—Original Article—

EUS-guided hepaticogastrostomy in patients with obstructive jaundice after failed or impossible endoscopic retrograde drainage: A multicenter, randomized phase II Study

Mariola Marx[1], Fabrice Caillol[1], Aurélie Autret[2], Jean-Philippe Ratone[1], Christophe Zemmour[2], Jean Marie Boher[2], Christian Pesenti[1], Erwan Bories[1], Marc Barthet[3], Bertrand Napoléon[4], Marc Giovannini[1]

[1]Division of Gastroenterology, Paoli-Calmettes Institute, Marseille, France; [2]Division of Biostatistics, Paoli-Calmettes Institute, Marseille, France; [3]Division of Gastroenterology and Hepatology, Hôpital Nord, Marseille, France; [4]Division of Gastroenterology and Hepatology, Hôpital Jean Mermoz, Lyon, France

ABSTRACT

Background and Objectives: Over the last two decades, EUS-guided hepaticogastrostomy (EUS-HGS) has emerged as a therapeutic alternative for patients with biliary obstruction and failed ERCP. Percutaneous transhepatic biliary drainage (PTBD) as the gold standard is associated with relevant morbidity and need for re-intervention. The aim of our work was to evaluate in a phase II study the safety and efficacy profile of EUS-HGS. A PTBD arm was considered a control group. **Patients and Methods:** We conducted a prospective, randomized, noncomparative phase II study in three French tertiary centers involving patients with benign or malignant obstructive jaundice after failure of ERCP. Patients were randomized to either PTBD or EUS-HGS. **Results:** Fifty-six patients (mean age 64 years) have been included between 2011 and 2015. Twenty-one underwent PTBD and thirty-five were drained using EUS-HGS. An interim analysis after the inclusion of 41 patients revealed an unexpected high 30-day morbidity rate for PTBD (13 out of 21 patients), justifying to stop randomization and inclusion in this control arm in 2013. The primary objective was reached with 10 out of the 35 EUS-HGS patients (28.6%) having observed complications (90%-level bilateral exact binomial confidence interval [CI] [16.4%–43.6%], left-sided exact binomial test to the objectified 50% unacceptable rate $P = 0.0083$). Both methods achieved comparable technical success rate (TSR) and clinical success rate (CSR) (TSR: PTBD 100% *vs.* EUS-HGS 94.3%, $P = 0.28$; CSR: PTBD 66.7% *vs.* EUS-HGS 80%, $P = 0.35$). Long-term follow-up showed EUS-HGS patients being at lower risk for re-intervention (relative risk = 0.47, 95% CI [0.27–0.83]). **Conclusion:** In cases of ERCP failure, EUS-HGS is a valuable alternative for biliary drainage with a high TSR and CSR. PTBD is associated with an unacceptable 30-day morbidity rate, whereas EUS-HGS seems to have a decent safety profile, suggesting that it may be the treatment of choice in appropriately selected patients.

Key words: biliary stenting, EUS, hepaticogastrostomy, obstructive jaundice, percutaneous transhepatic biliary drainage

Access this article online

Quick Response Code:

Website: www.eusjournal.com

DOI: 10.4103/EUS-D-21-00108

How to cite this article: Marx M, Caillol F, Autret A, Ratone JP, Zemmour C, Boher JM, *et al*. EUS-guided hepaticogastrostomy in patients with obstructive jaundice after failed or impossible endoscopic retrograde drainage: A multicenter, randomized phase II Study. Endosc Ultrasound 2022;11:495-502.

Address for correspondence

Dr. Mariola Marx, Division of Gastroenterology, Paoli-Calmettes Institute, Marseille, France.

E-mail: mariolamarx@gmx.de

Received: 2021-04-19; **Accepted:** 2022-04-24; **Published online:** 2022-10-05

INTRODUCTION

Biliary stenting by ERCP is the recommended palliative treatment for malignant biliary obstruction.[1] However, this classical retrograde access fails in 5%–20% when papillary cannulation turns out to be technically difficult or if the papilla cannot be reached because of ampullary or duodenal tumor infiltration, an indwelling duodenal stent, or altered anatomy due to previous surgery such as gastrectomy or Whipple procedure.[2,3] Percutaneous transhepatic biliary drainage (PTBD) is an accepted and efficient salvage strategy with a complication rate of about 20% - 30%.[4] Regarding costs, high morbidity and mortality rates as well as quality of life, biliary decompression by surgical anastomosis became nowadays a less important alternative, especially in palliative situations.[5,6]

EUS-guided biliary drainage (EUS-BD) is a progressing and increasingly used method, creating a transduodenal (EUS-guided choledochoduodenostomy [EUS-CDS]) or transgastric (EUS-guided hepaticogastrostomy [EUS-HGS]) bypass to the common bile duct or the left intrahepatic duct.[7-9] In the context of duodenal obstruction or altered anatomy, transgastric access by EUS-HGS is often the preferred and only feasible endoscopic treatment option. However, it remains one of the most complex therapeutic EUS interventions. Despite growing global experience and a good cumulative technical success rate (TSR) and clinical success rate (CSR) of 95% and 92%, respectively, only a few studies tried to evaluate or compare the safety and efficacy of EUS-BD to PTBD as second-line therapy after failed ERCP.[10-18] Meta-analysis of these data indicates that EUS-BD may be associated with a decreased risk of procedure-related complications and re-interventions whereas demonstrating equal or better functional success rates when compared to PTBD.[19-21]

The principal aim of our work was to evaluate in a prospective randomized phase II study the postprocedural safety profile during the 1st month after EUS-HGS in patients with obstructive jaundice after failed ERCP or inaccessibility of the papilla.

PATIENTS AND METHODS

Study setting

We conducted a controlled, randomized, prospective, noncomparative phase II trial in three different French centers with tertiary referral function. The randomization ratio was 1:1 with stratification by indication, benign versus malignant, and by center. Permutation block sizes were sampled among 4 or 6. The method of BD was randomized as PTBD (Group A, control arm) and EUS-HGS (Group B, experimental arm).

Patients

Patients of 18–80 years of age were eligible for inclusion if they had obstructive jaundice due to a benign or malignant stenosis of the common or left bile duct with impossible retrograde BD due to failed biliary cannulation or inaccessible papilla. ERCP using a double-balloon enteroscope was not attempted. The Karnofsky index had to be equal or superior to 50%. Diagnoses were confirmed by cross-section imaging and biochemical analysis. We obtained informed consent from all patients after the discussion of risks, alternatives, and benefits of both techniques, EUS-HGS and PTBD. The study was approved by our institutional review board (NCT01499537).

The exclusion criteria were an isolated stenosis of the right bile duct or a concomitant stenosis of the right bile duct if not drained before, previous PTBD or laparotomy 10 days prior to randomization, presence of ascites, coagulation disorder, or imperative anticoagulation/antithrombotic therapy that could not be stopped for intervention.

Study endpoints

The primary endpoint of our study was the morbidity rate 1 month after BD, defined as occurrence of at least one procedure-related complication. Adverse events were classified according to the Common Terminology Criteria for Adverse Events (v 4.0), but not divided into early and late complications.

Technical feasibility and efficacy were considered the secondary endpoints: the technical success was defined as correct bile duct puncture with stent or drain placement confirmed by fluoroscopy, while clinical success was indicated by a >50% decrease of the plasma bilirubin level after 15 days. Further secondary outcomes were procedure-related death, length of hospital stay, and time to the removal of external BD.

Long-term survival and the need for additional interventions in case of recurrent biliary obstruction after the index procedure have been assessed

retrospectively. For these analyses, patients with benign stenosis have been excluded.

Procedures

Procedures have been described in our previous publications. Some details regarding the protocol have to be specified.[8,22-24]

EUS-guided hepaticogastrostomy

EUS-HGS was performed under general anesthesia in the supine position with combined fluoroscopic and ultrasound guidance using a curved linear array echoendoscope (EG3830UT, ED-3490TK). All procedures were done with CO2 insufflation. The tip of the echoendoscope and the inflated balloon were positioned in the middle part of the lesser curvature of the stomach. After exclusion of intervening vessels by color flow Doppler, the distal part of the left hepatic bile duct was punctured with a 19G needle (EchoTip® Access Needle, Cook® Ireland Ltd., Limerick, Ireland). Bile was aspirated to confirm correct positioning within the bile duct. Then, we injected contrast dye to obtain a cholangiogram. Next, the needle was exchanged over a 0.035" guidewire (Jagwire™, Boston Scientific®, USA). A 6-Fr cystotome (Endo-Flex®, Voerde, Germany) allowed enlargement and coagulation of the needle tract. Finally, we deployed a dedicated 8- or 10-cm partially covered metal stent in the left hepatic bile duct (70% covered and 30% uncovered; GIOBOR™ biliary stent, Taewoong Medical, Korea).

To reduce the risk of bile leak, a 6- or 7-Fr nasobiliary drain (Cook Medical®) was attempted to place at the end of the procedure. Removal was scheduled after 48 h.

All procedures were performed by experienced endoscopists. A dose of prophylactic broad-spectrum antibiotic was given during or just after the procedure. Patients were admitted for overnight observation to monitor early complications.

Percutaneous transhepatic biliary drainage

Ultrasound-guided puncture of the biliary tree was performed with a Chiba needle (Neff percutaneous, 21 G) using an access set with a hydrophilic coating and a nitinol guidewire and catheter (Cook Medical®). A cholangiogram was obtained by contrast dye injection. Then, we changed for a hydrophilic guidewire (Jagwire™ 0.035", Boston Scientific®) which was placed in the intrahepatic bile ducts. If the guidewire passed the malignant stenosis, a self expandable metallic stent was deployed, followed by an additional 8.5Fr external plastic drain. In cases of an impassable stenosis, we placed an external 8.5-Fr drain in the intrahepatic biliary ducts. A few days later, we performed a second attempt to deploy an internal stent, once the intrahepatic ducts were not dilated anymore. Both, a right-sided intercostal and a left-sided subxiphoid access, were allowed and chosen at the endoscopist's discretion.

At one of the study centers, placement of percutaneous hepatic drains is traditionally performed by gastroenterologists, while radiologists provided PTBD procedures at the other two institutes. Periprocedural antibiotic prophylaxis and surveillance were the same as for EUS-BD patients.

Follow-up

Clinical examination, a comprehensive metabolic panel, blood clotting test, and complete blood count were recorded at baseline and 15 days after the procedure. Complications were followed for 30 days.

Study design, hypotheses, and sample size

The main objective of this study was the evaluation of the morbidity rate during the 30 days after BD using EUS-HGS. By first assuming an unacceptable rate p_0 = 30% (presumed rate in the PTBD control group), and a desirable rate p_1 = 15% (expected 50%-decrease for the EUS-HGS group), 55 patients were initially planned to be included in the EUS-HGS arm, following a 2-stage phase II Simon plan to reject the null hypothesis of an unacceptable regimen at the significance level α = 0.05 with an 80% power. The 30%-morbidity rate null hypothesis was based on retrospective studies. Therefore we included a PTBD control-group to validate these results.

In 2013, after the inclusion of respectively 21 PTBD and 20 EUS-HGS patients, a very high unexpected number of complications were observed in the PTBD group (13 patients). For safety reasons, it was thus decided to stop randomization and to only include patients in the EUS-HGS experimental arm.

Study design and hypotheses were therefore reconsidered, using a classical exact one-stage phase II design and assuming respectively an unacceptable

EUS-HGS morbidity rate p_0 = 50% and a desirable rate p_1 = 30%. A total of 37 evaluable patients in the EUS-HGS group were then necessary to reject the null hypothesis of an unacceptable regimen at the significance level α = 0.05 with an 80% power by using a left-sided exact binomial test.

Statistical analyses

Baseline characteristics were summarized using frequencies (percentage) for categorical variables and means with standard deviations, medians, and ranges for continuous variables. The categorical data of the two arms were compared using the Chi-square or exact Fisher tests. Continuous variables were compared using Wilcoxon tests.

The primary analysis compared the morbidity rate 1 month after BD of the EUS-HGS arm to the theoretical value of 50% by a left-sided exact binomial test. Associated 90%-level bilateral exact binomial confidence interval (CI) was estimated.

The overall survival was measured from the day of first BD until death. Patients still alive were right-censored at the day of last medical follow-up. Overall survival was estimated using the Kaplan − Meier method and compared between groups by the log-rank test. The relative risk (RR) of re-intervention in the EUS-HGS group compared to the PTBD group was estimated with the 95%-level bilateral Wald's CI.

Statistical analyses were performed using SAS, version 9.3 (SAS Institute, Cary, NC, USA), or R, version 4.0.3 (Vienna, Austria). $P < 0.05$ was considered statistically significant.

RESULTS

Patients

Between 2011 and 2015, we evaluated 65 patients with obstructive jaundice secondary to benign or malignant stenosis of the common bile duct or the left hepatic duct after failed ERCP. Nine patients were excluded [Figure 1]. The detection of ascites was the main exclusion criterion in five patients, and four patients finally had successful classical retrograde drainage. Altogether, 56 patients were randomized to treatment by PTBD (Group A; *n* = 21 patients) or EUS-HGS (Group B; *n* = 35 patients). Thirteen of them died and three did not appear for their consultation after 1 month, so that follow-up according to the protocol was completed for 40 subjects.

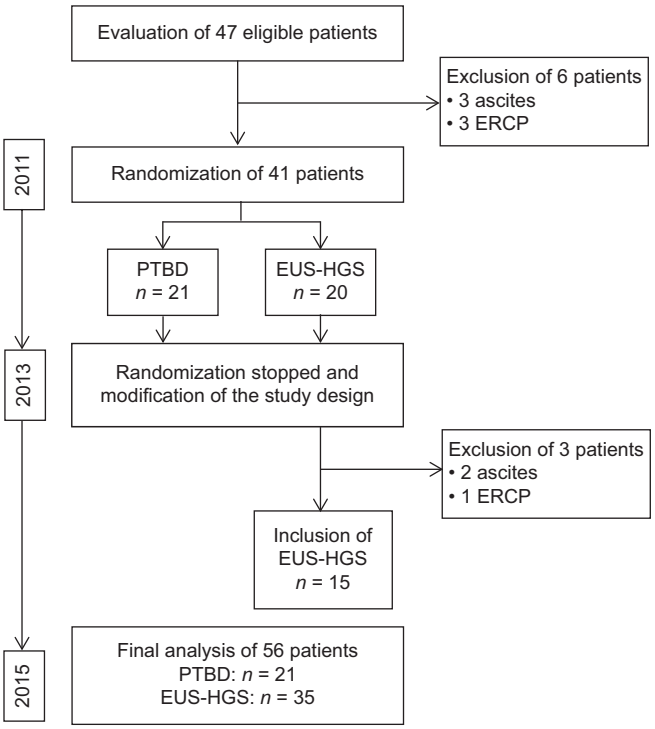

Figure 1. Flow chart of patient inclusion. Randomization was stopped in 2013 due to safety concerns. PTBD: Percutaneous transhepatic biliary drainage; EUS-HGS: EUS-guided hepaticogastrostomy

Baseline characteristics at inclusion [Table 1] were similar in both the groups except sex ratio (PTBD: ♀11/♂10 *vs.* EUS-HGS: ♀7/28♂; P = 0.01). The mean age was 64 years (PTBD: 66 [+/-9.8] *vs.* EUS-HGS: 64 [+/11.2]; P = 0.67). The principal indication for BD was malignancy (PTBD 19/21 [90.5%] *vs.* EUS-HGS 35/35 [100%]; P = 0.63); only two patients in arm A presented with a benign stenosis. There was no significant difference concerning vital parameters, presence of fever, bilirubin plasma level, or kidney failure. Liver enzymes (alanine aminotransferase) were slightly but significantly higher in the EUS-BD group compared to the PTBD group (median 107.0 [26.00–819.0] *vs.* 55.00 [24.00–428.0]; P = 0.04).

Outcomes

After the inclusion of 41 patients, it was decided to stop randomization owing to a very high unexpected complication rate in the PTBD arm. Actually, 13 patients undergoing percutaneous drainage suffered at least one procedure-related adverse event during the follow-up of 30 days (13/21, 61.9%).

Table 1. Patients' characteristics at inclusion

Characteristic	PTBD (*n*=21)	EUS-HGS (*n*=35)	*P**
Age (years), mean±SD	66±9.8	64±11.2	0.67
Sex, *n* (%)			
Female	11 (52)	7 (20)	0.01
Male	10 (48)	28 (80)	
KI, mean±SD	74±17.3	75±154	0.83
Laparotomy (previous), *n* (%)	8 (38)	14 (40)	0.89
Indication, *n* (%)			
Benign	2 (9.5)	0 (0)	0.26
Malignant	19 (90.5)	35 (100)	
ABP, median (minimum-maximum)			
Systolic	120 (100-160)	125 (100-155)	0.38
Diastolic	75 (50-90)	70 (50-90)	0.48
HR, median (minimum-maximum)	80 (55-119)	79 (50-107)	0.57
T°, median (minimum-maximum)	36.8 (36.0-38.2)	36.5 (36.0-39.5)	0.08
Bilirubin†, mean±SD	82±56	108±87	0.41
ALAT, median (minimum-maximum)	55 (24-428)	107 (26-819)	0.04
Creatinine, mean±SD	69.6±40.7	72.8±35.1	0.35

*χ^2 or exact Fisher's or Wilcoxon's test; †Conjugated. PTBD: Percutaneous transhepatic biliary drainage; EUS-HGS: EUS-guided hepaticogastrostomy; KI: Karnofsky index; ABP: Arterial blood pressure; HR: Heart rate; T°: Temperature; ALAT: Alanine aminotransferase; SD: Standard deviation

Ten out of the 35 (28.6%) EUS-HGS patients suffered a 30-day complication. The primary objective was then reached because this morbidity rate was very significantly lower than the null objective of 50% (90%-level bilateral exact binomial CI [16.4%–43.6%]; left-sided exact binomial test to 50%, $P = 0.0083$).

The occurrence of specific adverse events in both groups is detailed in Table 2. Thirteen patients died before the end of follow-up 30 days after intervention. Seven of them were deemed procedure related. There was no statistical significance in terms of procedure-related mortality in patients treated by PTBD compared to EUS-HGS (PTBD 14.3% *vs.* EUS-HGS 11.4%; $P = 1$).

Technical success was achieved in 20/20 patients (100%) treated by PTBD and in 33/35 patients (94.3%) undergoing EUS-BD, without significant difference between these two groups ($P = 0.28$). Efficacy, as indicated by the number of patients with a >50% decrease in plasma bilirubin after 15 days, was comparable in PTBD and EUS-HGS patients (per protocol analysis; PTBD: 10/15 [66.7%] *vs.* EUS-HGS: 20/25 [80%]; $P = 0.35$). The results are summarized in Table 2. Fourteen of 21 patients with percutaneous BD got an external drain; the mean delay until their removal was 10 days, and three of them were not removed at all. In contrast, ablation of the 15/35 nasobiliary drains placed during EUS-HGS was carried out after a mean of 3 days ($P < 0.001$). Hospitalization was shorter in EUS-HGS patients than in patients with percutaneous drainage, 8 *versus* 12 days, nevertheless this difference was statistically not significant ($P = 0.11$).

Survival and recurrent biliary obstruction

The retrospectively analyzed median follow-up was comparable in both groups [PTBD: median 104 months; EUS-HGS: 89 months; $P = 0.95$, Table 3]. Analysis of overall survival [Figure 2] showed no significant difference of survival probability in patients treated by PTBD or EUS-HGS ($P = 0.71$).

During the long-term follow-up, 51.2% of the patients with malignant stenosis (21/41) had at least one re-intervention for recurrent biliary obstruction. Ten of 27 patients [10/27, 37%, Figure 3] had additional BD in the EUS-HGS group and 11/14 patients (79%) in the PTBD group ($P = 0.02$), with a lower RR of re-intervention for patients treated by EUS-HGS (0.47, 95% CI [0.27–0.83]). The median number of re-interventions was higher in the PTBD group, but not statistically significant (EUS-HGS: median 1, range 1–3; PTBD: median 2, range 1–4, $P = 0.29$).

DISCUSSION

Since its first description in 2001, EUS-BD has emerged as innovative endotherapy over the last two decades. Combining echoendoscopy and fluoroscopy, this technique allows creating a biliodigestive anastomosis

Table 2. Outcomes after a follow-up of 30 days

Endpoint	PTBD	EUS-HGS	*P**
Primary outcome, *n* (%)			
Morbidity† (CI[I])	13/21 (61.9) (41.7-79.4)	10/35 (28.6) (16.4-43.6)	
Bleeding	5 (23.8)	3 (8.6)	
Bile leak	1 (4.8)	0 (0.0)	
Cholangitis	3 (14.3)	1 (2.9)	
Peritonitis	1 (4.8)	1 (2.9)	
Sepsis	6 (28.6)	7 (20.0)	
Secondary outcome, *n* (%)			
Technical success	20/20 (100)	33/35 (94.3)	0.28
Clinical success‡	10/15 (66.7)	20/25 (80.0)	0.35
Procedure-related death	3/21 (14.3)	4/35 (11.4)	1
External drain$, *n* (%)	14/21 (67)	15/35 (43)	
Removal (days), mean±SD	10±8.7	3±1.4	<0.001
Hospital stay (days), mean±SD	12±9.2	8±6.2	0.11

*χ^2 or exact Fisher's or Wilcoxon's test; †Defined as ≥ 1 procedure-related AE within 30 days after index procedure; ‡>50% decrease in plasma bilirubin at day 15; $Percutaneous drain in PTBD group and nasobiliary drain in EUS-HGS group; [I]Bilateral exact binomial 90% CI. PTBD: Percutaneous transhepatic biliary drainage; EUS-HGS: EUS-guided hepaticogastrostomy; CI: Confidence interval; SD: Standard deviation; AE: Adverse event

Table 3. Long-term outcomes after biliary drainage

Endpoint	PTBD	EUS-HGS	*P**
Follow-up (days), median (range)	104 (18-1029)	89 (3-629)	0.95
Patients with re-intervention for recurrent biliary obstruction†, *n* (%)	11/14 (79)	10/27 (37)	0.02
Number of re-interventions per patient, median (range)	2 (1-4)	1 (1-3)	0.29

*χ^2 or exact Fisher's or Wilcoxon's test; †After index procedure. PTBD: Percutaneous transhepatic biliary drainage; EUS-HGS: EUS-guided hepaticogastrostomy

with a stent between the biliary tree and the gastrointestinal tract. It is nowadays an accepted alternative for biliary decompression in obstructive jaundice when ERCP as the gold standard fails. However, the fear of adverse events has impeded this challenging procedure to be established in clinical practice and PTBD often remains the second-line treatment of choice due to its widespread availability.

Nevertheless, the last years have been marked by a considerable technical progress and growing experience in the field of EUS-BD and recent studies even suggest a lower rate of complications after EUS-BD compared to PTBD. In retrospectively analyzed data of 25 EUS-BD and 26 PTBD patients, Bapaye *et al.* revealed significantly more complications in the PTBD group (EUS-BD 5/25 *vs.* PTBD 12/26, $P < 0.05$). Similarly, in a retrospective study of 73 patients, Khashab *et al.* found PTBD to be associated with a higher adverse event rate (index procedure: 39.2 *vs.* 18.2%; all procedures including re-interventions: 80.4 *vs.* 15.7%).[13,15]

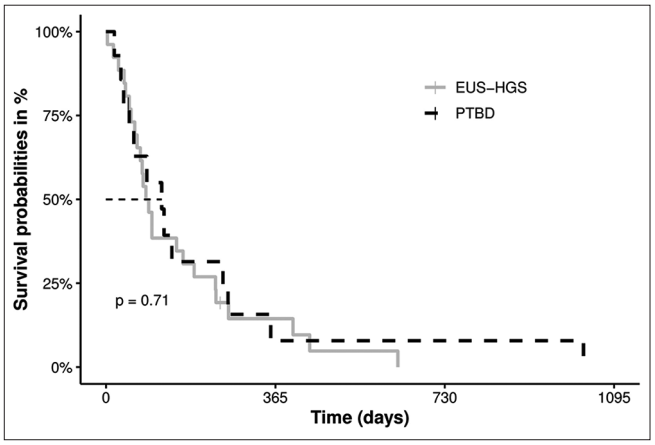

Figure 2. Overall survival probabilities according to the Kaplan–Meier estimate. PTBD: Percutaneous transhepatic biliary drainage; EUS-HGS: EUS-guided hepaticogastrostomy

These data correlate with the results of our present work. Despite a similar technical and functional success in both groups (EUS-HGS: TSR 94.3% CSR 80% *vs.* PTBD: TSR 100% CSR 66.7%, $P > 0.05$), an interim analysis 2 years after the beginning of inclusion (EUS-HGS $n = 20$; PTBD $n = 21$) showed that PTBD was associated with a very high and unacceptable 30-day morbidity rate, with 13 patients having suffered at least one procedure-related adverse event. At the end of the study, the procedural morbidity after 1 month of follow-up was hence 61.9% (90%-level CI [41.7%–79.4%]) in PTBD patients and 28.6% in EUS-HGS patients (90%-level CI [16.4%–46.3%]).

Two other studies compared the standard technique of PTBD to EUS-BD after unsuccessful ERCP, using

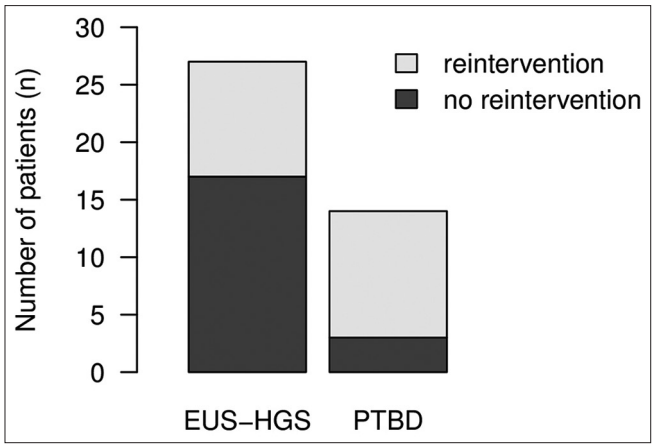

Figure 3. Re-intervention for recurrent biliary obstruction. PTBD: Percutaneous transhepatic biliary drainage; EUS-HGS: EUS-guided hepaticogastrostomy

exclusively procedures with a transgastric access by HGS. Sportes *et al.* did not find a significant difference regarding TSR, CSR, and AE rate, whereas the overall re-intervention rate was significantly lower and the length of hospital stay was shorter in the EUS-BD group (re-intervention 2 *vs.* 21; hospital stay 8 *vs.* 15 days).[16] Ogura *et al.* performed EUS-HGS as first-line treatment in gastric cancer patients with a comparable success and AE rate. Nevertheless, given the relative severity of adverse events in the PTBD group, the authors concluded that EUS-BD might be the procedure of choice for gastric cancer patients with inability to perform ERCP.[25]

A major inconvenience of PTBD is the need for multiple re-interventions and the likelihood of long-term external catheter drainage, affecting quality of life, particularly in palliative patients with limited life expectancy. A cost-effective analysis by Khashab *et al.* reported twice as high the total charges of PTBD compared to EUS-BD, mainly due to a significantly higher rate of re-intervention (80.4% *vs.* 15.7%). Similarly, we found a significantly higher rate of patients needing re-interventions for recurrent biliary obstruction in the PTBD group (37% *vs.* 79%, $P = 0.28$). The RR of PTBD patients for re-intervention is almost twice the RR of EUS-HGS patients (EUS-HGS RR 0.47, 95% CI [0.27–0.83]).

A recent study of Sharaiha *et al.* assessed the issue of patient comfort in a total of 60 individuals. They could show that EUS-BD patients experienced less postprocedural pain compared to the PTBD group (Pain Visual Analog Scale 4.1 *vs.* 1.9, $P = 0.016$).[18] In our present work, 14/21 PTBD patients got an external drain during the index intervention, which could be removed after a mean of 10 days in 14 patients. In contrast, nasobiliary drains placed in 15/35 EUS-BD patients were more transient and all removed after a mean of 3 days ($P < 0.001$). These results suggest that EUS-HGS might be perceived as being a less invasive procedure. However, we did not include rendezvous procedures in the PTBD group. This technique does not need external drainage and may be more comfortable than classical percutaneous drainage.

A relevant limitation of our study was to stop randomization at an early stage so that the number of included patients was not equal in both groups and, maybe for this reason, some endpoints did not reach the significance level. Nevertheless, we took this decision with regard to patient safety and our final results confirm that EUS-BD is safer than PTBD as alternative therapy following failed or impossible retrograde BD. As consequence, in our institute's current practice, EUS-BD has replaced PTBD as salvage approach after unsuccessful ERCP for palliative management whenever the patient is eligible.

Strong points of our study were the similarity of patients and the homogeneity of the EUS procedures which were all performed by a transgastric access. Of all known EUS-BD entities (EUS-HGS, EUS-CDS, EUS-rendezvous technique, and EUS with anterograde stent placement), EUS-HGS has the broadest application, even in case of duodenal obstruction or postsurgical altered anatomy, and the advantage of bypassing the tumor site which may delay stent dysfunction from tumor tissue stent ingrowth. Today, its scope is even extending to the drainage of the right liver.[26]

Our study design provided a sufficiently long patient follow-up of 30 days which seems important for the correct review of procedure-related complications as recent trials reported notably a significant difference in the occurrence of late adverse events in favor of EUS-BD.[17,18]

CONCLUSION

The results of this prospective study suggest that EUS-HGS is a valuable second-line treatment in cases of unsuccessful retrograde BD. Its high rate of technical and functional success is comparable to

PTBD. Even if it remains one of the most technically complex EUS interventions with a nonnegligible morbidity, EUS-HGS however seems an interesting alternative in terms of patient safety to PTBD which was associated with a very high morbidity rate in this study. Provided that operator expertise and well-trained surgical backup is available, EUS-HGS may be the treatment of choice after failure of ERCP in appropriately selected patients, especially in cases of duodenal obstruction or altered anatomy.

Financial support and sponsorship
Nil.

Conflicts of interest
Marc Giovannini is a Founding 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.

REFERENCES

1. 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;50:910-30.
2. Ekkelenkamp VE, de Man RA, Ter Borg F, *et al.* Prospective evaluation of ERCP performance: Results of a nationwide quality registry. *Endoscopy* 2015;47:503-7.
3. Enochsson L, Swahn F, Arnelo U, *et al.* Nationwide, population-based data from 11,074 ERCP procedures from the Swedish Registry for Gallstone Surgery and ERCP. *Gastrointest Endosc* 2010;72:1175-84.e1-3.
4. Nennstiel S, Weber A, Frick G, *et al.* Drainage-related complications in percutaneous transhepatic biliary drainage: An analysis over 10 years. *J Clin Gastroenterol* 2015;49:764-70.
5. Artifon EL, Sakai P, Cunha JE, *et al.* Surgery or endoscopy for palliation of biliary obstruction due to metastatic pancreatic cancer. *Am J Gastroenterol* 2006;101:2031-7.
6. Gouma DJ, Busch OR, Van Gulik TM. Pancreatic carcinoma: Palliative surgical and endoscopic treatment. *HPB (Oxford)* 2006;8:369-76.
7. Giovannini M, Moutardier V, Pesenti C, *et al*. Endoscopic ultrasound-guided bilioduodenal anastomosis: A new technique for biliary drainage. *Endoscopy* 2001;33:898-900.
8. Bories E, Pesenti C, Caillol F, *et al*. Transgastric endoscopic ultrasonography-guided biliary drainage: Results of a pilot study. *Endoscopy* 2007;39:287-91.
9. Burmester E, Niehaus J, Leineweber T, *et al*. EUS-cholangio-drainage of the bile duct: Report of 4 cases. *Gastrointest Endosc* 2003;57:246-51.
10. Wang K, Zhu J, Xing L, *et al.* Assessment of efficacy and safety of EUS-guided biliary drainage: A systematic review. *Gastrointest Endosc* 2016;83:1218-27.
11. Artifon EL, Aparicio D, Paione JB, *et al.* Biliary drainage in patients with unresectable, malignant obstruction where ERCP fails: Endoscopic ultrasonography-guided choledochoduodenostomy versus percutaneous drainage. *J Clin Gastroenterol* 2012;46:768-74.
12. Bill JG, Darcy M, Fujii-Lau LL, *et al.* A comparison between endoscopic ultrasound-guided rendezvous and percutaneous biliary drainage after failed ERCP for malignant distal biliary obstruction. *Endosc Int Open* 2016;4:E980-5.
13. Bapaye A, Dubale N, Aher A. Comparison of endosonography-guided vs. percutaneous biliary stenting when papilla is inaccessible for ERCP. *United European Gastroenterol J* 2013;1:285-93.
14. 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;14:1011-9.e3.
15. 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;60:557-65.
16. Sportes A, Camus M, Greget M, *et al.* Endoscopic ultrasound-guided hepaticogastrostomy *versus* percutaneous transhepatic drainage for malignant biliary obstruction after failed endoscopic retrograde cholangiopancreatography: A retrospective expertise-based study from two centers. *Therap Adv Gastroenterol* 2017;10:483-93.
17. Torres Ruiz F, de la Mora-Levy J, Alonso-Larraga J, *et al.* Su1337 biliary drainage in malignant obstruction: A comparative study between EUS-guided vs. percutaneous drainage in patients with failed ERCP. *Gastrointest Endosc* 2016;83:AB356.
18. Sharaiha RZ, Kumta NA, Desai AP, *et al.* Endoscopic ultrasound-guided biliary drainage versus percutaneous transhepatic biliary drainage: Predictors of successful outcome in patients who fail endoscopic retrograde cholangiopancreatography. *Surg Endosc* 2016;30:5500-5.
19. 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:E1563-73.
20. Sharaiha RZ, Khan MA, Kamal F, *et al.* Efficacy and safety of EUS-guided biliary drainage in comparison with percutaneous biliary drainage when ERCP fails: A systematic review and meta-analysis. *Gastrointest Endosc* 2017;85:904-14.
21. Baniya R, Upadhaya S, Madala S, *et al.* Endoscopic ultrasound-guided biliary drainage versus percutaneous transhepatic biliary drainage after failed endoscopic retrograde cholangiopancreatography: A meta-analysis. *Clin Exp Gastroenterol* 2017;10:67-74.
22. 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;6:329-35.
23. Caillol F, Bories E, Zemmour C, *et al.* Palliative endoscopic drainage of malignant stenosis of biliary confluence: Efficiency of multiple drainage approach to drain a maximum of liver segments. *United European Gastroenterol J* 2019;7:52-9.
24. Giovannini M. EUS-guided hepaticogastrostomy. *Endosc Ultrasound* 2019;8:S35-9.
25. Ogura T, Okuda A, Miyano A, *et al.* EUS-guided versus percutaneous biliary access in patients with obstructive jaundice due to gastric cancer. *Dig Liver Dis* 2019;51:247-52.
26. Caillol F, Rouy M, Pesenti C, *et al*. Drainage of the right liver using EUS guidance. *Endosc Ultrasound* 2019;8:S50-6.