Surg Endosc (2017) 31:422–429
DOI 10.1007/s00464-016-4993-8

Best options for preoperative biliary drainage in patients with Klatskin tumors

Jung Hyun Jo[1] · Moon Jae Chung[1] · Dai Hoon Han[2] · Jeong Youp Park[1] · Seungmin Bang[1] · Seung Woo Park[1] · Si Young Song[1] · Jae Bock Chung[1]

Received: 23 December 2015 / Accepted: 17 May 2016 / Published online: 10 June 2016

Abstract
Summary background data Operative treatment combined with PBD has been established as a safe management strategy for Klatskin tumors. However, controversy exists regarding the preferred technique for PBD among percutaneous transhepatic biliary drainage (PTBD), endoscopic biliary stenting (EBS), and endoscopic nasobiliary drainage (ENBD). This study aimed to identify the best technique for preoperative biliary drainage (PBD) in Klatskin tumor patients.
Methods This study evaluated 98 Klatskin tumor patients who underwent PBD prior to operation with a curative aim between 2005 and 2012. The PTBD, EBS, and ENBD groups included 43, 42, and 13 patients, respectively. Baseline characteristics, technical success rate, complications of PBD, and surgical outcomes were compared.
Results Initial technical success rates (97.3 %, PTBD; 90.2 %, endoscopic methods, including EBS and ENBD) and mean duration until biliary decompression (31.0, PTBD; 28.7, EBS; 35.8 days, ENBD) were not significantly different between the groups. Total frequency of complications did not significantly differ between the EBS group (42.9 %) and the PTBD (27.9 %, $p = 0.149$) and ENBD (15.4 %, $p = 0.072$) groups. The ENBD group showed a significantly higher rate of conversion to other methods (76.9 %) than the PTBD (4.7 %, $p < 0.0001$) and EBS (35.7 %, $p = 0.009$) groups.
Conclusions PTBD, EBS, and ENBD showed comparable results regarding initial technical success rates, complication rates, and surgical outcomes. As Klatskin tumor patients must undergo PBD prior to 3 weeks before surgery, PTBD and ENBD are uncomfortable and disadvantageous in terms of compliance. EBS was the most suitable method for initial PBD in terms of compliance among Klatskin tumor patients.

Keywords Klatskin tumors · Preoperative biliary drainage · Percutaneous transhepatic biliary drainage · Endoscopic biliary stenting · Endoscopic nasobiliary drainage

✉ Moon Jae Chung
MJCHUNG@yuhs.ac

[1] Division of Gastroenterology, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea

[2] Department of Surgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Cholangiocarcinoma is a rare malignant tumor that originates from the epithelial cells of the bile duct system. Cholangiocarcinoma can be classified according to their anatomical locations as intrahepatic, perihilar, and distal cholangiocarcinoma. Perihilar cholangiocarcinoma, also called Klatskin tumor, is the most common type, accounting for approximately 50–60 % of all cases [1], and can be defined as a tumor located above the junction of the cystic duct up to and including the second-order biliary branches of the right and left bile ducts. The 5-year survival rates for patients with perihilar cholangiocarcinoma are reported to be between 20 and 40 % [2, 3]. About 80 % of Klatskin tumors are diagnosed as unresectable or metastatic tumors, for which palliative chemotherapy or chemoradiation therapy is considered [4]. Except for liver transplantation in highly selective patients, surgical resection, if possible, is the only curative treatment strategy.

Almost all Klatskin tumor patients present with obstructive jaundice due to bile duct tumor masses. Therefore, biliary drainage by percutaneous or endoscopic means is necessary for palliative therapy and preemptive treatment for curative surgery. Proper biliary decompression can allow curative surgery or palliative therapy and prevent life-threatening biliary sepsis in patients. Although there is controversy about the risks and benefits of preoperative biliary drainage (PBD) [5–8], the consensus among experts is that PBD should be considered before surgery [9].

Generally, there are three options for PBD: percutaneous transhepatic biliary drainage (PTBD), endoscopic biliary stenting (EBS), and endoscopic nasobiliary drainage (ENBD). PTBD is widely used for PBD in Klatskin tumor patients scheduled for surgery because of its high technical success rate, low incidence of ascending cholangitis, easy multiple drainage, and ease of performing cholangiography [10, 11]. However, PTBD is invasive and uncomfortable for patients and is associated with risks of catheter dislodgement and catheter tract recurrence, which is a severe life-threatening complication [12, 13]. The incidence of PTBD catheter tract recurrence was 5.2 % in a previous study including 445 patients with perihilar and distal cholangiocarcinoma [13]. EBS and ENBD are performed with endoscopic retrograde cholangiopancreatography (ERCP). EBS is a less invasive and the more physiologically similar option, enabling the internal drainage of bile into the bowel. However, EBS can be accompanied by ERCP-related complications, such as post-ERCP pancreatitis and ascending cholangitis. ENBD is less invasive than PTBD and is reportedly associated with a lower incidence of ascending cholangitis than EBS [12]. However, an indwelling ENBD catheter may cause discomfort because of nasopharyngeal irritation and may decrease patient daily life activities over a period of 3 weeks until surgery [14]. Moreover, ENBD is associated with risks of tube dislodgement and ERCP-related complications.

As controversies exist concerning the optimal technique for PBD in Klatskin tumor patients before surgery, this study aimed to compare the efficacies and safety of PTBD, EBS, and ENBD for PBD in Klatskin tumor patients before curative surgery.

Patients and methods

Study population

This study included 98 Klatskin tumor patients who underwent PBD prior to operation with a curative aim at Severance Hospital between June 2005 and January 2012. The median patient age was 63.5 years (range 29–82 years), and the study population comprised 60 men (61.2 %) and 38 women (38.8 %).

Planned hilar resections included hilar plate resection with or without hemihepatectomy, as well as caudate lobectomy. A right hepatectomy and caudate lobectomy with extrahepatic bile duct resection were indicated for Bismuth type I, II, and IIIa tumors. A left hepatectomy and caudate lobectomy with extrahepatic bile duct resection were indicated for Bismuth type IIIb tumors. A right or left trisectionectomy and caudate lobectomy with extrahepatic bile duct resection were indicated for Bismuth type IV tumors.

Preoperative biliary drainage

The primary method for PBD was determined by the attending doctor on the basis of the anatomical tumor location, Bismuth classification, accessibility of the method, and general patient condition. Of the 98 patients, 43 underwent PTBD, 42 underwent EBS, and 13 underwent ENBD. The patients were divided into the PTBD, EBS, and ENBD groups according to the drainage method used initially.

The patients were referred to the Department of Interventional Radiology for PTBD, and all PTBD procedures were performed under ultrasound guidance. The diameter of the placement tubes was generally 7–10 Fr. The diameters were dilated up to 18 Fr in cases requiring percutaneous transhepatic cholangioscopy. All endoscopic procedures for EBS and ENBD were performed by experienced endoscopists (M. J. Chung, J. Y. Park, S. Bang, S. W. Park, S. Y. Song) while the patient was under conscious sedation with intravenous propofol and midazolam. In EBS, the tube diameter was 7–10 Fr, and a straight or pigtail-type tube was placed. A pigtail-type tube with a 7-Fr diameter was used in all ENBD cases.

Definitions of variables

We evaluated median patient age, gender, Bismuth tumor classification [15], drained area of the liver, and preoperative portal vein embolization (PVE) as baseline characteristics. We defined major hepatectomy as unilateral trisectionectomy, unilateral hepatectomy including caudate lobectomy, or a more extensive hepatectomy. The total serum bilirubin level and indocyanine green (ICG) retention rate at 15 min were evaluated as initial laboratory data. Patients with a total serum bilirubin level >2.0 mg/dL were considered to have jaundice.

Complications after PBD were evaluated, including tube dislocation after PTBD, post-ERCP pancreatitis, and cholangitis. Ipsilateral and contralateral segmental cholangitis occurring after PBD was evaluated. The initial technical success rate, duration until biliary decompression, biliary decompression rate, and rate of conversion to other PBD methods were evaluated to assess the technical and clinical outcomes of PBD. Conversion to another PBD method was defined as a change from the initial PBD method to another method owing to failure of biliary decompression or occurrence of complications. We defined biliary drainage as ineffective when reduced total serum bilirubin level after the biliary drainage was >5.0 mg/dL or rate of biliary decompression was <0.1 mg/dL/day.

Variables related to surgical and oncologic outcomes, including the extent of surgical resection, operation time, bleeding and transfusion during surgery, curative resection, tumor recurrence, postoperative hospital days, recurrence-free survival, and overall survival, were evaluated.

Statistical analysis

Data were analyzed using the χ^2, Fisher's exact, and Student's *t* tests to compare variables between the groups, and a *p* value of <0.05 was considered statistically significant. Kaplan–Meier analysis with log-rank tests and multivariate Cox regression were used for survival analysis. The starting point of survival was set as the time of surgery. Statistical analyses were performed using Predictive Analytics Software Statistics version 18.

Results

This study included 98 Klatskin tumor patients, of whom 43 (43.9 %) underwent PTBD, 42 (42.9 %) underwent EBS, and 13 (13.2 %) underwent ENBD for PBD (Table 1). There were no significant differences in gender distribution, drained area, and preoperative PVE rate among the three groups. Median age was significantly lower in the ENBD group than in the PTBD group (58.9 vs. 65.0 years, $p = 0.046$), and no significant difference was observed between the other groups. Tumor location, as indicated by Bismuth classification, was significantly different between the PTBD and EBS groups ($p = 0.020$). The PTBD group showed type IV tumors more often than the EBS group (39.5 vs. 14.3 %), and the EBS group showed type I and II tumors more often than the PTBD group (16.7 and 21.4 % vs. 7.0 and 4.7 %, respectively). No significant differences were found in initial laboratory data, including maximum total serum bilirubin level before PBD, and preoperative ICG retention rate at 15 min.

Overall complications occurred in 12 (27.9 %), 18 (42.9 %), and two (15.4 %) patients in the PTBD, EBS, and ENBD groups, respectively, and no significant differences were found between these groups. Ipsilateral and contralateral segmental cholangitis was observed, respectively, in two (4.7 %) and five (11.6 %) PTBD patients, seven (16.7 %) and five (11.9 %) EBS patients, and one (7.7 %) and one (7.7 %) ENBD patients. There were no significant differences in the rates of cholangitis after PBD between the groups (Table 2).

Tube dislocation was found in 11.6 % of the PTBD patients, and self-removal of the catheter was reported by 7.7 % of the ENBD patients. Stent migration was not observed in the EBS group. Post-ERCP pancreatitis was observed only in the EBS group (14.3 %); however, this difference was not significant in comparison with the ENBD group ($p = 0.149$). There were no major complications, such as retroperitoneal perforation requiring surgery after ERCP or catheter tract metastasis and portal vein injury, associated with PTBD.

Table 2 shows the postoperative morbidity and mortality rates. The morbidity rates were 34.9 % (15/43), 33.3 % (14/42), and 15.4 % (2/13) in the PTBD, EBS, and ENBD groups, respectively, and no significant differences were found between the groups. Moreover, in-hospital death rates were 11.6 % (5/43), 9.5 % (4/42), and 0 % (0/13) in the PTBD, EBS, and ENBD groups, respectively, and no significant differences were found between the groups. The presence of bile leakage, liver abscess, intra-abdominal abscess, sepsis, and hepatic insufficiency did not differ significantly between the groups.

The technical and clinical features of PBD are presented in Table 3. There was no significant difference in the initial technical success rates between the groups (97.3 %, PTBD; 87.5 %, EBS; 100 %, ENBD), and there was no significant difference between patients who underwent percutaneous drainage and patients who underwent an endoscopic method, including EBS and ENBD (97.3 %, PTBD; 90.2 %, endoscopic method; $p = 0.249$). No significant differences were found in the duration until biliary decompression (31.0, PTBD; 28.7, EBS; 35.8 days, ENBD) and the rate of biliary decompression per day (0.34, PTBD; 0.34, EBS; 0.26 mg/dL/day, ENBD) between the groups. The rates of conversion to another PBD method were 4.7, 35.7, and 76.9 % in the PTBD, EBS, and ENBD groups, respectively. The ENBD group had a significantly higher rate of conversion to another PBD method than the PTBD and EBS groups ($p < 0.001$ and $p = 0.009$, respectively). Moreover, the EBS group had a significantly higher rate of conversion to another PBD method than the PTBD group ($p < 0.001$). Two PTBD patients converted to EBS, and 15 EBS patients converted to PTBD. Of the ENBD patients, four converted to PTBD and six converted to EBS. The reasons for conversion were tube dislocation in one patient, procedure-related complication such as cholangitis in 12 patients and pancreatitis in two patients,

Table 1 Baseline characteristics

	PTBD group ($n = 43$)	EBS group ($n = 42$)	ENBD group ($n = 13$)	p value (PT:EB/EB:EN/PT:EN)
Median age, years (range)	65.0 (40–82)	61.1 (29–80)	58.9 (42–77)	0.141/0.590/0.046
Male sex	29 (67.4 %)	23 (54.8 %)	8 (61.5 %)	0.270/0.667/0.745
Bismuth classification				
Type I/II/IIIa/IIIb/IV	3/2/16/5/17	7/9/13/6/6	2/2/4/1/4	0.020/0.804/0.539
Drained area				
Unilateral/bilateral	37/6	37/5	9/3	0.778/0.356/0.392
Preoperative PVE	13 (30.2 %)	8 (19.0 %)	2 (15.4 %)	0.232/1.000/0.477
Initial laboratory data				
T. bil >2.0 mg/dL, number of patients	39 (90.7 %)	39 (92.9 %)	11 (84.6 %)	0.717/0.582/0.615
T. bil (mg/dL), mean (SD)	9.5 (±6.7)	7.7 (±5.3)	8.3 (±6.3)	0.126/0.975/0.128
ICG R15 (%), mean (SD)	17.6 (±17.2)	14.9 (±12.2)	12.4 (±5.7)	0.603/0.627/0.299

PTBD percutaneous transhepatic biliary drainage, *EBS* endoscopic biliary stenting, *ENBD* endoscopic nasobiliary drainage, *PVE* portal vein embolization, *T. bil* total bilirubin, *ICG R15* indocyanine green retention rate at 15 min, *PT* PTBD, *EB* ENBD, and *EN* ENBD

Table 2 Complications of PBD and postsurgical morbidities

	PTBD group ($n = 43$)	EBS group ($n = 42$)	ENBD group ($n = 13$)	p value (PT:EB/EB:EN/PT:EN)
Complications of PBD	12 (27.9 %)	18 (42.9 %)	2 (15.4 %)	0.149/0.072/0.361
Ipsilateral segmental cholangitis	2 (4.7 %)	7 (16.7 %)	1 (7.7 %)	0.072/0.423/0.670
Contralateral segmental cholangitis	5 (11.6 %)	5 (11.9 %)	1 (7.7 %)	0.968/0.670/0.688
Tube dislocation	5 (11.6 %)	0 (0 %)	1 (7.7 %)	0.023/0.070/0.688
Post-ERCP pancreatitis	–	6 (14.3 %)	0 (0 %)	-/0.317/-
Postsurgical morbidities	15 (34.9 %)	14 (33.3 %)	2 (15.4 %)	0.880/0.304/0.303
Bile leakage	3 (7.0 %)	5 (11.9 %)	2 (15.4 %)	0.483/0.664/0.580
Liver abscess	0 (0 %)	1 (2.4 %)	0 (0 %)	0.494/1.000/-
Intra-abdominal abscess	3 (7.0 %)[a]	2 (4.8 %)[a]	0 (0 %)	1.000/1.000/1.000
Sepsis	2 (4.7 %)	4 (9.5 %)[a]	0 (0 %)	0.433/0.562/1.000
Hepatic insufficiency	4 (9.3 %)	2 (4.8 %)[a]	0 (0 %)	0.676/1.000/0.563
In-hospital death	5 (11.6 %)[a]	4 (9.5 %)[a]	0 (0 %)	1.000/0.562/0.580

PBD preoperative biliary drainage, *PTBD* percutaneous transhepatic biliary drainage, *EBS* endoscopic biliary stenting, *ENBD* endoscopic nasobiliary drainage, *ERCP* endoscopic retrograde cholangiopancreatography, *PT* PTBD, *EB* ENBD, and *EN* ENBD

[a] Postsurgical morbidity data include duplicate cases

and ineffective biliary drainage in 12 patients (four patients in EBS group and eight patients in ENBD group).

Table 4 shows the surgical and oncologic outcomes. Extent of hepatectomy, operation time, bleeding amount, and red blood cell (RBC) transfusion during surgery did not differ significantly between the groups. The PTBD group had a higher rate (66.7 vs. 50.0 %, $p = 0.121$) and higher amount (558 vs. 296 mL, $p = 0.064$) of RBC transfusion than the EBS group, although these differences were not statistically significant. The curative resection rates were 86, 71.4, and 84.6 % in the PTBD, EBS, and ENBD groups, respectively, and no significant differences were observed. Moreover, tumor recurrence after curative resection and postoperative hospital days did not differ significantly between the groups.

The median recurrence-free periods were 16.3, 16.0, and 19.6 months in the PTBD, EBS, and ENBD groups, respectively, and there were no significant differences between the groups. The median overall survivals were 26.0, 19.9, and 27.1 months in the PTBD, EBS, and ENBD groups, respectively, and no significant differences were observed.

Table 3 Clinical outcomes and rates of conversion to another PBD method

	PTBD group ($n = 43$)	EBS group ($n = 42$)	ENBD group ($n = 13$)	p value (PT:EB/EB:EN/PT:EN)
Initial technical success rate[a]	36/37 (97.3 %)	42/48 (87.5 %)	13/13 (100 %)	0.132/0.326/1.000
Duration until biliary decompression (days), mean (range)	31.0 (4–112)	28.7 (4–162)	35.8 (8–122)	0.715/0.541/0.675
Rate of biliary decompression (mg/dL/day)	0.34 (±0.4)	0.34 (±0.37)	0.26 (±0.25)	0.918/0.470/0.523
Rate of conversion to another PBD method	2 (4.7 %)	15 (35.7 %)	10 (76.9 %)	0.000/0.009/0.000
Conversion procedure				
PTBD	–	15	4	
EBS	2	–	6	
ENBD	0	0	–	

PBD preoperative biliary drainage, *PTBD* percutaneous transhepatic biliary drainage, *EBS* endoscopic biliary stenting, *ENBD* endoscopic nasobiliary drainage, *PT* PTBD, *EB* ENBD, and *EN* ENBD

[a] Patient with failed PTBD for initial PBD underwent PTBD again. Six patients with failed EBS converted to PTBD

Table 4 Surgical and oncologic outcomes

	PTBD group ($n = 43$)	EBS group ($n = 42$)	ENBD group ($n = 13$)	p value (PT:EB/EB:EN/PT:EN)
Major hepatectomy	35 (81.4 %)	29 (69.0 %)	9 (69.2 %)	0.187/1.000/0.443
Operation time (min), mean	554 (±156)	553 (±181)	529 (±216)	0.992/0.684/0.684
Bleeding amount (mL), mean	1662 (±1692)	1179 (±943)	1603 (±1639)	0.111/0.246/0.246
RBC transfusion rate	28 (66.7 %)	21 (50.0 %)	6 (46.2 %)	0.121/0.808/0.183
RBC transfusion amount (mL), mean	558 (±890)	296 (±478)	288 (±391)	0.064/0.389/0.956
Curative (R0) resection	37 (86.0 %)	30 (71.4 %)	11 (84.6 %)	0.099/0.477/1.000
Tumor recurrence after curative resection	25/37 (67.6 %)	17/30 (56.7 %)	8/11 (72.7 %)	0.359/0.478/1.000
Postoperative hospital days, mean	26.8 (±17.9)	27.3 (±20.4)	27.5 (±14.6)	0.896/0.983/0.902
Median recurrence-free period, months (range)	16.3 (0.1–98.1)	16.0 (0.1–96.3)	19.6 (2.9–79.8)	0.069/0.068/0.073
Median overall survival, months (range)	26.0 (0.1–98.1)	19.9 (0.1–96.3)	27.1 (4.3–90.4)	0.370/0.287/0.672

PTBD percutaneous transhepatic biliary drainage, *EBS* endoscopic biliary stenting, *ENBD* endoscopic nasobiliary drainage, *RBC* red blood cell, *PT* PTBD, *EB* ENBD, and *EN* ENBD

Adjuvant chemotherapy was performed in patients with high risk of tumor recurrence, such as lymphovascular invasion, perineural invasion, or hepatic invasion on histologic examination of surgical specimens, and concurrent chemoradiation therapy was performed in patients who did not undergo R0 resection or were accompanied with a positive regional lymph node. Adjuvant chemotherapy was performed in 20 PTBD patients (46.5 %), 19 EBS patients (45.2 %), and six ENBD patients (46.2 %). Adjuvant concurrent chemoradiation therapy was performed in four PTBD patients (9.3 %), seven EBS patients (16.6 %), and two ENBD patients (15.4 %). There were no significant differences in the rates of adjuvant chemotherapy and concurrent chemoradiation therapy between the groups (Table 5).

Kaplan–Meier analysis and multivariate Cox regression were used to compare recurrence-free survival and overall survival between patients who received adjuvant chemotherapy (chemotherapy group, $n = 45$), those who received adjuvant concurrent chemoradiation therapy (chemoradiation group, $n = 13$), and those who did not receive any adjuvant anticancer treatment (supportive care group, $n = 40$). Multivariate Cox regression was performed with gender, age, and the method of PBD as the co-variables. The median recurrence-free survival was 17.6, 17.5, and 15.7 months in the chemotherapy, chemoradiation, and supportive care groups, respectively, and no significant difference was observed. Moreover, the median overall survivals were 26.0, 29.5, and 18.7 months in the chemotherapy, chemoradiation, and supportive care

Table 5 Survival analysis using Cox regression according to postoperative management strategy

	Supportive care ($n = 40$)	Chemotherapy ($n = 45$)	Chemoradiation ($n = 13$)	p value (SC:CT/SC:CR/CT:CR)
Median recurrence-free period, months (range)	15.7 (0.1–81.9)	17.6 (0.9–98.1)	17.5 (9.4–27.9)	0.683/0.602/0.566
Median overall survival, months (range)	18.7 (0.1–81.9)	26.0 (8.4–98.1)	29.5 (15.6–38.5)	0.077/0.576/0.715

SC supportive care, *CT* chemotherapy, *CR* chemoradiation

groups, respectively, and no significant difference was observed.

Discussion

We aimed to report our experience with Klatskin tumor patients, which may be helpful to determine the best option for PBD before curative surgery. Although PBD combined with curative surgery has been established as a safe management strategy for Klatskin tumors, controversy exists regarding the preferred method for PBD, because each method has its advantages and disadvantages.

PTBD has been considered a suitable technique for PBD. Kloek et al. [11] reported that PTBD could outperform EBS in terms of the initial technical success rate (100 vs. 81 %, $p = 0.020$), incidence of cholangitis (9 vs. 48 %, $p < 0.05$), and drainage period (11 vs. 15 weeks, $p < 0.05$) in 101 Klatskin tumor patients who underwent PBD (90 cases with PTBD and 11 cases with EBS). Walter et al. [10] also reported that PTBD was better than EBS with respect to technical success rate (98 vs. 78 %, $p = 0.04$) and time to successful biliary decompression (44 vs. 61 days, $p = 0.045$) in 129 Klatskin tumor patients (42 cases with PTBD and 87 cases with EBS).

However, in this study, there were no significant differences in initial technical success rate, duration until biliary decompression, and incidence of cholangitis between the PTBD and EBS groups. On the other hand, tube dislocation was observed in 11 % of the PTBD patients, a considerably high incidence, considering that stent migration was not observed in the EBS group. Initial technical success rates, function, and rates of complications for ERCP-associated procedures can differ depending on the experience of an endoscopist and the performance of a hospital [16, 17]. According to Asia–Pacific consensus recommendations for endoscopic and interventional management of hilar cholangiocarcinoma [18], endoscopic biliary drainage for a Klatskin tumor is classified as grade 5 procedure, which is the most difficult, and should be performed by an experienced endoscopist in light of recorded complication rates. In our study, all ERCP procedures were performed by five experienced endoscopists (M. J. Chung, J. Y. Park, S. Bang, S. W. Park, and S. Y. Song) who each had previously performed over 1000 ERCP procedures and also had a high yearly volume of more than 1000 ERCP procedures performed in total. This might be one reason for the differences between previous reports and our results.

Moreover, there are concerns about the serious complications of PTBD. Kawakami et al. [12] reported that PTBD caused portal vein injury (4/48, 8.4 %) and catheter tract metastasis (3/48, 6.3 %) in Klatskin tumor patients who underwent PTBD for PBD. Takahashi et al. [13] reported that the incidence of catheter tract recurrence in cholangiocarcinoma patients was 5.2 % (23/445) and that patients with catheter tract recurrence had poorer prognosis than those without catheter tract recurrence (median overall survival, 22.8 vs. 27.3 months, $p = 0.095$). Accordingly, PTBD cannot be considered superior to EBS in terms of efficacy and safety.

Kawakami et al. [12] reported that tube occlusion with cholangitis was significantly less frequent in an ENBD group than in an EBS group (10 vs. 60 %, $p < 0.0001$) and the total number of major complications including retroperitoneal perforation, portal vein injury, and catheter tract recurrence was significantly lower in the ENBD group than in the PTBD group (1.7 vs. 14.6 %, $p < 0.01$). The conversion rate was not significantly higher in the ENBD group than in the EBS and PTBD groups (21.7 vs. 95 % vs. 4.17 %).

In our study, no significant differences in the frequency of cholangitis and other complications were observed between the three groups. On the other hand, the conversion rate was significantly higher in the ENBD group (76.9 %) than in the PTBD (4.7 %, $p < 0.0001$) and EBS groups (35.7 %, $p = 0.009$). Although not statistically significant, tube dislocation occurred more frequently in the ENBD group than in the EBS group (7.7 vs. 0 %, $p = 0.070$).

In previous studies, the duration of PBD varied from 10 to 32 days, and when considering the number of patients in each group, the average duration of PBD was 21.9 days [14]. In our study, the average duration of PBD was 30.7 days. Approximately more than 3 weeks were needed to resolve the jaundice in patients. In this period, patients experience nasal irritation and limitations in their ordinary life due to the nasal catheter. Although there might be differences therein with a more experienced endoscopist, an external drainage catheter, as in ENBD, can be relatively uncomfortable and is exposed to greater danger of dislocation, compared with an internal drainage catheter, leading to lower safety and patient compliance. Considering that patients must undergo PBD for 3 weeks on average, it would be hard for us to recommend ENBD as the first option for PBD.

As mentioned above, previous studies have reported that, compared with other methods, EBS has a lower initial success rate, higher rate of cholangitis, and higher conversion rate [10, 11, 19]. In the present study, unlike that in previous studies, the initial technical success rate of EBS was not significantly lower than that of PTBD and ENBD. The EBS group had a significantly lower conversion rate than the ENBD group ($p = 0.009$). No significant differences in the cholangitis rate were observed between the groups. Similarly, in a study including 129 Klatskin tumor patients, Walter et al. [10] reported that the cholangitis rate did not differ significantly between the EBS and PTBD groups (25 vs. 21 %; $p = 0.34$).

EBS can be helpful in terms of bleeding control in patients undergoing surgery. Yoshida et al. [20] reported that preoperative bile replacement in biliary cancer patients who underwent external PBD improved serum liver enzyme levels and prothrombin time–international normalized ratio. Hirano et al. [21] reported that the frequency of RBC transfusion during surgery was significantly higher in a PTBD group than in an EBS group (21/67 vs. 7/74, $p = 0.001$), and median overall survival was significantly higher in the EBS group than in the PTBD group (59.4 vs. 31.4 months, $p = 0.004$). In our study, although not statistically significant, the EBS group tended to have a lower rate (50 vs. 66.7 %, $p = 0.121$) and lower amount (296 vs. 558 mL, $p = 0.064$) of RBC transfusion than the PTBD group. These results show that internal drainage by EBS has an advantage of bleeding control in surgery over external drainage by PTBD or ENBD, by improving the hemostatic condition of patients.

Percutaneous transhepatic biliary drainage introduces a higher risk of tube dislocation than other methods and greater risk of catheter tract metastasis, as reported by previous studies [13]. Thus, PTBD should be selected for PBD after careful consideration of the risks and benefits for the patients. ENBD has disadvantages in terms of patient compliance, showing a higher conversion rate than other methods due to discomfort among patients because of the long-term placement of the nasal catheter for about 3 weeks before surgery [14]. On the other hand, in our study, EBS had a similar risk of cholangitis as PTBD and had a lower conversion rate than ENBD. In our study, considering the risk of severe complications in PTBD and the high conversion rate of ENBD, EBS was found to be the most suitable method for PBD in terms of safety and patient compliance in Klatskin tumor patients.

Each method of the PBD has different advantages and disadvantages. It is important to consider various factors of the patient and disease status for the choice of the best option for PBD. PTBD might be a good option in terms of effectiveness. However, there is a possibility of severe complications and discomfort due to the invasive external catheter. While ENBD is a less invasive method compared with PTBD and effective enough for biliary decompression, maintenance nasal catheter might cause irritability of nasopharynx and lower the quality of the patient's life. EBS is a more comfortable way for the patients to maintain PBD than other methods, because it does not require an external catheter. In previous studies, there were some concerns about safety due to the higher rates of complications of EBS such as stent occlusion, stent migration, or ascending cholangitis. However, our results showed that EBS is safe enough and has similar or fewer complications compared with other methods in this study, and in terms of effectiveness, there were no significant differences among these three options. When the patient's quality of life is taken seriously, EBS would be the best option of PBD for the patients suffering with Klatskin tumor.

Our study has several limitations. First, this was a retrospective single-center study. In addition, a considerably lower number of patients underwent ENBD, compared with the other PBD methods. Second, there might be selection bias for the initial PBD methods. The median age of the ENBD patients was significantly lower than that of the PTBD patients. ENBD was associated with discomfort from the nasal catheter, and therefore, the attending physician might select ENBD in younger patients with a better general condition and compliance. Third, the proportion of tumor types, according to Bismuth classification, differed between the PTBD and EBS groups. This difference stems from certain characteristics, such as anatomical accessibility, of each PBD method. Fourth, no severe complications, such as portal vein injury and catheter tract recurrence, were observed, unlike that in previous studies. This retrospective study included patients who underwent curative surgery, and therefore, patients who experienced life-threatening complications before surgery may not have been included.

In conclusion, all PBD methods including PTBD, EBS, and ENBD showed comparable results in terms of initial technical success rates, duration until biliary decompression, complication rates, surgical outcomes, and postoperative morbidity and mortality. The ENBD group showed the highest rate of conversion to another PBD method.

Since Klatskin tumor patients must undergo PBD for more than 3 weeks before surgery, PTBD and ENBD can be uncomfortable and disadvantageous procedures for PBD. EBS was the most suitable method for initial PBD in terms of compliance in Klatskin tumor patients. Future prospective large-scale studies are needed to confirm these results.

Compliance with ethical standards

Disclosures Jung Hyun Jo, Moon Jae Chung, Dai Hoon Han, Jeong Youp Park, Seungmin Bang, Seung Woo Park, Si Young Song, and Jae Bock Chung have no conflicts of interest or financial ties to disclose.

References

1. Valero V 3rd, Cosgrove D, Herman JM, Pawlik TM (2012) Management of perihilar cholangiocarcinoma in the era of multimodal therapy. Expert Rev Gastroenterol Hepatol 6:481–495
2. Jarnagin WR, Fong Y, DeMatteo RP, Gonen M, Burke EC, Bodniewicz BJ, Youssef BM, Klimstra D, Blumgart LH (2001) Staging, resectability, and outcome in 225 patients with hilar cholangiocarcinoma. Ann Surg 234:507–517 **(discussion 517–509)**
3. Silva MA, Tekin K, Aytekin F, Bramhall SR, Buckels JA, Mirza DF (2005) Surgery for hilar cholangiocarcinoma; a 10 year experience of a tertiary referral centre in the UK. Eur J Surg Oncol 31:533–539
4. Valle J, Wasan H, Palmer DH, Cunningham D, Anthoney A, Maraveyas A, Madhusudan S, Iveson T, Hughes S, Pereira SP, Roughton M, Bridgewater J, Investigators ABCT (2010) Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med 362:1273–1281
5. Cherqui D, Benoist S, Malassagne B, Humeres R, Rodriguez V, Fagniez PL (2000) Major liver resection for carcinoma in jaundiced patients without preoperative biliary drainage. Arch Surg 135:302–308
6. Hochwald SN, Burke EC, Jarnagin WR, Fong Y, Blumgart LH (1999) Association of preoperative biliary stenting with increased postoperative infectious complications in proximal cholangiocarcinoma. Arch Surg 134:261–266
7. Rea DJ, Munoz-Juarez M, Farnell MB, Donohue JH, Que FG, Crownhart B, Larson D, Nagorney DM (2004) Major hepatic resection for hilar cholangiocarcinoma: analysis of 46 patients. Arch Surg 139:514–523 **(discussion 523–515)**
8. Kawasaki S, Imamura H, Kobayashi A, Noike T, Miwa S, Miyagawa S (2003) Results of surgical resection for patients with hilar bile duct cancer: application of extended hepatectomy after biliary drainage and hemihepatic portal vein embolization. Ann Surg 238:84–92
9. Ratti F, Cipriani F, Ferla F, Catena M, Paganelli M, Aldrighetti LA (2013) Hilar cholangiocarcinoma: preoperative liver optimization with multidisciplinary approach. Toward a better outcome. World J Surg 37:1388–1396
10. Walter T, Ho CS, Horgan AM, Warkentin A, Gallinger S, Greig PD, Kortan P, Knox JJ (2013) Endoscopic or percutaneous biliary drainage for Klatskin tumors? J Vasc Interv Radiol 24:113–121
11. Kloek JJ, van der Gaag NA, Aziz Y, Rauws EA, van Delden OM, Lameris JS, Busch OR, Gouma DJ, van Gulik TM (2010) Endoscopic and percutaneous preoperative biliary drainage in patients with suspected hilar cholangiocarcinoma. J Gastrointest Surg 14:119–125
12. Kawakami H, Kuwatani M, Onodera M, Haba S, Eto K, Ehira N, Yamato H, Kudo T, Tanaka E, Hirano S, Kondo S, Asaka M (2011) Endoscopic nasobiliary drainage is the most suitable preoperative biliary drainage method in the management of patients with hilar cholangiocarcinoma. J Gastroenterol 46:242–248
13. Takahashi Y, Nagino M, Nishio H, Ebata T, Igami T, Nimura Y (2010) Percutaneous transhepatic biliary drainage catheter tract recurrence in cholangiocarcinoma. Br J Surg 97:1860–1866
14. Paik WH, Loganathan N, Hwang JH (2014) Preoperative biliary drainage in hilar cholangiocarcinoma: when and how? World J Gastrointest Endosc 6:68–73
15. Bismuth H, Nakache R, Diamond T (1992) Management strategies in resection for hilar cholangiocarcinoma. Ann Surg 215:31–38
16. Ekkelenkamp VE, de Man RA, Ter Borg F, Borg PC, Bruno MJ, Groenen MJ, Hansen BE, van Tilburg AJ, Rauws EA, Koch AD (2015) Prospective evaluation of ERCP performance: results of a nationwide quality registry. Endoscopy 47:503–507
17. Williams EJ, Taylor S, Fairclough P, Hamlyn A, Logan RF, Martin D, Riley SA, Veitch P, Wilkinson ML, Williamson PR, Lombard M (2007) Risk factors for complication following ERCP; results of a large-scale, prospective multicenter study. Endoscopy 39:793–801
18. Rerknimitr R, Angsuwatcharakon P, Ratanachu-ek T, Khor CJ, Ponnudurai R, Moon JH, Seo DW, Pantongrag-Brown L, Sangchan A, Pisespongsa P, Akaraviputh T, Reddy ND, Maydeo A, Itoi T, Pausawasdi N, Punamiya S, Attasaranya S, Devereaux B, Ramchandani M, Goh KL, Asia-Pacific Working Group on Hepatobiliary C (2013) Asia–Pacific consensus recommendations for endoscopic and interventional management of hilar cholangiocarcinoma. J Gastroenterol Hepatol 28:593–607
19. Kawakami H, Kondo S, Kuwatani M, Yamato H, Ehira N, Kudo T, Eto K, Haba S, Matsumoto J, Kato K, Tsuchikawa T, Tanaka E, Hirano S, Asaka M (2011) Preoperative biliary drainage for hilar cholangiocarcinoma: which stent should be selected? J Hepatobiliary Pancreat Sci 18:630–635
20. Yoshida Y, Ajiki T, Ueno K, Shinozaki K, Murakami S, Okazaki T, Matsumoto T, Matsumoto I, Fukumoto T, Usami M, Ku Y (2014) Preoperative bile replacement improves immune function for jaundiced patients treated with external biliary drainage. J Gastrointest Surg 18:2095–2104
21. Hirano S, Tanaka E, Tsuchikawa T, Matsumoto J, Kawakami H, Nakamura T, Kurashima Y, Ebihara Y, Shichinohe T (2014) Oncological benefit of preoperative endoscopic biliary drainage in patients with hilar cholangiocarcinoma. J Hepatobiliary Pancreat Sci 21:533–540