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Comparative efficacy of endoscopic ultrasound-guided biliary drainage versus endoscopic retrograde cholangiopancreatography as first-line palliation in malignant distal biliary obstruction: a systematic review and meta-analysis

Shravya Reddy Ginnaram[a], Sudeep Nugooru[a], Dawood Tahir[a], Kara Devine[a], Ali Raza Shaikh[b], Pradeep Yarra[c], James Walter[d]

Jefferson Abington Hospital, PA; Thomas Jefferson University Hospital, Philadelphia, PA; Saint Louis University Medical Center, St. Louis, MO; Jefferson Einstein Hospital, Philadelphia, PA, USA

Abstract

Background Malignant distal biliary obstruction (MDBO) is a challenging clinical condition commonly managed with endoscopic retrograde cholangiopancreatography (ERCP). However, endoscopic ultrasound-guided biliary drainage (EUS-BD) has emerged as an alternative, especially in complex cases where ERCP fails or is deemed risky. This study aimed to compare the efficacy, safety and cost-effectiveness of EUS-BD vs. ERCP in the palliation of MDBO.

Methods We conducted a systematic review and meta-analysis, following PRISMA guidelines. Three databases were searched up to December 2023, including MEDLINE/PubMed, OVID and the Cochrane Central Register of Controlled Trials, for studies comparing EUS-BD with ERCP. Primary outcomes were technical and clinical success rates, while secondary outcomes included procedural times, hospital stay duration, 30-day mortality, reintervention rates, and adverse events such as pancreatitis.

Results Seven studies involving 1245 patients met the inclusion criteria. The meta-analysis revealed that EUS-BD had a technical success rate of 92%, compared to 85% for ERCP. Clinical success rates were similar for both EUS-BD and ERCP, at approximately 89%. EUS-BD was associated with a significantly lower incidence of pancreatitis (2% vs. 10% for ERCP).

Conclusions EUS-BD offers a viable and potentially superior alternative to ERCP for the primary palliation of MDBO, particularly in terms of technical success and a lower risk of pancreatitis. These findings support the adoption of EUS-BD in clinical settings equipped to perform this technique, though future research should focus on long-term outcomes and further economic analysis to solidify these recommendations.

Keywords Malignant distal biliary obstruction, endoscopic ultrasound-guided biliary drainage, endoscopic retrograde cholangiopancreatography, meta-analysis

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Correspondence to: Shravya Reddy Ginnaram, M.D, 1200 Old York Rd, Abington, PA 19001, USA, e-mail: shravyaginnaram@gmail.com

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Introduction

Approximately 70% of newly diagnosed pancreatic cancers, including pancreatic head adenocarcinoma, cholangiocarcinoma in the lower third of the common bile duct, ampullary carcinoma, or lymph node involvement and metastases, present with some form of biliary obstruction. Biliary decompression is crucial for symptomatic relief, and to facilitate the administration of neoadjuvant or palliative chemotherapy in cases of advanced or inoperable disease [1].

Endoscopic retrograde cholangiopancreatography (ERCP)-guided transpapillary stenting is the recognized first-line

palliative treatment for malignant distal biliary obstruction (MDBO). However, ERCP comes with its challenges, including a significant risk of pancreatitis, which has an incidence of up to 3.47% and associated mortality of 3.08%, as well as cholecystitis, cholangitis, stent dysfunction and migration, with a combined incidence rate of 28-36%. Complications are exacerbated by malignant infiltration of the duodenum or papilla, or in cases of surgically modified anatomy that precludes transpapillary stenting [2].

Endoscopic ultrasound-guided biliary drainage (EUS-BD) offers alternative transluminal and transpapillary stenting approaches, including intrahepatic hepaticogastrostomy (EUS-HGS) or extrahepatic choledochoduodenostomy (EUS-CDS), and rendezvous (EUS-RV) techniques [3]. Initially introduced by Giovannini *et al* in 2001 using plastic stents, the evolution to self-expandable metal stents was marred by complications including cholangitis, biliary peritonitis, and duodenal perforation. The introduction of lumen-apposing metal stents, and more recently electrocautery-enhanced lumen-apposing metal stents (Hot AXIOS or AXIOS-EC™, Boston Scientific Marlborough, MA, USA), has simplified EUS-CDS techniques, enabling a free-hand, single-step, and exchange-free procedure that reduces operative time and theoretically minimizes the risk of bile leak and peritonitis [4-6].

Through several randomized controlled trials (RCTs) and meta-analyses, EUS-BD has established itself as a viable second-line option in the management of MDBO when ERCP fails [7,8]. Despite its successes, the evidence supporting the use of EUS-BD as a primary treatment option for MDBO remains limited. This systematic review and meta-analysis aimed to assess and compare the efficacy of EUS-BD and ERCP in the initial palliative management of MDBO, potentially redefining treatment paradigms based on efficacy, safety, and procedural outcomes.

Materials and methods

Data sources and search strategy

This systematic review and meta-analysis was conducted in strict adherence to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines, as outlined by Page (2020) [9]. The PRISMA checklist was followed to ensure comprehensive and transparent reporting of our findings (See Supplementary Table 1). MEDLINE/Pubmed, OVID and the Cochrane Central Register of Controlled Trials were searched from database inception through December 2023. No time restriction was used in the search, but the language was restricted to English only. We began by creating search phrases using the Boolean operators "OR" and "AND" to form a keyword, and we applied these keywords in searches across titles, abstracts and URLs. To broaden our search, we also reviewed the reference lists of the articles we selected. All citations retrieved from the search were transferred to Zotero 6.0.30 Reference Manager and duplicates were removed. Seven studies were included in the meta-analysis.

[a]Department of Internal Medicine, Jefferson Abington Hospital, Abington, PA (Shravya Reddy Ginnaram, Sudeep Nugooru, Dawood Tahir, Kara Devine); [b]Department of Hematology/Oncology, Thomas Jefferson University Hospital, Philadelphia, PA (Ali Raza Shaikh); [c]Department of Gastroenterology and Hepatology, Saint Louis University Medical Center, St. Louis, MO (Pradeep Yarra); [d]Department of Gastroenterology and Hepatology, Jefferson Einstein Hospital, Philadelphia, PA (James Walter)

Study selection

All citations were screened by 2 reviewers (DT and KD). The selection strategy for the studies employed the Population, Interventions, Control, and Outcome (PICO) framework to determine eligibility for inclusion in our research. Discrepancies between reviewers were resolved through discussion or, if necessary, consultation with a third reviewer to reach consensus.

Inclusion criteria included adult patients aged between 18 and 70 years, and both male and female participants. Eligible studies included randomized controlled trials (RCT) and retrospective studies. Studies compared outcomes of EUS-BD vs. ERCP as a palliative intervention among patients with MDBO. Exclusion criteria included animal studies, studies not conducted within medical settings, and non-English manuscripts. These criteria were designed to ensure a focused and relevant analysis of interventions for MDBO, using high quality evidence from appropriate clinical settings.

Primary outcomes focused on technical success and clinical success. Secondary outcomes focused on mean procedural time, median procedural time, length of hospital stay, general adverse events, specifically pancreatitis, and 30-day mortality.

Data extraction and risk of bias

Two independent reviewers (SG and AS) extracted the data on year of publication, study design, inclusion criteria, primary endpoints and follow-up time, using a data extraction form. We adhered to the Cochrane Handbook for Systematic Reviews of Interventions guidelines, focusing on critical aspects such as random-sequence generation, allocation concealment, blinding, outcome assessment, and selective reporting [10]. For evaluating RCTs, we utilized the Cochrane risk of bias tool outlined in version 6.0 of the Cochrane handbook [11]. This tool identifies 5 bias types: performance, selection, detection, reporting and attrition biases. RCTs were categorized as having high risk, some concerns, or low risk of bias, based on these criteria. For quality appraisal of retrospective cohort studies, the Newcastle-Ottawa scale was used [12].

Statistical analysis

The data obtained from the included studies was analyzed using Microsoft Excel and R. We conducted a common and random-effects meta-analysis, utilizing the standardized mean difference to quantify the effect size. This approach allows for

comparing mixed-treatment interventions against a placebo group, by examining their direct and indirect impacts on the outcomes. The summary estimates were graphically illustrated using forest plots. Inconsistencies within our model were assessed using the I^2 statistic, aiming for a 95% confidence level.

Results

Study characteristics

Quality of included studies

Using the Cochrane risk of bias tool, most randomized controlled trials demonstrated low to moderate risk, with robust scores in sequence generation and blinding, as shown in Supplementary Fig. 1, and 2. Retrospective studies, assessed via the Newcastle-Ottawa scale and displayed in Supplementary Table 2, also scored highly, particularly in selection and outcome measures.

Primary outcomes

Technical success

The meta-analysis suggested a possible higher technical success rate for EUS-BD over ERCP (Fig. 2), with a common effects model (CEM) odds ratio (OR) of 1.77 (95% confidence interval [CI] 1.00-3.14) and a random effects model (REM) OR of 1.37 (95%CI 0.51-3.70). However, wide confidence intervals encompassing 1 imply substantial uncertainty. The influence of individual studies varied; notable was the study by Dhir

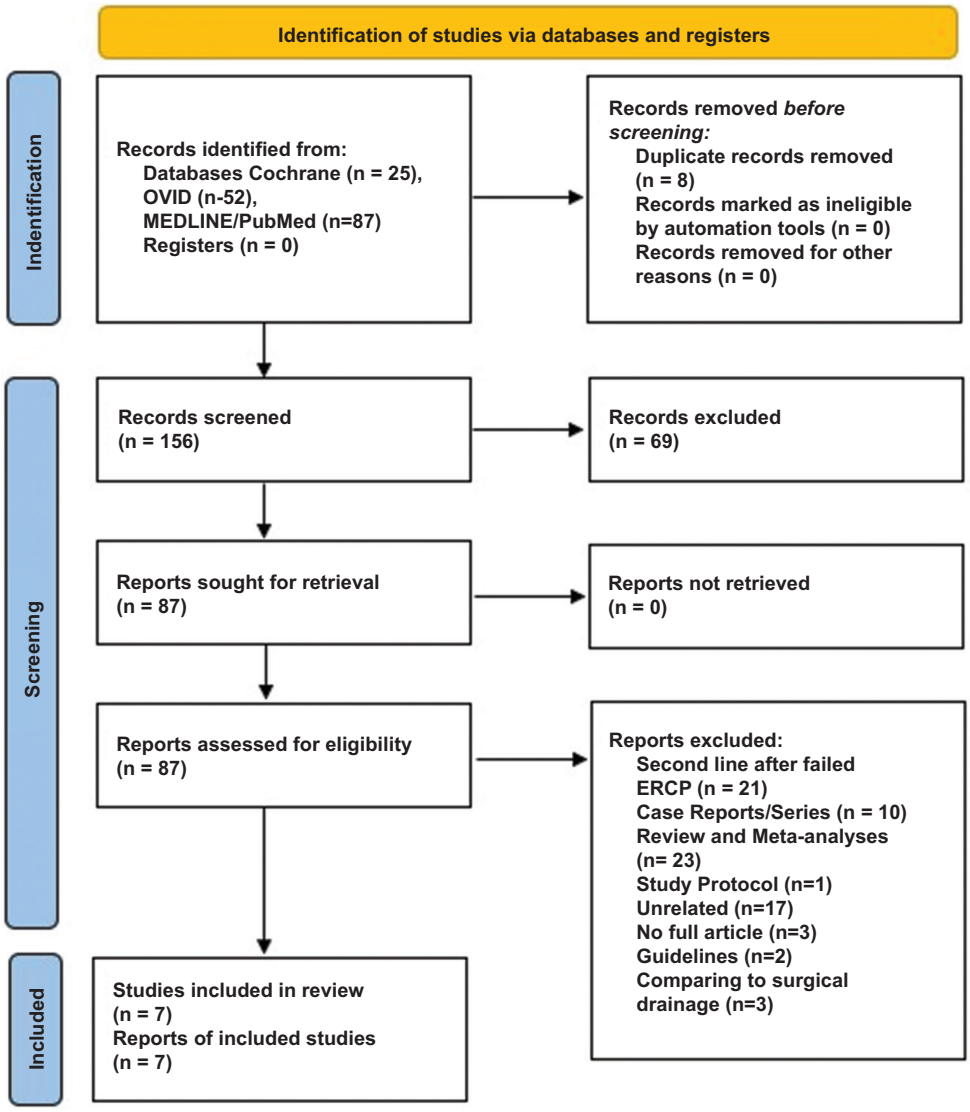

Figure 1 The preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 flow diagram of included studies
ERCP, endoscopic retrograde cholangiopancreatography

Table 1 Comprehensive overview of baseline demographics

‘	Study Name, Year [ref.]	Design	Groups	Age (Years)	M/F	Primary Pancreatic Cancer	Ampullary Cancer	Cholangiocarcinoma	Metastases to Pancreas	Distant Metastasis	Size of Mass (mm)	CBD Diameter (mm)	Total Bilirubin (mg/dL)
1	Teoh *et al.*, 2023 [13]	RCT	EUS-BD	75.1	32/47	76	N/A	3	30	33	36	15.9	N/A
			ERCP	72.1	41/35	73	N/A	3	24	35	36	16.8	N/A
2	Nakai *et al.*, 2019 [14]	Retrospective	EUS-BD	71	53/47	28	N/A	2	4	11	31	13	4.5
			ERCP	69	48/52	21	N/A	2	2	5	35	13	4.3
5	Paik *et al.*, 2018 [15]	RCT	EUS-BD	64.8	41/23	38	3	N/A	N/A	N/A	N/A	15.7	8.3
			ERCP	68.4	26/35	40	5	N/A	N/A	N/A	N/A	15.0	7.7
3	Bang *et al.*, 2018 [16]	RCT	EUS-BD	69.4	17/16	33	N/A	N/A	0	8	31.3	13.3	12.5
			ERCP	69.2	23/11	31	N/A	N/A	3	7	28.6	12.5	12.1
4	Park *et al.*, 2018 [17]	RCT	EUS-BD	66.8	9/5	14	N/A	N/A	0	N/A	N/A	N/A	7.5
			ERCP	65.4	8/6	12	N/A	N/A	2	N/A	N/A	N/A	9.9
6	Dhir *et al.*, 2015 [18]	Retrospective	EUS-BD	66.72	46/58	79	10	N/A	N/A	N/A	N/A	N/A	13.4
			ERCP	63.7	49/55	82	14	N/A	N/A	N/A	N/A	N/A	12.6
7	Kawakubo *et al.*, 2015 [19]	Retrospective	EUS-BD	71	8/18	25	N/A	N/A	6	N/A	26.8	13.7	7.5
			ERCP	68	30/26	43	N/A	N/A	18	N/A	30.8	12.1	5.1

CBD, common bile duct; , RCT, randomized controlled trial; EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography

et al [18], which heavily weighted (36.8% in the CEM and 24.6% in the REM) and impacted the overall result. Variability in the studies was moderate (I^2=49%, P=0.08), suggesting that differences were not merely due to chance, yet not significant enough to discredit the pooled estimate.

Clinical success

The analysis indicated no significant difference in clinical success rates, with a CEM OR of 0.79 (95%CI 0.43-1.43) and an REM OR of 0.80 (95%CI 0.43-1.47) (Fig. 3). The confidence intervals spanning 1 reflect substantial uncertainty. Notably, the study by Dhir *et al* [18], held the greatest weight (41.5% in CEM and 43.7% in REM), significantly influencing the meta-analysis. The studies exhibited negligible heterogeneity (I^2=0%, P=0.82), suggesting that any differences in outcomes were consistent with chance. For a detailed analysis of publication bias of primary outcomes, see Supplementary Fig. 3 and 4.

Secondary outcomes

Adverse events

This plot compared the rates of adverse events between EUS-BD and ERCP (Fig. 4). The CEM showed an OR of 0.80 (95%CI 0.53-1.20), while the REM had a very similar OR of 0.81 (95%CI 0.51-1.27). Both confidence intervals cross the null value, suggesting that there was no statistically significant difference in adverse event rates between the 2 procedures. The heterogeneity was low (I^2=21%, P=0.28), indicating that there was little variability among the study results, and they were fairly consistent.

Adverse events – pancreatitis

This analysis assessed the occurrence of pancreatitis following EUS-BD vs. ERCP (Fig. 5). The CEM indicated an OR of 0.09 (95%CI 0.02-0.34), demonstrating a significantly lower rate of pancreatitis with EUS-BD. The REM was consistent, with an OR of 0.10 (95%CI 0.03-0.39). These results are statistically significant and suggest a strong protective effect of EUS-BD against pancreatitis compared to ERCP. The heterogeneity among studies was nonexistent (I^2=0%, P=0.94), pointing to a consistent effect across different studies.

Procedural time

The forest plot analyzing mean times indicated no substantial difference between EUS-BD and ERCP, as reflected by a CEM OR of 1.53 (95%CI 0.97-2.42) and a REM OR of

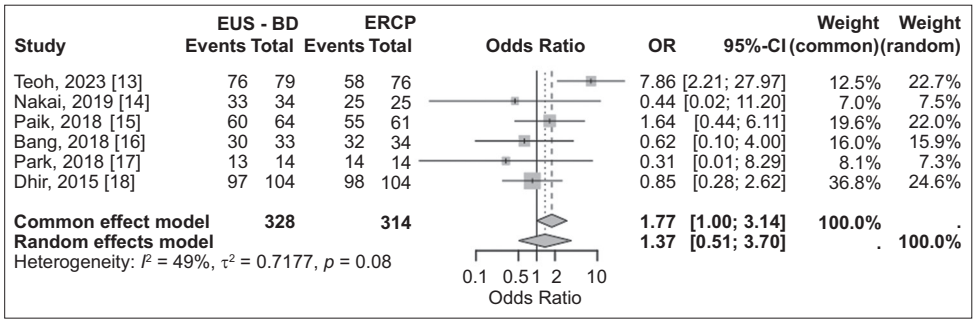

Figure 2 Forest plot comparing technical success
EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval

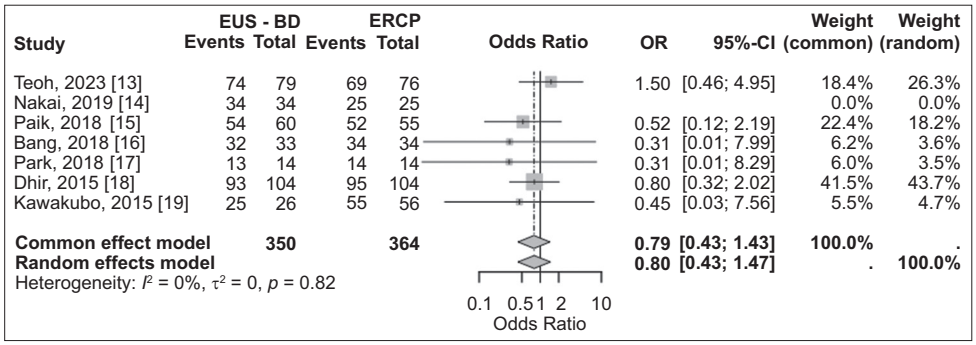

Figure 3 Forest plot comparing clinical success
EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval

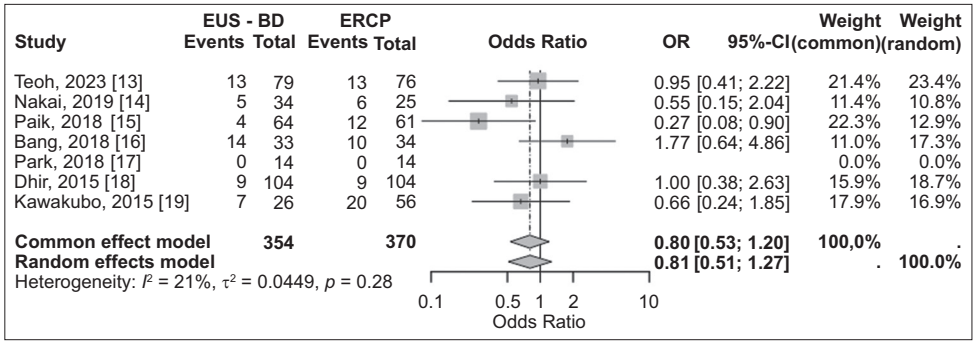

Figure 4 Forest plot comparing adverse events
EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval

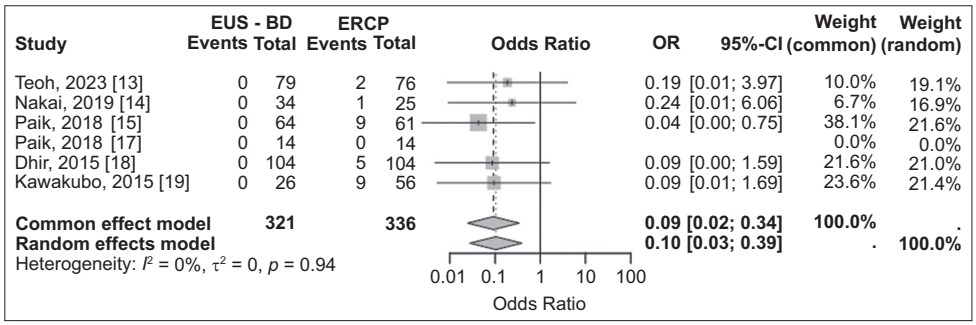

Figure 5 Forest plot comparing incidence of pancreatitis as an adverse event
EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval

1.52 (95%CI 0.96-2.40). Both confidence intervals are close to the null value and overlap it, implying significant uncertainty. The studies included showed minimal heterogeneity (I^2=0%, P=0.49), suggesting that the variation in outcomes was probably due to chance.

The forest plot focusing on median times suggests EUS-BD is associated with lower odds compared to ERCP, CEM OR of 0.54 (95%CI 0.32-0.92), indicating statistical significance. The REM showed an OR of 0.59 (95%CI 0.19-1.86), but with a wide CI that included 1, indicating uncertainty. There was significant heterogeneity among the studies (I^2=75%, P=0.02), which suggests that the variability in outcomes is more than would be expected by chance and may impact the reliability of the pooled estimate. For a detailed analysis of procedural times, see Supplementary Fig. 5,6.

Duration of hospital stay

The forest plot examining hospital stay durations compared EUS-BD and ERCP with a CEM OR of 0.84 (95%CI 0.31-2.25) and an identical REM OR at 0.84 (95%CI 0.31-2.25). The confidence intervals are wide and include 1, suggesting no clear difference between the procedures regarding the length of hospital stay. The heterogeneity across the included studies was negligible (I^2=0%, P=0.80), indicating a consistent effect size across studies. For a detailed analysis of the duration of hospital stay, see Supplementary Fig. 7.

30-day mortality

The plot presents data on 30-day mortality for EUS-BD vs. ERCP, showing a CEM OR of 0.62 (95%CI 0.17-2.30), with the same OR for the REM. The confidence interval is wide and crosses the null value, indicating no statistically significant difference between the 2 procedures in terms of mortality at 30 days. There was no reported heterogeneity (I^2=NA), implying consistent findings across the studies included. For a detailed analysis of 30-day mortality, see Supplementary Fig. 8.

Reintervention rates

This analysis compared reintervention rates between EUS-BD and ERCP. The CEM showed an OR of 0.58 (95%CI 0.36-0.92), indicating a statistically significant result that suggests lower reintervention rates for EUS-BD. The REM OR was 0.64 (95%CI 0.33-1.24), which includes 1 within the confidence interval, pointing to a lack of statistical significance and greater uncertainty. There was moderate heterogeneity (I^2=34%, P=0.18), suggesting that the differences in reintervention rates observed may not be entirely attributable to chance, but also not significant enough to suggest inconsistency across studies. For a detailed analysis of re-intervention rates, see Supplementary Fig. 9.

Discussion

This systematic review and meta-analysis provide a comprehensive comparison of the efficacy of EUS-BD vs. ERCP in the primary palliation of MDBO. Regarding primary procedural outcomes, the higher technical success rate observed for EUS-BD in our analysis aligns with previous studies, indicating its potential as a viable alternative to ERCP, especially in complex cases where ERCP is deemed technically challenging. These cases often involve altered surgical anatomy or malignant infiltration obstructing the duodenal papilla, conditions under which EUS-BD has shown superior adaptability [20]. A recent meta-analysis of 7887 patients, including 155 studies, showed that clinical outcomes are best (8.8% total adverse events) when biliary drainage is conducted using the natural orifice or major duodenal papilla via EUS-RV [21]. Nevertheless, the wide confidence intervals in our results reflect significant variability among studies, suggesting that while EUS-BD has promise, its performance is highly dependent on specific patient and clinical conditions.

Clinical success rates were comparable between EUS-BD and ERCP, indicating that both techniques are effective for symptom relief when they are technically successful. Secondary outcomes, including procedural time, duration of hospital stay, 30-day mortality and reinterventions, were not statistically significant, though some of them showed trends but with significant heterogeneity. In a patient-centered care approach, with the above similarity of outcomes between these 2 procedures, selection of a technique should be customized to the patient's specific clinical situation, adverse events and cost effectiveness, without sacrificing palliative outcomes.

In our study, a critical advantage of EUS-BD over ERCP was its association with a lower risk of pancreatitis, which is a major concern with ERCP, and contributes significantly to healthcare costs—over $200 million annually in the U.S. alone—as well as being a primary cause of litigation related to ERCP procedures. According to a meta-analysis of 89 RCTs, the risk profile for pancreatitis included precut sphincterotomy, pancreatic sphincterotomy, difficult cannulation, pancreatic duct injection, and sphincter of Oddi dysfunction [22] Notably, our results demonstrate a significantly lower incidence of pancreatitis with EUS-BD compared to ERCP, echoing previous findings that EUS-BD may offer a safer profile, with a reported cumulative total adverse event rate of 17% [6,23].

As a second line approach after failed ERCP, the economic benefit extends beyond the initial procedure costs, as despite EUS-BD having higher initial charges, it generally incurs lower overall expenses, with fewer reinterventions compared to percutaneous transhepatic biliary drainage, as demonstrated in cost-effectiveness analyses [24,25]. The significantly lower incidence of pancreatitis with EUS-BD not only highlights its clinical safety, but also promises substantial theoretical economic advantages, despite the lack of any direct head-to-head comparisons with ERCP.

The adoption of EUS-BD in healthcare systems is shaped by factors including the availability of specialized technology and expert endoscopists. This confines its use to well-resourced tertiary care centers [26]. However, it has been shown that the advanced training required for EUS is easier to master compared to ERCP, with 82% of fellows achieving technical competence in EUS procedures after a 1-year endoscopy fellowship, compared to 60% with ERCP procedures [27]. The cost of equipment and the need for specialized training create barriers to the widespread adoption of EUS methods, but also represent areas where targeted investments can facilitate broader use.

Despite these promising findings, our study is not without limitations. The heterogeneity in some of the analyzed outcomes suggests varying study designs, methodologies and patient populations, which could influence the generalizability of the results. Additionally, the moderate heterogeneity observed in the reintervention rates indicates that other factors, possibly related to the procedural expertise or healthcare setting, might impact these outcomes.

In conclusion, while our analysis supports the use of EUS-BD as an effective alternative to ERCP, especially in reducing the risk of pancreatitis and potentially lowering reintervention rates, both techniques remain valuable tools in the management of MDBO. Future research should focus on performing randomized control trials or head-to-head comparisons to evaluate long-term outcomes, patient-reported quality of life measures, and cost-effectiveness analyses to further delineate their roles in clinical practice. As the field advances, it will be crucial for ongoing updates to clinical guidelines to incorporate new evidence, ensuring optimal patient outcomes through informed, evidence-based decision-making.

Summary Box

What is already known:

- Malignant distal biliary obstruction (MDBO) is commonly managed using endoscopic retrograde cholangiopancreatography (ERCP)
- ERCP is associated with a significant risk of complications such as pancreatitis, cholangitis, and stent dysfunction
- Endoscopic ultrasound-guided biliary drainage (EUS-BD) has emerged as an alternative, particularly in cases where ERCP fails or is deemed risky

What the new findings are:

- EUS-BD demonstrated a higher technical success rate (92%) compared to ERCP (85%)
- Both EUS-BD and ERCP had similar clinical success rates, approximately 89%
- EUS-BD was associated with a significantly lower incidence of pancreatitis (2%) compared to ERCP (10%)
- EUS-BD offers a viable and potentially superior alternative to ERCP for the primary palliation of MDBO, especially in terms of technical success and safety profile

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Supplementary material

Supplementary Table 1 PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
		TITLE	
Title	1	Identify the report as a systematic review.	Page 1
		ABSTRACT	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 3
		INTRODUCTION	
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective (s) or question (s) the review addresses.	Page 5
		METHODS	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 5-6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pages 5-6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool (s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 6-7
Effect measures	12	Specify for each outcome the effect measure (s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pages 5-6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice (s). If meta-analysis was performed, describe the model (s), method (s) to identify the presence and extent of statistical heterogeneity, and software package (s) used.	Page 7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A

(*Contd...*)

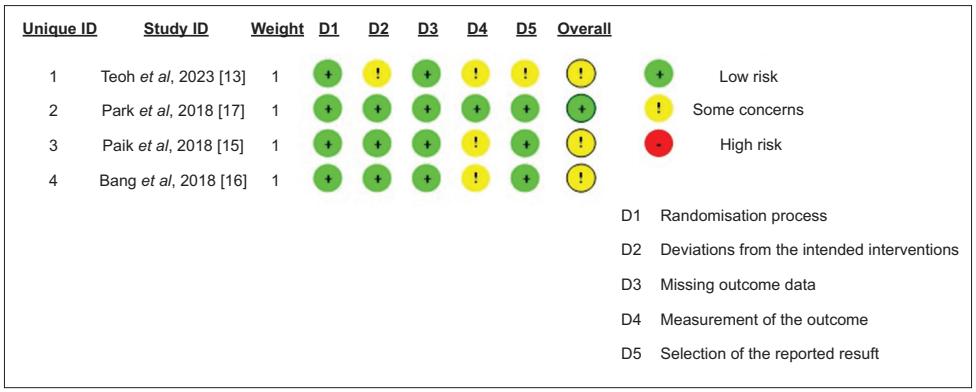
Supplementary Table 1 (*Continued*)

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Pages 6-7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
		RESULTS	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 23
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 23
Study characteristics	17	Cite each included study and present its characteristics.	Page 22
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Pages 28-29
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Pages 9-11
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Pages 28-29
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Pages 9-11
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Pages 9-11
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Pages 35-36
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
		DISCUSSION	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 12-14
	23b	Discuss any limitations of the evidence included in the review.	Page 14
	23c	Discuss any limitations of the review processes used.	Page 14
	23d	Discuss implications of the results for practice, policy, and future research.	Pages 14-15
		OTHER INFORMATION	
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 1
Competing interests	26	Declare any competing interests of review authors.	Page 1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

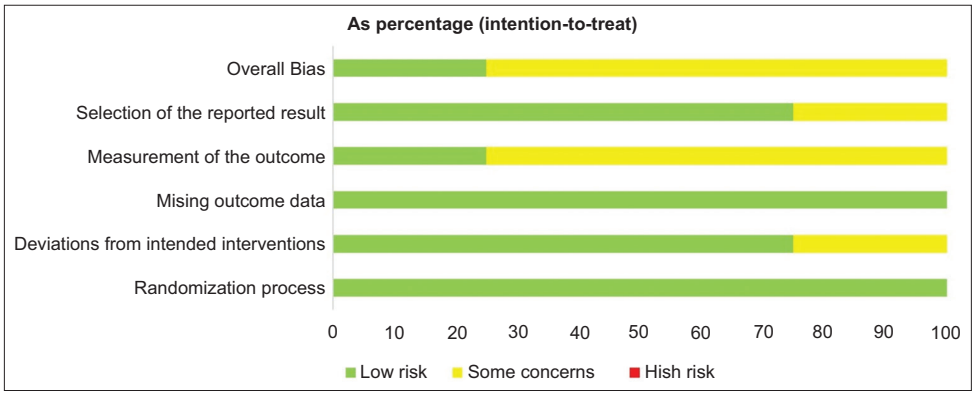
Supplementary Table 2 Newcastle-Ottawa scale to assess quality of retrospective cohort studies

Study, Year [ref.]	Number of stars awarded in each domain				AHRQ Quality Standard
	Selection	Comparability	Outcome	Overall	
Nakai *et al*., 2019 [14]	3	1	2	6/9	Good
Dhir *et al*., 2015 [18]	4	1	1	6/9	Good
Kawakubo *et al*., 2015 [19]	3	1	3	7/9	Good

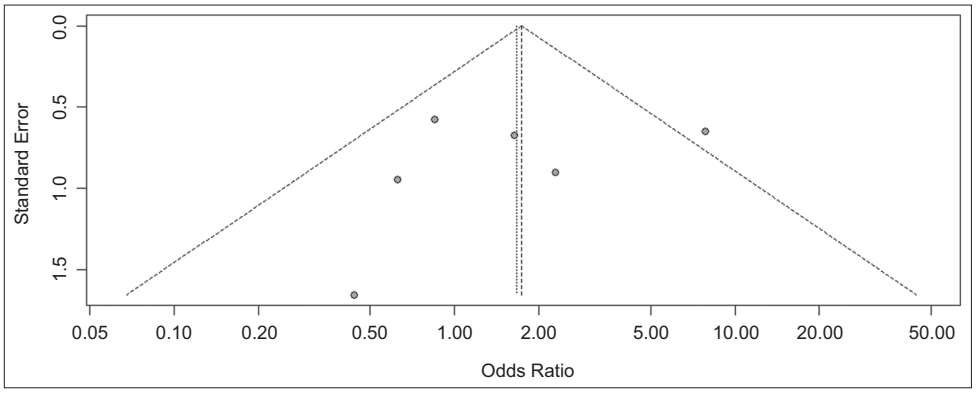
AHRQ, Agency for Healthcare Research and Quality



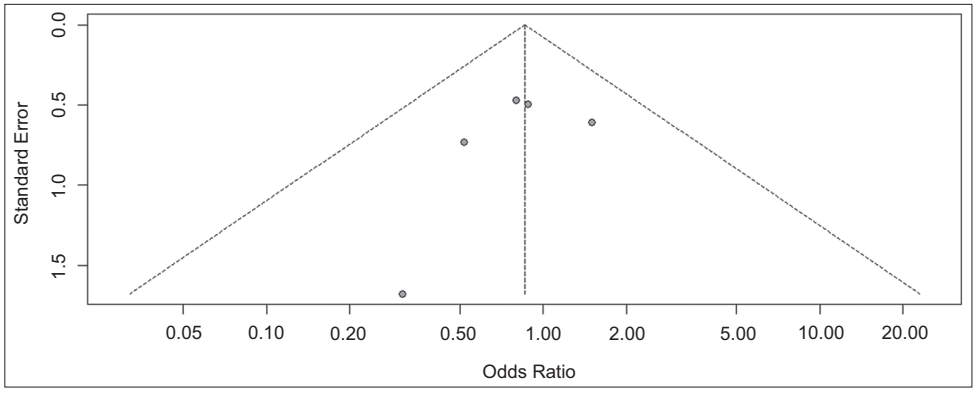
Supplementary Figure 1 Cochrane risk of bias (ROB-2) tool to assess quality of randomized controlled trials



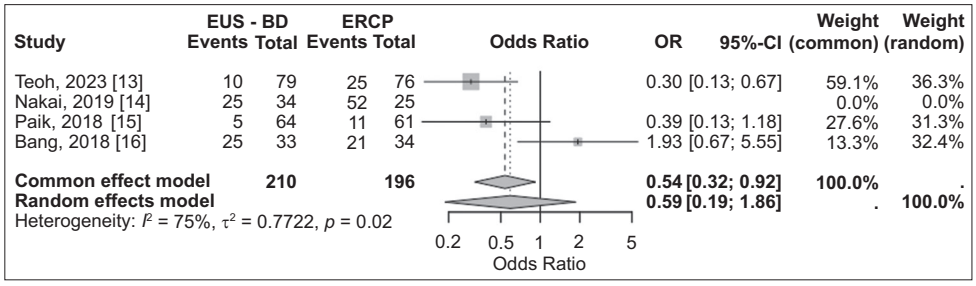
Supplementary Figure 2 Cochrane risk of bias (ROB-2) "intention to treat" quality assessment of included studies



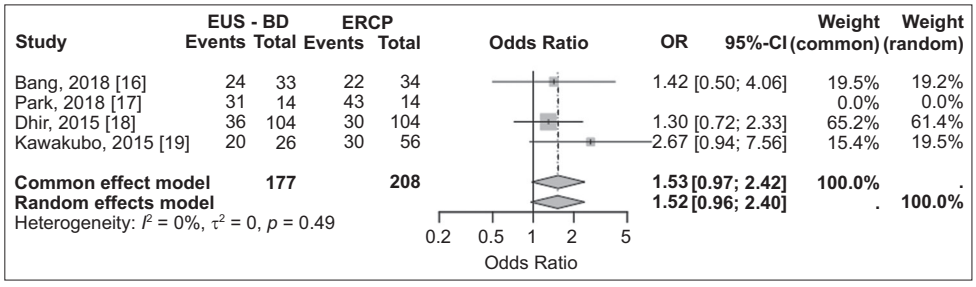
Supplementary Figure 3 Funnel plot comparing technical success rates



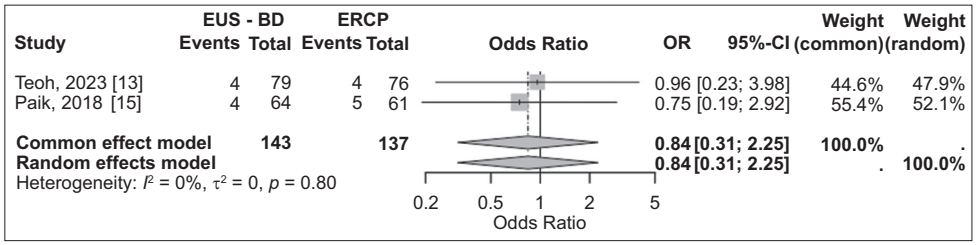
Supplementary Figure 4 Funnel plot comparing clinical success rates



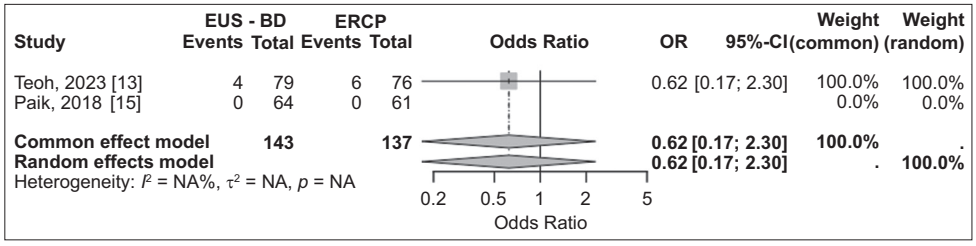
Supplementary Figure 5 Forest plot comparing median procedural time
EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval



Supplementary Figure 6 Forest plot comparing mean procedural time
EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval

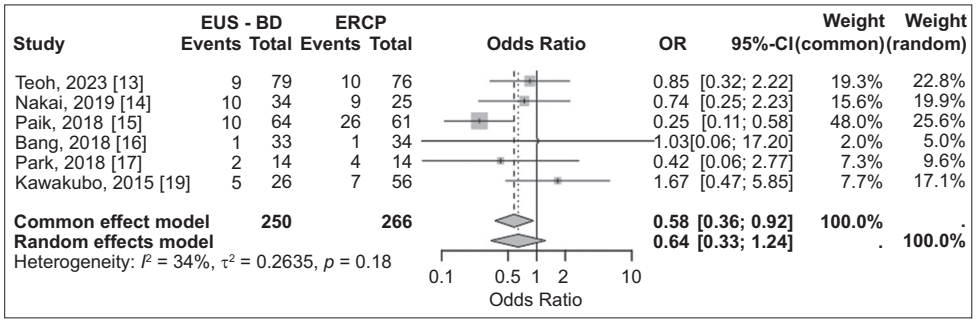


Supplementary Figure 7 Forest plot comparing duration of hospital stay
EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval



Supplementary Figure 8 Forest plot comparing 30-day mortality

EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval



Supplementary Figure 9 Forest plot comparing reintervention rates

EUS-BD, endoscopic ultrasound-guided biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; OR, odds ratio; CI, confidence interval