Review

Endoscopic Ultrasound

OPEN

EUS-guided gallbladder drainage as a rescue in distal malignant biliary obstruction: A systematic review with meta-analysis

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Abstract

Patients with distal malignant biliary obstruction (dMBO) needing biliary drainage (BD) undergo ERCP as a first approach. EUS–guided gallbladder drainage (EUS-GBD) is now accepted as a rescue alternative for the palliation of jaundice in those patients with dMBO who fail ERCP and cannot undergo EUS-BD. This is a systematic review with meta-analysis for evaluating the efficacy and safety of EUS-GBD in this scenario. A comprehensive search through the main database platforms was conducted to May 2024. Pooled estimates were obtained using a fixed-effects model with the generic inverse variance method. Study quality was evaluated using the Newcastle-Ottawa quality assessment scale (NOS). Heterogeneity was evaluated with I^2 statistic. Clinical success, adverse events (AEs) rate, and reintervention rate were the main outcomes. Sensitivity analyses were also conducted. Eight studies including 183 patients were identified. Pooled clinical success was 89% (95% CI, 84%–93%). The pooled clinical success of full-text publication was 88% (95% CI, 83%–93%; I^2 = 0%). Reintervention rate was 8% (95% CI, 4%–12%; I^2 = 0%). The overall AE rate was 10% (95% CI, 6%–15%; I^2 = 0%). The NOS allocated moderate quality in 7 studies. In conclusion, our findings confirm that EUS-GBD in dMBO is a feasible, effective, and safe technique as rescue therapy after failure of ERCP or EUS-BD.

Keywords: EUS; ; EUS-GBD; LAMS; Gallbladder drainage; Malignant biliary obstruction; Distal

INTRODUCTION

The evolution of therapeutic EUS during the past decade led to novel solutions in different conditions, such as in cases of biliary drainage in distal malignant biliary obstruction (dMBO).[1] Patients with dMBO needing biliary drainage (BD) undergo ERCP with transpapillary stent placement as a first approach.[2] Percutaneous transhepatic BD (PTBD) and EUS-guided BD are valuable alternatives in case of ERCP failure, preferring the EUS-guided approach when feasible.[3] Indeed, a meta-analysis of 10 studies, including 5 RCTs, comparing EUS-BD with PTBD showed comparable clinical success (90.0% *vs.* 88.7%, respectively; P = 0.51) but significant differences in adverse event (AE) rate (10.0% *vs.* 27.3%, P = 0.01) favoring EUS-BD.[4] However, technical issues encountered when performing ERCP or EUS-BD could lead to moving to other rescue procedures, such as EUS-guided gallbladder drainage (EUS-GBD) or percutaneous transhepatic biliary drainage (PT-BD). PT-BD has the disadvantage of inserting an external drainage catheter, increasing a potential source of infection and decreasing the oncologic patients' quality of life (QoL). Although the use of PT-BD or PT-GBD over the EUS approaches is still debated, the overall safer profile of the EUS-guided over the percutaneous procedures is leading to prefer the EUS approach when available.[4–6] Therefore, EUS-GBD is now accepted as a rescue alternative for the palliation of jaundice in patients with dMBO who fail ERCP and cannot undergo EUS-BD for technical reasons.[7,8] EUS-GBD is minimally invasive and easier to perform than other EUS-BD once the patency of the cystic duct has been ascertained.[9] The aim of this study is to perform a systematic review with meta-analysis of the studies assessing the efficacy and safety of EUS-GBD as rescue therapy in patients with dMBO.

METHODS

Data sources and search strategy

We performed this systematic review with meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-

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Endoscopic Ultrasound (2025) 14:2

Received: 13 June 2024; **Accepted**: 16 December 2024.

Published online: 23 April 2025

http://dx.doi.org/10.1097/eus.0000000000000108

Analyses statement (PRISMA).[10] Two authors (G.E.M.R., G.V.) conducted a comprehensive search among the main database platforms, such as Scopus, MEDLINE (PubMed platform), EMBASE, and Web of Science Core Collection (Clarivate) to May 2024. The strings used for the search included the terms EUS-GBD, dMBO, and biliary drainage (details in Supplementary Materials, http://links.lww.com/ENUS/A366). To identify additional studies, abstracts of international conferences were screened, and the online search was supplemented with manual searches of the reference lists of reviews and studies retrieved. When the results of the same cohort were analyzed in more than one publication, only the most recent and complete data were included in the meta-analysis. In addition, a hand cross-reference check from the retrieved studies was performed to identify duplicated reports.

Inclusion and exclusion criteria

Two authors (G.E.M.R. and L.F.) assessed the eligibility of the studies, and the discordances in the eligibility assessment of individual studies were solved by discussion with the other coauthors. Studies were included in the meta-analysis if they met the following criteria[1]: patients were suffering from dMBO,[2] EUS-GBD was performed as a rescue treatment in the management of dMBO after ERCP and/or EUS-BD failure/unfeasibility,[3] data on efficacy and/or safety of EUS-GBD were extractable. We excluded (1) studies in which the indication for EUS-GBD was acute cholecystitis, (2) case series with less than 5 patients, and (3) case reports and review articles.

Data extraction and quality assessment

Studies and patients' variables were extracted from all eligible studies. Study-level data included the name of the first author, publication year, region where the study was conducted, design, number of centers (single *vs*. multicenter), definition of clinical success, adverse events rate, type of stents placed (lumen apposing metal stent [LAMS], or self-expandable metal stent [SEMS]), procedure time, duration of follow-up, and reintervention rate. Patient- and technical-level data included type of neoplasia, oncologic stage (resectable/unresectable), concomitant gastric outlet obstruction, anatomical approach (transgastric and transduodenal), type of stent, and double-pigtail stents placement.

All studies were assessed for study quality according to a checklist based on a modified version of the Newcastle-Ottawa quality assessment scale, with discrepancies resolved by consensus among researchers.[11] Studies were graded using the following parameters: (1) representativeness of the cohort, (2) selection, (3) ascertainment of exposure, (4) assessment of outcomes, (5) confounders, and (6) adequacy of follow-up evaluation. Each parameter was scored 0 or 1 (Supplementary Table 1, http://links.lww.com/ENUS/A366). Studies with total scores of 6 or greater were classified as high quality, scores between 4 and 5 classified as moderate quality, and scores lower than 4 classified as low quality.

Outcomes and statistical analysis

The primary outcome of interest was the efficacy of EUS-GBD, broadly defined as clinical success by the decrease in post-procedure bilirubin. Secondary outcomes were safety (AE rate) and reintervention rate.

Pooled estimates were obtained using a fixed-effects model with the generic inverse variance method. Heterogeneity was assessed with the I^2 statistic. We performed subgroup analyses according to the definition of clinical success, type of failure as first approach, tumor staging (resectable *vs*. nonresectable), route of LAMS placement, and number of centers involved (single center *vs*. multicentric). Significant differences among subgroups were evaluated using the interaction test (Test Q di Cochran). We calculated pooled rates with 95% confidence intervals (CIs) for clinical success, adverse events rate, and reintervention rate. When pre- and post-procedure bilirubin was extractable, we calculated standardized mean difference (SMD) with 95% CI to compare pre- and post-levels. We did not evaluate the publication bias as the total number of studies was insufficient. All the statistics were processed using the statistical software STATA (Statistics and Data Science, version 18, College Station, TX).

RESULTS

The search strategy through the databases identified 982 articles; after applying selection criteria, 9 studies with 185 patients were considered eligible for qualitative analysis. One eligible study[12] included 23 patients with dMBO in the full publication, but individual data were not fully extractable. Therefore, data were provided by authors, causing exclusion from the quantitative analysis (meta-analysis) because only 2 patients had EUS-GBD after failed ERCP (none after failed EUS-CDS or EUS-HGS) among the 23 patients with dMBO. Finally, 8 studies with 183 patients were included in the quantitative analyses (details in Supplementary Figure 1, http://links.lww.com/ENUS/A366). The number of patients per study varied from 7[13] to 48,[14] with an overall pooled age of 68.39 (95% CI, 59.75–77.04) years. When exploring age distribution according to the geographical area to whom studies belonged to, we found no significant differences between patients included in those studies from European countries and those from extra-European (EE) countries, even if EE countries showed a slight younger age (65.77 *vs*. 71.36 years, $P = 0.53$; Supplementary Figure 2, http://links.lww.com/ENUS/A366). The exploration of gender among studies showed a homogeneous distribution (Supplementary Figure 3, http://links.lww.com/ENUS/A366)

Studies included in meta-analysis

All studies were retrospective: 5 studies were full publications,[14–18] 4 single-arm retrospective studies,[14–16,18] and 1 retrospective comparative study of EUS-GBD *versus* US-BD.[17] Three studies were abstracts presented during international conferences.[13,19,20] Three studies were single-center,[13,15,18] and only one study was from eastern world (Japan, Asia).[15] Only one study used a single route of drainage in 100% of cases (transgastric).[17] The studies included mainly patients with unresectable stage, even if 2 studies[14,17] included a minimal percentage of patients in resectable stage as well. Table 1 summarizes the characteristics of the studies. The quality assessment using the modified NOS allocated moderate quality in 6 studies, showing only 1 study[13] with low quality (Supplementary Table 2, http://links.lww.com/ENUS/A366).

Efficacy—clinical success

Efficacy, evaluated in terms of pooled clinical success, was 89% (95% CI, 84%–93%; $I^2 = 0\%$, $P = 0.544$) [Figure 1]. Four studies[13,14,16,17] reported the serum bilirubin levels before EUS-GBD with a mean difference of 9.81 mg/dL (95% CI, 3.83–15.78; $I^2 = 0\%$, $P = 0.468$; Supplementary Figure 4, http://links.lww.com/ENUS/A366). On the other hand, 3 studies[13,14,16] showed data regarding bilirubin levels after the procedure, reporting a pooled mean difference of 2.98 (95% CI, 0.91–4.85; $I^2 = 0\%$, $P = 960$; Supplementary Figure 5, http://links.lww.com/ENUS/A366). When the abstracts were removed from the analysis, the pooled clinical success was 88% (95% CI, 83%–93%; $I^2 = 0\%$, $P = 0.527$) [Figure 2]. Sensitivity analysis, including

Table 1

Characteristics of included studies (n = 8).

Author	Centers	Geographical area	Age	Gender (M/F)	Tumor stage	Type of previous failure	EUS-GBD, n	Clinical success, %	Definition of clinical success	Route of drainage, %		Comments	Follow-up	NOS score
										Transgastric	Transduodenal			
Imai et al.[15]	Single center	Japan, Asia	67.3 ± 13.9	8/4	Unresectable (100%)	ERCP, then EUS-RVS, EUS-CDS, and EUS-HGS	12	91.7	Decrease in bilirubin levels to <50% of the pretreatment value within 2 wk	58.3	41.7	EUS-GBD with PC-SEMS (Wallflex, 8 × 60 mm)	NA	4
Chang et al.[18]	Single center	USA, America	63.1 (range, 41–80)	5/4	Unresectable (100%)	ERCP and EUS-RV	9	77.8	Symptom and post-procedural liver chemistry improvement	44.4	55.6	LAMS	130.7 d	4
Paleti et al.*[13]	Single center	USA, America	67 ± 13.3	5/2	NA	ERCP	7	100	NA	NA	NA	LAMS	NA	3
Issa et al.[16]	Multicenter	USA, America	68 ± 13	15/13	Unresectable (100%)	ERCP and EUS-BD (not specified)	28	92.6	Decrease in serum bilirubin of >50% within 2 wk	46	54	After both ERCP and EUS-BD failure. 26 pts with LAMS (EC-LAMS n = 20 and LAMS n = 6) and 2 pts with SEMS	33 (3–64) mo	5
Lambin et al.*[19]	Multicenter	France, Europe	NA	NA	NA	ERCP	28	78.6	NA	NA	NA	EC-LAMS	3.6 ± 5.0 mo (mean)	4
Binda et al.[14]	Multicenter	Italy, Europe	74.3 ± 11.7	23/25	Resectable 1/48 (1.5%) Unresectable† 47/48 (97.9%)	ERCP and EUS-CDS	48	81.3	Reduction of bilirubin blood level of 50% within 2 wk after the procedure	58.3	41.7	LAMS and other stents	122 ± 161 d (mean)	4
Debourdeau et al.[17]	Multicenter	France, Europe	70.16 ± 11.06	22/19	Resectable 3/41 (7.3%) Unresectable 38/41 (92.7%)	ERCP	41 (EUS-GBD) 37 (EUS-BD)	87.8 (EUS-GBD) 89.2 (EUS-CDS)	Defined by a >50% decrease in total bilirubin levels at day 7 or normalization at day 28 (<48 lmol/L)	100%	0%	EUS-GBD *vs.* EUS-BD. EC-LAMS (Hot AXIOS stent; Boston Scientific, Marlborough, MA)	5.2 (1.21, 48.09) mo (median)	5
Korani*[20]	Multicenter	U.K., Europe	70 (range, 37–80)	NA	NA	ERCP	10	100	Decrease in serum bilirubin of >50% within 30 d post-procedure	70%	30%	LAMS. Additional pigtail stents were inserted through LAMS in 3 procedures; 5 patients were alive at 6 mo, showing all LAMS patent.	6 mo (median)	5

EUS-BD: EUS–guided biliary drainage; EUS-CDS: EUS-guided choledocoduodenostomy; EUS-GBD: EUS–guided gallbladder drainage; EUS-RV: EUS–guided rendez-vous; LAMS: Lumen apposing metal stent; SEMS: Self-expandable metal stent.

*Abstracts. NA: Not available.

†Authors declared missing data regarding patients' stage.

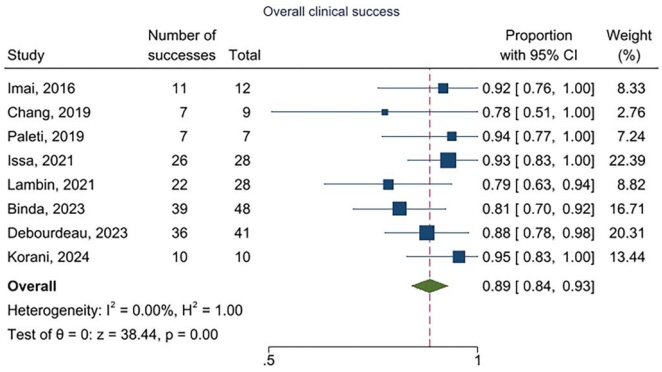

Figure 1. Forest plot for pooled rate of clinical success after EUS-GBD in dMBO among 8 included studies.

only studies with the most common definition of clinical success (decrease of bilirubin level >50% after at least 7 days from EUS-GBD), showed a pooled clinical success of 90% (95% CI, 85%–95%; I^2 = 0%, P = 0.452; Supplementary Figure 6, http://links.lww.com/ENUS/A366). On the other hand, in the 3 studies in which the definition was either not available[13,19] or vague (including symptoms and liver laboratory tests improvement[18]), the pooled rate was 84% (95% CI, 74%–95%; I^2 = 0%, P = 0.370). Single-center studies included 28 patients, showing a pooled clinical success of 90% (95% CI, 80%–100%; I^2 = 0%, P = 0.604), whereas multicenter studies included 155 patients showing a pooled clinical success of 88% (95% CI, 83%–93%; I^2 = 24.79%, P = 0.128; Supplementary Figure 7, http://links.lww.com/ENUS/A366). When removing the only one low-quality study,[13] the pooled clinical success was 88% (95% CI, 83%–93%; I^2 = 0%, P = 0.483; Supplementary Figure 8, http://links.lww.com/ENUS/A366). Subgroup analyses for tumor staging showed slight differences in clinical success, even if not significant (P = 0.24), among those studies including only unresectable tumors compared to those including both (85% *vs.* 91%, respectively) [Figure 3]. Subgroup analysis according to the route of LAMS (stomach or duodenum) was not possible due to the lack of individual data and extractable outcomes in the included studies.

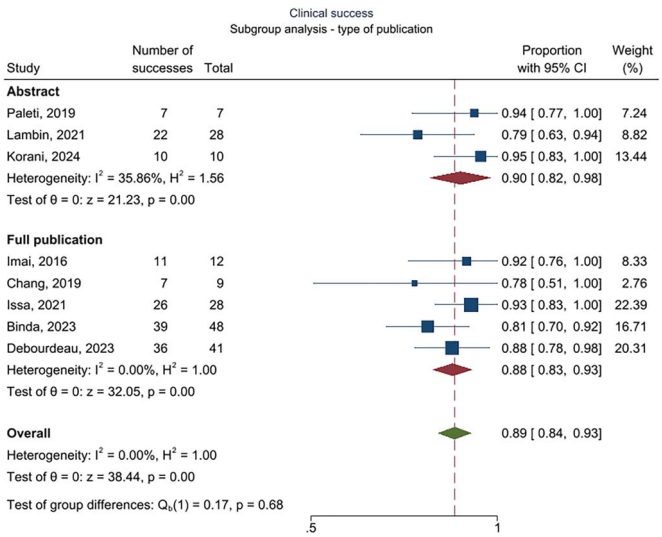

Figure 2. Subgroup analysis (abstracts *vs.* full-paper publications) showing the pooled rate of clinical success after EUS-GBD in dMBO.

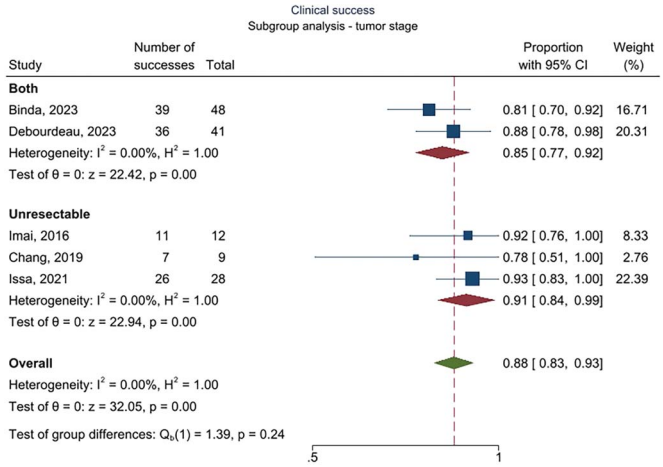

Figure 3. Subgroup analysis for clinical success according to patients' tumor stage (unresectable *vs.* both resectable and unresectable).

Safety

The safety was evaluated as the overall pooled rate of AEs, which was 10% (95% CI, 6%–15%; I^2 = 0%, P = 0.893) [Figure 4]. The removal of the abstracts from the analysis showed a pooled AE of 10% (95% CI, 6%–15%; I^2 = 0%, P = 0.733) [Figure 5]. Single-center studies showed a pooled AE rate of 8% (95% CI, 2%–17%; I^2 = 0%, P = 0.645), whereas multicenter studies showed a pooled AE rate of 11% (95% CI, 6%–16%; I^2 = 0%, P = 0.806; Supplementary Figure 9, http://links.lww.com/ENUS/A366) with no significant differences (P = 0.53). When removing the only one low-quality study,[13] the pooled AE rate was 10.8% (95% CI, 6.1%–15.4%; I^2 = 0%, P = 0.847; Supplementary Figure 10, http://links.lww.com/ENUS/A366) among the studies with moderate quality. One study included EUS-GBD with SEMS placement[15] and other 2[14,16] using both SEMS and LAMS, so subgroup analysis showed similar AE rate between studies using only LAMS (9%; 95% CI, 3%–14%; I^2 = 0%) compared to the previous

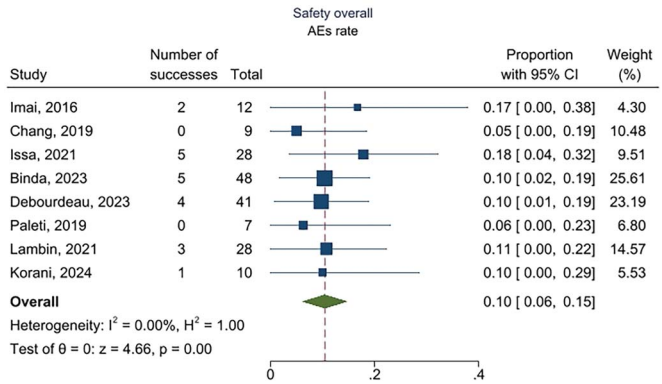

Figure 4. Forest plot for pooled rate of adverse events (safety) after EUS-GBD in dMBO.

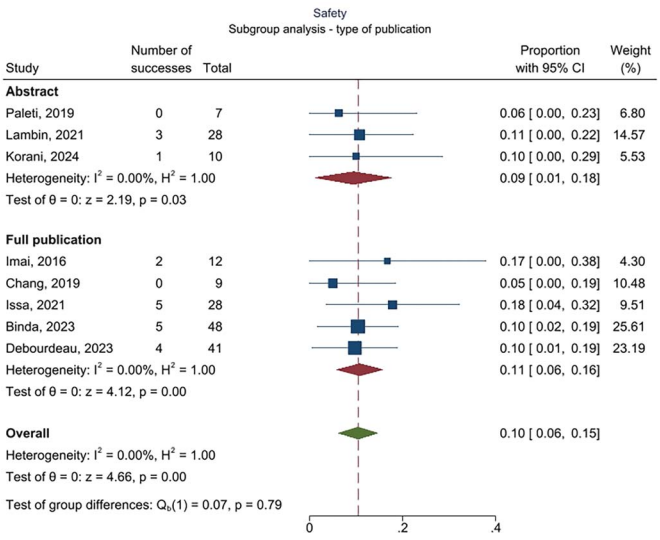

Figure 5. Subgroup analysis (abstracts *vs.* full-paper publications) showing the pooled rate of adverse events (safety) after EUS-GBD in dMBO.

(13%; 95% CI, 6%–20%; P = 0.37; Supplementary Figure 11, http://links.lww.com/ENUS/A366).

Adverse events (AEs)

Specifically, Imai et al. and Issa et al.[15,16] reported the highest AE rate (16.7% and 17.9%, respectively), showing stent dysfunction due to food impaction (Issa, n = 3) and tumor growth (Imai, n = 1). The residual AEs from the latter 2 studies were conservatively managed bleedings (n = 2, Issa) and peritonitis (n = 1, Imai). Binda et al.[14] reported 5 AEs (10.4%), 3 intraprocedural (2 bleedings and one dislodgement) and 2 delayed (>24 hours, 1 stent occlusion and 1 buried stent, both managed with LAMS-in-LAMS technique). The comparative study[17] reported a lower AE rate of EUS-GBD compared to EUS-BD (9.76% *vs.* 24.32%), showing 1 stent dislodgement, 1 bacteremia, and 2 bleedings in the EUS-GBD group. Eventually, Lambin et al.[19] showed 1 cholangitis, 1 septic shock, and 1 stent obstruction (AE rate = 10.7%), whereas Korani et al.[20] reported no immediate AEs, but in 1 case, LAMS dysfunction occurred due to impacted gallstones requiring endoscopic reintervention. Details are reported in Table 2.

Reintervention rate

Overall pooled reintervention rate was 8% (95% CI, 4%–12%; I^2 = 0%) [Figure 6] among 7 out of 8 studies in which data were extractable. Subgroup analyses considering previous reported covariates

Table 2

Adverse events among included studies (n = 7).

Author	AE rate, n/N (%)	Details on AEs and management after EUS-GBD	Deaths
Imai et al.6[15]	2/12 (16.7)	Adverse events (n = 2): • One peritonitis ➔ conservative treatment • One stent dysfunction due to tumor grown with cystic duct entrapment ➔ PTBD	—
Chang et al.[18]	0	No procedural adverse events	4 deaths for tumor progression
Paleti et al.*[13]	0	No procedural adverse events	—
Issa et al.[16]	5/28 (17.9)	Adverse events (delayed, >24 h) (n = 5): • 3 cases of food impaction➔ reintervention ➔ cholecystitis • 2 bleedings ➔ one needing clip of ulcer inside the GBD and the other self-solving	10 deaths (36%) at the time of paper writing
Lambin et al.*[19]	3/28 (10.7)	Adverse events (n = 3): • 1 stent obstruction • 1 cholangitis • 1 septic shock	—
Binda et al.[14]	5/48 (10.4)	Adverse events (n = 5): • 3 intraprocedural ➔ 2 bleedings (endoscopy/conservative) and 1 dislodgement (PTC) • 2 delayed (>15 d) ➔ 1 stent occlusion and 1 buried stent ➔ both with second LAMS	—
Debourdeau et al.[17]	EUS-GBD: 4/41 (9.76) EUS-BD: 9/37 (24.32)	Significant adverse events (n = 4) • 1 LAMS dislodgment within an hour postprocedure, leading to biliary peritonitis and necessitating surgical treatment and intensive care unit admission (AGREE grade IVa) • 2 bleeding • 1 bacteremia	No deaths among EUS-GBD group
Korani*[20]	1	No immediate adverse events occurred. One patient with additional pigtail had blocked LAMS within the first week from gallstones requiring reintervention.	Only 1 death was recorded within 30 d, which was no procedure-related.

AEs: Adverse events; AGREE: Classification for adverse events gastrointestinal endoscopy; EUS-BD: EUS–guided biliary drainage; EUS-GBD: EUS–guided gallbladder drainage; LAMS: Lumen apposing metal stent; PTBD: Percutaneous transhepatic biliary drainage; PTC: Percutaneous transhepatic cholangiogram.

*Abstracts.

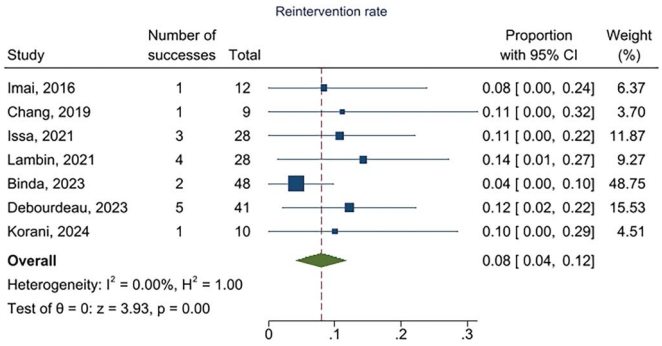

Figure 6. Forest plot for pooled reintervention rate.

did not show significant differences, even if those studies in which patients underwent EUS-GBD after failure of both ERCP and EUS-BD had a lower rate (6%; 95% CI, 1%–11%) compared to those after ERCP failure alone (13%; 95% CI, 5%–20%; *P* = 0.14; Supplementary Figure 12, http://links.lww.com/ENUS/A366). In addition, removing the only study using a single route of drainage (transgastric),[17] the reintervention rate of the other studies was 6% (95% CI, 2%–11%). Studies using LAMS showed a reintervention rate of 12% (95% CI, 5%–19%), whereas those using SEMS or both had a rate of 6% (95% CI, 1%–11%; *P* = 0.12).

DISCUSSION

Endoscopic treatment of jaundice in cases of dMBO still requires ERCP with stent placement as a primary approach. Nevertheless, ERCP can fail in 10%–20% of cases for dMBO, especially when the tumor leads to duodenal stenosis or involvement of the major papilla. Additionally, failure may occur in cases with the presence of a duodenal stent or further technical complexities in biliary cannulation.[2] EUS-BD showed similar efficacy to PTBD but lower postprocedural AEs.[21,22] Unfortunately, even EUS-BD can fail due to technical conditions, such as in cases of a common bile duct <15 mm in diameter, the absence of safe EUS-window due to vessels or further structures, or in case of altered anatomy.[23–25] When EUD-BD also fails or is not feasible in patients with dMBO, in patient with gallbladder still *in situ*, EUS-GBD becomes a valuable option if a patent cystic duct is ascertained. Our meta-analysis is an update that includes the latest evidence in the literature involving 183 patients with dMBO. Our analysis found a pooled clinical success rate of 89%, similar to the EUS-BD known from the literature.[26] Notably, one of the included studies[17] is the only study comparing EUS-GBD to EUS-BD (CDS) in the setting of dMBO when ERCP fails. This retrospective multicenter study demonstrated that drainage with EUS-GBD yields comparable clinical success rates to EUS-CDS (87.8% *vs.* 89.2%, *P* = 0.8). However, we explored potential sources of differences influencing the results through subgroup analyses. Firstly, we evaluated clinical success by considering studies according to the abstract or full-paper form. Our subgroup analysis confirmed similar clinical success rates (88% for full-paper publications), compared to the overall pooled rate (89%). However, a subgroup analysis exploring clinical success among studies including only unresectable patients and those including both resectable and unresectable showed slight differences, even if not significant (91% *vs.* 85%, *P* = 0.24), suggesting to better explore this perspective in future studies. The transduodenal route of stent insertion could not technically impact future surgery, so this could lead endosonographers to consider resectable patients. Moreover, stratifying the studies according to the definition of clinical success, clinical success moved from 90% (95% CI, 85%–95%) in the standard definition (decrease >50% of bilirubin after EUS-GBD) to 84% (95% CI, 74%–95%) among studies with other definitions. Anyway, we explored data regarding the technical aspects of EUS-GBD, finding that Imai et al. from Japan used PC-SEMS for EUS-GBD,[15] which were also used in a few cases (*n* = 2) by Issa et al. from the United States[16] together with different types of LAMS ("electro-cautery"[EC]-LAMS and "cold" LAMS). Furthermore, the route of LAMS placement was mostly balanced among the studies, except in the study by Korani et al.,[20] which used transgastric approach in 70% of patients, and Debourdeau et al.,[17] which used only the transgastric approach. A slight inclination to use the transgastric approach was seen also in Binda et al.[14] and Imai et al.,[15] which used it in most cases, meaning 58.3% in both studies. EUS-GBD is confirmed to be a safe procedure, as shown by the pooled rate of AEs of 10%, with only one serious AE reported,[17] specifically a stent dislodgement causing peritonitis requiring surgery and intensive care unit management. The latter AE was the only one needing surgery, and no further severe AE or procedure-related deaths were reported among the studies [Table 2]. The pooled AE rate was similar when including only full-paper publications compared to the abstracts AE rate (11% *vs.* 9%, respectively), with no statistical differences (*P* = 0.79). Subgroup analysis showed slightly lower AE rate among studies using only LAMS compared to those using SEMS or both (9% *vs.* 13%), suggesting that the use of SEMS could increase the rate of AEs, probably increasing procedure time, due to more steps, and the technical difficulty, even if this difference was not significant (*P* = 0.37). However, our study showed a reintervention rate of 8%, which is similar to previous meta-analysis (9.3%),[7] but our analysis included more studies (7 *vs.* 3) and an extremely higher number of patients (176 *vs.* 49), giving our results more robustness, considering that oncologic patients need to have long-term clinical benefit from this procedure, so confirming with more robustness a lower reintervention rate has a clinical impact. Moreover, we found slight but not significant (*P* = 0.14) differences between studies with previous ERCP failure and those with both EUS-BD and ERCP failure (13% *vs.* 6% reintervention rate).

Differently from the previously published meta-analysis by Kamal et al.,[7] our study included a higher number of studies (9) in the qualitative analysis and in the quantitative analysis (8 *vs.* 5) and, consequently, a higher number of patients (183 *vs.* 104) despite our exclusion criteria being more restrictive. In particular, we included 2 additional abstracts,[19,20] one additional full-paper[17] and the full-paper version[14] of one study, which was previously included in its abstract form,[27] permitting us to evaluate in our analysis additional relevant data not shown in the abstract form, such as reintervention rate (a main outcome), tumor stage, and more details on AEs. Indeed, 2 studies[14,17] included a few patients at a resectable stage, which were not discussed in the previous meta-analysis, whereas we explored it through a subgroup analysis. Unfortunately, individual data on outcomes were not extractable, so we cannot give any specific recommendations. The percentage of males and females was also evaluated among studies, showing a similar distribution, suggesting no difference in term of outcomes. Mean age among studies slightly changed between extra-European patients, which were younger, compared to European people, which were older (71.36 *vs.* 65.77 years), even it was not significant (*P* = 0.53). Furthermore, we performed a more in-depth item-by-item evaluation of the AEs, analyzing the type and the associated management. Other additional values of our study are surely the subgroup analyses, which the other authors did not perform and that can provide additional insights, especially using the statistical evaluation of differences among subgroups. In fact, a lower AE rate was seen among single-center studies compared to multicenter studies (8% *vs.* 11%, *P* = 0.53), probably due to the different expertise among the endosonographers of the centers in the multicentric studies leading to include patients from low-

volume centers with high risk of AEs. However, all the studies regarding EUS-GBD in this specific subset of patients (dMBO) are retrospective; they individually included few patients, so future researches need to go beyond these limitations through novel and well-designed prospective studies. In addition, our study suggests to evaluate and specify outcome of those patients with resectable stage, in order to produce more robust data. Therefore, we should be careful in interpreting our results, and randomized controlled trials on this topic should be encouraged for confirmation. In conclusion, our findings confirm that EUS-GBD in dMBO is an effective and safe technique as rescue therapy after failure of ERCP or EUS-BD, with low reintervention rate, and furthermore, it could be used for patients at resectable stage.

Acknowledgment

None.

Source of Funding

There is no financial support to this study.

Ethical Approval

Not applicable.

Informed Consent

Not applicable.

Conflict of Interest

Giuseppe Vanella: lecture fees from Boston Scientific and travel grants from Euromedical. Carlo Fabbri: consultant per Boston scientific, lecturer per steris e Q3 medical. Todd H. Baron is a consultant for Cook Endoscopy, Boston Scientific, Olympus, Medtronic, ConMed, and WL Gore. All the other authors have no conflict of interest to declare.

Data Availabitiy Statement

No additional data is available.

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