

# Comparison of short-term efficiency of endoscopic biliary drainage and percutaneous transhepatic biliary drainage in the treatment of obstructive jaundice caused by hilar cholangiocarcinoma: a propensity score matching analysis

Dalong Zhu

the First Affiliated Hospital of Xinjiang Medical University

Musitafa Zayier

the First Affiliated Hospital of Xinjiang Medical University

Alimu Tulahong

the First Affiliated Hospital of Xinjiang Medical University

Abuduhaiwaier Abuduhelili

the First Affiliated Hospital of Xinjiang Medical University

Fashun Lu

the First Affiliated Hospital of Xinjiang Medical University

Bo Ran

the First Affiliated Hospital of Xinjiang Medical University

Tiemin Jiang

the First Affiliated Hospital of Xinjiang Medical University

Yingmei Shao

the First Affiliated Hospital of Xinjiang Medical University

Tuerganaili Aji (✉ [tuergan78@sina.com](mailto:tuergan78@sina.com))

the First Affiliated Hospital of Xinjiang Medical University

---

## Research Article

**Keywords:** Hilar cholangiocarcinoma, Obstructive jaundice, Endoscopic biliary drainage, Percutaneous suprahepatic biliary drainage, Propensity score matching analysis

**Posted Date:** April 18th, 2022

**DOI:** <https://doi.org/10.21203/rs.3.rs-1562381/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)



## Abstract

**Background:** For patients with obstructive jaundice caused by cholangiocarcinoma (CCA), drainage methods, including endoscopic biliary drainage (EBD) and percutaneous suprahepatic biliary drainage (PTBD), may be applied. Here, this study aims to compare short-term efficiency of primary EBD and PTBD during the treatment process of obstructive jaundice caused by hilar cholangiocarcinoma (HCCA).

**Methods:** Clinical data of 114 patients with obstructive jaundice caused by HCCA were retrospectively analyzed from January 2016 to December 2020. According to treatment options, the patients were divided into EBD group ( $n=37$ ) and PTBD group ( $n=77$ ), and 19 pairs of patients were obtained after propensity score matching (PSM) analysis. Liver function, technical success rate, postoperative complications and hospitalization expenses were compared between groups.

**Results:** After PSM analysis all baseline parameters were comparable . Among PTBD group patients, technical success was observed in 75 cases (97.40%), which was found in 26 cases in EBD group (70.27%). The difference in technical success rate between groups was significant ( $P<0.001$ ). Compared with EBD group, postoperative total bilirubin was significantly decreased in PTBD group ( $P=0.019$ ), and there was significant difference in the decrease degree between groups ( $P=0.041$ ). The incidence of postoperative complications ( $P=0.049$ ) and acute pancreatitis (  $P=0.046$ ) in EBD group were higher than those in PTBD group.

**Conclusion:** Compared with EBD, PTBD had higher success rate, greater decrease in total bilirubin level and lower incidence rate of overall postoperative complications and acute pancreatitis. Therefore, PTBD may be given priority in the treatment of obstructive jaundice caused by HCCA.

## Introduction

In recent years, incidence rate of cholangiocarcinomas (CCA) in most countries has shown an upward trend, and the number of cases is also gradually increasing [1]. Among different types of CCA, hilar cholangiocarcinoma (HCCA) is the most common in clinical settings, accounting for approximately 60% CCA [2, 3]. HCCA, as one of the most malignancies in the biliary tracts, originates from the mucosal epithelium of common hepatic duct, left and right hepatic ducts and their confluence, also known as Klatskin tumor [4]. Due to no specificity, most patients are always hospitalized with jaundice related clinical manifestations including yellow stained skin and sclera, pruritus and abdominal pain [5–8], and obstructive jaundice caused by malignant lesions invading the biliary duct is the main type. In addition to causing these symptoms, jaundice can also cause intestinal barrier failure and increased intestinal permeability may be found in some patients, thus increasing the risk of complications such as cholangitis, sepsis and liver and kidney failure [9, 10]. It has been demonstrated that preoperative hyperbilirubinemia is main risk factor for poor prognosis of HCCA patients [11–13]. Hyperbilirubinemia not only increases hepatocyte apoptosis but also inhibits hepatocyte regeneration, and studies have shown that biliary drainage can improve reduce hepatocyte apoptosis, improve hepatocyte regeneration, and reduce liver function damage[14–16]. Therefore, rapid, safe and effective biliary drainage is crucial for such patients.

As the most applied technique for jaundice reduction, biliary drainage mainly referred to endoscopic biliary drainage (EBD) and percutaneous transhepatic biliary drainage (PTBD). So far, there has been few studies focusing on the application of these above two surgical methods during the treatment process of HCCA, and comparative analysis with regard to their short-term efficiency is still needs further exploration. Herein, this study aims to compare short-term efficiency of EBD and PTBD in the treatment of obstructive jaundice caused by HCCA, which may be valuable for medical professionals to make accurate treatment plans in such cases.

## Methods

### Patients selection

A retrospective study involving 226 patients with HCCA who underwent EBD or PTBD at the Department of Hepatobiliary and *Echinococcosis* Surgery, Digestive and Vascular Surgery Center, the First Affiliated Hospital of Xinjiang Medical University from January 2016 to December 2020 was conducted. Study patients were selected according to the following eligibility indications: (i) Age greater than 18 years old without gender limitations; (ii) Preoperative diagnosis of HCCA through imaging; (iii) Biochemical examination, especially serum bilirubin and direct bilirubin index, suggested obstructive jaundice; (iv) Received primary EBD or PTBD due to obstructive jaundice caused by HCCA. However, patients were excluded from the study according to the following criteria: (i) Exploratory laparotomy was performed before operation; (ii) Received preoperative chemotherapy, radiotherapy and other anti-tumor treatment; (iii) Contraindications or poor tolerance to EBD or PTBD treatment; (iv) Biochemical examination suggested non-obstructive jaundice; (v) Patients with congenital malformations of the biliary system; (vi) Severe impaired liver functions and grade C Child-Pugh classification; (vii) Patients with biliary stones or other benign biliary strictures; (viii) Patients with previous surgical history of common biliary duct; (ix) Patients accompanied with biliary tract infection or pancreatitis at admission; (x) Woman patients with pregnancy. All patients routinely underwent preoperative abdominal US, abdominal CT, and magnetic resonance cholangiopancreatography (MRCP).

According to different modes of biliary drainage, the patients were divided into EBD group ( $n=68$ ) and PTBD group ( $n=158$ ). Among these patients, 26 cases were excluded due to previous surgical history of common biliary duct including ten cases in EBD group and 16 cases in PTBD group. Moreover, seven patients in EBD group were also excluded due to benign hepatobiliary diseases. Due to incomplete postoperative clinical data, 29 patients, including five cases in EBD group and 24 cases in PTBD group, were also excluded. In addition, 31 patients with non-obstructive jaundice were excluded, who were included five cases in EBD group and 26 cases in PTBD group. Ten patients, including three cases in EBD group and seven cases in PTBD group, were excluded due to poor liver functions, which were classified into Child-Pugh grade C. One patient was excluded due to combined PTBD and EBD therapy, and eight patients in PTBD group were excluded due to open surgery before PTBD. Then, 114 patients were included in this study, including 37 cases in EBD group and 77 cases in PTBD group, among whom 11 patients in EBD group and two patients in PTBD group failed operation. Two group patients were 1:1 matched using

propensity score matching (PSM) analysis [17], and 19 pairs of HCCA patients were used for further analysis. Detailed study diagram was shown in Fig.1.

## **Operation techniques**

In EBD group, duodenoscopy was used to cut the Oddi sphincter at the duodenal papilla, and the contrast catheter was inserted. Then, contrast agent was injected to develop the biliary duct and pancreatic duct. When the obstruction site was confirmed, the guide wire was inserted along the contrast catheter. Finally, the stent or nasobiliary duct was inserted along the guide wire after the guide wire retrogradely passes through the obstruction site.

In PTBD group, dilated biliary duct was punctured under digital subtraction angiography (DSA) monitoring. After extracting the bile, the guide wire was inserted into the biliary duct along the puncture needle. Then, a stent or drainage tube for internal drainage or internal and external drainage was placed after the guide wire passes through the obstruction site. If the guide wire failed to pass through the obstruction site, external drainage was performed.

## **Data collection and follow up**

General situation of the patients, including gender, age, body mass index (BMI), hypertension, diabetes, coronary heart disease (CAD), hepatitis was collected through reviewing medical records. In addition, collected indicators for liver function were as follows: Child-Pugh grading, Bismuth-Corlette classification, preoperative and postoperative total bilirubin (TBIL), aspartate aminotransferase (AST), alanine aminotransferase (ALT),  $\gamma$ -Glutamyl transpeptidase ( $\gamma$ -GGT) and alkaline phosphatase (ALP).

Postoperative complications were included electrolyte disorder, acute pancreatitis, biliary bleeding, biliary tract infection, falling of stent/drainage tube, bile leakage and hypoproteinemia. Clinical data related to patient hospitalization, such as postoperative hospital stay, hospitalization expenses and operation time were also collected.

The PTBD group should wait for 2-4 hours after operation until the anesthetic reaction disappears, and patients without nausea and vomiting and other uncomfortable symptoms can gradually resume a liquid or semi-liquid light diet. In the EBD group, fasting was routine after operation, and the diet should be decided according to the blood biochemical indexes of patients in the early morning of the next day. If the indexes of white blood cell, serum amylase and serum lipase were not high, the liquid or semi-liquid light diet could be resumed gradually.

The liver function related indexes such as TBIL, AST and ALT were measured again at the same time of drainage in both groups to assess the drainage effect. Patients were observed at postoperative follow-up from this biliary drainage until discharge or until the next surgical intervention.

## **Definition of Events**

Technical success is defined as the successful placement of a stent or catheter for drainage at the site of malignant lesion invasion. Definition of acute pancreatitis: (i) The patient suddenly presents with acute persistent mid-upper abdominal pain. (ii) Serum amylase exceeds the upper limit of normal by more than 3 times. (iii) Imaging changes of pancreatic inflammation such as pancreatic enlargement and peripancreatic exudation on ultrasound or CT examination. The diagnosis of acute pancreatitis can be confirmed by meeting two of the above three diagnostic criteria. Bile duct infection was defined as a patient with a temperature  $> 38.5^{\circ}\text{C}$  and no other demonstrable cause, along with biochemical evidence of cholestasis and infection (increased C-reactive protein and white blood cells). Procedure-related biliary bleeding after biliary drainage was defined as bleeding that required blood transfusion or additional intervention, or bleeding that resulted in a 2 g/dL drop in hemoglobin levels. Definition of stent or drainage tube dislodgement: (i) stent dislodgement: postoperative patients undergoing abdominal X-ray or endoscopic retrograde cholangiopancreatography (ERCP) clearly have a biliary stent that is not in its original position and has partially dislodged or completely dislodged; (ii) drainage tube dislodgement: postoperative patients with drainage tubes dislodged from the puncture site due to loose or damaged body surface drainage tube fixation devices. Bile leak is defined as a patient presenting with postoperative signs of peritoneal irritation, bile aspirated by laparotomy or bile accumulation in the abdominal cavity found by reoperation.

## PSM analysis

In order to avoid confounding factors and differences caused by intrinsical baseline characteristics, matched patients was selected to compare the short-term efficiency between groups through PSM analysis [17]. Logistic regression model including 14 variables was used to estimate propensity score, which were as follows: gender, age, BMI, hypertension, diabetes, CAD, hepatitis, Child-Pugh grading, Bismuth-Corlette type [18], preoperative TBIL, preoperative AST, preoperative ALT, preoperative  $\gamma$ -GGT and preoperative ALP. The nearest neighbor matching method was used to 1:1 match the two group patients within 0.02 standard deviation without replacement.

## Statistical analysis

Statistical analysis was performed using SPSS version 26.0 (SPSS Inc, Chicago, IL, USA). Quantitative data confirming to normal distribution were presented as the mean  $\pm$  standard deviation, and statistical comparison between groups was made by Student's  $t$  test. Relatively, quantitative data without normal distribution were presented with the median (Q1, Q3), and statistical comparison between groups was made by Mann-Whitney U test or Wilcoxon rank sum test. Qualitative data were presented with ratio or percentage (%), and statistical comparison between groups was made by Chi square test or Fisher exact probability test. Statistical significance was set at the 5% level and  $P < 0.05$  was considered statistically significant.

# Results

## Clinical characteristics of study cohort

A total of 114 patients were included in this study before PSM analysis, among whom 44 cases had multiple comorbidity including hypertension, diabetes, cardiovascular diseases or hepatitis. The incidence of hypertension in PTBD group patients was significantly higher than that in EBD group patients (33.77% VS 13.51%,  $P=0.023$ ). The baseline characteristics of patients between groups were unbalanced and incomparable. Thus, PSM analysis was applied to make the baseline characteristics between groups comparable, and 19 pairs of patients were successfully matched. Then, differences in all variables between groups were not statistically significant ( $P\geq0.05$ ), which were used for analysis. Detailed clinical characteristics of these patients were shown in Table 1.

### **Comparison of technical success rate between groups**

These patients who had operation failure were not re-checked after operation, and their liver functions and postoperative complications were unlikely to further evaluate. Therefore, in order to perform PSM analysis, 114 patients were selected as study subjects for determining the technical success rate. Among PTBD group patients, successful operation was observed in 75 cases (97.40%), which was found in 26 cases in EBD group (70.27%). The difference in technical success rate between groups was obviously significant ( $P<0.001$ ). Due to the special location and complex anatomy of HCCA lesions, different types were also compared, and HCCA classification was based on Bismuth-Corlette classification system. The success rate of patients in PTBD group (34/34, 100.00%) was higher than that of patients in EBD group (15/21, 71.43%). The difference in technical success rate between two group patients who belonged to type I was statistically significant ( $P= 0.002$ ). However, there was no statistical difference in technical success rate of two group patients who were classified to other types ( $P\geq0.05$ ), which was shown in Table 2.

### **Comparison of postoperative complications between groups**

The incidences of overall postoperative complications and acute pancreatitis were significantly higher in EBD group patients than that in PTBD group patients (73.68% VS 36.84,  $P=0.039$ ). However, there were no statistical differences in other postoperative complications between groups ( $P\geq0.05$ ). Complications related to electrolyte disorder, biliary tract infection and hypoproteinemia were more common in EBD group than that in PTBD group. In contrast, biliary bleeding was more commonly seen in PTBD group than that in EBD group. Detailed aspects with regard to postoperative complications were seen in Table 3.

### **Comparison of treatment efficiency**

Both inter-group and intra-group comparison of treatment efficiency were conducted in this study. In EBD group patients, there was statistical significance in  $\gamma$ -GGT level before and after operation [311.70 U/L (122.63±593.50) U/L VS 162.40 U/L (88.53±529.60) U/L,  $P=0.003$ ]. However, there were no statistical differences in other variances before and after operation ( $P\geq0.05$ ) (Table 4). Strikingly, there were significant differences in all variances in PTBD group patients ( $P<0.05$ ) (Table 5). Compared with EBD group, postoperative TBIL was significantly decreased in PTBD group [(307.34±113.34)  $\mu$ mol/L VS (233.51±107.49)  $\mu$ mol/L,  $P=0.019$ ], and the decrease degree of TBIL level in PTBD group patients was also more significant [(8.49±149.18)  $\mu$ mol/L VS (87.74±63.59)  $\mu$ mol/L,  $P=0.041$ ] (Table 6).

## **Comparison of operation duration and hospitalization expenses between groups**

There were no statistical differences in operation duration [EBD group VS PTBD group, 45.00 min (40.00–90.00) min VS 30.00 min (25.00–55.00) min,  $P=0.102$ ], postoperative hospitalization [EBD group VS PTBD group, 5.00 d (4.00–9.00) VS 7.00 d (5.00–17.00) d,  $P=0.265$ ] and expenses [EBD group VS PTBD group, 32701.14 RMB (25784.77–47424.61) RMB VS 30619.35 RMB (22988.21–36476.45) RMB,  $P=0.601$ ] between groups (Table 7).

## **Follow-up treatment in 38 patients**

**EBD group:** 6 patients had only one EBD; 3 patients had EBD again; 7 patients had PTBD; and 3 patients had radical resection of HCCA.

**PTBD group:** 10 patients received PTBD just once; 2 patients underwent PTBD again; 1 patient underwent EBD; 2 patients underwent transcatheter arterial chemoembolization (TACE); 1 patient underwent left liver resection with caudate lobectomy; and 3 patients underwent radical resection of HCCA.

## **Discussion**

Unlike previous studies that compared other aspects of PTBD and EBD, this study took short-term efficiency as the main observation index. This study demonstrated that technical success rate of patients in PTBD group was obviously higher than that of patients in EBD group, which was consistent with previous studies [19, 20]. Our current study also made comparison of technical success rate of patients who were classified into different types, which showed that technical success rate of patients in PTBD group who were type I was also significantly higher than that of patients in EBD group. Whereas, there was no statistical difference in technical success rate of patients belonging to other types. It was believed that the distinct difference in technical success rate between groups was mainly attributed to the intrinsic differences of EBD and PTBD. The length of common endoscopes that is sued in EBD is usually more than 100 cm, which is difficult for surgeons to operate in clinical work. In contrast, PTBD directly punctures the intrahepatic biliary duct through abdominal wall tissue and a small part of hepatic parenchyma, and the operation path only ranges from 20 cm to 30 cm. Therefore, compared with EBD, the operation path is significantly shorter and the operation difficulty is relatively small. Additionally, if the guide wire can not pass through the narrow segment during EBD process, the operation may not be continued and may inevitably fail. However, the guide wire can be used for internal drainage or internal and external drainage through the narrow segment during PTBD process. If the guide wire can not pass through the narrow segment, external drainage is still practicable, which also improves the success rate. The head end of guide wire used both in EBD and PTBD is generally coated with hydrophilic coating. It was demonstrated that compared with EBD that retrogrades into the biliary tract, PTBD is easier to pass through the biliary obstruction site and surgical success rate is relatively higher.

With regard to postoperative complications, the incidences of overall complications and acute pancreatitis in EBD group were higher than those of PTBD group, which was also consistent with previous studies [19–

21]. The reason why the incidence of acute pancreatitis in EBD group was higher than that in PTBD group may be that the surgical process of EBD needs to pass through the Oddi's sphincterotomy and retrograde into the common biliary duct and even the guide wire may enter the main pancreatic duct. In contrast, the surgical process of PTBD anterogradely enters the common biliary duct. When the obstruction was serious, external drainage may be performed and the guide wire may not even enter the common biliary duct. As a result, the incidence of acute pancreatitis in EBD group was higher than that in PTBD group. Kim km et al., also demonstrated in a total of 106 cases including 62 performed PTBD and 44 performed EBD that the incidence of biliary tract infection in EBD was higher than that in PTBD, which was in agreement with our studies that the incidence of cholangitis in EBD group was higher than that in PTBD group. The reason why the incidence of biliary tract infection in EBD group was higher than that in PTBD group may be that the contrast medium needs to be injected into the biliary tract during EBD surgical process. Clinically, one side of biliary tract is always drained, and the other side cannot be drained, thus resulting in residual of the contrast medium, which then may increase the risk of biliary tract infection. In this current study, there was great difference in the incidence of electrolyte disorders between groups. It is generally considered that the incidence of electrolyte disorders in PTBD is higher than that in EBD. Patients who performed PTBD reduce jaundice through external drainage and a large amount of bile may be introduced out of the body during this process, thus long-term bile loss may cause electrolyte disorders and even malnutrition. However, results of our study was contradictory to the convention, which may be due to the fact that patients who performed PTBD were managed with the concept of accelerated rehabilitation after operation during perioperative period. Besides, shorter drainage time may also contribute to relatively lower risk of biliary tract infection in PTBD group. Importantly, there were no significant difference in the incidences of other complications between groups. Due to small sample size, the differences in other complications between groups was not statistically significant, which were still necessary to expand the sample size in our further studies.

It has been shown in previous studies that both PTBD and EBD had excellent drainage effect [22, 23]. Yongjiang Ba et al., have also demonstrated that the serum bilirubin level significantly decreased after preoperative biliary drainage through PTBD and EBD operation ( $332.14 \pm 186.85$  VS  $161.42 \pm 93.11$ , VS  $303.17 \pm 182.72$  VS  $126.87 \pm 75.96$ ,  $P=0.001$ ), but there was not significant difference in the decrease degree of bilirubin ( $176.30 \pm 106.76$  VS  $170.72 \pm 93.74$ ,  $P=0.810$ ). Similarly, our study displayed that total bilirubin level obviously decreased after PTBD. However, the decrease of total bilirubin after EBD was not statistically significant. More importantly, there was not only significant difference in total bilirubin between groups after operation, but there also existed evident difference in the decrease degree of bilirubin between groups. It was believed that relatively lower bilirubin decrease in EBD group may be closely associated with higher occurrence rate of acute pancreatitis and biliary tract infection after operation. Taken together, PTBD showed superior drainage effects in patients with obstructive jaundice than EBD in the short run.

This present study reported that differences in postoperative hospitalization time and expenses between groups were not statistically significant, which may be the reason that this study only included the relevant data of patients who performed primary EBD or PTBD in our department. In addition,

follow-up treatment process of these patients was not limited and there may be patients who underwent multiple operations at one time. Therefore, comparability of these above indexes may not reliable, and it still needed to collect and analyze the cases that performed primary PTBD or EBD in each hospitalization to make the results more accurate and reliable. Collectively, this study indicated that compared with EBD, PTBD was more efficient and safer in the treatment of obstruction caused by HCCA.

In terms of short-term treatment efficiency, PTBD was superior than EBD, which presented with higher technical success rate and lower incidence of overall postoperative complications. Therefore, PTBD may be preferred in the treatment of obstructive jaundice caused by HCCA. As for the long-term efficiency, some studies have indicated that compared with EBD, downstage rate of patients who successfully undergo transplantation after PTBD was also higher [21, 24, 25]. However, Wiggers JK et al., showed that PTBD has not superiority in this down-staging process [26]. In future studies, more prospective and randomized studies need to further explore long-term efficiency of EBD and PTBD in reducing jaundice caused by various hepatobiliary diseases.

## Conclusion

In summary, although this current study was a single-center study with small number of samples and there may still exist some deviations, it was demonstrated that PTBD was more efficient and safe for patients with obstructive jaundice caused by HCCA than EBD, which may provide references for medical professionals to make accurate treatment plans to deal with HCCA patients accompanied with obstructive jaundice in their clinical work.

## Abbreviations

CCA=cholangiocarcinoma, EBD=endoscopic biliary drainage, PTBD=percutaneous suprahepatic biliary drainage, HCCA=hilar cholangiocarcinoma, PSM=propensity score matching, MRCP=magnetic resonance cholangiopancreatography, DSA=digital subtraction angiography, BMI=body mass index, CAD=coronary heart disease, TBIL=total bilirubin, AST=aspartate aminotransferase, ALT=alanine aminotransferase,  $\gamma$ -GGT= $\gamma$ - Glutamyl transpeptidase, ALP=alkaline phosphatase, ERCP=endoscopic retrograde cholangiopancreatography, TACE=transcatheter arterial chemoembolization.

## Declarations

### Ethical approval and consent to participate

Design of this study and management of patients were in accordance with the Helsinki Declaration and approved by the Human Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University. Written and signed informed consent for anonymous collection and analysis of clinical data was obtained from all patients before operation in this retrospective cohort. Patients under the age of 18 were not included in this study.

## **Consent for publication**

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published. All patients signed written informed consent for publication of relevant data.

## **Availability of data and materials**

The datasets used/analyzed during the current study are within the manuscript and more data could be available from the corresponding author on reasonable request.

## **Conflicts of interest**

The author declare that there was no conflicts of interest.

## **Funding**

National Natural Science Foundation of China (81960377).

## **Author contributions**

DaLong Zhu: Conception and design; Acquisition of data; Analysis and interpretation of data; Drafting the article.

Musitafa Zayier: Acquisition of data; Drafting the article.

Alimu Tulahong: Acquisition of data; Analysis and interpretation of data.

Abuduhaiwaier Abuduhelili: Acquisition of data; Drafting the article.

Fashun Lu: Acquisition of data.

Bo Ran: Analysis and interpretation of data; Critical revision of manuscript.

Tiemin Jiang: Analysis and interpretation of data; Critical revision of manuscript.

Yingmei Shao: Conception and design; Critical revision of manuscript.

Tuerganaili Aji: Conception and design; Critical revision of manuscript; Final approval of the version to be submitted.

## **Acknowledgements**

None.

## **References**

1. Florio AA, Ferlay J, Znaor A, Ruggieri D, Alvarez CS, Laversanne M, Bray F, McGlynn KA, Petrick JL: **Global trends in intrahepatic and extrahepatic cholangiocarcinoma incidence from 1993 to 2012.** CANCER-AM CANCER SOC 2020, **126**(11):2666–2678.
2. de Jong MC, Marques H, Clary BM, Bauer TW, Marsh JW, Ribero D, Majno P, Hatzaras I, Walters DM, Barbas AS *et al*: **The impact of portal vein resection on outcomes for hilar cholangiocarcinoma.** CANCER-AM CANCER SOC 2012, **118**(19):4737–4747.
3. Khan AS, Dageforde LA: **Cholangiocarcinoma.** SURG CLIN N AM 2019, **99**(2):315–335.
4. KLATSKIN G: **ADENOCARCINOMA OF THE HEPATIC DUCT AT ITS BIFURCATION WITHIN THE PORTA HEPATIS. AN UNUSUAL TUMOR WITH DISTINCTIVE CLINICAL AND PATHOLOGICAL FEATURES.** AM J MED 1965, **38**:241–256.
5. Dondossola D, Ghidini M, Grossi F, Rossi G, Foschi D: **Practical review for diagnosis and clinical management of perihilar cholangiocarcinoma.** WORLD J GASTROENTERO 2020, **26**(25):3542–3561.
6. Nagino Masato HSYH: **Clinical practice guidelines for the management of biliary tract cancers 2019: the 3rd English edition.** J HEPATO-BIL-PAN SCI 2020.
7. Lleo A, Colapietro F, Maisonneuve P, Aloise M, Cravotto V, Ceriani R, Rimassa L, Badalamenti S, Donadon M, Pedicini V *et al*: **Risk Stratification of Cholangiocarcinoma Patients Presenting with Jaundice: A Retrospective Analysis from a Tertiary Referral Center.** CANCERS 2021, **13**(9):2070.
8. Molina V, Sampson J, Ferrer J, Sanchez-Cabus S, Calatayud D, Pavel MC, Fondevila C, Fuster J, García-Valdecasas JC: **Tumor de Klatskin: Diagnóstico, evaluación preoperatoria y consideraciones quirúrgicas.** Cirugía Española 2015, **93**(9):552–560.
9. Ding JW, Andersson R, Soltesz VL, Parsson H, Johansson K, Wang W, Bengmark S: **Inhibition of bacterial translocation in obstructive jaundice by muramyl tripeptide phosphatidylethanolamine in the rat.** J HEPATOL 1994, **20**(6):720–728.
10. Stelios F Assimakopoulos CDSC: **Pathophysiology of increased intestinal permeability in obstructive jaundice.** WORLD J GASTROENTERO 2007(48):6458–6464.
11. Belghiti J, Hiramatsu K, Benoist S, Massault P, Sauvanet A, Farges O: **Seven hundred forty-seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection.** J Am Coll Surg 2000, **191**(1):38–46.
12. Wronka K, Grąt M, Stypułkowski J, Bik E, Patkowski W, Krawczyk M, Zieniewicz K: **Relevance of Preoperative Hyperbilirubinemia in Patients Undergoing Hepatobiliary Resection for Hilar Cholangiocarcinoma.** J CLIN MED 2019, **8**(4):458.
13. William R. Jarnagin MGYF: **Improvement in Perioperative Outcome After Hepatic Resection.** ANN SURG 2002.
14. Ratti F, Cipriani F, Ferla F, Catena M, Paganelli M, Aldrighetti LAM: **Hilar Cholangiocarcinoma: Preoperative Liver Optimization with Multidisciplinary Approach. Toward a Better Outcome.** WORLD J SURG 2013, **37**(6):1388–1396.
15. Lalisan Toar J M SRSN: **Profile of hepatocyte apoptosis and bile lakes before and after bile duct decompression in severe obstructive jaundice patients.** Hepatobiliary Pancreat Dis Int 2010, **9**(3):520.

16. Ozturk N, Ozturk G, Cerrah S, Atamanalp SS, Gul MA, Aksungur N, Bakan N, Bakan E: **Evaluation of liver function by means of serum cytokeratin 18 and hepatocyte growth factor levels in patients with obstructive jaundice.** ACTA CHIR BELG 2018, **118**(3):167–171.
17. Abadie A, Imbens GW: **Matching on the Estimated Propensity Score.** ECONOMETRICA 2016, **84**(2):781–807.
18. PAUL A, KAISER GM, MOLMENTI EP, SCHROEDER T, VERNADAKIS S, OEZCELIK A, BABA HA, CINCINNATI VR, SOTIROPOULOS GC: **Klatskin Tumors and the Accuracy of the Bismuth-Corlette Classification.** The American surgeon 2011, **77**(12):1695–1699.
19. Kloek JJ, van der Gaag NA, Aziz Y, Rauws EAJ, van Delden OM, Lameris JS, Busch ORC, Gouma DJ, van Gulik TM: **Endoscopic and Percutaneous Preoperative Biliary Drainage in Patients with Suspected Hilar Cholangiocarcinoma.** J GASTROINTEST SURG 2010, **14**(1):119–125.
20. Kawakami H, Kuwatani M, Onodera M, Haba S, Eto K, Ehira N, Yamato H, Kudo T, Tanaka E, Hirano S et al: **Endoscopic nasobiliary drainage is the most suitable preoperative biliary drainage method in the management of patients with hilar cholangiocarcinoma.** J GASTROENTEROL 2011, **46**(2):242–248.
21. Kim KM, Park JW, Lee JK, Lee KH, Lee KT, Shim SG: **A Comparison of Preoperative Biliary Drainage Methods for Perihilar Cholangiocarcinoma: Endoscopic versus Percutaneous Transhepatic Biliary Drainage.** GUT LIVER 2015, **9**(6):791.
22. Ba Yongjiang YPLJ: **Percutaneous transhepatic biliary drainage may be the preferred preoperative drainage method in hilar cholangio- carcinoma.** Endoscopy international open 2020.
23. Park SY, Park CH, Cho SB, Lee WS, Kim JC, Cho CK, Joo YE, Kim HS, Choi SK, Rew JS: **What is appropriate procedure for preoperative biliary drainage in patients with obstructive jaundice awaiting pancreaticoduodenectomy?** Surg Laparosc Endosc Percutan Tech 2011, **21**(5):344–348.
24. Komaya K, Ebata T, Yokoyama Y, Igami T, Sugawara G, Mizuno T, Yamaguchi J, Nagino M: **Verification of the oncologic inferiority of percutaneous biliary drainage to endoscopic drainage: A propensity score matching analysis of resectable perihilar cholangiocarcinoma.** SURGERY 2017, **161**(2):394–404.
25. Hirano S, Tanaka E, Tsuchikawa T, Matsumoto J, Kawakami H, Nakamura T, Kurashima Y, Ebihara Y, Shichinohe T: **Oncological benefit of preoperative endoscopic biliary drainage in patients with hilar cholangiocarcinoma.** J HEPATO-BIL-PAN SCI 2014, **21**(8):533–540.
26. Wiggers JK, Groot Koerkamp B, Coelen RJ, Doussot A, van Dieren S, Rauws EA, Schattner MA, van Lienden KP, Brown KT, Besselink MG et al: **Percutaneous Preoperative Biliary Drainage for Resectable Perihilar Cholangiocarcinoma: No Association with Survival and No Increase in Seeding Metastases.** ANN SURG ONCOL 2015, **22**(S3):1156–1163.

## Tables

**Table 1** Detailed clinical aspects of study cohort

Overall cohort (n=114)			PSM cohort (n=38)			
Variances	EBD group (n=37)	PTBD group (n=77)	P	EBD group (n=19)	PTBD group (n=19)	P
Sex				0.936		
Male	20 (54.05%)	41±53.25%		10±52.63%	8±42.11%	0.746
Female	17 (45.95%)	46±46.75%		9±47.37%	11±57.89%	
Age (year)	65.97±12.12	65.44±11.57	0.822	63.21±12.12	64.89 ±8.95	0.624
BMI (Kg/m <sup>2</sup> )	23.54±3.91	23.47±3.62	0.927	24.18±3.71	24.99±3.97	0.536
hypertension	5 (13.51%)	26±33.77%	0.023	3±15.79%	0±0.00%	0.230
diabetes	3 (8.11%)	14±18.18%	0.157	1±5.26%	0±0.00%	1.000
CAD	1 (2.70%)	5±6.49%	0.396	0±0.00%	0±0.00%	
hepatitis	2 (5.41%)	6±7.79%	0.640	1±5.26%	0±0.00%	1.000
Child-Pugh stage				1.000		
A	0 (0.00%)	0±0.00%		0±0.00%	0±0.00%	
B	37 (100.00%)	77±100.00%		19±100.00%	19±100.00%	
Bismuth-Corlette type				0.579		
I	21 (56.76%)	34±44.16%		11±57.89%	8±42.11%	
II	7 (18.92%)	27±35.06%		2±10.53%	7±36.84%	
IIIa	1±2.70%	7±9.09%		1±5.26%	2±10.53%	
IIIb	5 (13.51%)	7±9.09%		4±21.05%	1±5.26%	
IV	3±8.11%	2±2.60%		1±5.26%	1±5.26%	
Pre-TBIL (μmol/L)	312.61±115.67	326.06±110.90	0.551	315.83±97.31	321.25±96.38	0.862
Pre-AST (U/L)	118.90±85.59-192.10±223.02	97.20±62.06-204.16	0.428	132.00±68.90±211.00	83.20±55.10±234.60	0.904
Pre-ALT (U/L)	154.74±71.48-238.97	111.55±62.95-204.16	0.161	113.50±63.05±232.50	85.16±51.00±189.67	0.629
Pre-γGGT (U/L)	378.50±193.28±586.90	392.75±200.22±736.00	0.586	311.70±122.63±593.50	348.07±139.00±550.00	0.904
Pre-ALP (U/L)	478.78±350.36±798.40	405.00±281.00±611.35	0.075	501.06±245.70	435.39±150.61	0.254

PSM: Propensity score matching; EBD: Endoscopic biliary drainage; PTBD: Percutaneous transhepatic biliary drainage; BMI: Body mass index; CAD: Coronary artery disease; Pre-TBIL: Preoperative total bilirubin; Pre-AST: Preoperative aspartate aminotransferase; Pre-ALT: Preoperative alanine aminotransferase; Pre-GGT: Preoperative  $\gamma$ -glutamyl transpeptidase; Pre-ALP: Preoperative alkaline phosphatase.

**Table 2** Comparison of technical success rate between groups

EBD group (n=37)		PTBD group (n=77)		P	
	Events/total	Technical success rate (%)	Events/total	Technical success rate (%)	
All stages	26/37	70.27%	75/77	97.40%	0.001
I	15/21	71.43%	34/34	100%	0.002
II	5/7	71.43%	26/27	96.30%	0.101
IIIa	1/1	100%	7/7	100%	
IIIb	4/5	80.00%	7/7	100%	0.417
IV	1/3	33.33%	1/2	50.00%	1.000

EBD: Endoscopic biliary drainage; PTBD: Percutaneous transhepatic biliary drainage.

**Table 3** Comparison of postoperative complications between groups

Complications	EBD group (n=19)		PTBD group (n=19)		P
	Events/total	Incidence rate (%)	Events/total	Incidence rate (%)	
Overall complications	14/19	73.68	7/19	36.84%	0.049
Electrolyte disturbance	7/19	36.84%	4/19	21.05%	0.476
Acute pancreatitis	5/19	26.32%	0/19	0.00%	0.046
Hemobilia	1/19	5.26%	3/19	15.79%	0.604
Biliary tract infection	8/19	42.11%	2/19	10.53%	0.062
Stent/drainage tube dropout	0/19	0.00%	0/19	0.00%	
Biliary leakage	0/19	0.00%	0/19	0.00%	
Hypoproteinemia	6/19	31.58%	4/19	21.05%	0.714

EBD: Endoscopic biliary drainage; PTBD: Percutaneous transhepatic biliary drainage.

**Table 4** Comparison of treatment efficiency in EBD group patients (n=19) before and after treatment

<b>Variances</b>	<b>Preoperative</b>	<b>postoperative</b>	<b>P</b>
TBIL (μmol/L)	315.83±97.31	307.34±113.34	0.807
AST (U/L)	132.00±68.90±211.00±	73.30±46.30±139.10±	0.059
ALT (U/L)	113.50±63.05±232.50±	105.27±44.87±163.53±	0.053
γGGT (U/L)	311.70±122.63±593.50±	162.40±88.53±529.60±	0.003
ALP (U/L)	501.06 ±245.70	456.83 ±305.65	0.321

EBD: Endoscopic biliary drainage; TBIL: Total bilirubin; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; γGGT: γ-glutamyl transpeptidase; ALP: Alkaline phosphatase.

**Table 5** Comparison of treatment efficiency in PTBD group patients (n=19) before and after treatment

<b>Variances</b>	<b>Preoperative</b>	<b>postoperative</b>	<b>P</b>
TBIL (μmol/L)	321.25±96.38	233.51±107.49	±0.001
AST (U/L)	83.20±55.10±234.60±	48.20±34.90±113.00±	0.001
ALT (U/L)	85.16±51.00±189.67±	56.16±43.00±101.39±	0.001
γGGT (U/L)	348.07±139.00±550.00±	193.70±79.00±331.27±	±0.001
ALP (U/L)	435.39 ±150.61	309.66±120.98	±0.001

PTBD: Percutaneous transhepatic biliary drainage; TBIL: Total bilirubin; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; γGGT: γ-glutamyl transpeptidase; ALP: Alkaline phosphatase.

**Table 6** Comparison of treatment efficiency between groups

<b>Variances</b>	<b>EBD group (n=19)</b>	<b>PTBD group (n=19)</b>	<b>P</b>
Post-TBIL (μmol/L)	307.34±113.34	233.51±107.49	0.019
Decrease of TBIL (μmol/L)	8.49±149.18 8.46	87.74±63.59	0.041
Post-AST (U/L)	73.30±46.30±139.10±	48.20±34.90±113.00±	0.398
Post-ALT (U/L)	105.27±44.87±163.53±	56.16±43.00±101.39±	0.184
Post-γGGT (U/L)	162.40±88.53±529.60±	193.70±79.00±331.27±	0.936
Post-ALP (U/L)	456.83 ±305.65	309.66±120.98	0.066

EBD: Endoscopic biliary drainage; PTBD: Percutaneous transhepatic biliary drainage; Post-TBIL: Postoperative total bilirubin; Post-AST: Postoperative aspartate aminotransferase; Post-ALT: Postoperative

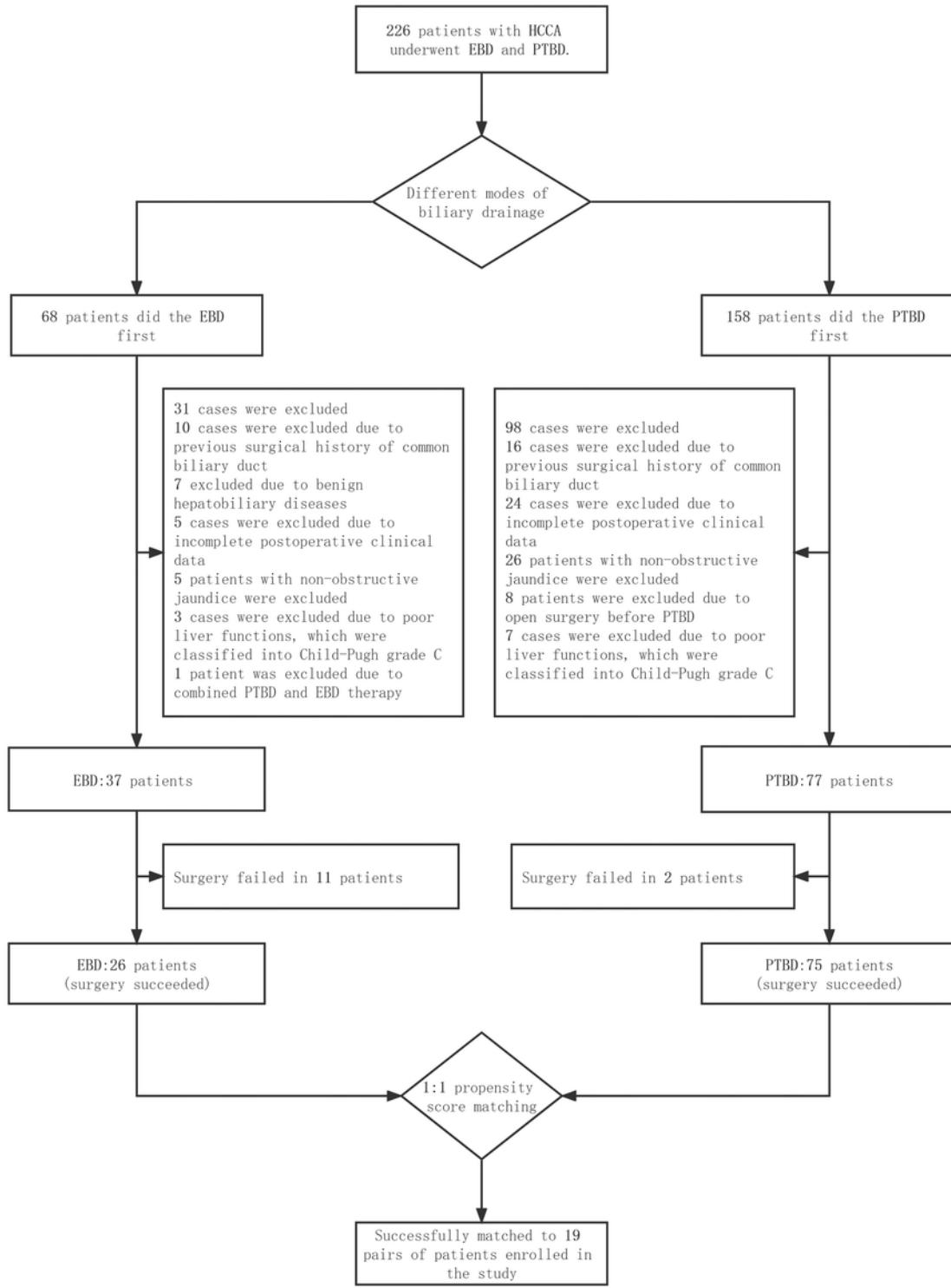
alanine aminotransferase; Post-GGT: Postoperative  $\gamma$ -glutamyl transpeptidase; Post-ALP: Postoperative alkaline phosphatase.

**Table 7** Comparison of operation duration and hospitalization expenses between groups

Variances	EBD group (n=19)	PTBD group (n=19)	P
Operation duration (min)	45.00 (40.00-90.00)	30.00 (25.00-55.00)	0.102
Postoperative Hospitalization time (day)	5.00 (4.00-9.00)	7.00 (5.00-17.00)	0.265
Hospitalization costs (RMB)	32701.14 (25784.77-47424.61)	30619.35 (22988.21-36476.45)	0.601

EBD: Endoscopic biliary drainage; PTBD: Percutaneous transhepatic biliary drainage.

## Figures



**Figure 1**

Study diagram of subjects used in this study.