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SYSTEMATIC REVIEW

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Efficacy and safety of endoscopic nasobiliary drainage versus percutaneous transhepatic cholangial drainage in the treatment of advanced hilar cholangiocarcinoma: a systematic review and meta-analysis

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Abstract

Objective To evaluate and compare the efficacy and safety of Endoscopic Nasobiliary Drainage (ENBD) and Percutaneous Transhepatic Cholangiography Drainage (PTCD) in patients with advanced Hilar Cholangiocarcinoma (HCCA) through a meta-analysis of clinical studies.

Methods We searched Chinese and English databases, including China National Knowledge Infrastructure (CNKI), Wanfang database, PubMed, Embase, Scopus, and Web of Science, for relevant literatures on PTCD and ENBD for advanced HCCA clinical trials. Two investigators independently screened the literatures, and the quality of the included studies was evaluated using the Newcastle-Ottawa Scale (NOS). The primary endpoint was the success rate of biliary drainage operation, while secondary endpoints included Total Bilirubin (TBIL) change, acute pancreatitis, biliary tract infection, hemobilia, and other complications. R software was used for data analysis.

Results A comprehensive database search, based on predefined inclusion and exclusion criteria, yielded 26 articles for this study. Analysis revealed that PTCD had a significantly higher success rate than ENBD [OR (95% CI) = 2.63 (1.98, 3.49), Z=6.70, $P<0.05$]. PTCD was also more effective in reducing TBIL levels post-drainage [SMD (95%CI) =-0.13 (-0.23, -0.03), Z=-2.61, $P<0.05$]. While ENBD demonstrated a lower overall complication rate [OR (95%CI) = 0.60 (0.43, 0.84), Z=-2.99, $P<0.05$], it was associated with a significantly lower incidence of post-drainage biliary hemorrhage compared to PTCD [OR=3.02, 95%CI: (1.94-4.71), Z= 4.89, $P<0.01$].

Conclusions This meta-analysis compares the efficacy and safety of ENBD and PTCD for palliative treatment of advanced HCCA. While both are effective, PTCD showed superiority in achieving successful drainage, reducing TBIL, and lowering the incidence of acute pancreatitis and biliary infections. However, ENBD had a lower risk of post-drainage bleeding. Clinicians should weigh these risks and benefits when choosing between ENBD and PTCD for individual patients. Further research is needed to confirm these findings and explore long-term outcomes.

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Keywords Endoscopic nasobiliary drainage (ENBD), Hilar cholangiocarcinoma (HCCA), Meat-analysis, Percutaneous transhepatic cholangial drainage (PTCD)

Introduction

Hilar cholangiocarcinoma (HCCA), a highly aggressive malignant tumor of the digestive system, is also known as Klatskin tumor after its detailed description by Klatskin in 1965 [1–3]. Representing 60%-70% of all intrahepatic and extrahepatic biliary tract tumors, HCCA carries a grim prognosis, with a median survival time of less than 6 months for patients without radical resection [4, 5].

The disease's hallmark is bile duct obstruction, leading to increased pressure, bile capillary expansion, and reversed bile flow into the bloodstream. This can result in liver failure, biliary tract infections, sepsis, and septic shock, the primary causes of death in HCCA patients [6, 7].

Effective biliary drainage is crucial for managing HCCA. It promotes the excretion of metabolic waste and toxins, reduces liver cell damage, and ultimately improves quality of life and prolongs survival [4, 8]. Two minimally invasive biliary drainage methods are commonly employed: endoscopic nasobiliary drainage (ENBD) [9, 10] and percutaneous transhepatic cholangial drainage (PTCD) [3, 8].

PTCD involves placing a puncture needle under ultrasound or X-ray guidance through the skin into the bile duct above the obstruction site to drain bile externally [11, 12]. This approach offers several advantages: simplicity, low technical requirements, ease of implementation in primary hospitals, avoidance of general anesthesia, and fewer surgical contraindications [13, 14]. However, PTCD also presents limitations, including the need for prolonged drainage tube placement, potential for infection, and patient discomfort.

ENBD, an endoscopic technique based on Endoscopic Retrograde Cholangiopancreatography (ERCP), involves inserting a nasobiliary drainage tube into the common bile duct and guiding it through the duodenum, stomach, esophagus, pharynx, and throat, ultimately exiting through the nose [15–19]. This method facilitates both endoscopic diagnosis and treatment.

While PTCD was once the preferred biliary drainage method for advanced HCCA, ENBD has emerged as a viable alternative with the advancements in endoscopic technology [3, 20]. Both methods aim to relieve biliary obstruction and reduce pressure, but their effectiveness and impact on patient prognosis remain unclear.

This meta-analysis aims to evaluate and compare the efficacy and safety of PTCD and ENBD in treating HCCA by synthesizing data from published clinical studies. Our goal is to provide robust evidence-based guidance for clinicians in selecting the most appropriate minimally invasive biliary drainage method for their HCCA patients.

Methods

Literature retrieval strategy

We conducted the literature search through six widely used databases: PubMed, Scopus, Embase, Web of Science, Wanfang, and China National Knowledge Infrastructure (CNKI). We strictly followed the PICOS principle, and the search terms included "klatskin tumor, hilar cholangiocarcinoma, endoscopic nasobiliary drainage, percutaneous transhepatic cholangial drainage, TBIL change after biliary drainage, acute pancreatitis after biliary drainage, biliary tract infection, hemobilia, patient survival". We used a combination of MeSH terms and free text words, and adjusted the search strategy according to the characteristics of different databases from inception to August 31, 2023 (Search strategies are provided in the Supporting document).

Eligibility criteria

Inclusion criteria: (1) HCCA patients who could not undergo radical resection surgery; (2) comparison of two techniques: PTCD and ENBD, and (3) randomized controlled trials (RCTs), cohort study and case-control study. The exclusion criteria were included: (1) the sample size was less than 10; (2) not supported by appropriate data in the study; (3) animal experiments, reviews, and case reports and (4) low-quality studies assessed using Newcastle-Ottawa tool (The total score is 9, with a score greater than or equal to 6 indicating a high quality of the literature).

Studies had to report at least one predefined primary or secondary endpoint (e.g., success rate of biliary drainage procedures, change in TBIL, incidence of acute pancreatitis, etc.). Studies comparing only two methods but not reporting any relevant end points were excluded.

Two researchers (HZ and CL) independently screened according to the inclusion and exclusion criteria. If there were different opinions, the inclusion was discussed with the third researcher (MS). According to the literature data extraction table set in advance, the relevant data of the final included studies were extracted. The detailed flow-chart for the literature search and selection strategy was exhibited in Fig. 1.

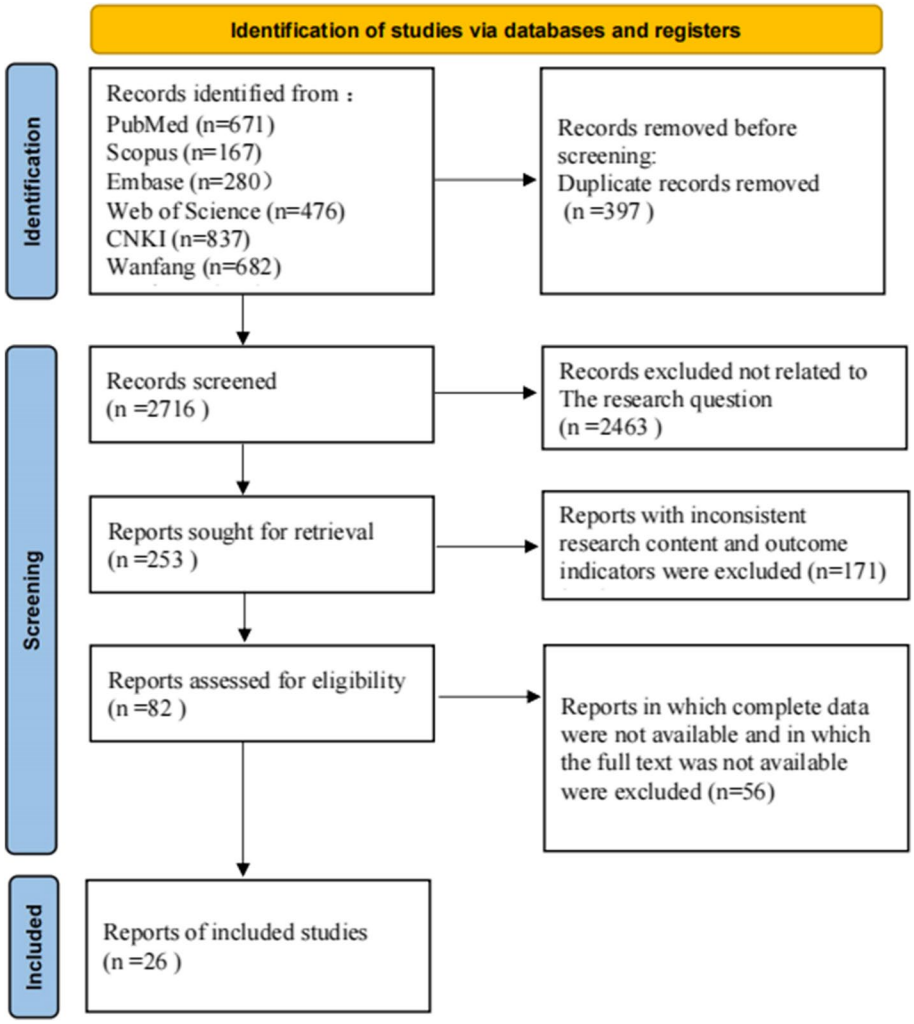

Fig. 1 Modified Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram of the literature search

Information extraction

The contents of data extraction included: (1) basic information of literature: author, country, publication time, research type, total sample size, etc. (2) Outcome indicators: the success rate of drainage, the change of TBIL after drainage, the occurrence of complications after drainage (acute pancreatitis, biliary tract infection, hemobilia), and the survival of patients after drainage. The primary endpoint of this study was success rate of biliary drainage operation. Secondary endpoints included Total Bilirubin (TBIL) change after biliary drainage, acute pancreatitis after biliary drainage, biliary tract infection, hemobilia and other complications.

Statistical analysis

We used R (Version 4.1.2) within the RStudio (Version 1.4.1) for statistical analysis. The following R packages were utilized 'meta', 'metafor'. The Cochran's Q test will be used to assess the heterogeneity and I^2 will be calculated to quantify inconsistency. If I^2>50%, a fixed effects model will be used, otherwise, a random effects model will be used. The odds ratio (OR) and 95% confidence interval (CI) will be calculated to analyze the dichotomous variables. Standardized mean difference (SMD) will be calculated to analyze the continuous variables. Funnel plot was used to evaluate the publication bias of the studies included in the meta-analysis.

Results

Study characteristics

After applying the inclusion and exclusion criteria, a total of 26 studies published between 2007 and 2023 were selected for this review (Fig. 1). These studies had a combined sample size of 2533, with 1295 participants in the ENBD group and 1238 in the PTCD group.

The majority of the studies were conducted in China (n=24), followed by South Korea (n=1) and Canada (n=1). The basic characteristics of the included studies are presented in Table 1.

Success rate of biliary drainage operation

We included 15 studies in the analysis of drainage success rates, with a total sample size of 1500 cases (798 in the ENBD group and 702 in the PTCD group). The heterogeneity analysis revealed low heterogeneity (I^2=0, P>0.05), allowing us to combine the effect sizes using a fixed-effect model. The meta-analysis results showed a significant difference in drainage success rates between the two groups [OR (95%CI) = 2.63 (1.98, 3.49), Z=6.70, P<0.01] (Fig. 2), indicating that PTCD is more effective than ENBD in achieving successful biliary drainage.

Changes of total bilirubin (TBIL) after biliary drainage

Sixteen studies were included to analyze the change of TBIL after ENBD and PTCD drainage, with a total sample of 1575 patients, including 820 patients in the ENBD group and 755 patients in the PTCD group. The heterogeneity of the results was analyzed (I^2=0<50%, P>0.1), indicating that the heterogeneity was not obvious. The effect size was combined by fixed effect model, and the results of Meta-analysis showed that the difference was statistically significant [SMD (95%CI) =-0.13 (-0.23, -0.03), Z=-2.61, P<0.05] (Fig. 3), suggesting that PTCD was more effective than ENBD in the change of TBIL after biliary drainage.

Complications after biliary drainage

This meta-analysis included 25 studies comparing complications after ENBD and PTCD, with a total sample of 2534 cases (1298 ENBD and 1236 PTCD). The main

Table 1 Basic characteristics of the included literatures

Author	Year	Location	Study type	Age		Gender[a]		Success rate		PTCD/ENBD[b]	NOS score
				PTCD	ENBD	Male	Female	PTCD	ENBD		
Cai et al.	2010	China	Retrospective	65.20±10.10	60.30±8.90	12/20	13/15	92.00%	80.00%	25/35	8[24]
Chen et al.	2023	China	Retrospective	50.41±15.28	52.87±13.96	42/38	68/45	-	-	110/83	7[1]
Chen et al.	2020	China	Retrospective	64.65±14.78	67.23±11.74	31/52	26/36	82.40%	81.80%	57/88	7[25]
Ding et al.	2012	China	Retrospective	59.90±13.60	61.20±14.3	52/49	30/64	85.58%	70.80%	82/133	8[29]
Gong et al.	2019	China	Retrospective	59.28±5.79	60.63±5.81	26/25	22/22	89.58%	76.60%	48/47	7[26]
Huang et al.	2016	China	Retrospective	58.80±6.50	58.70±6.30	39/42	23/26	95.20%	82.40%	62/68	8[11]
Lee et al.	2007	South Korea	Retrospective	67.20±1.10	66.80±2.90	46/23	20/11	97.70%	93.90%	66/34	9[36]
Li et al.	2016	China	Retrospective	63.30±12.10	64.92±12.71	33/32	27/21	-	-	60/53	8[37]
Liang et al.	2020	China	Retrospective	61.30±6.90	62.20±7.30	24/19	18/17	85.70%	63.90%	42/36	7[38]
Liu et al.	2023	China	RCT	54.58±2.65	54.60±2.67	24/25	18/17	-	-	42/42	8[19]
Liu et al.	2017	China	Retrospective	-	-	-	-	95.56%	91.53%	45/59	7[39]
Meng et al.	2023	China	Retrospective	67.74±5.98	67.79±5.97	25/26	18/17	88.37%	69.77%	43/43	9[2]
Niu et al.	2017	China	Retrospective	61.20±11.40	58.40±9.60	20/22	16/10	-	-	36/32	9[13]
Shi et al.	2012	China	Retrospective	54.80±9.50	55.70±9.30	23/29	8/15	89.70%	86.40%	31/44	9[12]
Sui et al.	2017	China	Retrospective	61.40±13.70		26	33	-	-	27/32	9[28]
Thomas et al.	2012	Canada	Retrospective	66.00±10.60		24/54	19/33	98.00%	78.00%	42/87	8[31]
Wan et al.	2019	China	Retrospective	56.83±4.52	56.95±4.61	19/21	15/13	88.20%	67.60%	34/34	9[23]
Wang et al.	2019	China	Retrospective	61.04±6.94	60.98±6.91	21/20	23/24	86.36%	68.18%	44/44	8[40]
Wang et al.	2018	China	Retrospective	61.10±2.80	61.30±2.50	16/17	15/14	93.50%	77.40%	31/31	7[27]
Zhang et al.	2022	China	Retrospective	55.53±3.94	56.02±3.04	24/22	17/19	-	-	41/41	8[41]
Zhang et al.	2017	China	Retrospective	49.50±20.50		63	50	85.90%	85.70%	71/42	8[18]
Zhang et al.	2017	China	Retrospective	48.08±0.05	48.11±0.01	48/43	27/27	-	-	75/70	7[42]
Zhang et al.	2016	China	Retrospective	60.24±6.16	60.72±6.45	18/17	16/16	-	-	34/33	8[43]
Zhang et al.	2011	China	Retrospective	63.40±6.37	59.40±6.45	13/14	12/11	88.00%	68.00%	25/25	8[30]
Zheng et al.	2018	China	Retrospective	60.20±4.80	61.40±4.30	28/30	22/22	86.00%	67.30%	50/52	9[32]
Zhu et al.	2020	China	Retrospective	70.80±14.30	68.10±15.70	22/24	18/18	-	-	40/42	8[14]

[a] PTCD/ENBD

[b] Sample size

-not reported

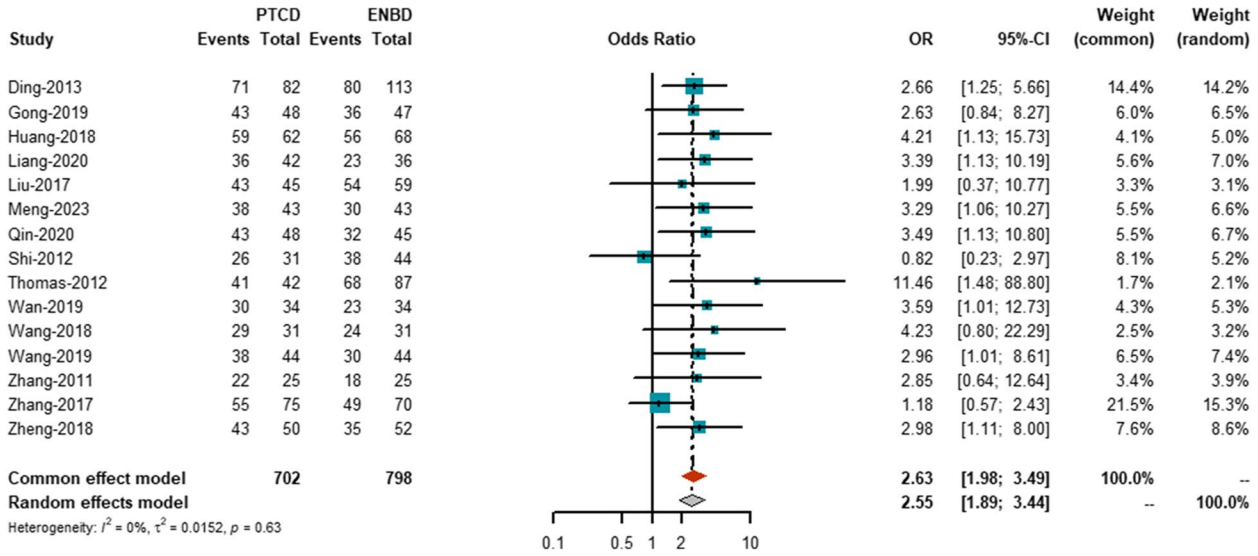

Fig. 2 Forest plots of the success rate of biliary drainage operation meta-analysis

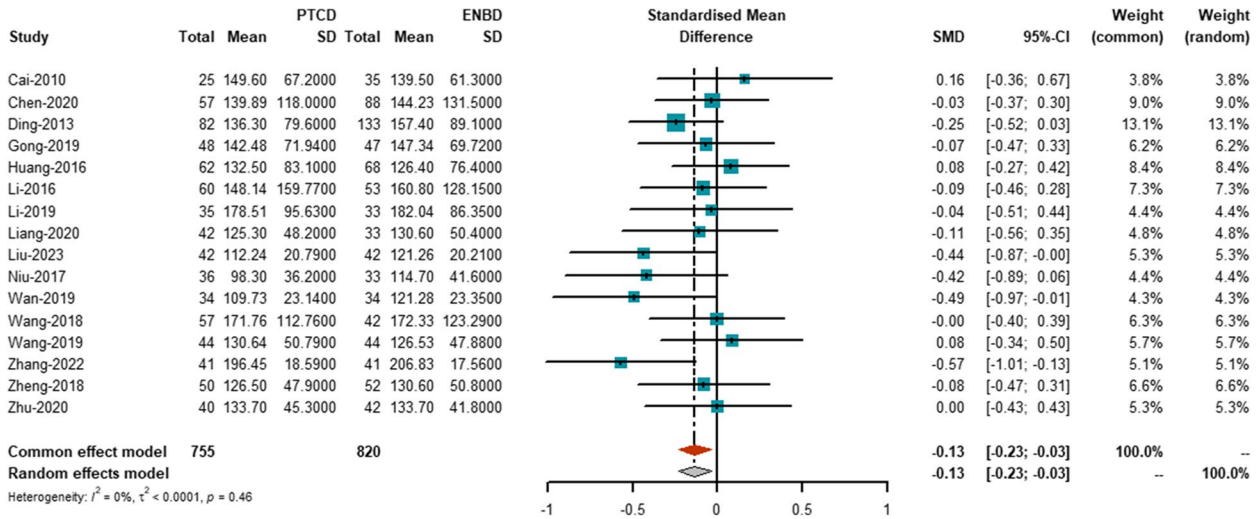

Fig. 3 Forest plots of the effect of biliary drainage meta-analysis

complications analyzed were acute pancreatitis, biliary tract infection, and biliary tract hemorrhage.

Heterogeneity analysis revealed significant heterogeneity among the studies (I^2>50%, P<0.05). Therefore, a random-effects model was employed to combine effect sizes. The meta-analysis results showed statistically significant differences between ENBD and PTCD [OR (95% CI) = 0.60 (0.43, 0.84), Z = -2.99, P<0.05] (Fig. 4), indicating that ENBD is associated with a higher incidence of overall complications after biliary drainage compared to PTCD.

Subsequently, we conducted a subgroup analysis focusing on the occurrence of hemobilia after biliary drainage. This analysis included 16 studies with a total sample size of 1700 cases (883 ENBD and 817 PTCD). Heterogeneity analysis for hemobilia showed no significant heterogeneity (I^2 = 16.3% < 50%, P =0.27>0.1). Consequently, a fixed-effect model was used to combine the effect sizes. The meta-analysis results for hemobilia revealed a statistically significant difference [OR (95% CI) = 3.02 (1.94, 4.71), Z =4.89, P<0.01] (Fig. 5), suggesting that ENBD is associated with a lower incidence of hemobilia compared

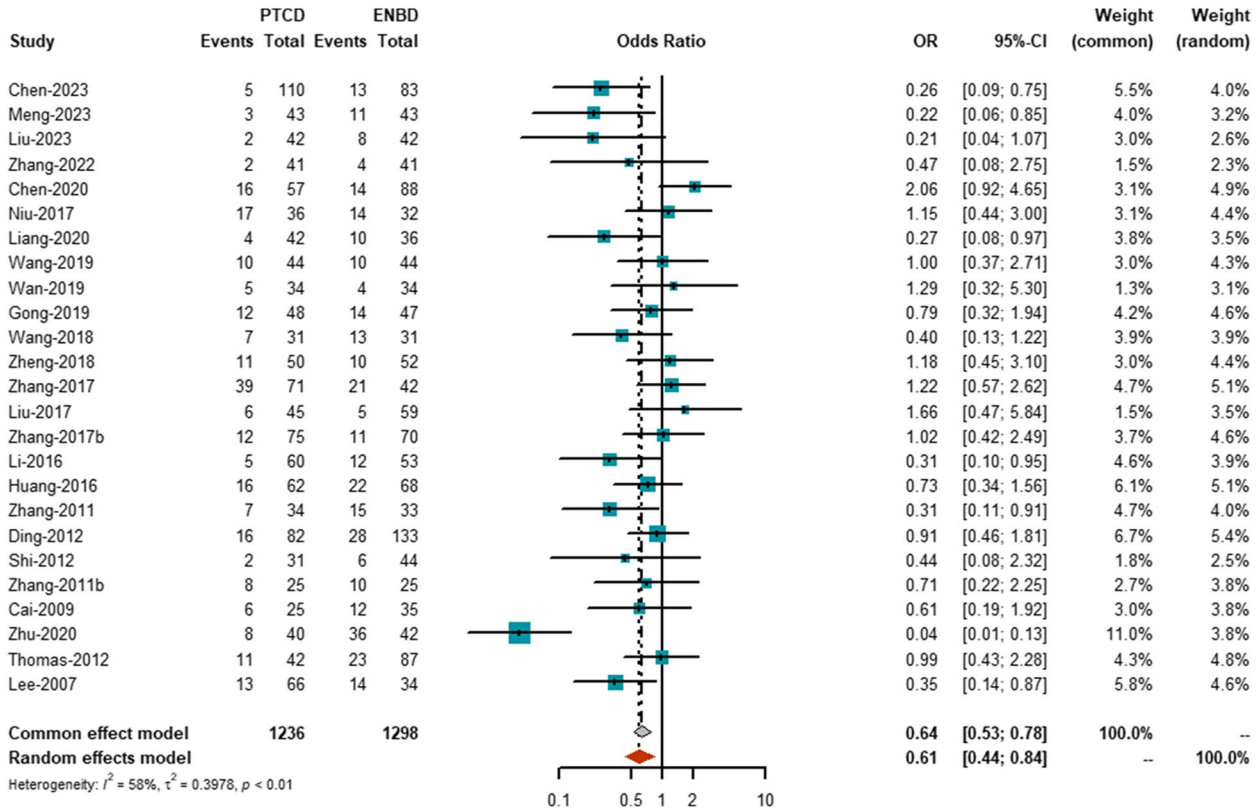

Fig. 4 Forest plots of complications after biliary drainage meta-analysis

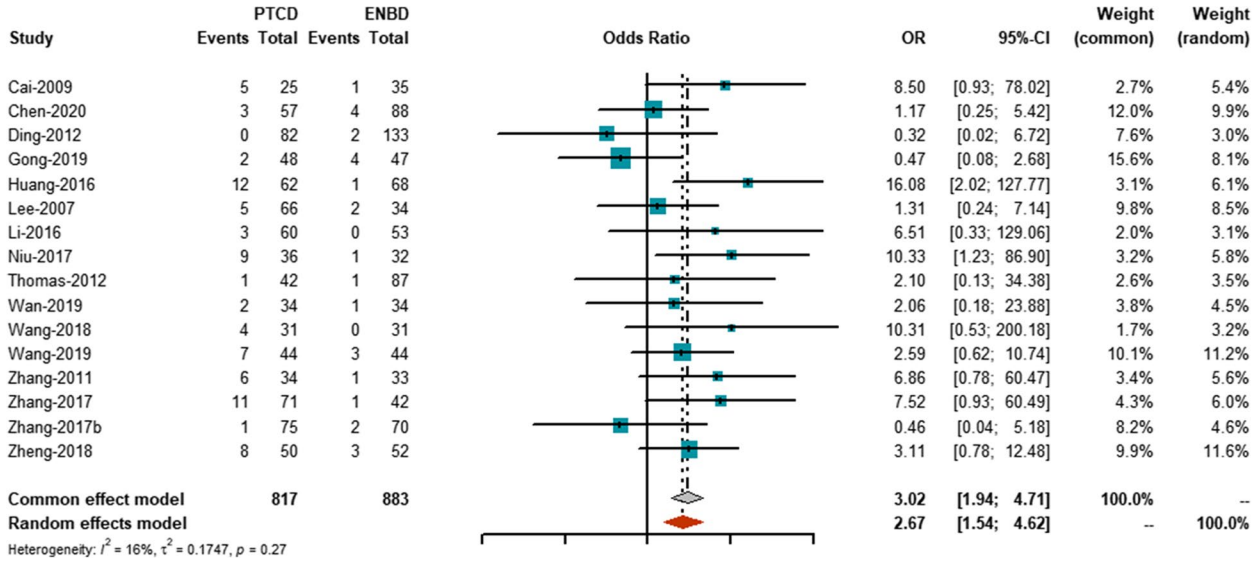

Fig. 5 Forest plots of biliary tract bleeding after biliary drainage meta-analysis

to PTCD. In conclusion, although ENBD appears to have a higher overall complication rate, it demonstrates a lower incidence of hemobilia compared to PTCD.

Publication bias and sensitivity analysis

We examined the publication shift of the included studies by funnel plot (Fig. 6), and the results showed that the funnel plot shape of drainage success rate, TBIL, and

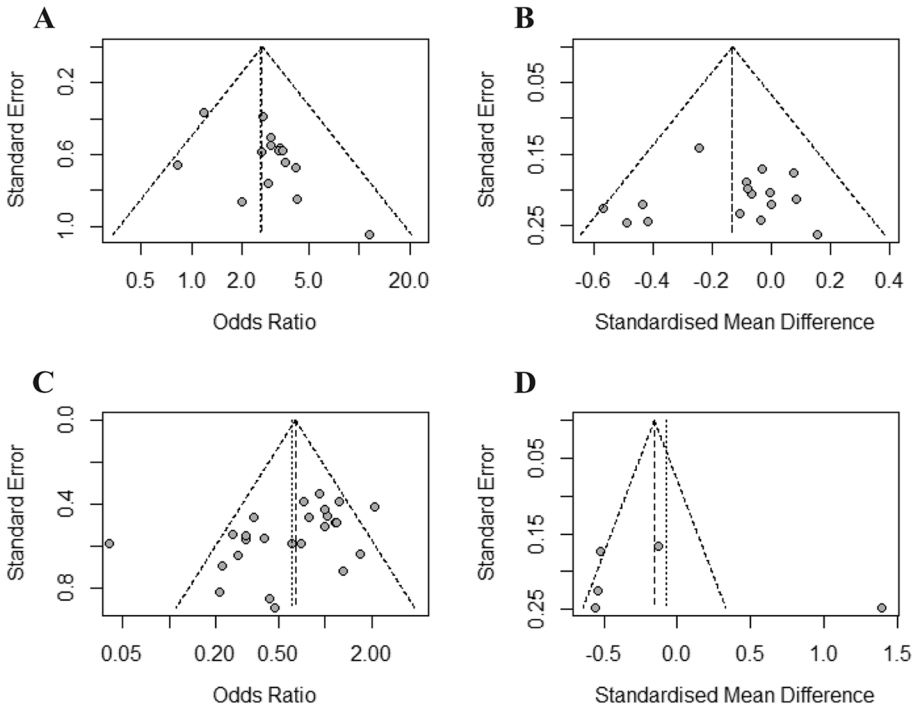

Fig. 6 Funnel plots of the meta-analysis. **A** 15 articles in the meta-analysis of the success rate of biliary drainage operation. **B** 16 articles in the meta-analysis of Changes of total bilirubin (TBIL) after biliary drainage. **C** 25 articles in the meta-analysis of postoperative complications. **D** 16 articles in the meta-analysis biliary tract bleeding after biliary drainage

postoperative complications showed basically symmetry. No significant publication bias was observed, and the results were highly reliable. Sensitivity analysis of effect size exhibited no significant difference for each data.

Discussion

In the treatment of patients with HCCA, PTCD compared endoscopic nasal biliary drainage ENBD have a higher success rate of surgery and a lower incidence of complications. In addition, PTCD in reducing total bilirubin TBIL level also shows advantage. These findings provide an important basis for clinical decision-making and help to improve the treatment outcomes of HCCA patients. Our results are consistent with previous reported basic literature [21, 22]. ENBD low success rate of surgery could be due to the following factors: first, ENBD operation process, and thread easily into the main pancreatic duct stent, cause the failure of operation [23, 24]. Secondly, biliary obstruction caused by HCCA belongs to high obstruction, which increases the difficulty of guidewire and catheter access to the obstruction site [16, 25, 26]. In addition, the duodenal papilla structure is not clear due to tumor invasion in some patients, which makes ENBD more difficult to perform [27, 28]. In contrast, PTCD is less difficult to perform, but its success rate is largely dependent on the condition of the bile duct [29, 30]. Regarding complications, we found that the incidence of postoperative complications of ENBD than PTCD. This may be due to the contrast agent entering the pancreatic duct and exudation during the ENBD procedure, which caused damage to the pancreas. Repeated operation may lead to duodenal papilla spasm and bile reflux into the pancreas. Prolonged procedural time may also increase the risk of complications in patients with Bismuth-Corlette type III or IV [31]. PTCD, by contrast, is the main complication of biliary tract bleeding, the incidence of 3% to 14%, may be related to improper puncture Angle control or puncture after bile extraction [32] too much too fast.

Although PTCD has shown advantages in several aspects, ENBD still has its unique value in some situations. ENBD postoperative nursing is relatively simple, patients life quality is higher. For patients without high-risk complications, ENBD can be used as the first choice for palliative jaundice reduction [33, 34]. In addition, PTCD can be used as an effective alternative after ENBD failure [35].

The limitations of this study is to include research quantity is limited, and most of the retrospective study, there may be a selection bias. More high-quality randomized controlled trials are needed to further verify our findings in the future. In addition, our analysis focuses on

the short-term effect, for the long-term outcome of evaluation still needs more research.

In a word, this meta-analysis for HCCA patients with biliary drainage method provides an important basis. PTCD in the success rate of surgery, complications and reduce TBIL level shows the advantage. However, in view of the two methods have their own characteristics, clinical doctors should consider when choosing the drainage method. When choosing between ENBD and PTCD, clinicians should carefully consider the individual patient's clinical situation and the potential risks and benefits. For patients at higher risk of post-drainage bleeding, ENBD may be the more appropriate choice. Conversely, patients at higher risk of complications such as acute pancreatitis or biliary infections may benefit from PTCD. Further research with larger sample sizes and longer follow-up periods is crucial to corroborate these findings and explore the long-term outcomes of these two interventional approaches.

Conclusions

This meta-analysis compares the efficacy and safety of ENBD and PTCD for palliative treatment of advanced HCCA. While both are effective, PTCD showed superiority in achieving successful drainage, reducing TBIL, and lowering the incidence of acute pancreatitis and biliary infections. However, ENBD had a lower risk of post-drainage bleeding. Clinicians should weigh these risks and benefits when choosing between ENBD and PTCD for individual patients. Further research is needed to confirm these findings and explore long-term outcomes.

Abbreviations

ENBD	Endoscopic Nasobiliary Drainage
PTCD	Percutaneous Transhepatic Cholangiography Drainage
HCCA	Hilar Cholangiocarcinoma
NOS	Newcastle-Ottawa Scale
TBIL	Total Bilirubin
OR	Odds Ratio
CI	Confidence Interval
SMD	Standardized Mean Difference

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-024-03397-3.

Supplementary Material 1.

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Authors' contributions

JY and XS were involved in the administrative support, reviewing, and revised the manuscript. HZ and CL was involved in the conception and design of the manuscript, and drafted the initial manuscript. XY was involved in data analysis. MS was involved in the collection and assembly of data. All authors contributed to the article and approved the submitted version.

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Availability of data and materials

Data is provided within the manuscript and supplementary information files.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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