—Original Article—

Efficacy and safety of EUS-guided biliary drainage for benign biliary obstruction – A systematic review and meta-analysis

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ABSTRACT

Background and Objectives: ERCP is the first line of treatment for benign and malignant biliary obstruction and EUS-guided biliary drainage (EUS-BD) is usually used for patients who have failed ERCP. Recently, several studies have evaluated the role of EUS-BD in the management of benign biliary obstruction. This meta-analysis evaluates the efficacy and safety of EUS-BD in the management of benign biliary obstruction. **Methods:** We reviewed several databases from inception to July 8, 2022, to identify studies evaluating the efficacy and safety of EUS-BD in the management of benign biliary obstruction. Our outcomes of interest were technical success, clinical success, and adverse events. Pooled rates with 95% confidence intervals (CIs) for all outcomes were calculated using a random effects model. Subgroup analyses were performed including patients with normal anatomy *versus* surgically altered anatomy (SAA). Heterogeneity was assessed by I^2 statistic. **Results:** We included 14 studies with 329 patients. The pooled rate (95% CI) of technical success was 88% (83%, 92%). The pooled rate (95% CI) of technical success for patients with SAA and normal anatomy was 92% (85%, 96%) and 83% (75%, 89%), respectively. The pooled rates (95% CI) of clinical success and adverse events were 89% (83%, 93%) and 19% (13%, 26%), respectively. We found low heterogeneity in most of the analyses. **Conclusions:** EUS-BD is an effective and safe option in patients with benign biliary obstruction and should be considered after a failed attempt at ERCP or when ERCP is not technically possible.

Key words: Benign biliary obstruction, endoscopic ultrasound, meta-analysis

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INTRODUCTION

ERCP with transpapillary stent placement is the first line of treatment to achieve biliary drainage (BD) in patients with malignant or benign biliary obstruction. Sometimes, ERCP is not possible due to reasons such as surgically altered anatomy (SAA) or gastric outlet obstruction.[1] EUS-guided BD (EUS-BD) is an effective alternative in cases of failed ERCP and has potential advantages over percutaneous transhepatic BD such as providing internal BD, which is more physiologic, and avoidance of an external catheter.[2-5] One meta-analysis evaluating the efficacy and safety of EUS-BD found that the rates of clinical success and adverse events were 87% and 18%, respectively.[6]

EUS-BD has been found to be a safe and effective method of providing BD in patients with benign as well as malignant biliary obstruction and also in patients with normal or SAA.[7,8] Traditionally, EUS-BD has mostly been used in patients with malignant biliary obstruction after failed ERCP or if ERCP is not technically possible.[9,10] Recently, several studies have shown that EUS-BD is also safe and effective in patients with benign biliary obstruction.[11,12] Previous meta-analyses evaluating the efficacy and safety of EUS-BD have largely focused on patients with malignant biliary obstruction.[6,13,14] To date, no meta-analysis has evaluated the role of EUS-BD in benign biliary obstruction. As such, we performed a meta-analysis to evaluate the efficacy and safety of EUS-BD in the management of benign biliary obstruction.

METHODS

Data sources and search strategy

We followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to conduct this meta-analysis. An experienced medical librarian (W. L-S.) performed a comprehensive search of MEDLINE (PubMed platform, NCBI), EMBASE (Embase.com, Elsevier), Web of Science Core Collection (Clarivate), and the Cochrane Central Register of Controlled Trials (Cochrane Library, Wiley) from inception to July 8, 2022. There was no restriction on language in conducting the search. The search included truncation-expanded keywords and database-specific subject terms for benign biliary diseases and EUS-guided BD. Full search strategies from all databases are provided in Supplementary Table 1. Two authors (F. K. and S. S.) independently reviewed the titles and abstracts of the retrieved articles and excluded those that did not provide data on our outcomes of interest. Full texts of the remaining articles were reviewed. We also reviewed the references of these articles to identify any additional study with relevant information. The screening results are illustrated in the form of a PRISMA flowchart in Figure 1.

Inclusion and exclusion criteria

Two authors (F. K. and M. A. K.) independently reviewed original studies based on the preestablished inclusion criteria that are detailed below. We only included studies that evaluated the efficacy and safety of EUS-guided BD in the management of benign biliary obstruction. We included peer-reviewed publications that comprised patients with normal anatomy as well as SAA which underwent any form of EUS-guided BD method such as hepaticoenterostomy, choledochoenterostomy, and rendezvous procedure. We excluded case reports, case series with fewer than five patients, and abstracts. We also excluded studies that included patients with benign as well as malignant biliary obstruction but did not separately report data on outcomes of interest for these patients. If there were multiple publications from the same cohort, we included only the most recent publication and/or the publication with more information. All articles were downloaded into EndNote X9 (Clarivate, Philadelphia, Pennsylvania, USA), a bibliographic database manager. Duplicate citations were removed using successive EndNote algorithms based on bibliographic information and subsequent visual inspection.

Data extraction

Two authors (F. K. and M. A. K.) independently assessed the eligibility of included studies and collected data using data extraction forms that were specifically designed for this study. Any disagreement between individual authors was resolved by a repeat review of data and discussion with a third reviewer (D. G. A.). Extracted data included year of publication, number of patients with normal anatomy *versus* SAA, indications for BD, technical success, clinical success, adverse events, method of BD, and types of stents used. These data are summarized in Table 1. The methods of BD included hepaticogastrostomy (placement of stent between stomach and intrahepatic bile duct), hepaticojejunostomy (placement of stent between jejunum and intrahepatic bile duct),

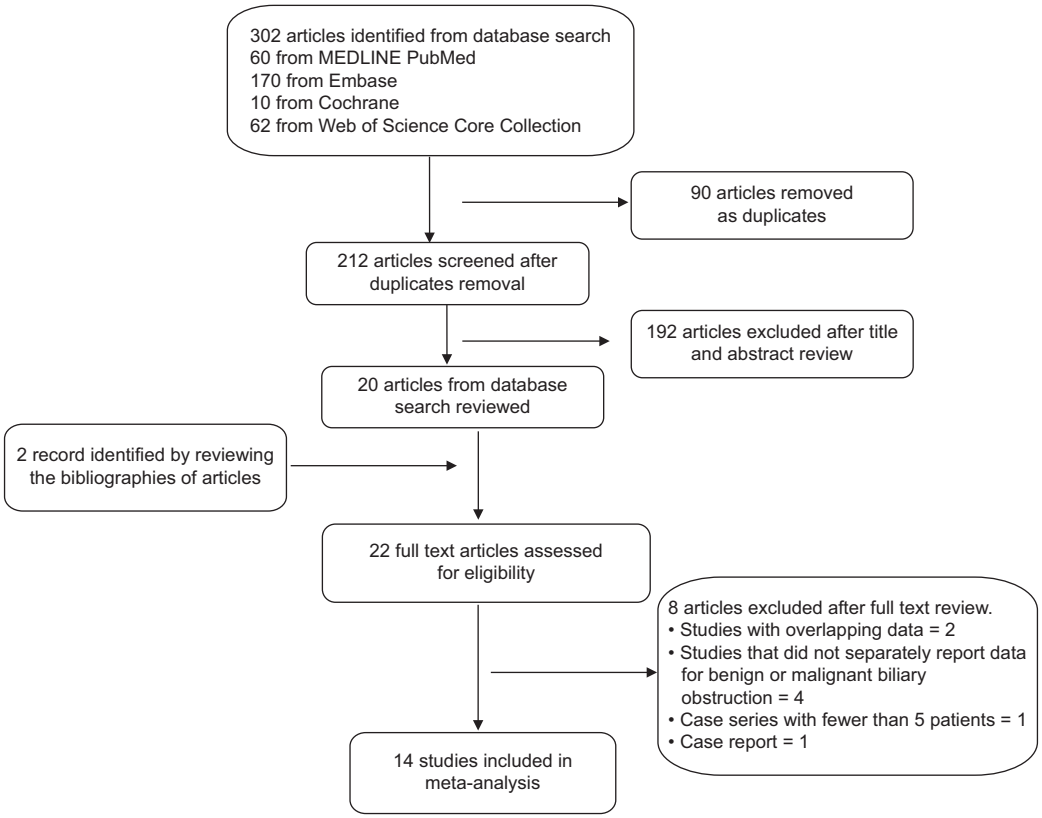

Figure 1. PRISMA flowchart. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

choledochojejunostomy (placement of stent between jejunum and common bile duct), and EUS rendezvous (bile duct is accessed through EUS and then wire is advanced into bile duct through major papilla into duodenum. Alongside wire, a duodenoscope is advanced to the major papilla. The biliary tree is then cannulated with a sphincterotome using the guidewire placed via EUS as a guide and then ERCP is completed) and choledochoduodenostomy (placement of stent between duodenum and bile duct) and EUS-guided methylene blue injection for identification of the major papilla.

Quality assessment

We assessed the quality of studies using the Methodological Index for Nonrandomized Studies (MINORS) criteria.[15] Noncomparative studies are scored on 8 items and comparative studies are scored on 12 items of MINORS criteria. Each item is scored from 0 to 2 (0 if not reported, 1 when reported but inadequate, and 2 when reported and adequate). Therefore, the ideal global score for noncomparative studies is 16. The quality of studies was classified as poor (score ≤5), fair (score 6–10), or high quality (≥11), as described previously.[16,17] Two authors (U. F. and Z. E.) independently performed the quality assessment, and any disagreement was discussed with a third reviewer (F. K.). The quality assessment of studies is summarized in Supplementary Table 2.

Data synthesis and statistical analysis

Our primary outcome of interest was the rate of technical success of EUS-guided BD among patients with benign biliary obstruction. The secondary outcomes were the rates of clinical success and adverse events. Subgroup analyses were performed including patients with normal anatomy *versus* SAA. As not all studies reported both technical and clinical success, which could lead to the impression that pooled clinical success was higher than pooled technical success, we performed a sensitivity analysis for technical success including studies that reported both technical and clinical success to address this concern. We calculated pooled rates with 95% confidence intervals (CIs) for outcomes of interest, and data were transformed using logit transformations. We assessed heterogeneity by I^2 statistics. $P < 0.1$ for Cochran's Q-test or an I^2 value > 50% indicated significant heterogeneity. We assessed publication bias by using funnel plots and Egger's test for the outcomes including 10 or

Table 1. Characteristics of studies

Study, year	Number of patients	SAA *versus* normal anatomy (*n*)	Definition of technical success	Definition of clinical success	Adverse events (*n*)	Types of stents used (*n*)	Indications for biliary drainage (*n*)
Hathorn *et al.*, 2022	85	SAA: 61 Normal: 24	Successful placement of a metal stent for biliary drainage	Appropriate decline in total serum bilirubin postprocedurally	Perforation: 1, abdominal pain: 4, bacteremia: 3, biloma: 2, fever: 1, hematemesis: 1, respiratory distress: 1, cholangitis: 6	Fully covered metal stents: 85	CBD stone: 28, benign postsurgical stricture: 32, cystic head of pancreas lesion causing obstruction: 1, pancreatitis: 9, occluded biliary stent: 1, primary sclerosing cholangitis: 4, inflammatory stricture: 6, indeterminant: 3
Matsunami *et al.*, 2021	57	SAA: 51 Normal: 6	Successful placement of plastic stent in the intrahepatic bile duct	No symptoms or no recurrence of cholangitis and additional drainage for 2 months after the procedure	Peritonitis: 4, bleeding: 2, cholecystitis: 2, pneumoperitoneum: 1	Plastic stents: 57	Bilioenteric anastomotic stricture: 28, intrahepatic bile duct stones: 8, CBD stones: 15, EtOH chronic pancreatitis: 2, WON: 1, idiopathic retroperitoneal fibrosis: 1, left lobe hepatic injury: 1, bile duct polyp: 1
Iwai *et al.*, 2021	7	SAA: 7	NA	NA	0	Metal stents: 2, plastic stents: 3	Cholangitis due to choledochojejunostomy stricture: 7
Bill *et al.*, 2021	36	Normal anatomy: 36	Achievement of deep biliary cannulation and performance of planned maneuver (removal of stones or stent placement)	NA	Pancreatitis: 6, bleeding: 1, perforation: 2, bile leak: 1	Fully covered metal stent*	Stones: 19, bile leak: 5, stricture: 12
Ueshima *et al.*, 2018	14	SAA: 14	Insertion of the dilation device into the intestine across a stricture site without the need for other dilation devices	After removal of stent, contrast medium flowing into the intestine across the anastomosis site without hepaticojejunostomy anastomotic stricture	Abdominal pain: 1	Covered metal stents: 14	Obstructive jaundice: 6, cholangitis: 8
Pizzicannella *et al.*, 2019	12	SAA: 12	EUS-guided fully covered metal stent placement from the left intrahepatic duct into the stomach or the jejunum	NA	Recurrent cholangitis: 3, bleeding: 1	Fully covered metal stents: 12	Acute cholangitis: 12
Ogura *et al.*, 2019	26	SAA: 21 Normal anatomy: 5	Stent deployment under EUS guidance	Decrease in serum bilirubin concentration to<75% of preprocedural values within 30 days after stent deployment or resolved cholangitis	Abdominal pain: 2	Plastic stents: 3, metal stents: 23	Anastomotic biliary stricture: 17, bile duct stones: 5, inflammatory biliary stricture: 3, acute pancreatitis prevention: 1

Contd...

Table 1. Contd...

Study, year	Number of patients	SAA *versus* normal anatomy (n)	Definition of technical success	Definition of clinical success	Adverse events (*n*)	Types of stents used (*n*)	Indications for biliary drainage (*n*)
Martinez *et al.*, 2019	27	Normal anatomy: 27	Selective biliary cannulation	NA	Abdominal pain: 1, bile leak: 1, pancreatitis: 1, pneumomediastinum: 1	NA	Bile duct stones: 20, benign stenosis: 5, biliary leak: 2
James *et al.*, 2018	20	SAA: 20	Completion of EUS-guided biliary stent placement from left intrahepatic duct into the gastrointestinal tract	NA	Pancreatitis: 1, abdominal pain: 1, cholangitis: 1	Fully covered metal stents: 20	CBD stone: 8, benign postsurgical stricture: 7, chronic pancreatitis: 3, inflammatory stricture: 1, bile leak: 1
Tang *et al.*, 2016	10	Normal anatomy: 10	NA	NA	Not separately reported for benign and malignant diseases	NA	Benign obstruction: 10, bile leak: 1, biliary dilation: 1
Miranda-Garcia *et al.*, 2016	7	Altered anatomy: 7	NA	NA	Bleeding: 3, stent migration: 3	Fully covered metal stents: 7	Recurrent cholangitis: 3, jaundice: 4
Consiglieri *et al.*, 2015	11	Normal anatomy: 11	Access to the CBD, identification of the papilla orifice, transpapillary deep cannulation, and optimal drainage of the contrast or fluids	Resolution of the symptoms and normalization of biochemical parameters	Abscess: 1	NA	Choledocholithiasis: 10, pancreatic stricture: 1
Iwashita *et al.*, 2016	8	Normal anatomy: 8	NA	NA	Pancreatitis: 1	NA	Biliary stones: 7, chronic pancreatitis: 1
Kawakubo *et al.*, 2013	9	Normal anatomy: 9	Successful biliary cannulation using an EUS-rendezvous technique	NA	Pancreatitis: 1	NA	Choledocholithiasis: 9

*Stent selection was at the discretion of the attending endoscopist. Fully covered metal stent was most commonly used. NA: Not available or not applicable; SAA: Surgically altered anatomy; WON: Walled off necrosis; CBD: Common bile duct; *n*: Number of patients

more studies. If publication bias was detected, the effect size was recalculated using Duval and Tweedie's "trim-and-fill" test based on the linear model. The statistical analysis was performed using comprehensive meta-analysis software.

RESULTS

The search strategy produced 302 articles, 90 of which were removed after being identified as duplicates [Figure 1]. From the remaining 212 articles, 192 were removed after title and abstract review. Two additional relevant articles were identified from review of bibliographies. Full texts of these 22 articles were reviewed. One case report and one case series with fewer than five patients were ultimately excluded. Four studies were excluded because these did not separate data between patients with benign or malignant biliary obstruction. Two studies with overlapping data were excluded.

Overall, 14 studies with 329 patients were included in the final analysis.[11,12,18-29] One hundred and ninety-three patients had SAA and 136 patients had normal anatomy. Among the studies that reported numerical data with regard to the selected method for BD, 56% underwent hepaticogastrostomy, 6% hepaticojejunostomy, 2% choledochojejunostomy, 29% EUS rendezvous, 1% choledochoduodenostomy, 1% hepaticoduodenostomy, and 4% underwent EUS-guided methylene blue injection for identification of the major papilla.

Technical success

The pooled rate (95% CI) of technical success was 88% (83%, 92%), I^2 = 10% [Figure 2]. Egger's test showed no publication bias (P = 0.07). On subgroup analysis including patients with SAA, the rate (95% CI) of technical success was 92% (85%, 96%), I^2 = 0% [Supplementary Figure 1a]. When we performed a subgroup analysis of patients with normal anatomy, the rate (95% CI) of technical success was 83% (75%, 89%), I^2 = 0% [Supplementary Figure 1b]. On sensitivity analysis including studies that reported both technical and clinical success, the pooled rate (95% CI) of technical success was 92% (88%, 95%) [Supplementary Figure 2].

Clinical success

The pooled rate (95% CI) of clinical success was 89% (83%, 93%), I^2 = 0% [Figure 3]. On subgroup analysis including patients with SAA, the rate (95% CI) of clinical success was 89% (75%, 96%), I^2 = 25% [Supplementary Figure 3a]. When we performed a subgroup analysis including patients with normal anatomy, the rate (95% CI) of clinical success was 91% (66%, 98%), I^2 = 0% [Supplementary Figure 3b].

Adverse events

The pooled rate (95% CI) of adverse events was 19% (13%, 26%), I^2 = 36% [Figure 4]. Egger's test did not detect publication bias (P = 0.45). On subgroup analysis including patients with SAA, the rate (95% CI) of adverse events was 22% (9%, 43%), I^2 = 63% [Supplementary Figure 4a]. When we performed a subgroup analysis including patients with normal anatomy, the rate (95% CI) of adverse events was 21% (14%, 31%), I^2 = 0% [Supplementary Figure 4b].

DISCUSSION

Our meta-analysis demonstrates that EUS-BD is a safe and effective option in patients with benign biliary obstruction. ERCP is the gold standard treatment for biliary obstruction, and the use of EUS-BD is typically reserved for patients who have failed ERCP or where ERCP is technically not possible. Several meta-analyses have demonstrated the efficacy and safety of EUS-BD in the management of malignant biliary obstruction.[6,13,14] Our meta-analysis supports the use of EUS-BD to achieve BD in patients with benign biliary obstruction as well. In our study, we found that the rate of technical success was 87% (81%, 92%), which is comparable to the reported technical success of EUS-BD for malignant biliary obstruction.[5,6]

ERCP in patients with SAA can be challenging. We found that the rate of technical success of EUS-BD in cases of SAA was 92% (85%, 96%), far better than that seen when attempting ERCP in patients with SAA with a single-balloon enteroscope (SBE). One can argue for using EUS-BD as a first-line treatment to achieve BD in SAA cases given its high success rate and substantially shorter procedure time compared to SBE-assisted ERCP. However, the rate of adverse events with SBE-assisted ERCP is lower compared to EUS-BD. In a meta-analysis including 15 studies, Inamdar *et al.* showed that the rate of adverse events with SBE-assisted ERCP was 6.5%.[30] We found that the rate of adverse events of EUS-BD for SAA was 22% (9%, 43%).

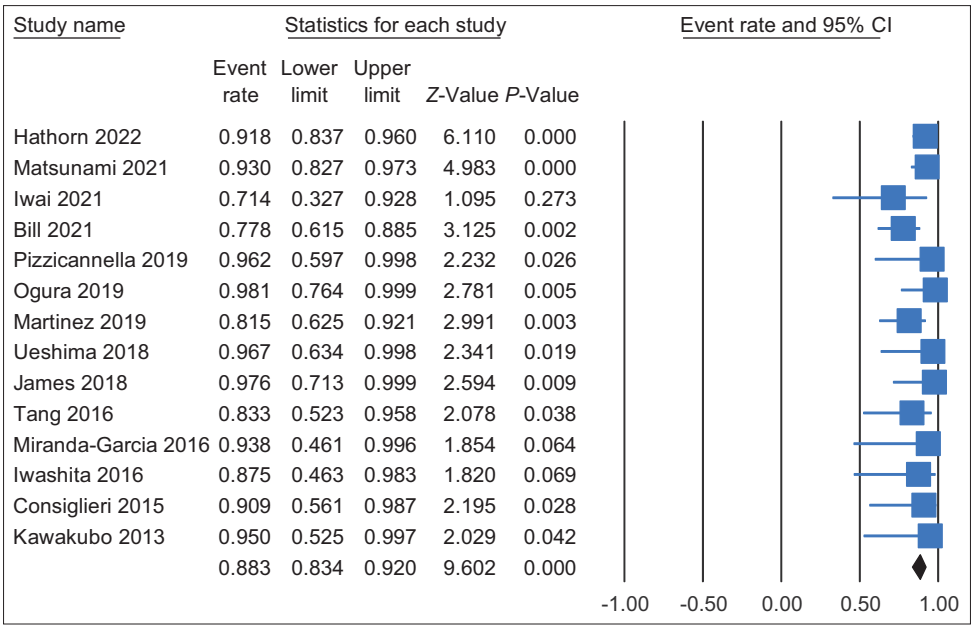

Figure 2. Rate of technical success of EUS-guided biliary drainage for benign biliary obstruction. CI: Confidence interval

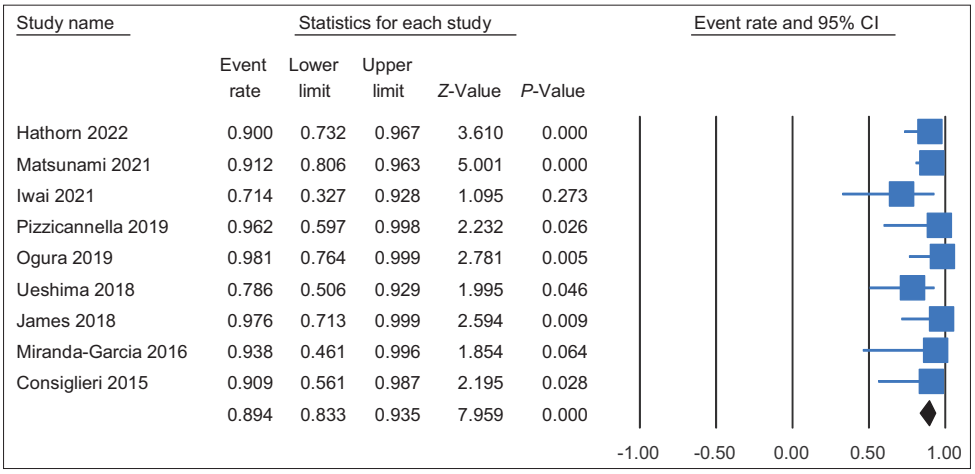

Figure 3. Rate of clinical success of EUS-guided biliary drainage for benign biliary obstruction. CI: Confidence interval

In patients with normal anatomy and benign biliary obstruction, ERCP sometimes cannot be performed due to reasons such as inability to identify papilla, failed cannulation, and benign gastric outlet obstruction by conditions such as pancreatic walled-off necrosis or peptic ulcer disease. EUS offers a variety of options in these cases to achieve BD including EUS-guided rendezvous, hepaticogastrostomy, choledochoduodenostomy, and EUS-guided methylene blue injection for identification of papilla. We found that the rate of technical success of EUS BD in patients with normal anatomy was high at 83% (75%, 89%). However, the rate of adverse events was also high at 21% (14%, 31%), suggesting the need for ongoing selection, in most patients, after attempts at ERCP as first-line treatment for benign biliary obstruction.

Methods of BD varied across the studies included in our meta-analysis. Hepaticogastrostomy was the most commonly used method and EUS rendezvous was the second most commonly used method of BD. Hepaticogastrostomy and hepaticojejunostomy are useful in patients with SAA.[31] These can be technically challenging in patients with benign biliary obstruction because biliary system is nondilated. Furthermore, these methods offer one advantage over EUS rendezvous by avoiding the risk of pancreatitis. The potential complications of hepaticogastrostomy and hepaticojejunostomy include bile peritonitis,

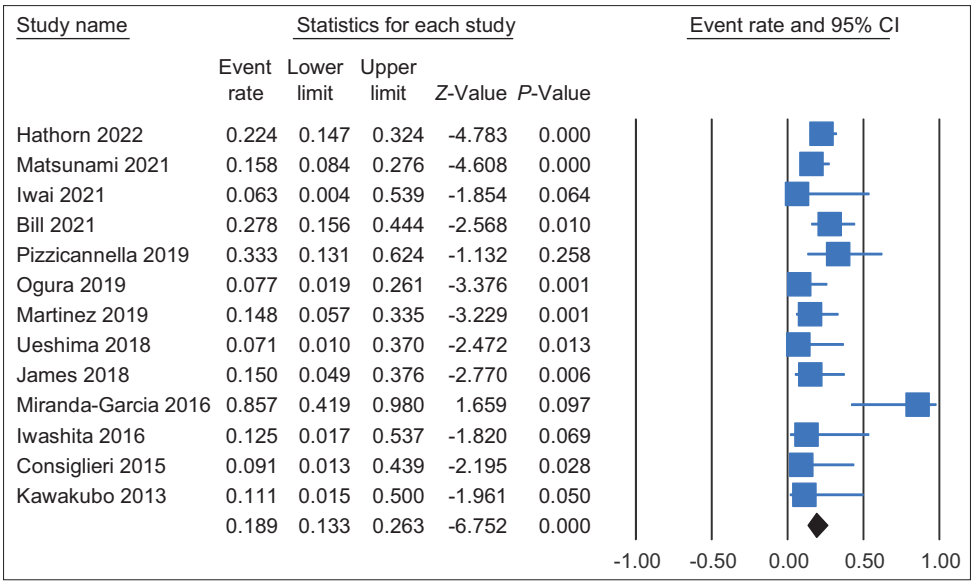

Figure 4. Rate of adverse events of EUS-guided biliary drainage for benign biliary obstruction. CI: Confidence interval

pneumoperitoneum, bleeding, and stent dislodgement.[31] EUS rendezvous represents a method of natural BD in patients with normal anatomy with benign biliary obstruction. Like any ERCP procedure, there is a risk of pancreatitis associated with ERCP after EUS rendezvous.

This is the first systematic review and meta-analysis to evaluate the efficacy and safety of EUS-BD for benign biliary obstruction. Our comprehensive literature search identified a large number of relevant studies to evaluate the usefulness of EUS-BD in patients with SAA as well as normal anatomy. We found low heterogeneity in most of the analyses. More than half of the studies included in our meta-analysis were rated as of fair quality based on MINORS criteria [Supplementary Table 2]. Our meta-analysis has several limitations. All of the included studies were observational which have intrinsic shortcomings with risks of measured and unmeasured confounding. We found evidence of clinical heterogeneity across studies. Types of stents (metal *versus* plastic) used varied across the studies [Table 1]. The methods to achieve EUS-BD such as hepaticoenterostomy, choledochoenterostomy, and EUS rendezvous also varied across the studies. As numerical data were not consistently reported for each of these techniques, we could not perform subgroup analyses based on the methods of BD.

CONCLUSION

Our meta-analysis demonstrated that EUS-BD is an effective and safe approach in patients with benign biliary obstruction and should be considered after a failed attempt at ERCP or when ERCP is not technically possible.

Supplemental material

Supplementary information is linked to the online version of the paper on the *Endoscopic Ultrasound* website.

Financial support and sponsorship

Nil.

Conflicts of interest

Douglas G. Adler is a Co-Editor in Chief of the journal. This article was subject to the journal's standard procedures, with peer review handled independently of the editor and his research group.

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SUPPLEMENTARY TABLE 1. FULL SEARCH STRATEGIES (ALL SEARCHED PERFORMED AUGUST 12, 2021)

Embase (Embase.com, Elsevier)

Query	Results
'biliary tract drainage'/exp OR hepatoenterostom* OR hepatojejunostom* OR hepatogastrostom* OR hepaticoenterostom* OR hepaticojejunostom* OR hepaticogastrostom* OR 'hepato enterostom*' OR 'hepato jejunostom*' OR 'hepato gastrostom*' OR 'hepatico enterostom*' OR 'hepatico jejunostom*' OR 'hepatico gastrostom*' OR 'bilioenteric anastomos*' OR 'biliary drainage*' OR 'biliary tract drainage*' OR 'bili digestive anastomos*' OR 'biliary bypass*' OR 'biliary enteric anastomos*' OR 'biliary intestinal anastomos*' OR 'bilidigestive anastomosis*' OR 'bilidigestive shunt*' OR 'biliodigestive anastomosis*' OR 'biliointestinal anastomosis*' OR choledochostom* OR 'bile duct bypass*' OR choledochojejunostom* OR 'choledoco jejunostom*' OR choledocojejunostom* OR choledojejunostom* OR 'choledoco duodenostom*' OR choledochoduodenostom* OR choledocoduodenostom* OR hepatogastr* OR hepaticogastr* OR hepatojejun* OR hepaticojejun*	37,473
'interventional ultrasonography'/exp OR 'endoscopic ultrasonography'/exp OR echoendoscop* OR 'endoscopic echograph*' OR 'endoscopic ultrasonograph*' OR 'endoscopic ultrasound*' OR endosonograph* OR 'eus' OR 'interventional ultrasonograph*' OR 'interventional ultrasound*' OR 'intravascular ultrasonograph*' OR 'echo endoscop*' OR 'ultrasonic endoscop*'	58,616
#1 AND #2	3202
benign AND ('obstructive bile duct disease'/exp OR 'cholelithiasis'/exp OR cholestas* OR 'biliary stasis' OR obstruct* OR stricture* OR stenos* OR stone* OR cholelithas*)	30,181
#3 AND #4	240
#5 AND ('Editorial'/it OR 'Letter'/it OR 'Note'/it OR 'Review'/it)	36
#5 NOT ('editorial'/it OR 'letter'/it OR 'note'/it OR 'review'/it)	204
#7 AND ('case report'/de OR 'meta analysis'/de OR 'meta analysis topic'/de OR 'practice guideline'/de OR 'systematic review'/de OR 'systematic review topic'/de)	59
#7 NOT ('case report'/de OR 'meta analysis'/de OR 'meta analysis topic'/de OR 'practice guideline'/de OR 'systematic review'/de OR 'systematic review topic'/de)	145
#9 NOT ([animals]/lim NOT [humans]/lim)	144

MEDLINE (PubMed, National Center for Biotechnology Information, National Library of Medicine)

Search number	Query	Results
1	"Choledochostomy"[Mesh] OR ("Drainage"[Mesh] AND "Biliary Tract"[Mesh]) OR Hepatoenterostom* OR hepatojejunostom* OR hepatogastrostom* OR Hepaticoenterostom* OR hepaticojejunostom* OR hepaticogastrostom* OR Hepato-enterostom* OR hepato-jejunostom* OR hepato-gastrostom* OR Hepatico-enterostom* OR hepatico-jejunostom* OR hepatico-gastrostom* OR bilioenteric-anastomos* OR biliary-drainage* OR biliary-tract-drainage* OR bili-digestive-anastomos* OR biliary-bypass* OR biliary-enteric-anastomos* OR biliary-intestinal-anastomos* OR bilidigestive-anastomosis* OR bilidigestive-shunt* OR biliodigestive-anastomosis* OR biliointestinal-anastomosis* OR choledochostom* OR bile-duct-bypass* OR Choledochojejunostom* OR Choledoco-jejunostom* OR Choledocojejunostom* OR Choledojejunostom* OR Choledoco-duodenostom* OR Choledochoduodenostom* OR choledocoduodenostom* OR hepatogastr* OR hepaticogastr* OR hepatojejun* OR hepaticojejun*	26,095
2	"Ultrasonography, Interventional"[Mesh] OR "Endosonography"[Mesh] OR echoendoscop* OR endoscopic-echograph* OR endoscopic-ultrasonograph* OR endoscopic-ultrasound* OR endosonograph* OR "eus" OR interventional-ultrasonograph* OR interventional-ultrasound* OR intravascular-ultrasonograph* OR echo-endoscop* OR ultrasonic-endoscop*	51,852
3	benign AND ("Cholestasis"[Mesh] OR "Cholelithiasis"[Mesh] OR Cholestas* OR biliary-stasis OR obstruct* OR stricture* OR stenos* OR stone* OR cholelithas*)	17,069
4	#1 AND #2	1336
5	#3 AND #4	77
6	#5 NOT ("animals"[mesh] NOT "humans"[mesh])	77
7	#6 NOT ("case reports"[Publication Type] OR "comment"[Publication Type] OR "editorial"[Publication Type] OR "guideline"[Publication Type] OR "introductory journal article"[Publication Type] OR "meta analysis"[Publication Type] OR "news"[Publication Type] OR "retracted publication"[Publication Type] OR "review"[Publication Type] OR "systematic review"[Publication Type])	53

Cochrane Central Register of Controlled Trials (CochraneLibrary.com platform, Wiley, Issue 18 of 12, August 2021)

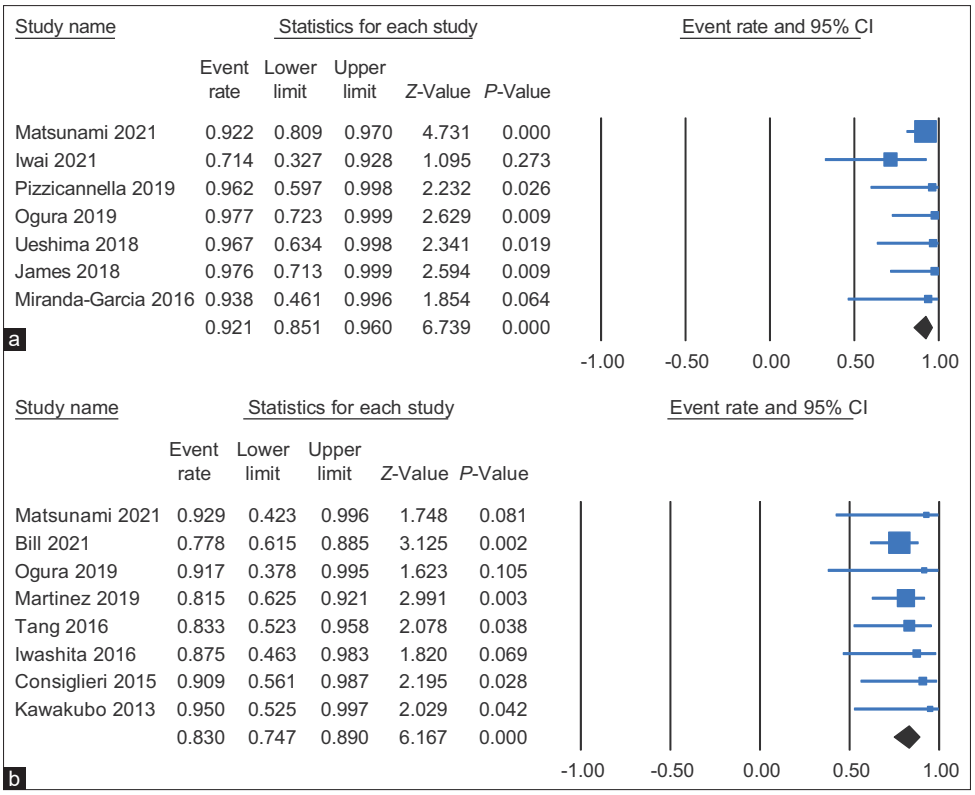
ID	Search	Hits
#1	[mh "Choledochostomy"] OR ([mh "Drainage"] AND [mh "Biliary Tract"]) OR Hepatoenterostom* OR hepatojejunostom* OR hepatogastrostom* OR Hepaticoenterostom* OR hepaticojejunostom* OR hepaticogastrostom* OR Hepato-enterostom* OR hepato-jejunostom* OR hepato-gastrostom* OR Hepatico-enterostom* OR hepatico-jejunostom* OR hepatico-gastrostom* OR bilioenteric-anastomos* OR biliary-drainage* OR biliary-tract-drainage* OR bili-digestive-anastomos* OR biliary-bypass* OR biliary-enteric-anastomos* OR biliary-intestinal-anastomos* OR bilidigestive-anastomosis* OR bilidigestive-shunt* OR biliodigestive-anastomosis* OR biliointestinal-anastomosis* OR choledochostom* OR bile-duct-bypass* OR Choledochojejunostom* OR Choledoco-jejunostom* OR Choledocojejunostom* OR Choledojejunostom* OR Choledoco-duodenostom* OR Choledochoduodenostom* OR choledocoduodenostom* OR hepatogastr* OR hepaticogastr* OR hepatojejun* OR hepaticojejun*	1645
#2	[mh "Ultrasonography, Interventional"] OR [mh "Endosonography"] OR echoendoscop* OR endoscopic-echograph* OR endoscopic-ultrasonograph* OR endoscopic-ultrasound* OR endosonograph* OR "eus" OR interventional-ultrasonograph* OR interventional-ultrasound* OR intravascular-ultrasonograph* OR echo-endoscop* OR ultrasonic-endoscop*	4334
#3	#1 AND #2	120
#4	benign AND ([mh "Cholestasis"] OR [mh "Cholelithiasis"] OR Cholestas* OR biliary-stasis OR obstruct* OR stricture* OR stenos* OR stone* OR cholelithas*)	1607
#5	#3 AND #4	12
#6	Trials matching "#5 - #3 AND #4"	9

Web of Science Core Collection (Web of Science Platform, Clarivate, Editions = Arts & Humanities Citation Index, Emerging Sources Citation Index [previous 5 years], Conference Proceedings Citation Index, Science Citation Index-EXPANDED, and Social Science Citation Index)

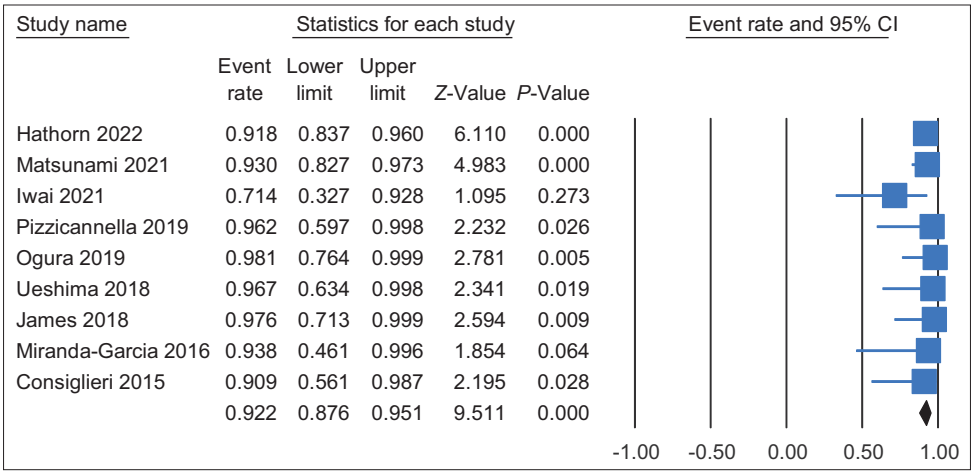
Search	Results
benign AND (Cholestas* OR biliary-stasis OR obstruct* OR stricture* OR stenos* OR stone* OR cholelithas*) (Topic) AND echoendoscop* OR endoscopic-echograph* OR endoscopic-ultrasonograph* OR endoscopic-ultrasound* OR endosonograph* OR "eus" OR interventional-ultrasonograph* OR interventional-ultrasound* OR intravascular-ultrasonograph* OR echo-endoscop* OR ultrasonic-endoscop* (Topic) AND Hepatoenterostom* OR hepatojejunostom* OR hepatogastrostom* OR Hepaticoenterostom* OR hepaticojejunostom* OR hepaticogastrostom* OR Hepato-enterostom* OR hepato-jejunostom* OR hepato-gastrostom* OR Hepatico-enterostom* OR hepatico-jejunostom* OR hepatico-gastrostom* OR bilioenteric-anastomos* OR biliary-drainage* OR biliary-tract-drainage* OR bili-digestive-anastomos* OR biliary-bypass* OR biliary-enteric-anastomos* OR biliary-intestinal-anastomos* OR bilidigestive-anastomosis* OR bilidigestive-shunt* OR biliodigestive-anastomosis* OR biliointestinal-anastomosis* OR choledochostom* OR bile-duct-bypass* OR Choledochojejunostom* OR Choledoco-jejunostom* OR Choledocojejunostom* OR Choledojejunostom* OR Choledoco-duodenostom* OR Choledochoduodenostom* OR choledocoduodenostom* OR hepatogastr* OR hepaticogastr* OR hepatojejun* OR hepaticojejun* (Topic) AND Letters or Editorial Materials or Review Articles (Exclude – Document Types)	55

Supplementary Table 2. Methodological index for nonrandomized studies score for methodological quality assessment of included studies

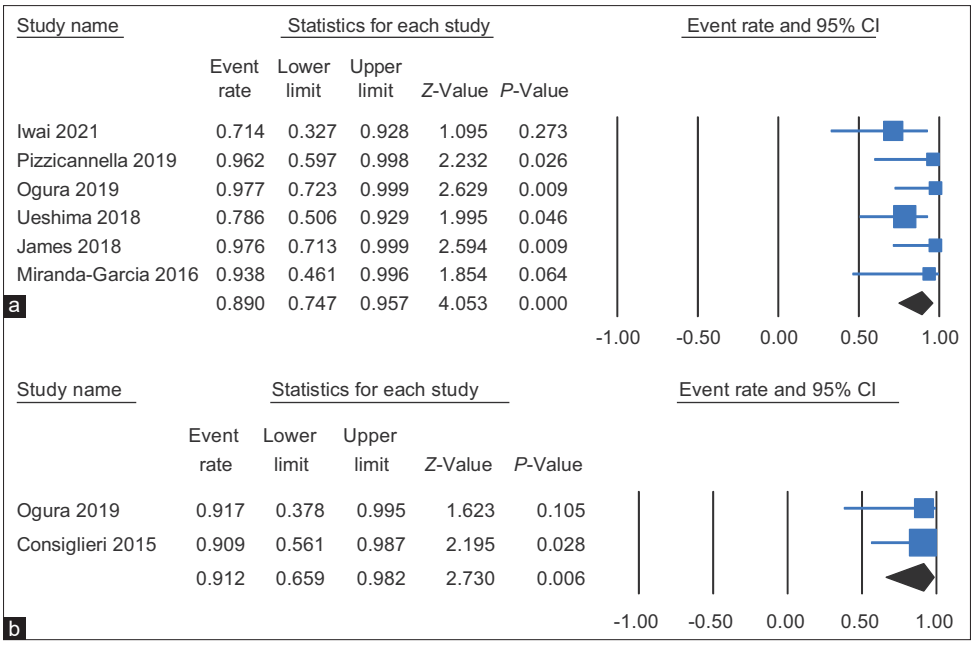
Study	Clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss to follow-up <5%	Prospective calculation of the study size	Total score
Hathorn *et al.*	2	2	1	2	0	2	2	0	11
Bill *et al.*	2	2	2	2	0	0	2	0	10
Martinez *et al.*	2	2	1	2	0	0	2	0	9
Consiglieri *et al.*	2	2	2	2	0	1	2	0	11
Miranda-García *et al.*	1	2	2	2	0	1	2	0	10
Iwai *et al.*	2	2	1	2	0	2	2	0	11
James *et al.*	2	2	2	2	0	2	2	0	12
Matsunami *et al.*	2	2	2	2	0	2	2	0	12
Tang *et al.*	2	2	2	2	0	0	2	0	10
Pizzicannella *et al.*	2	2	2	2	0	1	2	0	11
Ogura *et al.*	2	2	2	2	0	2	0	0	10
Ueshima *et al.*	2	2	2	2	0	0	2	0	10
Umeda *et al.*	2	2	1	2	0	1	2	0	10
Kawakubo *et al.*	1	2	2	2	0	1	2	0	10
Iwashita *et al.*	2	2	2	2	0	0	2	1	11



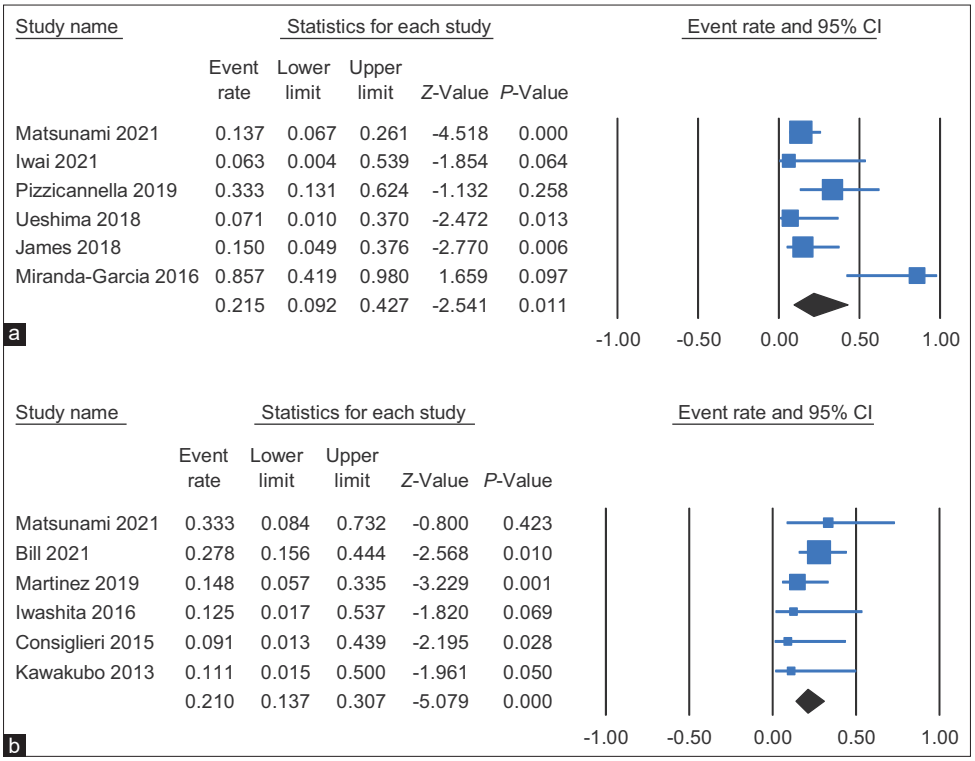
Supplementary Figure 1. (a) Rate of technical success of EUS-guided biliary drainage for benign biliary obstruction with SAA. (b) Rate of technical success of EUS-guided biliary drainage for benign biliary obstruction with normal anatomy. SAA: Surgically altered anatomy, CI: Confidence interval



Supplementary Figure 2. Rate of technical success of EUS-guided biliary drainage for benign biliary obstruction only including studies that reported both technical and clinical success. CI: Confidence interval



Supplementary Figure 3. (a) Rate of clinical success of EUS-guided biliary drainage for benign biliary obstruction with SAA. (b) Rate of clinical success of EUS-guided biliary drainage for benign biliary obstruction with normal anatomy. SAA: Surgically altered anatomy, CI: Confidence interval



Supplementary Figure 4. (a) Rate of adverse events of EUS-guided biliary drainage for benign biliary obstruction with SAA. (b) Rate of adverse events of EUS-guided biliary drainage for benign biliary obstruction with normal anatomy. SAA: Surgically altered anatomy, CI: Confidence interval