (P > 0.05 for all). Nine patients in the PBD group had previous abdominal surgery that included 5 cholecystectomies and 4 common bile duct explorations with T-tube drainage. Twelve patients in the undrained group had previous abdominal surgery, which included 6 appendectomies, 4 cholecystectomies and 2 cholecystectomies with common bile duct exploration. Furthermore, there was no significant difference in the TBIL levels at admission between the drained and undrained groups (294.2 ± 135.7 *vs* 254.0 ± 63.5, P = 0.126).

PBD techniques and liver function tests

In the PBD group, 23, 5 and 4 patients underwent PTCD, ENBD, and surgical drainage, respectively. In this study, 4 patients underwent surgical drainage through laparotomy and T-tube placement at the referring hospitals. No patient in this study underwent EBS. Six patients underwent PTCD twice each as a result of previous inadequate drainage. Drainage-related complications occurred in 8 patients (10.3%), with 3 cases of cholangitis and 4 of hemobilia following PTCD, and 1 case of hyperamylasemia following ENBD. All these adverse events were resolved after symptomatic treatment alone before surgery. The mean time between insertion of a biliary drainage catheter preoperatively and surgical resection was 15.3 ± 3.4 (d). PBD significantly improved liver function as evidenced by reduced TBIL (294.2 ± 135.7 *vs* 108.1 ± 60.6, P = 0.000), direct bilirubin (DBIL) (231.8 ± 87.0 *vs* 85.2 ± 57.4, P = 0.000), aspartate aminotransferase (AST) (132.1 ± 68.6 *vs* 86.1 ± 35.8, P = 0.000), alanine aminotransferase (ALT) (123.2 ± 79.1 *vs* 97.5 ± 62.4, P = 0.004), gamma-glutamyl transpeptidase (GGT) (531.2 ± 434.7 *vs* 357.6 ± 268.3, P = 0.000) and alkaline phosphatase (ALP) (502.1 ± 356.2 *vs* 343.5 ± 187.6, P = 0.001), although albumin (ALB) (36.7 ± 4.8 *vs* 34.8 ± 5.9, P = 0.213) levels remained unchanged.

Perioperative details

All patients in both groups had hilar bile duct resection. There were no significant differences in operation procedure (liver resection) between the two groups. Also, there were no significant differences between the drained and undrained groups in terms of caudate lobectomy, pedicle clamping, portal vein resection, hepatic artery resection, number of patients requiring blood transfusions and intraoperative blood transfusion volume (all P > 0.05).

Postoperative outcomes

Postoperative outcomes are outlined in Table 2. The number of patients with postoperative morbidity in the two groups was comparable (53.1% *vs* 58.7%, P = 0.626). No significant difference was found in the number of patients who had either infectious morbidity or non-infectious morbidity. Also, there was no significant difference in the incidence of individual complications. In addition, in a subgroup analysis (data not shown in table), there was a higher morbidity (84.6% *vs* 35.7%, P = 0.028) in patients undergoing right-sided hepatectomy without PBD than patients with PBD. However, in the left-sided hepatectomy group, patients had a higher morbidity (78.9% *vs* 40.6%, P = 0.018) in the drained group compared to the undrained group. However, there was no difference in the postoperative hospital stay between the two groups (16.5 *vs* 15, P = 0.221). Two patients in the drained group and 3 patients in the undrained group underwent reoperation. There was no significant difference in mortality (9.4% *vs* 4.3%, P = 0.673) between the two groups. In the drained group, 1 patient died of multiorgan failure (liver failure and renal failure) while another 2 patients died of septic shock. In the undrained group, one patient died from a massive gastrointestinal bleeding while another 1 patient died of multiorgan failure (liver failure and renal failure).

Logistic regression analyses

Several variables in this study were analyzed for their association with postoperative morbidity (Table 3). Univariate logistic regression showed that PBD was not a risk factor associated with postoperative morbidity. However, preoperative TBIL > 170 μmol/L (P = 0.021), preoperative AST > 100 U/L (P = 0.036), Bismuth-Corlette classification (P = 0.025) and extended liver resection (P = 0.018) were risk factors associated with postoperative morbidity on univariate logistic regression analysis. Furthermore, multivariate analysis identified preoperative TBIL > 170 μmol/L (OR = 13.690, 95%CI: 1.275-147.028, P = 0.031), Bismuth-Corlette classification (OR = 0.013, 95%CI: 0.001-0.166, P = 0.001) and extended liver resection (OR = 14.010, 95%CI: 1.130-173.646, P = 0.040) as three independent risk fac-

Table 3 The risk factors for postoperative complications *n* (%)

Variable	*n*	Incidence of complications	Univariate	Multivariate	
			P value	OR	*P* value
Age (yr)					
> 60	38	21 (55.3)	0.842		
≤ 60	40	23 (57.5)			
Sex					
Male	49	25 (51)	0.212		
Female	29	19 (65.5)			
PBD					
Yes	32	17 (53.1)	0.626		
No	46	27 (58.7)			
Concomitant diseases					
Yes	20	14 (70)	0.155		
No	58	30 (51.7)			
Previous abdominal surgery					
Yes	21	11 (52.4)	0.663		
No	57	33 (57.9)			
Preoperative TBIL					
> 170 μmol/L	48	32 (66.7)	0.021	13.690 (1.275-147.028)	0.031
≤ 170 μmol/L	30	12 (40)			
Preoperative AST					
> 100 U/L	47	31 (66)	0.036	1.138 (0.157-8.225)	0.898
≤ 100 U/L	31	13 (41.9)			
Preoperative ALT					
> 100 U/L	44	29 (65.9)	0.054	5.664 (0.595-53.905)	0.131
≤ 100 U/L	34	15 (44.1)			
Preoperative ALB					
> 35	41	26 (63.4)	0.189		
≤ 35	37	18 (48.6)			
Bismuth-Corlette stage					
Ⅰ and Ⅱ	24	9 (37.5)	0.025	0.013 (0.001-0.166)	0.001
Ⅲ and Ⅳ	54	35 (64.8)			
Extended liver resection					
Yes	12	11 (91.7)	0.018	14.010 (1.130-173.646)	0.04
No	66	33 (50)			
Caudate lobectomy					
Yes	20	12 (60)	0.707		
No	58	32 (55.2)			
Pedicle clamping					
Yes	43	22 (51.2)	0.300		
No	35	22 (62.9)			
Vascular resections					
Yes	19	13 (68.4)	0.225		
No	59	31 (52.5)			
Additional surgery					
Yes	6	3 (50)	0.742		
No	72	41 (56.9)			
Intraoperative blood transfusion					
Yes	35	19 (54.3)	0.644		
No	43	25 (59.5)			

TBIL: Total bilirubin; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALB: Albumin; PBD: Preoperative biliary drainage.

tors for postoperative complications.

Results of literature search

Fourteen studies were identified[5,10,14,18-20,31-37] using the defined search strategy (Table 4). Seven studies included patients who had curative resections only[5,14,18,20,31,33,37], while the remaining studies included both curative and palliative resection groups.

DISCUSSION

Currently, the only curative treatment for HCCA is radical surgical resection[3]. Patients with HCCA usually present with concomitant obstructive jaundice, which results in high surgical morbidity and mortality in those undergoing major hepatic resection[38,39]. Furthermore, postoperative liver failure is a common cause of in-hospital death after major hepatectomy in patients with obstructive jaundice[13,40]. PBD offers the advantage of being able to increase the tolerance of cholestatic liver to ischemia, improve the regeneration capacity of the liver and decrease blood loss, which may contribute to reducing morbidity and mortality. However, there were conflicting conclusions from various studies with regards to the benefits of

Table 4 Studies including resections for hilar cholangiocarcinoma with and without preoperative biliary drainage *n* (%)

Ref.	Year	Country	Design	Type of PBD	Surgical procedures for included patients	PBD	*n*	Morbidity	*P* value	Mortality	*P* value
Su *et al*[10]	1996	China	Retro	PTCD	CR and PR	Yes	33	17 (51.5)	NS	5 (15.2)	NS
						No	16	6 (37.5)		0	
Takada *et al*[37]	1996	Japan	Retro	PTCD	CR	Yes	24	NA	-	3 (12.5)	NS
						No	12	NA		6 (50)	
Hochwald *et al*[19]	1999	United States	Pro	PTCD	CR and PR	Yes	42	36 (85.7)	0.045	2 (4.8)	NS
				EBD		No	29	19 (65.5)		4 (14.3)	
Figueras *et al*[31]	2000	Spain	Retro	PTCD	CR	Yes	11	11 (100)	NS	1 (9)	NS
						No	9	6 (66)		2 (22.2)	
Parks *et al*[36]	2000	United Kingdom	Retro	PTCD	CR and PR	Yes	20	11 (55)	NS	1 (5)	NS
				EBD		No	27	11 (40.7)		1 (3.7)	
Gerhards *et al*[5]	2000	The Netherlands	Retro	PTCD	CR	Yes	93	59 (63)	NS	16 (17)	NS
				EBD		No	18	13 (72)		3 (17)	
Dinant *et al*[33]	2006	The Netherlands	Retro	PTCD	CR	Yes	83	56 (67.5)	NS	14 (16.7)	NS
				EBD		No	14	6 (42.9)		2 (14.3)	
Li *et al*[32]	2009	China	Retro	PTCD	CR and PR	Yes	55	20 (36.3)	NS	4 (7.3)	NS
						No	56	16 (28.6)		5 (8.9)	
Ferrero *et al*[18]	2009	Italy	Retro	PTCD	CR	Yes	30	21 (70)	NS	1 (3)	NS
				EBD		No	30	19 (63)		3 (10)	
				SD							
Ercolani *et al*[34]	2010	Italy	Retro	PTCD	CR and PR	Yes	44	25 (56.8)	NS	NA	-
				EBD		No	7	2 (28.5)		NA	
El-Hanafy *et al*[20]	2010	Egypt	Retro	PTCD	CR	Yes	46	27 (58.6)	0.001	5 (10.8)	NS
				EBD		No	54	11 (20.3)		3 (5.5)	
Yu *et al*[35]	2012	China	Retro	PTCD with bile re-infusion	CR and PR	Yes	48	14 (29.2)	0.036	1 (2.1)	NS
						No	39	20 (51.3)		2 (5.1)	
Farges *et al*[14]	2013	France and Belgium	Retro	PTCD	CR	Yes	180	123 (68.3)	NS	17 (9.4)	NS
				EBD		No	186	128 (68.8)		22 (11.8)	
Present study		China	Retro	PTCD	CR	Yes	32	17 (53.1)	NS	3 (9.4)	NS
				EBD		No	46	27 (58.7)		2 (4.3)	
				SD							

Retro: Retrospective; Pro: Prospective; PBD: Preoperative biliary drainage; PTCD: Percutaneous transhepatic cholangio-drainage; EBD: Endoscopic biliary drainage; SD: Surgical drainage; CR: Curative resection; PR: Palliative resection; NA: Not available; NS: Not significant.

PBD[14,19,20,31,35,41].

In our study, the two groups were comparable with respect to demographics, BMI, comorbidities and serum TBIL levels at admission. PBD-associated complications were low, occurring in 8 patients (10.3%), which may be because EBS was not used in our study[42]. This also illustrates that the drainage techniques and technology used at our center are feasible. The number of patients undergoing PVE before surgery was comparable between the drained and undrained groups. PBD followed by PVE prior to major hepatectomy is considered a safe management strategy[24-26].

The number of patients with postoperative complications was comparable, with 17 patients (53.1%) in the drained group and 27 patients (58.7%) in the undrained group; there was no significant difference in the number of patients who had either infectious complications or non-infectious complications. We found this result to be consistent with most of the studies that were reviewed in our systematic search. Most recently, a multicenter European study by Farges *et al*[14] reported that there was no significant difference in the rate of complications between drained and undrained groups of patients undergoing major liver resection. However, the infectious complications were not compared in this study and the risk factors for the overall complications were not analyzed. In our study, there was no significant difference in the number of patients with infectious complications between the two groups, which might be because most of them underwent PTCD (71.9%) as compared to endoscopic techniques (ENBD-15.6% and EBS-0%). EBS in particular has been shown to increase the infectious complication rate as compared to other drainage procedures[18,23,42,43]. Three studies[18-20] from our search reported higher infectious complications in patients who underwent PBD. Four studies[5,18,19,31] reported no significant difference in the non-infectious complication rates between the two groups. In our study, patients undergoing right-sided hepatectomy without PBD had a higher morbidity than patients with PBD, whereas contrary results were obained in the left-sided hepatectomy group. This is consistent with the study carried out by Farges *et al*[14]. Furthermore, while some studies have reported a longer stay in the drained group[20,31], other studies have shown no difference between the two groups[18,19]. In our study, there was no difference in the postoperative hospital stay, reoperation rate and mortality between the two groups.

While PBD was not a risk factor for postoperative complications, preoperative TBIL > 170 μmol/L, a higher Bismuth-Corlette classification and extended liver resection were found to be three independent risk factors for postoperative complications. In our study, PBD reduced the preoperative serum bilirubin level and other liver function indexes significantly as compared to those on admission. However, this did not translate into a significant reduction in the occurrence of postoperative complications, as compared to the undrained group. Previous studies have shown that preoperative bilirubin levels influence postoperative morbidity and mortality rates[18,34]. However, there is no consensus on the serum bilirubin cut-off level before surgery at which PBD should be undertaken. Some studies recommend undertaking PBD at a bilirubin cut-off of 51.3 μmol/L (3 mg/dL) to minimize complications following major surgery[11,12]. Other studies recommend a bilirubin cut-off of more than 85.5 μmol/L (5 mg/dL)[13]. The serum bilirubin level prior to surgery was 108.1 ± 60.6 μmol/L in our study. Farges *et al*[14] advised that major hepatectomy for jaundiced patients should be delayed until the serum bilirubin level had fallen below 50 μmol/L. Other studies have suggested that PBD should be performed and surgery should be delayed when the preoperative bilirubin level was higher than 171 μmol/L (10 mg/dL)[10,34]. Koyama *et al*[15] advised that adequate recovery of hepatic function depended not only on the duration of obstructive jaundice prior to decompression, but also on the duration of biliary decompression. Some studies have suggested 3-6 wk of preoperative drainage for obstructive jaundice, with even longer periods proposed with a prolonged biliary obstruction before decompression[8,15,16]. In our study, the PBD catheter remained *in situ* for a mean of 15.3 d. In light of the above, it is plausible that postoperative outcomes may have improved further, had we kept the PBD catheter *in situ* longer with a lower preoperative serum bilirubin level. However, we recommend PBD, prior to major hepatectomy, in patients with HCCA with a TBIL above 170 μmol/L.

Gerhards *et al*[5] had reported a higher Bismuth-Corlette classification was associated with postoperative morbidity. Also Li *et al*[32] reported that while PBD alleviated liver injury caused by hyperbilirubinemia, it did not decrease the postoperative morbidity and mortality and concomitant hepatectomy and Bismuth-Corlette classification were independent risk factors linked to surgical risks. This is explainable as a higher Bismuth-Corlette classification warrants a more extensive surgical resection, which resulted in higher morbidity[44]. Indeed, in our study, there were many patients with stage Ⅲ and Ⅳ tumors who underwent extended hepatectomy with caudate lobe resection and vascular resection.

We acknowledge the limitations of our study. First of all, our results derive from a retrospective study and are unavoidably subject to selection bias although a consecutive series was reported. Second, the sample size is relatively small, coming from a single center. Moreover, various factors such as the variable procedures for biliary drainage, treatment of patients at other centers prior to transfer to our center and failure of the initial drainage procedure may have contributed to biases in our study. However, as the baseline characteristics of patients prior to surgery were comparable between the drained and undrained groups, we hope that the effect of these factors on postoperative outcome was minimized. Currently, there continues to be a lack of consensus and recommendations on the use of PBD prior to major liver resection for HCCA. This has been highlighted by our study and review of literature. While an adequately powered randomized controlled trial at a single center may be currently unrealistic, in view of the rarity of this tumor, a multicenter study would go a long way in informing future practice.

In summary, short-term postoperative outcomes after major liver resection for HCCA are not improved by PBD, which is consistent with most of published evidence. Preoperative TBIL > 170 μmol/L and Bismuth-Corlette classification and extended liver resection might be three independent risk factors for postoperative complications. There is a need to undertake multicenter studies to inform future practice.

COMMENTS

Background

Whether preoperative biliary drainage (PBD) should be used in jaundiced patients with hilar cholangiocarcinoma (HCCA) undergoing major liver resection remains unclear.

Research frontiers

To investigate the role of PBD in patients with HCCA undergoing major liver hepatectomy using prospectively maintained database from a specialty center. A retrospective comparative analysis was performed comparing the perioperative and short-term postoperative outcomes of patients with PBD or not.

Innovations and breakthroughs

Based on the study, PBD does not improve short-term postoperative outcomes in patients with HCCA undergoing major liver resection. However, Preoperative total bilirubin (TBIL) > 170 μmol/L, Bismuth-Corlette classification and extended liver resection are three independent risk factors for postoperative complications.

Applications

The advantages of PBD was not found in this study; however, higher preoperative TBIL (> 170 μmol/L) was indeed a risk factor for postoperative complications. In addition, taking into account the nature of a retrospective study, there is a need to undertake well-designed, prospective multicenter studies to inform future practice.

Terminology

PBD is an important method for recovery of liver function in patients with obstructive jaundice, which includes the percutaneous transhepatic cholangiodrainage, endoscopic biliary stenting, endoscopic nasobiliary drainage and surgical drainage.

Peer review

This well-written study investigated the short-time postoperative outcomes and risk factors in jaundiced patients as result of HCCA with PBD or not. It may be of interest for hepatobiliary surgeons worldwide.

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