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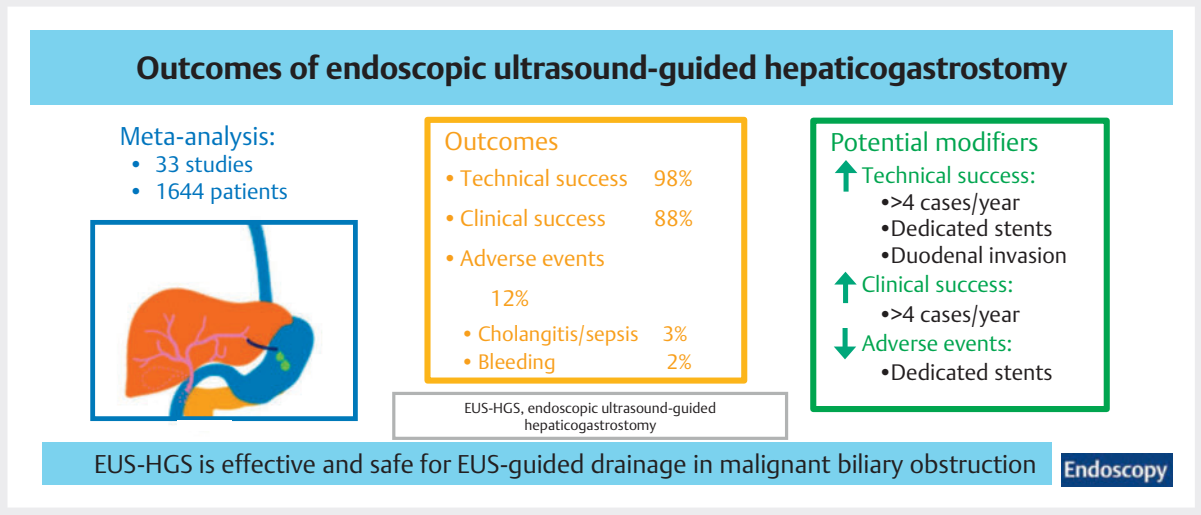
# Efficacy and safety of endoscopic ultrasound-guided hepaticogastrostomy: a meta-regression analysis

## GRAPHICAL ABSTRACT

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## ABSTRACT

**Background** Endoscopic ultrasound-guided hepaticogastrostomy (EUS-HGS) is a valid option for EUS-guided biliary drainage that has been increasingly used in the last decade. The aims of this study were to provide a systematic review with meta-analysis and meta-regression of the features and outcomes of this procedure.

**Methods** The MEDLINE, Scopus, Web of Science, and Cochrane databases were searched for literature pertinent to EUS-HGS. Meta-analysis of the proportions and meta-regression of potential modifiers of the main outcome measures were applied. The main outcome was technical success; secondary outcomes were clinical success and procedure-related adverse events (AEs).

**Results** 33 studies, including 1644 patients, were included in the meta-analysis. Malignant biliary obstruction (MBO) was the underlying cause in almost all cases (99.6%); the main indications for EUS-HGS were duodenal/papillary invasion (34.8%), surgically altered anatomy (18.4%), and hilar stenosis (16.0%). The pooled technical success of EUS-HGS was 97.7% (95%CI 96.1%–99.0%; $I^2$ = 0%), the intention-to-treat clinical success rate was 88.1% (95%CI 84.7%–91.2%; $I^2$ = 33.9%), and procedure-related AEs occurred in 12.0% (95%CI 9.8%–14.5%; $I^2$ = 20.4%), with cholangitis/sepsis (2.8%) and bleeding (2.3%) the most frequent. The rate of procedure-related AEs was lower with the use of dedicated stents on univariable meta-regression analysis. Meta-regression showed that technical success and clinical success rates were modified by the centers' experience (>4/year).

**Conclusions** EUS-HGS represents an effective and safe procedure for EUS-guided biliary drainage in patients with MBO. Future studies should address the impact of center experience, patient selection, and the use of dedicated stents to improve performance of this technique.


## Introduction

EUS-guided biliary drainage (EUS-BD) is one of the possible treatments for the relief of jaundice caused by malignant biliary obstruction (MBO) when endoscopic retrograde cholangiopancreatography (ERCP) has failed [1]. If the common bile duct cannot be cannulated, or the papilla is infiltrated or unreachable, EUS-BD provides a valuable alternative to percutaneous transhepatic biliary drainage (PTBD) [2]. The available evidence shows that EUS-BD is comparable with PTBD in terms of efficacy, although PTBD is burdened by a higher rate of re-intervention and a lower quality of life [3].

EUS-guided hepaticogastrostomy (EUS-HGS) was first described in 2003 [4, 5]; however, since its introduction, its use in clinical practice has been intermittent, slowly becoming more widespread in the last 10 years. The main reasons for this are: its technical complexity, requiring high technical skills in both ERCP and interventional EUS; the far from negligible rate of AEs that are often severe and require additional modalities (e. g. interventional radiology or surgery); and, for a long time, the lack of dedicated devices [6]. In more recent years, different types of stents have been designed in order to make this procedure safer and to overcome the limitations of the previously available devices. These stents are usually self-expandable metal stents (SEMSs), with a longer fully covered portion and an uncovered extremity for the intrahepatic side, and are provided with variable anti-migration systems [7, 8]. This step forward in tools and the paradigm change in biliopancreatic endoscopy have led to recent widespread use of the technique.

Despite the growing evidence on EUS-HGS, to date, the available meta-analyses have mainly focused on EUS-BD, including both EUS-HGS and EUS-choledochoduodenostomy (EUS-CDS), with comparative analysis among the two techniques [1, 9]. No meta-analysis has previously been performed to consider EUS-HGS alone and, as remarkable heterogeneity exists among studies, the outcomes of this technique may not be completely reliable.

We performed a systematic review with meta-analysis, aiming to evaluate the efficacy and safety of the EUS-HGS procedure. The main outcome was the rate of technical success; secondary outcomes were the rates of clinical success and adverse events (AEs). In addition, we aimed to identify potential modifiers of the efficacy and safety of EUS-HGS through meta-regression analysis [10].

## Methods

### Literature search strategy

A systematic search was made through Pubmed, Scopus, Web of Science and Cochrane databases until December 2022 that were relevant to EUS-HGS, without restriction criterion for the starting date. No search for grey literature was attempted. The meta-analysis was conducted and reported in accordance with the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) [11] and Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [12]. The native search for each database syntax is given in **Appendix 1s** (see online-only Supplementary material).

### Literature screening

One author (E.D.) conducted an initial screen to obtain a single list of articles from the queried databases. Once the list of articles had been obtained, the same author identified articles that were irrelevant by the title or abstract. Study selection was then accomplished through three levels of screening. First, reviews, letters, expert opinions, and editorials were excluded. Second, the abstracts of the retained studies were reviewed by two independent reviewers (C.B. and P.G.) and studies that reported the safety and efficacy of patients undergoing EUS-HGS as the only study population or in comparison to other treatments (i.

e. percutaneous drainage or other routes for EUS-BD) entered the subsequent screening level. For the final level of screening, the full text was obtained for any relevant articles and for those articles where a decision could not be made on the basis of the abstract. The reference lists of the selected articles were checked for additional studies by another investigator (C.C.).

## Inclusion and exclusion criteria

The final inclusion criteria were: (i) a study population that included patients treated with EUS-HGS for the treatment of biliary obstruction whether malignant or benign; (ii) adequate description of the study population; (iii) a complete description of the technical and clinical success rates, together with description of any post-procedural AEs. The following studies were excluded: (i) small cases series with <10 patients; (ii) studies including antegrade stenting; (iii) studies that did not provide sufficient data to evaluate the primary outcome. Where a study was followed by a more complete study or studies that included the original data set, the most recent, the largest, or the most complete report was used for the analysis. Such linked studies were identified on the grounds of authorship, institutions, design, length of follow-up, and study populations. Any divergences were resolved by discussion between the reviewers and a third investigator (A.C.).

## Data extraction and quality assessment

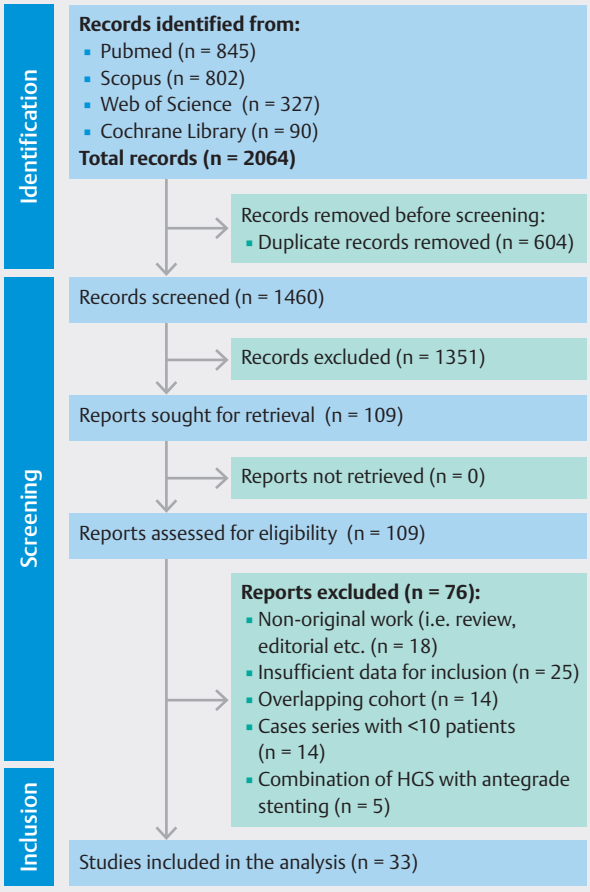
The extracted data included study period, design, and number of centers involved, study location, patient demographics, clinical characteristics, route of drainage, and the type of stent used. The number of procedures/year was calculated by dividing the total number of cases treated at each center by the study period in years. Technical success, clinical success, AEs, procedure-related mortality, 30-day all-cause mortality, hospital stay, re-intervention rate, and time to recurrence were all evaluated. Clinical success was evaluated both on an intention-to-treat (ITT) approach (the denominator being all attempted EUS-HGSs) and per successful procedure (the denominator being only patients where technical success was achieved). Prespecified AEs included only the following procedure-related complications: pneumoperitoneum, biliary leakage/peritonitis, stent malfunction/migration, perforation, bleeding, and cholangitis/sepsis. The quality of each selected study was assessed by two investigators (P.G. and C.C.) through the Cochrane tool (RoB-2) for randomized controlled trials (RCTs) [13] and the Newcastle–Ottawa scale (NOS) for observational studies [14]. Any divergences were resolved by discussion between reviewers and a third investigator (A.C.).

## Statistical analysis

The main outcome was the technical success of the procedure. Secondary outcomes were the rates of clinical success and procedure-related AEs. Dichotomous variables were estimated as pooled binomial proportions with 95%CIs applying random-effect models and the Freeman-Tukey double arcsine transformation to retain studies with proportions at 0 or 1 margins and ensuring admissible confidence intervals for the pooled proportions [15]. Continuous variables were pooled in weighted means with 95%CI, using random-effect models. When studies reported continuous variables as median and range or interquartile range (IQR), the mean and variance were estimated as proposed by Wan et al. [16]. Studies were not weighted for their quality.

Statistical heterogeneity was explored by Cochrane's *Q* and inconsistency ($I^2$) statistics [17]. Publication bias was evaluated with Egger's and Begg's tests [18, 19]. The meta-regression analysis included the following prespecified covariates: study characteristics (year, design, center volume); patient demographics (age, sex); proportion of patients with malignancy; indication for HGS (proportion of patients with surgically altered anatomy/hilar stenosis/duodenal invasion); presence of ascites; and procedure details (use of dedicated stents, transgastric route).

We performed the following post-hoc sensitivity analyses: by geographic reason, by study year (before vs. after 2015), and for subgroups of patients using exclusively metal stents, exclusively dedicated stents, or a transgastric approach. Meta-analysis was performed using Stata (StataCorp. 2017. Stata Statistical Software: release 15. College Station, Texas: StataCorp LLC) and the package "metafor" for R-Project 3.2.5 (R Core




▶ **Fig. 1** Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart for study identification, selection, and inclusion [12].

▶ **Table 1** Pooled analysis of the clinical features of the study populations submitted to endoscopic ultrasound-guided hepaticogastrostomy (EUS-HGS).

| | Number of studies | Weighted analysis (95%CI) | $I^2$, %* | Cochrane's Q; Wald-type/LR |
|---|---|---|---|---|
| **Clinical features** | | | | |
| Age, years | 33 | 66.4 (65.0–67.9) | 89.6 | 306.3 |
| Sex, male, % | 32 | 57.9 (54.4–61.3) | 29.8 | 46.6; 46.6 |
| Malignant biliary obstruction | 33 | 99.6 (97.5–99.9) | 53.7 | 69.11; 406 |
| Indication for EUS-HGS, % | | | | |
| ▪ Surgically altered anatomy, % | 30 | 18.4 (11.3–28.6) | 79.9 | 144.2; 302.2 |
| ▪ Hilar stenosis, % | 25 | 16.0 (2.3–60.5) | 76.1 | 100.4; 484.4 |
| ▪ Bismuth ≥III stenosis | 15 | 1.95 (1.93–1.98) | 25.4 | 18.8; 213.1 |
| ▪ Duodenal/papillary invasion (%) | 24 | 34.8 (24.3–47.0) | 80.3 | 116.7; 195.6 |
| Ascites present, % | 10 | 20.2 (14.3–27.6) | 73.5 | 34.0; 39.6 |
| **Procedure features** | | | | |
| Type of stent used, % | | | | |
| ▪ Metal stent | 33 | 99.9 (96.3–100) | 83.3 | 191.2; 1113.3 |
| ▪ Plastic stent | 33 | 8.3 (7.1–9.8) | 0 | 31.2; 765.9 |
| ▪ Dedicated stent | 31 | 42.6 (40.2–45.0) | 36.6 | 47.3; 1826.2 |
| Transgastric puncture/drainage, % | 32 | 99.9 (98.2–99.9) | 0 | 6.8; 334.9 |

* $I^2$ describes the amount of heterogeneity resulting from meta-analysis. A rough guide to interpretation is as follows: 0%-40%, might not be important; 30%–60%, may represent moderate heterogeneity; 50%–90%, may represent substantial heterogeneity; 75%–100%, considerable heterogeneity.

Team [2016], Vienna, Austria; available from: http://www.R-project.org).

## Results

### Literature search

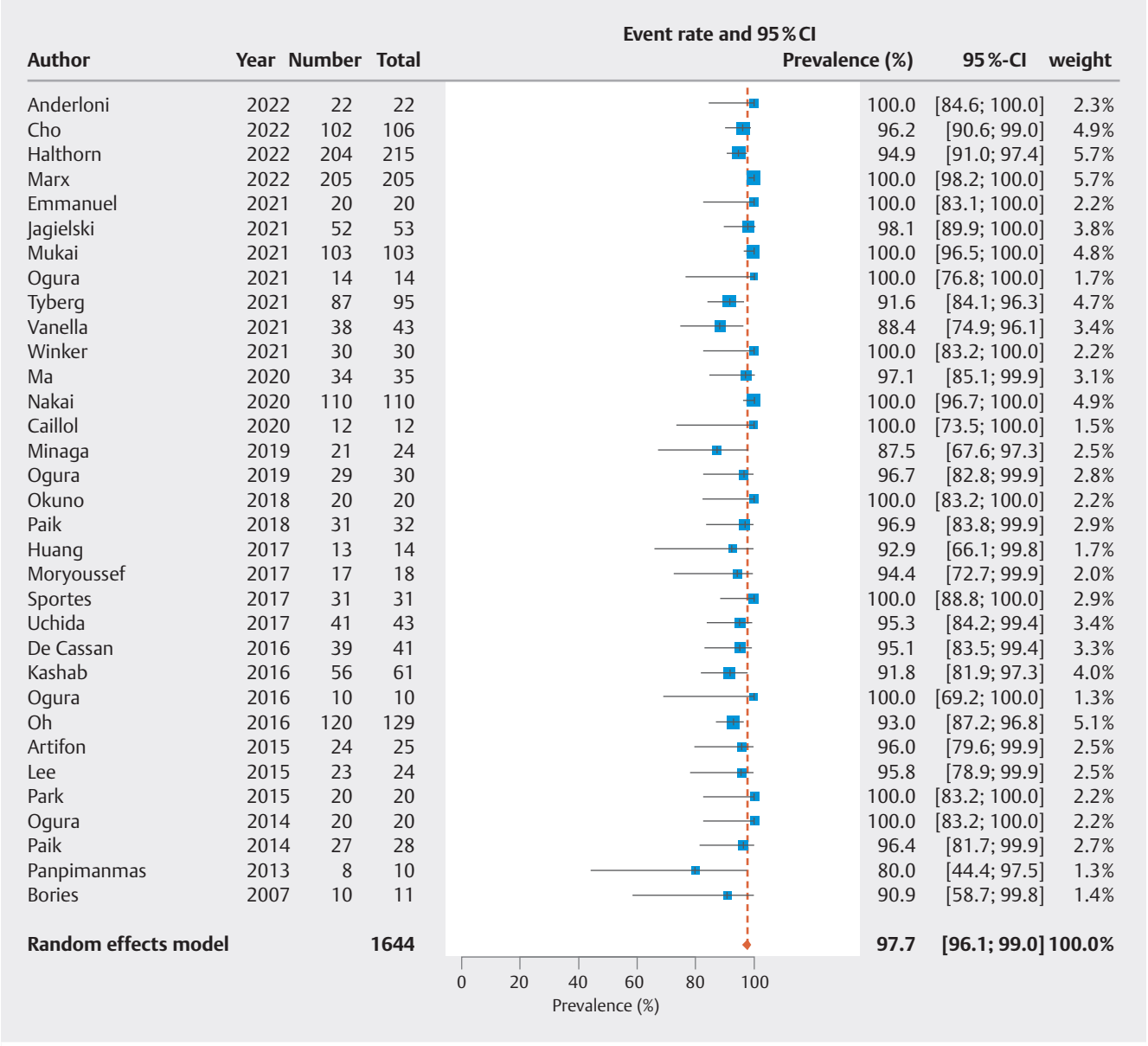
A total of 1460 articles were identified after the removal of duplicate records and, after assessment against the exclusion criteria, 1351 articles were rejected (▶ **Fig. 1**). The remaining 109 studies were assessed for eligibility, of which 76 were not included in the final analysis: in particular 14 studies were excluded because they were subsequently enlarged or included in larger multi-institutional analyses, 14 studies because they included <10 patients, and five studies because they combined HGS with antegrade stenting. Ultimately 33 studies, with 1644 patients, were included for the final analysis (**Table 1s**, see online-only Supplementary material). Among these, 13 were prospective studies, including five RCTs, and nine were multicenter studies. The overall quality of the included studies was deemed to be sufficient.

### Characteristics of included patients

From the 33 included studies, the mean age of the included patients varied from 57 [20] to 76 years [21] and the percentage of male patients from 40% [20] to 80% [22]. The cause of biliary obstruction was exclusively malignancy in 24 studies; in the remaining studies, malignant obstructions ranged from 60% [22] to 95% [23]. The proportion of patients with duodenal/papillary invasion and surgically altered anatomy ranged from 0% to 91% [20, 24] and 0% [20, 25, 26, 27] to 70% [28], respectively. The rate of patients with hilar stenosis was highly variable (0% [27, 29, 30, 31, 32, 33, 34] to 100% [20, 25, 26, 35, 36]). The transgastric approach was used exclusively in 24 studies, whereas the use of this approach ranged from 80% [21] to 97% [37] in the other studies; one study used only the transduodenal approach [38]. Pooled analysis of the clinical characteristics from the included studies is reported in ▶ **Table 1**.

### Meta-analyses of clinical outcomes

When evaluating the primary outcome, EUS-HGS showed a summary technical success of 97.7% (95%CI 96.1%–99.0%) (▶ **Fig. 2**), with no heterogeneity among studies ($I^2$ = 0%). The summary ITT and per-procedure clinical success rates were 88.1% (95%CI 84.7%–91.2%; $I^2$ = 33.9%) and 91.0% (95%CI 88.2%–93.3%; $I^2$ = 16.7%), respectively, with moderate-to-low heterogeneity among studies (▶ **Fig. 3**). Procedure-related AEs occurred at a summary rate of 12.0% (95%CI 9.8%–14.5%; $I^2$ = 20.4%) (▶ **Fig. 4**), with cholangitis/sepsis 2.8% (95%CI 1.5%–5.2%), bleeding 2.3% (95%CI 1.6%–3.3%), biliary leakage 1.6% (95%CI 0.9%–3.0%), and pneumoperitoneum 1.6% (95%CI 0.8%–3.0%) the most common (▶ **Table 2**). Procedure-related mortality was practically nil. The summary in-hospital stay was




▶ **Fig. 2** Forrest plots of meta-analysis for the technical success of endoscopic ultrasound-guided hepaticogastrostomy (EUS-HGS).

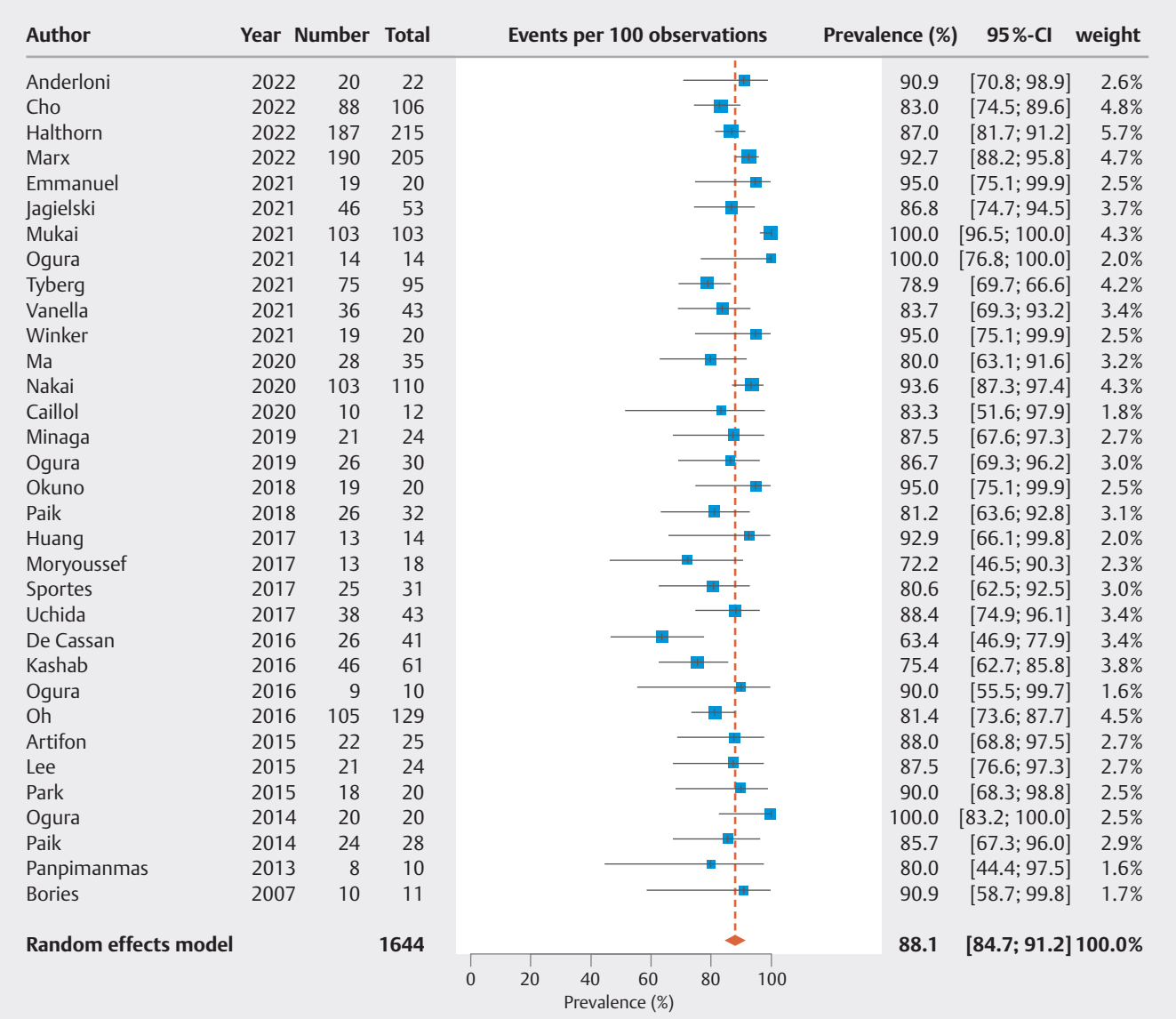
8.2 days (95%CI 5.3–11.0). Recurrence of biliary obstruction during follow-up occurred at a summary rate of 16.2% (95%CI 11.8%–21.8%), after a weighted mean time of 165 days (95%CI 115–195).

## Potential modifiers of the primary and secondary outcomes

Results from univariable meta-regression of studies and patients' features are reported in ▶ **Table 3**. On univariable meta-regression analysis, technical success was improved when centers had more experience (>4 cases/year; OR 2.12, 95%CI 1.23–3.67; $P=0.007$), in the presence of duodenal invasion (OR 6.56, 95%CI 1.18–36.4; $P=0.03$), and when dedicated HGS stents were used (OR 2.22, 95%CI 1.24–3.99; $P=0.007$). There was no evidence of publication bias for the primary outcome (Egger's test, $P=0.91$; Begg's test, $P=0.82$).

Regarding ITT clinical success, the only potential modifier identified was center experience (>4 cases/year), which was associated with an increased chance of clinical success (OR 1.47, 95%CI 1.01–2.13; $P=0.04$); this variable accounted for 11.5% of the heterogeneity found. No evidence of publication bias for this secondary outcome was found (Egger's test, $P=0.87$; Begg's test, $P=0.13$).

Finally, in terms of the rate of procedure-related AEs, the use of dedicated stents was the only variable associated with a reduced risk of AEs (OR 0.62, 95%CI 0.41–0.95; $P=0.03$) on univariable meta-regression analysis. There was no evidence of publication bias for this secondary outcome (Egger's test, $P=0.49$; Begg's test, $P=0.84$).




▶ **Fig. 3** Forrest plots of meta-analysis for the clinical success of EUS-HGS.

### Post-hoc sensitivity analysis

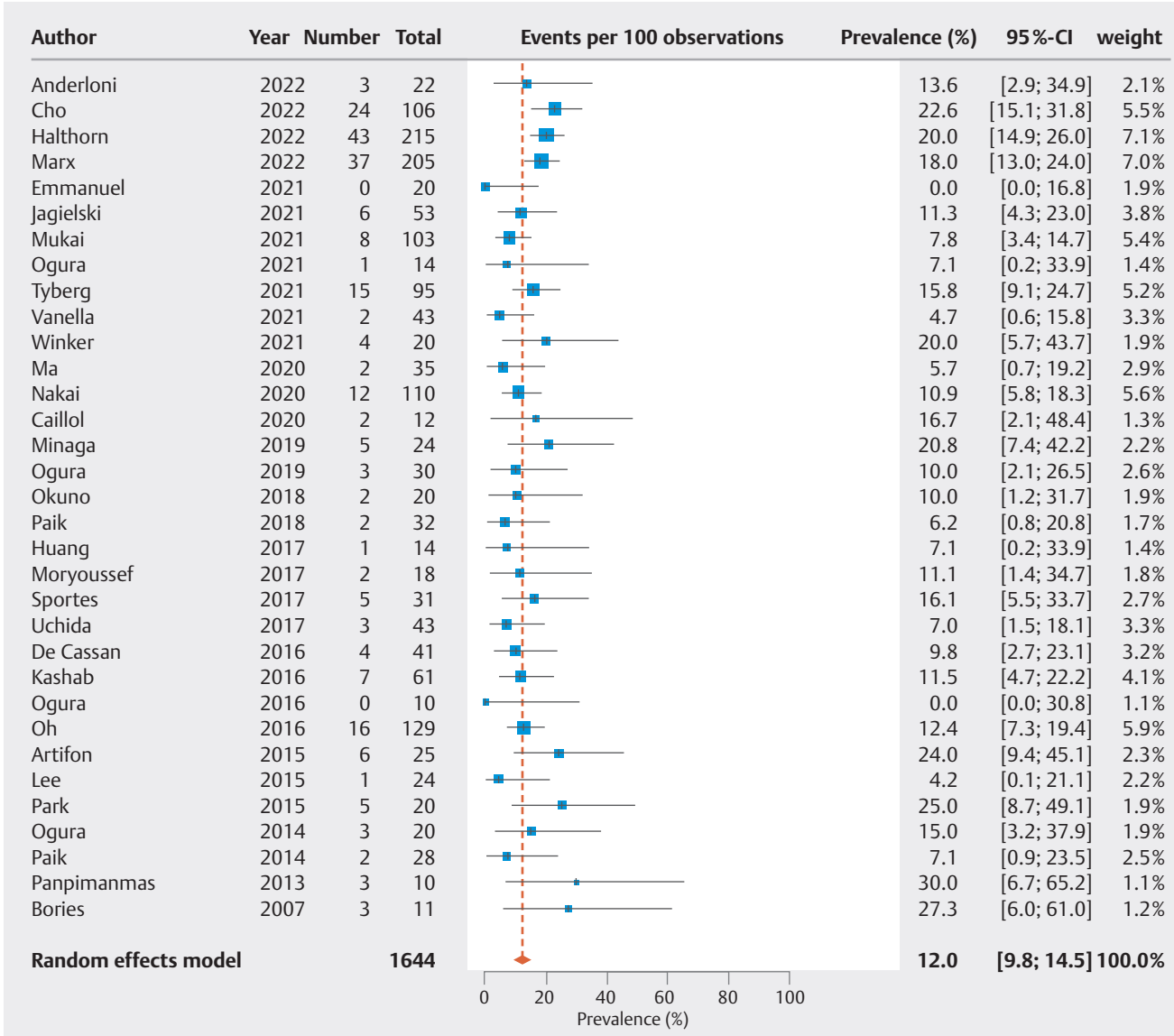
The post-hoc sensitivity analysis according to geographical area showed substantially overlapping results between studies performed in Asia, Europe, and North America (▶ **Table 4**). Of note, the number of studies conducted in North America was limited (n = 3).

More importantly, we performed a post-hoc sensitivity analysis separately evaluating studies where EUS-HGS was performed after 2015 vs. before 2015 and found that the rate of technical success was significantly higher in the former group (98.2% [95%CI 95.7%–99.2%] vs. 94.6% [95%CI 92.0%–96.3%]; $P$ = 0.02), as was the rate of clinical success (89.7% [95%CI 86.0%–92.5%] vs. 83.2% [95%CI 76.9%–88.0%]; $P$ = 0.04).

The post-hoc sensitivity analysis for studies using only metal stents or only a transgastric approach showed efficacy and safety overlapping with the overall estimates. When considering only dedicated stents, the rates of technical and clinical success were 99.1% (95%CI 97.3%–100%) and 88.0% (95%CI 81.8%–93.1%), respectively, while the complication rate was 10.7% (95%CI 6.6%–15.4%).

## Discussion

Since its introduction in 2003 [4, 5], EUS-HGS has been increasingly used for the relief of jaundice in patients affected by both distal and hilar MBO [6, 26]. We performed a meta-analysis to specifically investigate the efficacy and safety of EUS-HGS, followed by a meta-regression analysis in order to overcome the heterogeneity among the published studies and to identify potential modifiers of EUS-HGS outcomes. Our analysis showed that EUS-HGS has a high technical success rate 97.7% (95%CI 96.1%–99.0%; $I^2$ = 0%).




▶ **Fig. 4** Forrest plots of meta-analysis for adverse events of EUS-HGS.

Although this technique is currently considered very cumbersome, requiring a steep learning curve, the recent development of dedicated devices and improvement in procedural steps have allowed higher technical success rates to be achieved over the years[1, 29]. Indeed, when performed in expert hands, some technical tricks have been described to improve the success of the procedure: (i) dilation of the intrahepatic duct >5 mm with an interposed portion of hepatic parenchyma ≤3 cm is advisable; (ii) puncture of liver segment S3 is preferable over S2, because of the greater distance from the gastroesophageal junction, although puncture of S2 may allow an easier stent deployment; (iii) bile aspiration after intrahepatic puncture has been reported to reduce the rate of post-procedural AEs, such fever and abdominal pain[30]. Moreover, the choice of guidewire and its manipulation are crucial points, requiring a flexible tip to gain access and advance into the biliary tree, and adequate stiffness in order to easily advance the stent [39]. Last, but not least, in order to minimize the risk of stent misdeployment, the intrachannel release technique is recommended [40, 41].

Although high, the rate of clinical success was suboptimal, being 88.1% (95%CI 84.7%–91.2%; $I^2$ = 33.9%) and 91.0% (95% CI 88.2%–93.3%; $I^2$ = 16.7%) in the ITT and per-procedure analyses, respectively. When compared with other EUS-BD modalities, no significant differences in clinical success have been reported [42]. Regardless of the technique used, the achievement of clinical success may be affected by several patient and disease features, such as the presence of liver metastases and a complex hilar biliary stricture, although to date no clear correlations have been defined. As for other EUS-BD modalities [43], the future challenge will be to better define those patients who will substantially benefit from this type of treatment.

▶ **Table 2** Pooled analysis of clinical outcomes across the study population submitted to endoscopic ultrasound-guided hepaticogastrostomy.

| Outcome | Number of studies | Weighted analysis (95%CI) | $I^2$,%* | Cochrane's Q |
|---|---|---|---|---|
| Technical success, % | 33 | 97.7 (96.1–99.0) | 0 | 13.4 |
| Clinical success, % | | | | |
| ▪ Intention-to-treat | 33 | 88.1 (84.7–91.2) | 33.9 | 48.4 |
| ▪ Per-procedure | 33 | 91.0 (88.2–93.3) | 16.0 | 38.1 |
| Adverse events, % | | | | |
| ▪ Total (any) | 33 | 17.5 (14.7–20.8) | 30.8 | 46.2 |
| ▪ Total (prespecified) | 33 | 12.0 (9.8–14.5) | 20.4 | 40.2 |
| ▪ Pneumoperitoneum | 33 | 1.6 (0.8–3.0) | 0 | 17.2 |
| ▪ Biliary leakage/peritonitis | 33 | 1.6 (0.9–3.0) | 0 | 16.3 |
| ▪ Stent malfunction/migration | 33 | 1.3 (0.5–3.2) | 0 | 23.8 |
| ▪ Perforation | 33 | 0.1 (0.01–1.3) | 0 | 1.54 |
| ▪ Bleeding | 33 | 2.3 (1.6–3.3) | 0 | 14.8 |
| ▪ Cholangitis/sepsis | 33 | 2.8 (1.5–5.2) | 0 | 23.8 |
| Procedure-related mortality, % | 31 | 0.3 (0.06–1.7) | 0 | 1.6 |
| Hospital stay, days | 9 | 8.2 (5.3–11.0) | 97.5 | 325.9 |
| Any re-intervention, % | 28 | 16.2 (11.8–21.8) | 65.4 | 78.1 |
| Time to re-intervention, days | 14 | 165 (115–195) | 98.3 | 779.5 |

* $I^2$ describes the amount of heterogeneity resulting from meta-analysis. A rough guide to interpretation is: 0%–40%, might not be important; 30%–60%, may represent moderate heterogeneity; 50%–90%, may represent substantial heterogeneity; 75%–100%, considerable heterogeneity.

In our study, the overall rate of procedure-related AEs was 12.0% (95%CI 9.8%–14.5%; $I^2$ = 20.4%), mainly represented by cholangitis or sepsis, bleeding, biliary leakage, and pneumoperitoneum. Although not negligible, the overall rate of AEs is lower than for PTBD [3], while it is similar when compared with other EUS-BD techniques [42]. Indeed, despite high technical and clinical success rates, previous studies and meta-analyses have reported that PTBD is associated with higher rates of AEs and need for re-intervention than EUS-BD, mainly owing to an increased risk of stent dysfunction and stent dislodgement [3]. Moreover, the presence of an external catheter has been associated with abdominal pain at the insertion site and with lower quality of life [44].

When comparing EUS-CDS and EUS-HGS, there is actually no evidence of the superiority of one over the other in terms of technical success, clinical success, or AEs [45]; however, although the overall rate of complications is comparable, differences have been reported in the types of AEs. In a meta-analysis by Uemura and colleagues, higher rates of cholangitis were shown for EUS-CDS than for EUS-HGS (31% vs. 10% of AEs, respectively) [46]; however, other studies have not confirmed the same results [42]. In our analysis, the rate of cholangitis was relatively low at 2.8% (95%CI 1.5%–5.2%), comparable with previous studies and to the rate reported with ERCP [45].

Minimizing the rate of cholangitis is particularly important as it strongly impacts on oncologic outcomes and patient survival [47]. Stent patency is therefore crucial, generally defined as the time from stent deployment to stent dysfunction, and usually indicated by the time to re-intervention. Because the stent is generally far away from the MBO, EUS-HGSs have been assumed to have a lower risk of obstruction from tumor ingrowth/overgrowth; however, obstruction by clogging, by food, or by reactive tissue has been described [48]. In our analysis, the pooled incidence of recurrence of biliary obstruction was 16.2% (95%CI 11.8%–21.8%), after a weighted mean time of 165 days (95%CI 115–195). Our data are slightly lower than those reported in a recent meta-analysis, in which the rate of re-intervention for EUS-HGS was 20.9% (95%CI 16.3%–25.6%), being higher than that reported for EUS-CDS (15.8%, 95%CI 12.2%–19.5%) [42]. A subgroup meta-analysis from Mao et al. considering only fully covered SEMSs for EUS-HGS showed no significant difference in stent obstruction and re-intervention compared with EUS-CDS (OR 0.25, 95%CI 0.25–1.34; $P$ = 0.11; $I^2$ = 0%) [49]. According to recent data, an intragastric portion of the stent with a length of >3 cm and chemotherapy seem to be associated with a longer median stent patency [39].

The procedure-related mortality rate is our study was close to zero. This result is in line with the meta-analysis by Giri et al., which reported a pooled mortality incidence related to EUS-HGS of 0.2% (95%CI 0.0–0.5%) and of 0.1% (95%CI 0.0–0.4%) related to EUS-BD overall [42].

▶ **Table 3** Results from univariable meta-regression of the main outcomes considered.

| | Odds ratio (95%CI) | | |
|---|---|---|---|
| | **Technical success** | **Clinical success on ITT analysis** | **Procedure-related adverse events** |
| Study characteristics | | | |
| ▪ Publication year | 1.05 (0.97–1.13) | 1.06 (0.98–1.14) | 1.00 (0.94–1.06) |
| ▪ Prospective/RCT | 1.02 (0.6–1.75) | 1.06 (0.65–1.72) | 0.93 (0.61–1.41) |
| Center characteristics | | | |
| ▪ Procedures/year >4 | 2.12 (1.23–3.67) | 1.47 (1.01–2.13) | 0.74 (0.45–1.24) |
| Patient characteristics | | | |
| ▪ Sex, male | 3.13 (0.16–61.9) | 1.27 (0.10–15.8) | 0.11 (0.01–1.02) |
| ▪ Age | 1.03 (0.96–1.10) | 1.03 (0.97–1.09) | 1.00 (0.96–1.05) |
| ▪ Malignancy | 0.88 (0.14–5.49) | 0.88 (0.11–6.84) | 1.11 (0.26–4.71) |
| ▪ Surgically altered anatomy | 0.77 (0.20–2.88) | 0.69 (0.20–2.44) | 0.82 (0.29–2.37) |
| ▪ Hilar stenosis | 0.75 (0.27–2.08) | 0.71 (0.30–1.69) | 1.30 (0.64–2.64) |
| ▪ Duodenal invasion | 6.56 (1.18–36.4) | 2.62 (0.75–9.09) | 0.50 (0.18–1.36) |
| ▪ Ascites | 19.2 (0.06–6654) | 0.63 (0.02–25.4) | 0.08 (0.01–1.11) |
| Procedure details | | | |
| ▪ Use of dedicated stents | 2.22 (1.24–3.99) | 1.31 (0.79–2.19) | 0.62 (0.41–0.95) |
| ▪ Transgastric puncture/drainage | 0.58 (0.09–3.86) | 1.28 (0.43–3.85) | 1.00 (0.94–1.06) |

ITT, intention to treat; RCT, randomized controlled trial.
Results in bold indicate significant results ($P < 0.05$).

▶ **Table 4** Results of the post-hoc sensitivity analyses.

| | Number of studies | Percentage rate (95%CI) | | |
|---|---|---|---|---|
| | | **Technical success** | **Clinical success** | **Procedure-related adverse events** |
| Overall | 33 | 97.7 (96.1–99.0) | 88.1 (84.7–91.2) | 12.0 (9.8–14.5) |
| Region | | | | |
| ▪ Asia | 19 | 97.4 (95.0–98.7) | 90.5 (86.1–93.4) | 10.7 (7.9–14.2) |
| ▪ Europe | 10 | 98.4 (94.3–99.6) | 85.4 (78.4–90.4) | 14.4 (10.6–19.3) |
| ▪ Northern America | 3 | 94.4 (91.1–96.5) | 84.0 (77.0–89.2) | 18.6 (14.6–23.4) |
| Study year | | | | |
| ▪ Before 2015 | 14 | 94.6 (92.0–96.3) | 83.2 (76.9–88.0) | 13.1 (10.3–16.6) |
| ▪ After 2015 | 19 | 98.2 (95.7–99.2) | 89.7 (86.0–92.5) | 12.3 (9.5–15.9) |
| Procedure details | | | | |
| ▪ Only metal stents | 25 | 98.2 (96.7–99.3) | 87.9 (84.5–90.9) | 12.1 (9.2–15.3) |
| ▪ Only dedicated stents | 11 | 99.1 (97.3–100) | 88.0 (81.8–93.1) | 10.7 (6.6–15.4) |
| ▪ Only transgastric puncture | 24 | 97.3 (95.5–98.8) | 86.7 (83.0–90.1) | 12.3 (9.8–14.9) |

Interestingly, on meta-regression analysis, center experience (>4 cases/year) was found to be an independent modifier of both technical and clinical success. This threshold could be considered low for such a challenging technique; however, published data come mainly from referral centers, with highly skilled endoscopists. Moreover, over the years, the advancement of technical skills and the introduction of dedicated devices may have positively affected both the learning curve and patient selection. According to Oh et al., the procedure time shortened and the AE rate decreased after at least 24 overall procedures had been performed, reaching a plateau after 33 procedures [50]. In contrast, a later study reported a number of approximately 40 procedures to gain adequate experience in EUS-HGS [51]. All these data highlight how the learning curve to achieve proper expertise may be long and needs to be maintained over the years. To achieve this, centralization of such cases to expert hands in referral centers is mandatory, in order to optimize outcomes.

Duodenal invasion was also associated with higher technical success. This may be because duodenal obstruction is usually an expression of distal MBO. Although to date there have been no studies comparing the outcomes of EUS-HGS in patients with distal versus hilar MBO, it is reasonable to believe that the latter may be technically more challenging. In patients with distal MBO, EUS-CDS may be a valuable alternative for the relief of jaundice; however, emerging evidence supports the use of EUS-HGS in patients with combined distal MBO and gastric outlet obstruction, owing to the lower stent dysfunction rate of EUS-HGS compared with EUS-CDS; indeed duodenal invasion may be predictive of EUS-CDS dysfunction [52].

Finally, on meta-regression analysis, the use of dedicated stents was found to positively affect technical success and was the only variable associated with a reduced risk of procedure-related AEs (OR 0.62, 95%CI 0.41–0.95; $P=0.03$). Dedicated stents are partially covered metal stents, with an uncovered portion of variable length for intraductal drainage, and a fully covered part for the extrahepatic and intragastric portion; in addition, importantly, these devices are fitted with antimigration systems (i.e. anchoring flaps, asymmetric flared shape) [22]. Such hybrid stents aim to overcome the main limitations of uncovered and fully covered SEMSs, such as the risk of bile leakage, intrahepatic bile duct obstruction, and migration. On a post-hoc sensitivity analysis, the results when considering only dedicated stents were extremely satisfying, being 99.1% and 88.0% for technical and clinical success, respectively, while the complication rate was 10.7%.

Newly designed plastic stents specifically designed for EUS-HGS have also now been developed, which showing promising results, representing a valuable alternative to metal stents, especially when EUS-HGS is performed for benign indications [53, 54]. Our meta-regression did not show any superiority of metal stents over plastic ones. This may be due to the fact that the mean follow-up of the included studies was short (<6 months), affecting the reliability of this result on long-term outcomes.

Our post-hoc sensitivity analysis confirmed that the outcomes of EUS-HGS were superior for studies published after 2015, a landmark year for standardization of the technique and the availability of dedicated devices. Therefore, in the near future, the use of these dedicated devices should be recommended, as they increase the safety of this challenging procedure. As happened in recent years with lumen-apposing metal stents (LAMSs), the development of systems that may reduce the number of steps in the procedure (e.g. the integrated cystotome) is desirable.

The present study has some limitations. First, most of the studies were retrospective or non-randomized, which could lead to a lack of information regarding the stent design and technical issues, such as the length of the intragastric portion, and to selection bias. Moreover, the short follow-up period does not allow conclusions to be drawn on long-term outcomes, such as stent patency, this being beyond the aim of the current analysis. Second, some of the main results, such as the use of metal stents during EUS-HGS, the re-intervention rate, and the time to re-intervention, showed significant heterogeneity. Clinical success on ITT analysis and total AEs also showed moderate heterogeneity. The definitions of outcomes were variable among the studies and some issues, such as the use of chemotherapy and overall patient survival, were not included, thereby limiting the interpretation of the results as to the real efficacy of EUS-HGS. Finally, our meta-regression analysis was limited to those variables that have a plausibility to influence the clinical outcomes and had been commonly reported among most of the studies; however, it is likely that other known and unknown factors can influence the efficacy and safety of HGS and these aspects should be addressed by future prospective studies.

In conclusion, where ERCP and EUS-CDS are not feasible, EUS-HGS is a safe and effective procedure when performed in an expert setting. The development and spread of dedicated devices will positively affect the safety of the procedure going forward.

## Conflict of Interest

The authors declare that they have no conflict of interest.

## References


[1] Hedjoudje A, Sportes A, Grabar S et al. Outcomes of endoscopic ultrasound-guided biliary drainage: A systematic review and meta-analysis. United European Gastroenterol J 2019; 7: 60–68 doi:10.1177/2050640618808147

[2] Dumonceau JM, Tringali A, Papanikolaou IS et al. Endoscopic biliary stenting: indications, choice of stents, and results: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline – Updated October 2017. Endoscopy 2018; 50: 910–930 doi:10.1055/a-0659-9864

[3] Lee TH, Choi JH, Park do H et al. Similar efficacies of endoscopic ultrasound-guided transmural and percutaneous drainage for malignant distal biliary obstruction. Clin Gastroenterol Hepatol 2016; 14: 1011–1019.e3

[4] Burmester E, Niehaus J, Leineweber T et al. EUS-cholangio-drainage of the bile duct: report of 4 cases. Gastrointest Endosc 2003; 57: 246–251 doi:10.1067/mge.2003.85

[5] Giovannini M, Dotti M, Bories E et al. Hepaticogastrostomy by echo-endoscopy as a palliative treatment in a patient with metastatic biliary obstruction. Endoscopy 2003; 35: 1076–1078

[6] Paik WH, Park DH. Outcomes and limitations: EUS-guided hepaticogastrostomy. Endosc Ultrasound 2019; 8: S44–S49 doi:10.4103/eus.eus_51_19

[7] Nakai Y, Sato T, Hakuta R et al. Long-term outcomes of a long, partially covered metal stent for EUS-guided hepaticogastrostomy in patients with malignant biliary obstruction (with video). Gastrointest Endosc 2020; 92: 623–631.e1

[8] Anderloni A, Fugazza A, Spadaccini M et al. Single-session EUS-guided gastroenterostomy and hepaticogastrostomy using dedicated metal stents (with videos). Endosc Ultrasound 2021; 10: 214–215

[9] Minaga K, Ogura T, Shiomi H et al. Comparison of the efficacy and safety of endoscopic ultrasound-guided choledochoduodenostomy and hepaticogastrostomy for malignant distal biliary obstruction: Multicenter, randomized, clinical trial. Dig Endosc 2019; 31: 575–582 doi:10.1111/den.13406

[10] van Houwelingen HC, Arends LR, Stijnen T. Advanced methods in meta-analysis: multivariate approach and meta-regression. Stat Med 2002; 21: 589–624 doi:10.1002/sim.1040

[11] Brooke BS, Schwartz TA, Pawlik TM. MOOSE reporting guidelines for meta-analyses of observational studies. JAMA Surg 2021; 156: 787–788 doi:10.1001/jamasurg.2021.0522

[12] Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71 doi:10.1136/bmj.n71

[13] Higgins JP, Altman DG, Gøtzsche PC et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343: d5928 doi:10.1136/bmj.d5928

[14] Wells GA, Shea B, O'Connell D et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses – 2008. Accessed March 28, 2024: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

[15] Freeman MF, Tukey JW. Transformations related to the angular and the square root. Ann Math Stat 1950; 21: 607–611

[16] Wan X, Wang W, Liu J et al. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014; 14: 135 doi:10.1186/1471-2288-14-135

[17] Higgins JP, Thompson SG, Deeks JJ et al. Measuring inconsistency in meta-analyses. BMJ 2003; 327: 557–560 doi:10.1136/bmj.327.7414.557

[18] Egger M, Davey Smith G, Schneider M et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997; 315: 629–634

[19] Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994; 50: 1088–1101

[20] Panpimanmas S, Ratanachu-ek T. Endoscopic ultrasound-guided hepaticogastrostomy for advanced cholangiocarcinoma after failed stenting by endoscopic retrograde cholangiopancreatography. Asian J Surg 2013; 36: 154–158 doi:10.1016/j.asjsur.2013.04.007

[21] Ogura T, Chiba Y, Masuda D et al. Comparison of the clinical impact of endoscopic ultrasound-guided choledochoduodenostomy and hepaticogastrostomy for bile duct obstruction with duodenal obstruction. Endoscopy 2016; 48: 156–163 [published correction appears in Endoscopy 2016; 48: 163] doi:10.1055/s-0034-1392859

[22] Mukai S, Itoi T, Sofuni A et al. Urgent and early EUS-guided biliary drainage in patients with acute cholangitis. Endosc Ultrasound 2021; 10: 191–199

[23] De Cassan C, Bories E, Pesenti C et al. Use of partially covered and uncovered metallic prosthesis for endoscopic ultrasound-guided hepaticogastrostomy: Results of a retrospective monocentric study. Endosc Ultrasound 2017; 6: 329–335 doi:10.4103/2303-9027.209869

[24] Jagielski M, Zieliński M, Piątkowski J et al. Outcomes and limitations of endoscopic ultrasound-guided hepaticogastrostomy in malignant biliary obstruction. BMC Gastroenterol 2021; 21: 202

[25] Ogura T, Sano T, Onda S et al. Endoscopic ultrasound-guided biliary drainage for right hepatic bile duct obstruction: novel technical tips. Endoscopy 2015; 47: 72–75 doi:10.1055/s-0034-1378111

[26] Winkler J, Caillol F, Ratone JP et al. Feasibility of EUS-guided hepaticogastrostomy for inoperable malignant hilar biliary strictures. Endosc Ultrasound 2021; 10: 51–56 doi:10.4103/eus.eus_68_20

[27] Artifon EL, Marson FP, Gaidhane M et al. Hepaticogastrostomy or choledochoduodenostomy for distal malignant biliary obstruction after failed ERCP: is there any difference? Gastrointest Endosc 2015; 81: 950–959 doi:10.1016/j.gie.2014.09.047

[28] Huang P, Zhang H, Zhang XF et al. Comparison of endoscopic ultrasonography guided biliary drainage and percutaneous transhepatic biliary drainage in the management of malignant obstructive jaundice after failed ERCP. Surg Laparosc Endosc Percutan Tech 2017; 27: e127–e131 [published correction appears in Surg Laparosc Endosc Percutan Tech 2018; 28: 133] doi:10.1097/SLE.0000000000000485

[29] Ogura T, Higuchi K. Endoscopic ultrasound-guided hepaticogastrostomy: technical review and tips to prevent adverse events. Gut Liver 2021; 15: 196–205 doi:10.5009/gnl20096

[30] Fugazza A, Colombo M, Spadaccini M et al. Relief of jaundice in malignant biliary obstruction: When should we consider endoscopic ultrasonography-guided hepaticogastrostomy as an option? Hepatobiliary Pancreat Dis Int 2022; 21: 234–240

[31] Minaga K, Ogura T, Shiomi H et al. Comparison of the efficacy and safety of endoscopic ultrasound-guided choledochoduodenostomy and hepaticogastrostomy for malignant distal biliary obstruction: Multicenter, randomized, clinical trial. Dig Endosc 2019; 31: 575–582 doi:10.1111/den.13406

[32] Okuno N, Hara K, Mizuno N et al. Efficacy of the 6-mm fully covered self-expandable metal stent during endoscopic ultrasound-guided hepaticogastrostomy as a primary biliary drainage for the cases estimated difficult endoscopic retrograde cholangiopancreatography: A prospective clinical study. J Gastroenterol Hepatol 2018; 33: 1413–1421

[33] Sportes A, Camus M, Greget M et al. Endoscopic ultrasoundguided hepaticogastrostomy versus percutaneous transhepatic drainage for malignant biliary obstruction after failed endoscopic retrograde cholangiopancreatography: A retrospective expertisebased study from two centers. Therap Adv Gastroenterol 2017; 10: 483–493

[34] Khashab MA, Valeshabad AK, Afghani E et al. A comparative evaluation of EUS-guided biliary drainage and percutaneous drainage in patients with distal malignant biliary obstruction and failed ERCP. Dig Dis Sci 2015; 60: 557–565

[35] Caillol F, Rouy M, Pesenti C et al. Drainage of the right liver using EUS guidance. Endosc Ultrasound 2019; 8: (Suppl. 01): S50–S56 doi:10.4103/eus.eus_52_19

[36] Moryoussef F, Sportes A, Leblanc S et al. Is EUS-guided drainage a suitable alternative technique in case of proximal biliary obstruction? Ther Adv Gastroenterol 2017; 10: 537–544 doi:10.1177/1756283X17702614

[37] Ogura T, Nishioka N, Miyano A et al. Endoscopic ultrasound-guided hepaticogastrostomy combined with antegrade stenting using a double bare covered metal stent. Endoscopy 2019; 51: E24–E25

[38] Ma KW, So H, Cho DH et al. Durability and outcome of endoscopic ultrasound-guided hepaticoduodenostomy using a fully covered metal stent for segregated right intrahepatic duct dilatation. J Gastroenterol Hepatol 2020; 35: 1753–1760 doi:10.1111/jgh.15089

[39] Park DH. Endoscopic ultrasound-guided biliary drainage of hilar biliary obstruction. J Hepatobiliary Pancreat Sci 2015; 22: 664–668 doi:10.1002/jhbp.271

[40] Paik WH, Park DH, Choi JH et al. Simplified fistula dilation technique and modified stent deployment maneuver for EUS-guided hepaticogastrostomy. World J Gastroenterol 2014; 20: 5051–5059 doi:10.3748/wjg.v20.i17.5051

[41] Miyano A, Ogura T, Yamamoto K et al. Clinical impact of the intrascope channel stent release technique in preventing stent migration during EUS-guided hepaticogastrostomy. J Gastrointest Surg 2018; 22: 1312–1318

[42] Giri S, Mohan BP, Jearth V et al. Adverse events with endoscopic ultrasound-guided biliary drainage: a systematic review and meta-analysis. Gastrointest Endosc 2023; 98: 515–523.e18 doi:10.3390/cancers15112988

[43] Fabbri C, Binda C, Sbrancia M et al. Determinants of outcomes of transmural EUS-guided gallbladder drainage: systematic review with proportion meta-analysis and meta-regression. Surg Endosc 2022; 36: 7974–7985

[44] Barkay O, Mosler P, Schmitt CM et al. Effect of endoscopic stenting of malignant bile duct obstruction on quality of life. J Clin Gastroenterol 2013; 47: 526–531

[45] Miller CS, Barkun AN, Martel M et al. Endoscopic ultrasound-guided biliary drainage for distal malignant obstruction: a systematic review and meta-analysis of randomized trials. Endosc Int Open 2019; 7: E1563–E1573 doi:10.1055/a-0998-8129

[46] Uemura RS, Khan MA, Otoch JP et al. EUS-guided choledochoduodenostomy versus hepaticogastrostomy: a systematic review and meta-analysis. J Clin Gastroenterol 2018; 52: 123–130 doi:10.1097/MCG.0000000000000948

[47] Dumonceau JM, Kapral C, Aabakken L et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2020; 52: 127–149 doi:10.1055/a-1075-4080

[48] Ishiwatari H, Ishikawa K, Niiya F et al. Endoscopic ultrasound-guided hepaticogastrostomy versus hepaticogastrostomy with antegrade stenting for malignant distal biliary obstruction. J Hepatobiliary Pancreat Sci 2022; 29: 703–712

[49] Mao K, Hu B, Sun F et al. Choledochoduodenostomy Versus Hepaticogastrostomy in Endoscopic Ultrasound-guided Drainage for Malignant Biliary Obstruction: A Meta-analysis and Systematic Review. Surg Laparosc Endosc Percutan Tech 2021; 32: 124–132 doi:10.1097/SLE.0000000000000992

[50] Oh D, Park DH, Song TJ et al. Optimal biliary access point and learning curve for endoscopic ultrasound-guided hepaticogastrostomy with transmural stenting. Therap Adv Gastroenterol 2017; 10: 42–53

[51] James TW, Baron TH. Practical applications and learning curve for EUS-guided hepaticoenterostomy: results of a large single-center US retrospective analysis. Endosc Int Open 2019; 7: E600–E607 doi:10.1055/a-0867-9599

[52] Vanella G, Bronswijk M, van Wanrooij RL et al. Combined endoscopic mAnagement of BiliaRy and gastrIc OutLET obstruction (CABRIOLET Study): A multicenter retrospective analysis. DEN Open 2022; 3: e132 doi:10.1002/deo2.132

[53] Kitagawa K, Mitoro A, Minami R et al. Efficacy of a dedicated plastic stent in endoscopic ultrasound-guided hepaticogastrostomy during the learning curve: cumulative multi-center experience. Scand J Gastroenterol 2023; 58: 296–303

[54] Ohno A, Fujimori N, Kaku T et al. Feasibility and efficacy of endoscopic ultrasound-guided hepaticogastrostomy without dilation: a propensity score matching analysis. Dig Dis Sci 2022; 67: 5676–5684