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RESEARCH ARTICLE

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Endoscopic ultrasound-guided biliary rendezvous after failed cannulation, and comparison between benign vs malignant biliopancreatic disorders: outcomes at a single tertiary-care centre

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ABSTRACT

Background: Endoscopic ultrasound (EUS)-guided biliary rendezvous (RV) is an EUS-assisted technique described as a rescue method in cases of failed biliary cannulation *via* endoscopic retrograde cholangiography (ERC). Current literature remains unclear regarding its current role. The study aim was to evaluate the effectiveness for biliary EUS-RV, and comparison between benign vs malignant biliopancreatic disorders.

Methods: Retrospective observational study with prospective consecutive inclusion in a specific database from a tertiary-center. All patients with biliopancreatic diseases that underwent a EUS-assisted ERC between October-2010 and November-2022 for failed ERC were included. Main outcomes were technical/overall success. Secondary outcomes were safety, potential factors related to failure/success or safety; and a comparative analysis between EUS-RV and EUS-guided transmural drainage (TMD) in malignant cases.

Results: A total of 69 patients who underwent EUS-RV procedures, with benign and malignant pathologies ($n=40$ vs $n=29$), were included. Technical / overall success and related-adverse events (AEs) were 79.7% (95%CI, 68.3-88.4) / 74% (95%CI, 61-83.7) and 24% (95%CI, 15.1-36.5), respectively. Failed cases were mainly related with guidewire manipulation. Seven failed RV were successfully rescued by EUS-TMD. On multivariable analysis, EUS-RV and malignant pathology was associated with a greater failure rate (technical success: OR,0.21; 95%CI,0.05-0.72; $p=0.017$), and higher AEs rate (OR,3.46; 95%CI,1.13-11.5; $p=0.034$). Also, the EUS-TMD group had greater technical success (OR,16.96; 95%CI,4.69-81.62; $p<0.001$) and overall success (OR, 3.09; 95%CI,1.18-8-16; $p<0.026$) with a lower AEs rate (OR,0.30; 95%CI,0.11-0.78; $p=0.014$) than EUS-RV in malignant disorders.

Conclusions: EUS-RV is a demanding technique with better outcomes in benign than in malignant biliopancreatic diseases. Comparison of the EUS-TMD group on malignant disorders showed worse outcomes with EUS-RV. Given these findings, maybe EUS-RV is not the best option for malignant biliopancreatic disorders.

KEY MESSAGES

- Last international guidelines suggest Endoscopic Ultrasound (EUS)-guided assisted bile duct access (or biliary *rendezvous*) after a second failed Endoscopic Retrograde Cholangiography (ERC) in benign biliary disease, in high volume centers, but its current role in malignant disease is unclear.
- This study provides a larger number of EUS-guided biliary *rendezvous* cases than reported in previous studies, and offers new and relevant information, not available in the last clinical guidelines or systematic reviews
- The EUS-guided biliary *rendezvous* associates better effectiveness in benign than in malignant biliopancreatic disorders. When comparing EUS-guided *rendezvous* with EUS-biliary transmural drainage in malignant diseases, rendezvous has a lower success, and higher adverse events. Therefore, maybe EUS-guided *rendezvous* is not the best option for malignant disorders and might be reserved for benign cases.

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Introduction

Endoscopic ultrasound (EUS)-assisted bile duct access is an indirect technique performed using two endoscopes. It includes EUS-guided rendezvous (EUS-RV) using guidewire, or even colorant injection ('wireless' concept), as assistant techniques for failed endoscopic retrograde cholangiography (ERC). It is considered a technically demanding technique not free from adverse events (AEs). In particular, the technical success rates of EUS-biliary RV ranges between 72% and 96%, with a mean of 84-86% in expert hands, and with 10-34% safety [1,2].

Recently, the European Society of Gastrointestinal Endoscopy (ESGE) guidelines suggested EUS-RV after a second failed ERC in benign biliary disease, and with normal GI anatomy, in high-volume centres (weak recommendation, low-quality evidence, ESGE2021). But its current role in malignant disease is unclear, especially with recent improvements and new scientific evidence favouring the transmural (TMD) technique [1,3]. Surprisingly, the technical success of the EUS-RV technique in benign disease has been reported to be lower than in malignant disease, and AEs are more likely to occur (27%), owing to limited bile duct dilatation and technical difficulty in accessing [1,2].

In case of failed ERC, EUS-guided bile duct access techniques come in several varieties [3]. EUS-RV, although widely recognized, in real-clinical practice is performed in relatively few high-volume centres, and its standardization is still in the process of development. Also, the related literature is still sparse (i.e. 248 malignant cases reported in the latest ESGE guidelines), with mostly retrospective studies with small sample sizes (range; 13 to 58 cases), and long-term outcomes are limited. These are the main reasons why this procedure is not yet widely used twenty years after the demanding technique was initially reported (first EUS-biliary RV, by Mallery et al. in 2004) [4].

This is a review of our experience in EUS-assisted ERC over a decade, including long-term analysis. The main aim was to evaluate the effectiveness of EUS-guided assisted RV, with a comparison between benign vs. malignant groups. Additionally, a comparison analysis was made with all EUS-guided biliary TMD performed during the same study period for malignant disorders.

Material and methods

Study design

In this retrospective single-centre study, an EUS/ endoscopic retrograde cholangiopancreatography (ERCP) database maintained for the period between October 2010 and November 2022 was retrospectively reviewed.

The study was approved by our institutional ethics committee (PR240/12), Comitè Ètic d'Investigació Clínica, Hospital Universitari de Bellvitge) and conducted in accordance with the principles of the Declaration of Helsinki and the guidelines for Good Clinical Practice.

Participants

All consecutive EUS-guided assisted ERC cases were identified and included in this analysis. A previous ERC attempt was mandatory before attempting EUS-guided bile duct access. Exclusion criteria were transpapillary stent by standard ERC, EUS-guided pancreatic duct intervention, and lack of follow-up information.

All EUS-guided biliary TMD performed during the same study period for malignant disorders were also analysed as a subgroup for a comparative analysis. Figure 1 contains a detailed flowchart.

The following variables were reviewed before and after the interventional procedures: demographic and clinical data, procedure and technical details, follow-up data, incidents, and AEs.

Regarding the consent statement, all included patients provided a written informed consent before each procedure concerning to the intervention and data collection. Data was introduced in a prospectively maintained database. Authors had access to information that could identify individual participants during or after data collection.

Technique

Orotracheal intubation or deep sedation was provided according to the anesthesiologist's criteria. All EUS-guided biliary interventions were done by a single endoscopist with expertise in ERCP (since 2004), EUS (since 2006), and stenting (>15 years), and with nurses trained in both procedures. The learning curve period included stays at 3 centers, and animal-lab training from 2007 until 2010. Cases done during this period were not included in this study. Rectal indomethacin and antibiotics were routinely given in all cases. Procedures were performed with patients in the left-side or supine position.

A linear array echoendoscope (GF-UCT140-AL5, GF-UCT180 Olympus; or EG-580UT, Fujifilm) was advanced into the gastric cavity or duodenum and the biliary tree was identified by EUS. Under EUS guidance, the intra- or extrahepatic bile duct was accessed transgastrically/transduodenally, respectively, with a 19-G and/or 22-G fine-aspiration needle and confirmed by bile aspiration. Limited cholangiogram was obtained at the endoscopist's discretion. Doppler imaging was used to avoid interposal vessels.

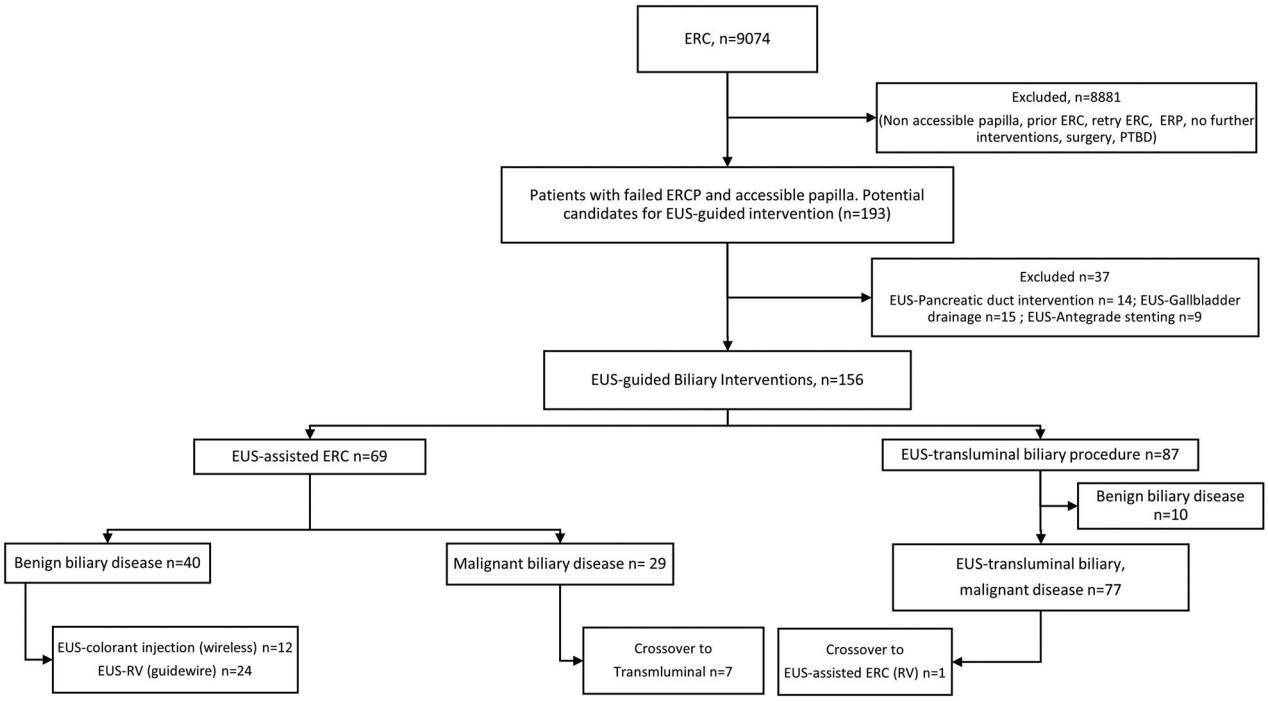

Figure 1. Patient flowchart of the study. EUS-guided interventional biliary procedures performed during the study period

All patients were monitored in the recovery room of the endoscopy unit for at least 1 h and admitted for 24 h of clinical observation.

EUS-guided assisted ERC:

i. EUS-guided colorant injection or 'wireless' RV: as noted in a previous report [5]. After contrast-medium injection to obtain a cholangiography, a sufficient amount (5-10 mL) of colorant (methylene blue or linoleic acid) was injected, depending on duct diameter and the presence of contrast fluid flow, into the small intestine, and monitored by fluoroscopy. If EUS-guided cholangiography was successful, the echoendoscope was withdrawn and ERC was immediately attempted. Papilla orifice identification was achieved using colorant flow. Once the papilla was reached, a sphincterotome, with a 0.025- or 0.035-inch guidewire, was used for direct cannulation. Secondly, if necessary, a precut with a needle-knife was attempted. If cannulation was not achieved after several attempts (3-4), an EUS-guided RV using guidewire, or a second ERC session, was considered.

ii. EUS-guided RV with guidewire: under fluoroscopic guidance, a guidewire was advanced through the needle and antegradely into the bile duct across the obstruction site to the enteral lumen. When a 19-G EUS needle was used, guidewires were mostly 0.035-inch (jagwire, Boston Sc) or 0.025-inch (Visiglide2, Olympus; or Revolution, angle-tipped, Boston Sc). Using a 22-G EUS-needle, a 0.018-inch needle (Novagold, Boston Sc) was used. Contrast injection was performed at the endoscopist's discretion. After guidewire passage through the papilla, echoendoscope was replaced by a duodenoscope thereby allowing conventional ERC to be performed. Generally, retrograde biliary cannulation was attempted alongside the antegrade guidewire using the monorail technique with a homemade modified 3.9/4.4F sphincterotome (small incision at the convex side, at the distal end). In case of failed RV the procedure was finished, or else the guidewire was coiled at the endoscopist's discretion, and transmural stenting was considered over the wire.

Finally, in both techniques and in accordance with findings, sphincterotomy, retrograde stent placement, or other maneuvers were considered.

Examples of various EUS-RV (benign or malignant disorders; long or short-scope position) are presented in Figure 2 andsupplementary figures (Figures S1–S3).

EUS-guided biliary TMD:

In transluminal cases (e.g. choledochoduodenostomy, hepaticogastrostomy), the entire procedure was performed using a linear echoendoscope. Interventional

technique and approach were as detailed in previous published reports [6,7].

With the introduction of biliary lumen-apposing metal stent (LAMS) at our unit in 2014, EUS-guided choledochoduodenostomy progressively gained major prominence to become the standard approach in cases of malignant distal biliary obstruction [8]. This change was natural following recognition that the procedure was less time-consuming and with increased confidence with this EUS-biliary TMD variant.

Follow-up

All laboratory, radiologic, surgical, and clinical findings after index procedures or repeat sessions were reviewed. All imaging parameters were reviewed and taken from the original written reports. The last available clinical follow-up was used to assess patients' responses to interventions.

Definitions

Technical success for EUS-RV: defined as successful biliary access with papilla identification or guidewire passage from the biliary system into the small bowel to allow conventional ERC to be performed.

Overall success, RV: included technical success and successful retrograde biliary cannulation.

Technical or clinical success for TMD (according to each clinical indication) or procedure time, defined as previously described [6,7]

Safety: defined as rate of AEs. AEs were recorded for all index and repeat procedures. AE severity was graded according to the AGREE-American Society for Gastrointestinal Endoscopy (ASGE) lexicon for endoscopic AEs.

Failed biliary cannulation with ERC was not standardized.

Study endpoints

The primary endpoint was to assess the effectiveness of the EUS-guided biliary RV (global and between either benign or malignant pathology), in terms of technical and overall success.

Secondary endpoints were to assess the safety, potential factors related to failure/success or safety;

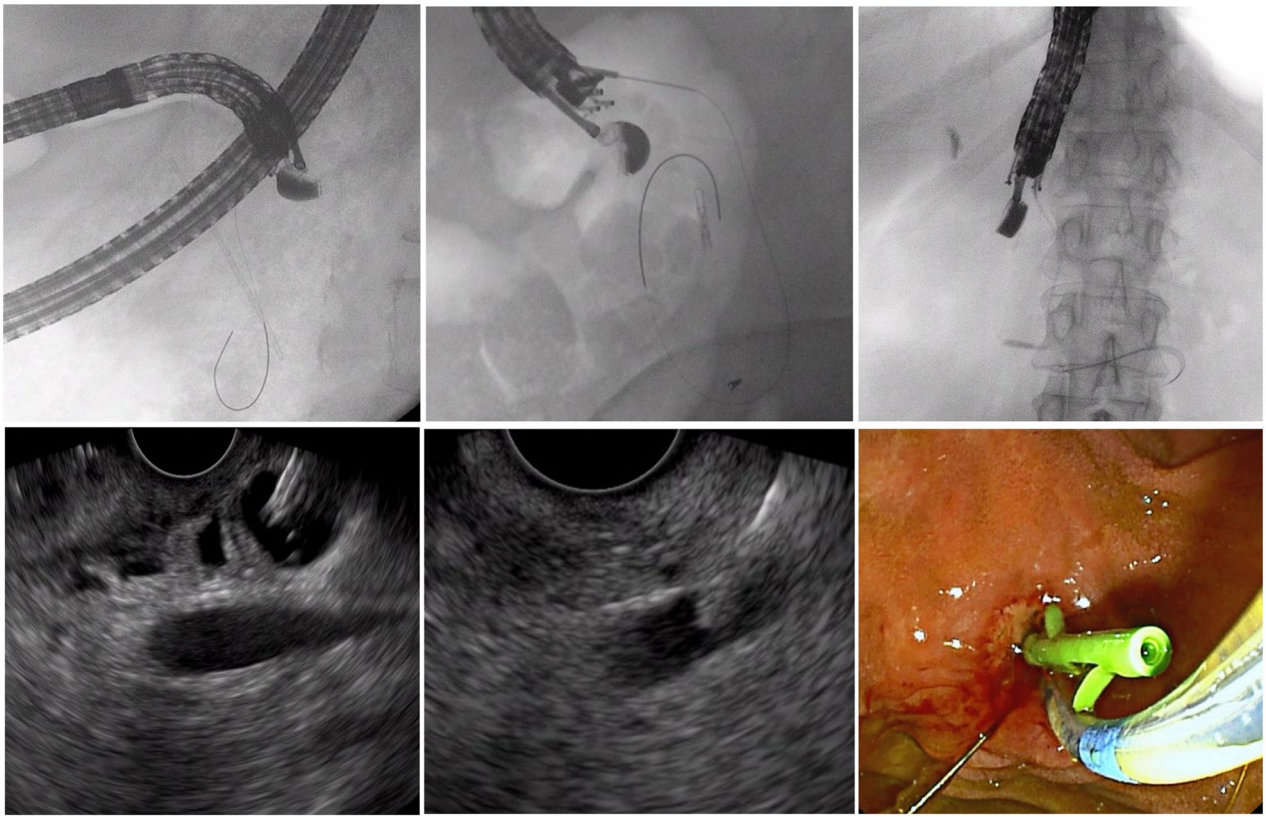

Figure 2. Examples of EUS-guided assisted ERC (Rendezvous guidewire type). **A**, Transduodenal and long-scope position: the extrahepatic bile duct is punctured from the bulb. **B**, Transduodenal short-scope position: the extra-hepatic bile duct is punctured from the bulb. **C**, Transduodenal short-scope position: the extra-hepatic bile duct is punctured from the second portion of the duodenum. **D**, **E**, EUS image during puncture of extrahepatic and intrahepatic bile duct. **F**, Rendezvous with the guidewire passed antegradely through the papilla.

and a comparative analysis between EUS-RV and EUS-TMD for malignant distal biliary obstruction cohort.

Statistical analysis

The number of cases and percentages were presented as categorical variables; continuous variables were shown as mean and standard deviation (SD), or median and interquartile rank (IQR), depending on whether the data distribution was normal. Categorical variables were compared using the chi-squared test (or Fisher's exact test if required). Quantitative variables were compared using the Student's *t*-test or Kruskal–Wallis test, according to application criteria.

Independent univariate logistic regression models were performed to identify variables associated with success/failure and safety. The models were repeated, adjusted for different clinical, technical, and analytical variables depending on the outcome analysed. These associations were estimated with odds ratio (OR) accompanied by 95% confidence interval (CI).

The level of statistical significance was set at <0.05. The statistical package used was R version 4.3.1 for Windows.

Table 1. Demographics and clinical data. EUS-guided assisted ERC.

Parameter	Global (*n* = 69)	Benign (*n* = 40)	Malignant (*n* = 29)
Age, mean (SD), years	73 (9.0)	75 (8.9)	70 (8.7)
Sex, *n* (%)			
Female	30 (43.4)	19 (47.5)	11 (37.9)
Male	39 (56.5)	21 (52.5)	18 (62.1)
CCI[¶], median (IQR)	7.0 (5–9)	5 (4–7)	9.5 (8–11)
Aetiology, *n* (%)			
Malignant	29 (42.0)	–	29 (100)
Pancreatic cancer	21 (30.4)	–	21 (72.4)
Gallbladder cancer	2 (2.9)	–	2 (6.9)
Cholangiocarcinoma	4 (5.8)	–	4 (13.8)
External tumoral compression (LN/M)	2 (2.9)	–	2 (6.9)
Benign	40 (58.0)	40 (100)	–
Choledocholithiasis	37 (53.6)	37 (92.5)	–
Biliary stricture	2 (2.9)	2 (5)	–
Chronic pancreatitis	1 (1.4)	1 (2.5)	–
Oncological status (resect/borderline/ palliative)	5 (7.2); 6 (8.7); 18 (26))	–	5 (17); 6 (20); 18 (62)
Clinical indication, *n* (%)			
Cholestasis	3 (4.3)	2 (5.0)	1 (3.4)
Cholangitis	34 (49.3)	31 (77.5)	3 (10.3)
Obstructive jaundice	29 (42.0)	4 (10.0)	25 (86.2)
Pancreatitis	3 (4.3)	3 (7.5)	0
Causes of failed ERC[¶], *n* (%)			
Surgically altered anatomy (with accessible papilla)	4 (5.8)	3 (7.5)	1 (3.5)
Cancer infiltration	27 (39.7)	–	27 (96.4)
Peri-ampullary diverticulum	22 (32.4)	22 (55.5)	0
Undetectable papilla	9 (13.2)	9 (22.5)	0
Other technical reasons*	6 (8.8)	6 (15.0)	0
Precut as an attempt for cannulation[‡], *n* (%)	22 (33.8)	7 (18.9)	15 (53.6)

Values are number (%) unless otherwise stated. [¶]Data missing for one patient. [‡]Data missing for four patients.
*Others include difficult papilla after failed cannulation using advanced techniques.
CCI: Charlson Comorbidity Index; ERC: endoscopic retrograde cholangiography.

Results

Demographics and procedure details for EUS-assisted ERC

A total of 69 (43.4% female; mean [SD] age, 73 [9.0] years) EUS-assisted ERC were performed out of 9,074 ERCP (0.7%). Demographic and clinical characteristics are shown in Table 1. (Visual abstract)

Benign disorders (40 patients [58%]) were more frequent than malignant (29 patients [42%]), with choledocholithiasis (*n* = 37) and pancreatic cancer (*n* = 21) as the most frequent in each category, respectively. The main reason for failed conventional ERC was peri-diverticular papilla (*n* = 22) and tumoral infiltration (*n* = 27) in the benign and malignant groups, respectively.

Concerning EUS-assisted ERC type, most procedures were EUS-RV using guidewire, in 75.4% (*n* = 52), EUS-assisted colorant injection in 17.4% (*n* = 12), and combined techniques in 7.2% (*n* = 5). In all EUS-RV cases in the malignant group, a guidewire was used.

Mean (SD) bile duct diameter and procedure time were 10.8 (3.3) mm and 92 min (IQR,71-110), respectively. A 19 G and 22 G needle size (*n* = 34 vs. *n* = 31; both needles in 4 cases) were used to access the bile duct in all procedures. Extrahepatic access (82.6%) was more frequently than intrahepatic puncture site (14.5%), and transduodenal with short-scope position (66%) was the most approach most frequently used. EUS-guided assisted ERC was done in the same session, after a failed ERC procedure, in almost half of the cases (47.8%), but in the malignant group this percentage increased to 79.3%.

Comparison of malignant and benign groups

Significant differences were encountered: wider bile duct diameter (mean (SD) 12.4[2.7] vs 9.7[3.2] mm; $p < 0.001$), longer procedure duration (median, 96 vs 82 mm; $p < 0.001$), shorter time from failed ERC to EUS-RV (2.14 [5.4] vs 18.9 [23] days; $p < 0.001$), greater use of 19 G needles (65.5 vs 37.5%; $p < 0.044$), and greater number of EUS-FNA in the same procedure (48.2 vs 20.2%) were detected for the malignant group (Table 2).

Table 2. Procedure details and clinical outcomes of EUS-guided assisted ERC.

Parameters	Global (*n* = 69)	Benign (*n* = 40)	Malignant (*n* = 29)	*p*
Procedure details:				
Bile duct diameter, mean (SD), mm	10.8 (3.3)	9.7 (3.2)	12.4 (2.7)	**<0.001**
Procedure duration*, median (IQR), min	92.0 (71–110)	82.5 (61–94)	96 (90–120)	**0.006**
EUS-assisted ERC type, *n* (%)				**<0.001**
EUS-guided RV (guidewire)	52 (75.4)	24 (60)	28 (96.5)	
EUS-guided colorant injection (wireless RV)m	12 (17.4)	12 (30)	0	
Combined procedures	5 (7.2)	4 (10)	1 (3.4)	
Needle size, *n* (%)				**0.044**
19 G	34 (49.2)	15 (37.5)	19 (65.5)	
22 G	31 (44.9)	23 (57.5)	8 (27.5)	
Both needle sizes	4 (5.8)	2 (5.0)	2 (6.9)	
Puncture site, *n* (%)				**0.013**
Intrahepatic	10 (14.5)	3 (7.5)	7 (24.13)	
Extrahepatic	57 (82.6)	37 (92.5)	20 (68.9)	
Both	2 (2.8)	0	2 (6.9)	
Approach route, *n* (%)				**0.003**
Transgastric	12 (17.4)	3 (7.5)	9 (31)	
Transduodenal:	55 (79.7)	37 (92.5)	18 (62.0)	
Both (gastric and duodenal)	2 (2.89)	0	2 (6.9)	
Scope-position (transduodenal)‡, *n*(%)				>0.99
Short-scope position	36 (66.0)	23 (57.5)	13 (44.8)	
Long-scope position	3 (5.5)	2 (5.0)	1 (3.4)	
Same session, *n* (%)	33 (47.8)	10 (25.0)	23 (79.3)	**<0.001**
Other session, *n* (%)	36 (52.2)	30 (75.0)	6 (20.7)	**<0.001**
Time from failed ERC, days, mean (SD) attempts attempt, *n*	11.9 (19.6)	18.9 (23.0)	2.14 (5.4)	**<0.001**
EUS-FNA at same procedure, *n* (%)	14 (20.2)	–	14 (48.2)	–
Clinical outcomes, *n* (%) [95%CI]:				
Overall technical success	55 (79.7) [68.3–88.4]	36 (90.0) [76–97]	19 (65.5) [46–82]	**0.028**
Overall success	51 (73.9) [61.0–83.7]	33 (82.5) [67–93]	18 (62.1) [42–79]	0.103
Overall adverse events rate	17 (24.6) [15.1–36.5]	6 (15.0) [6–30]	11 (37.9) [21–58]	0.058
Related mortality	4 (5.7)	1 (2.5)	3 (10.3)	–

Values are number (%) unless otherwise stated. *Data missing for 12 patients. ‡Data missing for 30 patients. Statistically significant results are indicated with bold text in the *p* value column.
ERC: endoscopic retrograde cholangiography; EUS: endoscopic ultrasound; FNA: fine-needle aspiration; RV: rendezvous.

Table 3. Comparison of clinical outcomes between groups.

EUS-guided assisted ERC: benign vs malignant						
		No	Yes	OR [95%CI]	*P* value	*N*
Overall technical success, n (%):	Benign	4 (10.0)	36 (90.0)	Ref.	Ref.	69
	Malignant	10 (34.5)	19 (65.5)	0.21 [0.05–0.72]	**0.017**	
Overall success, n (%):	Benign	7 (17.5)	33 (82.5)	Ref.	Ref.	69
	Malignant	11 (37.9)	18 (62.1)	0.35 [0.11–1.03]	0.067	
Overall adverse events rate, n (%):	Benign	34 (85.0)	6 (15.0)	Ref.	Ref.	69
	Malignant	18 (62.1)	11 (37.9)	3.46 [1.13–11.54]	**0.036**	
Comparison of outcomes between EUS-assisted ERC and EUS-transluminal groups, for malignant cases						
		No	Yes	OR [95%CI]	*P* value	N
Overall technical success, n (%):	Rendezvous	10 (37.0)	17 (63.0)	Ref.	Ref.	104
	Transmural	3 (3.90)	74 (96.1)	14.51 [3.96–70.13]	**<0.001**	
Overall success, n (%):	Rendezvous	11 (40.7)	16 (59.3)	Ref.	Ref.	104
	Transmural	14 (18.2)	63 (81.8)	3.09 [1.18–8.16]	**0.026**	
Overall adverse events rate, n (%):	Rendezvous	16 (59.3)	11 (40.7)	Ref.	Ref.	104
	Transmural	64 (83.1)	13 (16.9)	0.3 [0.11–0.78]	**0.017**	

Statistically significant results are indicated with bold text in the *p* value column. ERC: endoscopic retrograde cholangiography; EUS: endoscopic ultrasound.

Global outcomes for EUS-assisted ERC

Technical and overall success rates of EUS-assisted ERC were 79.7% (95%CI, 68.3–88.4) and 74% (95%CI, 61.9–83.7), respectively.

Failed RV-cases were mainly related to guidewire manipulation (30%, Table S1).

Analysis of malignant vs benign groups

Comparison of benign and malignant groups evidenced higher success for benign cases: a greater technical success of 90% (95%CI, 76–97) vs 65% (95%CI, 46–82), and overall success of 82% (95%CI, 67–93) vs 62% (95%CI, 42–79), (Table 2, 3).

Detailed information on EUS-assisted ERC technical success between malignant and benign groups is presented in Table S1.

Safety

Seventeen AEs were detected (24.5%; 95%CI, 15.1–36.5), with a higher rate for malignant cohort vs benign: 37.9% (95%CI, 21–58) vs 15% (95%CI, 6–30) (Table 3).

Most of the reported SAEs were perforation ($n=5$) or infection-related ($n=5$) and were detected as immediate or early-AEs (<7days). In the malignant group, most of the AEs where cholangitis and sepsis, likely related to failure to achieve adequate biliary drainage. All reported AEs, including severity (AGREE), timing, and type are detailed inSupplementary Table S2.

Related mortality was detected in 4 cases: 3 in the malignant group (2 perforation, 1 sepsis) vs. 1 in the benign group (1 pancreatitis).

Univariate and multivariate analysis

On univariate and multivariate analysis, malignant pathology was statistically associated with a greater possibility of failure rate (technical success OR,0.21; 95%CI, 0.05–0.72; $p=0.017$), and higher risk for AEs (OR,3.46; 95%CI, 1.13–11-5; $p=0.036$) for EUS-RV group. Concerning overall success, a non-significant trend was observed (OR,0.35; 95%CI, 0.11–1.03; $p=0.067$) (Tables 2, 3 and Figure S4).

No statistically significant differences in terms of puncture site, approach route, needle type, rendezvous type, anticoagulation, or albumin level were related to success or safety. Complete statistical results can be found inSupplementary material (Tables S3, S4).

Comparative analysis with EUS-TMD group for malignant disorders

A total of 87 (50.6% female; mean [SD] age, 71.8 [10.6] years) EUS-guided biliary TMD were performed during the same period as the included EUS-assisted ERC. This EUS-TMD group had significantly greater bile duct diameter (mean [SD]: 16.8 [3.9] vs 12.7 [2.6] mm, $p<0.001$) and higher Charlson comorbidity index (11[1.5] vs 9.46 [2.8], $p=0.028$) compared to the malignant EUS-RV group. Technical success, overall success, and adverse events for EUS-TMD were 96% (95%CI, 89–99), 81.8% (95%CI, 71–90), and 16.9% (95%CI, 9–27) respectively (Table 4).

Concerning outcomes comparison, better results were encountered for the EUS-TMD group: greater technical success (OR, 14.51; 95%CI, 3.96-70.13; $p<0.001$) and overall success (OR, 3.09; 95%CI, 1.18–8.16; $p=0.026$), and lower AEs rate (OR, 0.30; 95%CI, 0.11–0.78; $p=0.017$) (Table 3 and Figure S5).

It must be noted that seven failed EUS-RV were successfully rescued with EUS-TMD procedures, and only one failed transluminal drainage (choledochoduodenostomy) was rescued with RV [9].

Discussion

Although different methods of difficult biliary cannulation for improving the cannulation success rate in ERCP have been reported, a significant percentage of failed ERC still exists, even with expert endoscopists. In this scenario, EUS-guided interventions can improve the final success rate of endoscopic biliary drainage [10].

This is a retrospective study of patients from a single tertiary referral center who underwent EUS-assisted-ERC after unsuccessful ERC over an 11-year period. The number of EUS-RV ($n=69$, 0.76%) and/or EUS-guided biliopancreatic interventions (n-193, 2%) represents a low volume in a high-volume centre, with only 6.2 EUS-guided biliary RV cases annually. So, this serves to highlight the efficacy of standard ERC.

The EUS-guided RV technique is a technically demanding alternative technique and not free from AEs, due to several technical factors, as well as the lack of dedicated accessories [1,11]. Previous studies have reported that EUS-RV seems to be feasible after failed ERC, but there is wide variability in the reported success and AEs rates [2,12]. Although EUS-RV is one of the most widely practiced techniques, in our opinion, and in accordance with guidelines and reviews, EUS-RV should be considered after a failed ERC in centres where expertise is available, and preferably during the same session [1–3,12].

In our study, the technical success rate was 79% and the AEs rate was 24%. Table S5 contains a literature review of most EUS-RV studies compared with our study [13–30]. It includes 585 cases (19 studies), with a technical success rate of 85.4%, and AEs rate of 15.5%. The lack of standardization makes comparison of results difficult, where heterogeneity is noted. Recently, Yoon et al. summarized the outcomes of 525 cases in a meta-analysis, with most of the published series including only a small number of cases. The pooled rate for technical success was 88% (benign/malignant, 89/90%) and for overall AEs 14% [12].

Table 4. Comparison of baseline characteristics, procedure details, and outcomes between EUS-assisted ERC and transluminal groups, for malignant cases.

Parameters	EUS-assisted ERC malignant group ($n=27$)†	EUS-transluminal group ($n=77$)	*P*
Baseline and procedure details:			
Age, mean (SD), years	70.1 (10.4)	71.8 (10.6)	0.49
Sex, female, *n* (%)	10 (37.0)	39 (50.6)	0.32
CCI, mean (SD)¶	9.46 (2.8)	11 (1.5)	**0.028**
Bile duct diameter, mean (SD), mm	12.7 (2.6)	16.8 (3.9)‡	**<0.001**
Procedure duration, median (IQR), min	106 (55–215)	73 (23–160)*	–
EUS-assisted ERC type, n (%)			–
EUS-guided RV (guidewire)	26 (96.3)	–	
EUS-guided colorant injection (wireless RV)m	0	–	
Combined procedures	1 (3.7)	–	
EUS-Transluminal procedure/stent type, n (%)			–
Choledochoduodenostomy/stents	–	61 (79) / 7 plastic, 4 SEMS, 51 LAMS	
Choledocoantrostomy/stents	–	2 (2.5) / 2 plastic	
Hepaticogastrostomy/stents	–	12 (15.6) / 1 plastic / 11 SEMS	
Hepaticoduodenostomy/stents		2 (2.5) / 2 SEMS	
Time from failed ERC, days, mean (SD) attempts attempt, *n*	2.3 (5.6)	0.9 (2.9)	0.22
EUS-FNA at same procedure, *n* (%)	14 (51.8)	29 (37.6)	–
Conversion to the other method, *n* (%)	7 (26.0)	1 (1.3)	–
Clinical outcomes, *n* (%) [95%CI]:			
Overall technical success	17 (63) [42–81]	74 (96.1) [89–99]	**<0.001**
Overall success	16 (59) [39–78]	63 (81.8) [71–90]	**0.036**
Overall adverse events rate	11 (40.7) [22–61]	13 (16.9) [9–27]	**0.023**

†Two cases excluded to avoid overlapping (failed RV and salvage technique by EUS-choledochoduodenostomy in the same session). ¶Data missing for 57 patients. ‡Data missing for 22 patients. *Data missing for 19 patients. Statistically significant results are indicated with bold text in the *p* value column. CCI: Charlson Comorbidity Index; ERC: endoscopic retrograde cholangiography; EUS: endoscopic ultrasound; FNA: fine-needle aspiration; LAMS: lumen-apposing metal stent; SEMS: self-expandable metal stent; RV: rendezvous.

This current study included a greater number of patients, and the results were comparable to although more modest those revealed in these recent meta-analyses [2,12]. Rigorous data collection in prospective databases from a single centre (specially for AEs), a long study period including all consecutive cases after a learning curve period, and inclusion of a malignant group (predominantly palliative cases) may partially explain these differences. Regarding patients with normal anatomy vs surgically altered anatomy, this study includes only cases with accessible papilla, in accordance with dedicated literature suggesting that percutaneous transhepatic biliary drainage (PTBD) and EUS-biliary TMD seem to be better suited to this scenario [1,3,12].

EUS-RV is an example of an assisted or 'indirect' technique in which EUS facilitates the introduction of a guidewire towards the papilla to within reach of a duodenoscope without involving tract dilation or stent transmural placement. In addition, although the procedure may sound simple, it is a multiple-step process and can be challenging even for an experienced endoscopist [31]. The most challenging points during EUS-RV are: i) guidewire manipulation through a rigid long needle into the bile duct and across the stenosis/papilla with limited directional manoeuvrability, and limited needle angulation; ii) a complex endoscope exchange process that may cause guidewire loss; and iii) retrograde biliary cannulation (alongside or over-the-wire) [2,15]. In this study, in accordance with prior experience, the main cause of failed EUS-RV was the inability to advance the guidewire through the papilla. But in 3 cases a guidewire dislodgement during scope exchange was also noted, altering the overall success rate [11].

Concerning recommended approach routes (intra- or extrahepatic) and scope-positions (long or short), no robust data exists to recommend one over the other. Recent literature shows extrahepatic and short scope position as preferred because the shorter distance (biliary access point and obstruction) allows for better manoeuvrability while advancing the guidewire, while greater diameter of common bile duct (CBD) allows for easier targeting. Short-scope position is superior to long-scope because a duodenal bulb with long-position will obligate the guidewire advance upstream in the direction of the liver rather than to the distal CBD [12,31,32]. Similarly, extrahepatic/transduodenal route and short-scope position were more common in our study, in both groups. Although bile leak from the punctured biliary duct has been described as a potential AE with the extrahepatic approach, no cases were detected in our study [15,32].

According to a recent review, EUS-RV has the potential advantage of fewer AEs when compared with PTBD, percutaneous-RV, and EUS-BD [12,15]. In our study, the AEs and mortality rates were strikingly high in the malignant group, especially compared to the benign diseases group and the EUS-TMD technique. Most of the AEs reported in the RV-malignant group where cholangitis, perforation or sepsis, likely related to failure to achieve adequate biliary drainage. Also, the longer procedure time during the same failed ERC session (using precut-techniques), with a more demanding tight tumoral stenosis, high CCI index, and fragility for this malignant group, may explain these findings. In contrast, AEs for the RV/benign and EUS-TMD groups were similar to what is reported in the literature.

With the goal of reducing the cholangitis rate, after gaining more experience with this demanding procedure, cholangiogram (contrast injection) was progressively avoided without increasing the failure rate. In this manner, after a failed RV, the level of concern about an urgent PTBD was more acceptable.

Current international guidelines recommend RV techniques in benign diseases but they can also be used in malignant biliary diseases [1,12]. In particular, the latest ESGE guidelines state that EUS-RV should be the first-line approach following failed ERCP, over PTBD or EUS-BD, in benign diseases if expertise is available. Even so, two recent randomized studies, coming from India and presented as conference abstracts, have compared precut-papillotomy with EUS-RV in patients with difficult biliary cannulation showing comparable success and AEs rates, but with a higher pancreatitis rate in the precut group [33,34].

Comparing benign vs malignant cohorts, the technical success of EUS-RV in benign disease may be lower than in malignant disease, and AEs may be more likely to occur, owing to limited bile duct dilatation [1]. Interestingly, in our study, a small bile duct diameter was associated with the benign group, but shorter procedure time and a significantly higher technical success with a lower AEs rate was seen.

Our initially standard approach to EUS-guided biliary access for malignant distal biliary obstruction changed gradually from EUS-RV to EUS-biliary TMD. This decision was based on the progressive perception of shorter procedure time, superior technical success, lower AEs rates, and successful salvage transmural drainage after failed RV following the introduction of biliary LAMS at our unit in 2014 [8]. This attractive and effective EUS-transmural BD variant has gained greater prominence in malignant distal obstructions. This study provides a direct comparison between the two techniques, clearly favouring the EUS-TMD group (basically, choledochoduodenostomy, hepaticogastrostomy) over EUS-RV with greater success, shorter procedure duration, and better safety rates.

Thus, with our findings, we feel that EUS-transmural BD drainage may remain as the preferred approach over EUS-RV in malignant diseases. EUS-RV might be reserved for benign disease.

This study has some limitations, mainly owing to its retrospective design. First, because of a lack of data, patient discomfort, hospitalization, and cost comparison could not be assessed. Second, the variability of assisted techniques (colorant/guidewire) included in this study may have imposed a selection bias on the study population. Third, this technique may cause AEs related to the ERC or EUS-guided biliary access, but it is difficult to ensure causality; thus an overestimation of AEs related to EUS may have occurred. For this reason, two cases (EUS-RV and EUS-TMD in the same procedure) were excluded from the EUS-RV group for the comparison analysis with EUS-TMD. Fourth, this single-center study may not be applicable to other centers with different practice patterns. Lastly, the lack of a standardized or uniform protocol due to changes related to the long study period, with no specific follow-up, may have entailed a lack of some relevant data. Furthermore, comparison of RV and TMD was limited because of the non-randomized nature of the study and the step-up approach in which both techniques were used [35].

Among the strengths of this study are its rigorous design and analysis of specific and detailed data, inclusion of benign and malignant diseases, and consecutive inclusion during a long period with a single operator in a tertiary center, providing greater homogeneity in the results.

Conclusions

This study offers new and relevant information, not available in the latest guidelines or reviews. The EUS-RV technique is a technically demanding multi-step technique, with better effectiveness in benign than in malignant disorders. In case of failed ERC and accessible papilla, when comparing EUS-RV with EUS-biliary TMD in malignant diseases, EUS-RV has a lower success rate, higher AEs, and a worrying mortality rate.

Therefore, given these findings, maybe EUS-RV is not the best option for malignant disorders, and might be reserved for benign cases. Innovations with new devices are needed to simplify and improve the range of EUS-guided interventions.

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Author contributions statement

JBG conceived the project and designed the study. JBG, AGS, and SQ provided a critical review and participated in the design of the study. MM, BL, JB, and AGS promoted the enrolment of patients. DL, JGV, SM, SQ, MP, JE, AGS, and JBG carried out acquisition, analysis, and interpretation of data. VM, AGS, and JBG did the statistical analysis. AGS and JBG drafted the manuscript, interpreted the data, verified the underlying data, and critically reviewed the manuscript. JBG had final responsibility for the decision to submit for publication. All authors read, revised, and provided a critical review of the draft manuscript. All authors approved the final manuscript.

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Data availability statement

Data that support the findings of this study are available from the corresponding author [JBG] upon reasonable request.

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