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EUS-guided biliary drainage in patients with distal malignant biliary obstruction requires fewer interventions and has a lower cost compared to ERCP biliary drainage

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Abstract

Introduction Endoscopic retrograde cholangiopancreatography (ERCP) biliary drainage is considered the reference standard in patients with biliary obstruction, but it is not free of complications. EUS-guided biliary drainage (EUS-BD) is considered an alternative in patients with failed ERCP; however, data are scarce as to whether EUS-BD could be considered a first option.

Objective The aim of our study was to compare the need for reintervention and cost between ERCP biliary drainage vs. EUS-BD.

Material and methods We conducted a retrospective and comparative study of patients with distal malignant biliary obstruction with biliary drainage with ERCP + plastic stent (ERCP-PS) vs. ERCP + metal stent (ERCP-MS) vs. EUS-BD.

Results 124 patients were included, divided into three groups: ERCP-PS, 60 (48.3%) patients; ERCP-MS, 40 (32.2%) patients; and EUS-BD, 24 (19.3%) patients. The need for reinterventions (67 vs. 37 vs. 4%, respectively), the number of procedures [3 (1–10) vs. 2 (1–7) vs. 1 (1–2)], and the costs (4550 ± 3130 vs. 5555 ± 3210 vs. 2375 ± 1020 USD) were lower in the EUS-BD group. No differences in terms of complications were detected.

Conclusion EUS-BD requires fewer reinterventions and has a lower cost compared to drainage by ERCP with metal or plastic stents.

Keywords EUS-guided biliary drainage · ERCP · Pancreatic cancer

For more than three decades, drainage of the bile duct has been carried out using endoscopic retrograde cholangiopancreatography (ERCP) with a high success rate; however, it is not free of complications [1–3]. Pancreatitis, bleeding and perforation are the most common complications, with rates ranging from 3 to 15% [1–4]. When ERCP is not successful, other options may be taken, such as the use of advanced cannulation techniques, percutaneous drainage, surgery or drainage of the bile duct guided by endoscopic ultrasound (EUS) [5, 6].

EUS-guided biliary drainage EUS (EUS-BD) has been shown to have a high success rate and an acceptable complication rate. Two studies have compared the primary drainage of the biliary tract of EUS vs. ERCP; in one study, the adverse events and success rates were similar [7] and in the other study, lower adverse outcomes with no risk of pancreatitis, longer stent patency with less need for reintervention, and more preserved quality of life (QOL) were observed [8].

The aim of our study was to compare the need for reintervention and the costs between ERCP biliary drainage vs. EUS-BD.

Material and methods

This was a comparative retrospective study in which patients with unresectable cancer with secondary malignant distal obstruction of the bile duct, who underwent drainage guided by ERCP or EUS-BD, were included. Unresectability was confirmed by CT/MRI/EUS in all patients. We included

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patients older than 18 years with unresectable malignant obstruction of the distal bile duct, who were seen in our center in the period from December 2015 to December 2017. The final diagnosis of malignancy was based on the results from the histological specimen by EUS-FNA/FNB or by ERCP-guided biopsy forceps, clinical and radiological assessment, and follow-up for at least 6 months. The protocol was approved by the ethics committee of the institution and all patients provided signed informed consent. Data were obtained from clinical files (physical and electronic). Patients with incomplete information were excluded.

All EUS-BD procedures were performed by one of two endoscopists (F.T.A., M.A.R.L.) who had performed at least 30 procedures. ERCPs were performed by one of five staff physicians. All patients were submitted to a complete blood count, coagulation tests and were under sedation by an anesthesiologist. Patients with EUS-BD had orotracheal intubation. For EUS-BD a linear GF-UCT140 (Olympus Corp., Tokyo, Japan) with an Aloka SSD-5500 console (Aloka Co., Ltd., Tokyo, Japan) or a FUJI EG-530UT device with an SU-8000 console (Fujifilm Corporation, Minato-Ku, Tokyo, Japan) were used. All patients were hospitalized and observed for at least 4 h after the study to assess the development of possible complications.

Due to the design of the study, the criteria used to choose the initial drainage method was decided by the attending physician. The included patients were divided into three groups: Group 1 included patients with transpapillary drainage via ERCP with the placement of a plastic stent (ERCP-PS); Group 2 were patients with transpapillary drainage via ERCP with the placement of a self-expanded metal stent (group ERCP-MS); and Group 3 were all patients with previous ERCP failures and biliary drainage was performed by EUS-guided choledochoduodenostomy. Patients with two or more consecutive ERCPs with placement of PS and subsequent placement of SEMS were considered to be in Group 1. Patients with a single ERCP with PS placement and SEMS placement in the second procedure were considered to be in Group 2. This is because, in daily practice, it is common for the patient to be drained with a PS temporarily during the time in which the histological diagnosis is obtained. All patients in group 1 received one 10 Fr PS. In all patients in group 2, uncovered SEMS were placed. The study begins at the time of the first ERCP.

Definitions

Technical success was defined as the appropriate placement of one stent (plastic or metal) by ERCP or one metal stent by EUS. *Clinical success* was defined as the resolution of symptoms that caused the indication of the drainage of the biliary tract or a decrease in bilirubin by 50% or more in a lapse of 14 days [7, 9]. The costs were determined by the procedural fees, anesthesia, accessories (in ERCP groups, sphincterotome, guidewire, dilation device, plastic or metallic stent, in EUS-BD we used needle, guidewire, cystostome, dilation device and the metallic stent), medications, procedural facility fees, and hospital stay.

We considered complications as follows [10]: *perforation* was diagnosed when pneumoperitoneum was evident on imaging studies, associated with peritoneal signs. *Bleeding* was defined as any hemorrhagic event that required endotherapy, blood product transfusion, or inpatient observation. *Infection* was considered if any septic event occurred after the initial drainage (ERCP or EUS-guided) and was proven by new-onset fever, positive blood cultures, or positive fluid cultures. *Reintervention* was defined as the need for additional endoscopic, percutaneous, or surgical intervention to relieve jaundice in the presence of a dilated biliary duct system on imaging studies. In our center, dysfunctional PS are exchanged for another plastic stent or one SEMS, according to the endoscopist's criteria. Dysfunctional SEMS were treated by inserting a second SEMS within the occlusion (a covered model) or, in the case of a life expectancy ≤ 3 months, by inserting a plastic stent inside the SEMS. *Stent migration* was defined as the need to retrieve a stent from within the biliary tract or the enteral lumen. *Stent dysfunction* was considered when patient had recurrence of cholangitis because of stent occlusion caused by sludge (in plastic stents), or by tissue ingrowth/overgrowth or sludge (in metallic stents).

EUS-guided choledochoduodenostomy (EUS–CD) technique

After prophylactic administration of a 1 g single dose of intravenous ceftazidime, the dilated extrahepatic bile duct was visualized and punctured with a 19G needle (Flex 19; Boston Scientific Corporation, Natick, Mass) from the duodenal bulb. After the bile was aspirated, contrast medium was injected to obtain a cholangiogram and a 0.035-inch guide wire was inserted into the bile duct via the needle. After removal of the FNA needle, a cytostome 6F (ring knife MTW, Germany) was used. Then, a 4-mm biliary balloon dilator (Max Force, Microvasive, Boston, Massachusetts, USA) was used "over the wire" for dilation of the choledochoduodenal fistula. Finally, a fully covered metal stent (4 cm by 10 mm) was inserted.

Statistical analysis

The results were evaluated using descriptive statistics, including medians, ranges, and absolute and relative frequencies for data with non-parametric distributions. Differences between groups were tested using a χ^2 test or Mann–Whitney U test, as appropriate. A two-tailed p

value < 0.05 was considered indicative of statistical significance. All analyses were conducted using SPSS 20 (Chicago, Illinois, USA) for Mac.

Results

Overall, 124 patients were included, of which 52 (41.9%) were women with a mean age ± SD of 63.4 ± 13.4 years. The tumors for which drainage of the bile duct was indicated are shown in Table 1. For each patient, 2.4 ± 1.7 (median 2; 1–7) procedures were performed, with 55 (44.3%) patients requiring at least one reintervention during follow-up, and 49 (39.5%) patients requiring hospitalization, with an average inpatient stay of 6.8 ± 3 days (median of 0; 0–46 days). Baseline characteristics and procedure details at first ERCP procedure are shown in Table 1.

In Group I, 60 (48%) patients were included, whereas in Group II, 40 (32%) patients were included and in Group III, 24 (19.2%) patients were included. When comparing the groups, there were no differences in relation to technical success (Table 2). Clinical success was lower in patients with plastic stent (Table 2); when groups of ERCP-MS and EUS-BD were compared no differences were observed ($p = 0.17$).

Table 1 Baseline characteristics and procedure details of included patients

Variable	Group I ($n = 60$)	Group II ($n = 40$)	Group III ($n = 24$)	p value
Age, years, median (IQR)	61 (55–70)	64 (57–75)	64 (54–73)	0.66
Gender, male, *n* (%)	33 (55)	25 (62)	14 (56)	0.75
Type of malignancy[a]				0.19
Primary pancreatic cancer	42 (70)	24 (60)	19 (79.1)	
Ampulla's Vater carcinoma	8 (13.3)	5 (12.5)	3 (12.5)	
Distal cholangiocarcinoma	8 (13.3)	11 (27.5)	2 (8.4)	
Pancreatic neuroendocrine tumor	2 (3.4)	0	0	
Baseline total bilirubin, mg/dL, median (IQR)	4.4 (2–10.7)	3.7 (1.5–8.3)	20.7 (10–24.4)	0.07
Size of pancreatic mass, mm, median (IQR)	40 (25–55)	42 (27–57)	38 (30–45)	0.7
Common bile duct diameter, mm, median (IQR)	13 (9–18)	15 (10–19)	16 (11–19)	0.8

IQR interquartile range (25–75)

[a]All patients had unresectable tumors

Table 2 Comparison of outcome measures in included patients

Outcome measure	Group I ($n = 60$)	Group II ($n = 40$)	Group III ($n = 24$)	p value
Number of total procedures, median (min–max)	3 (1–10)	2 (1–7)	1 (1–2)	0.001
Need for reintervention, *n* (%)	40 (67)	15 (37.5)	1 (4.1)	0.001
Hospitalization, *n* (%)	26 (43.3)	20 (50)	4 (23.5)	0.18
Days in hospital, median (min–max)	0 (0–40)	1.5 (0–46)	0 (0–23)	0.18
Technical success, *n* (%)	60 (100)	40 (100)	24 (100)	–
Clinical success, *n* (%)	32 (53.3)	34 (85)	23 (95.8)	0.001
Complications, *n* (%)	8 (13.3)	9 (22)	4 (16.6)	0.23
Stent dysfunction	3	6	0	
Pancreatitis	2	3	0	
Stent migration	3	0	0	
Fever after procedure[a]	0	0	3	
Pneumoperitoneum[b]	0	0	1	
Costs, USD				
Mean (SD)	4550 (3130)	5555 (3210)	2375 (1020)	0.001
Median	3640	4750	1950	0.001
Min–max	1040–16,773	1950–15,600	1950–5570	

USD American dollars

[a]Only present by 24 h o less and only treated with paracetamol. No pain or other data of cholangitis was present in any of these 3 patients

[b]Only treated with NSAID by 24 h

The need for reinterventions and the number of procedures was lower in the EUS-BD group compared with the other groups (Table 2). Of the total patients, 8 (6.4%) required percutaneous drainage, 2 (3.3%) patients from group 1 and 6 (15%) patients from group 2. The requirement of the percutaneous drainage in these 8 patients were secondary to clinical failure in the follow-up.

Costs

The costs were lower in the EUS-BD group, compared to the rest of the groups (Table 2). There were no significant differences in costs when comparing patients in Group I (ERCP-PS) with those in Group II (ERCP-MS) ($p=0.12$).

Complications

The overall complication rate was 16.9% ($n=21$) and the most frequent complication was stent dysfunction ($n=9$; 7.2%). No differences in the complication rate were seen (Table 2).

Survival

There were no differences among groups regarding survival time ($p=0.2$; Fig. 1).

Discussion

According to our results, EUS-BD requires a smaller number of reinterventions and has lower costs, compared to drainage by ERCP using metal or plastic stents. The clinical success is lower in patients with ERCP-PS compared to patients with ERCP-MS and EUS-BD.

For a few years, EUS-BD has proven to be a useful alternative in patients with malignant distal bile duct obstruction and failed ERCP. In a short period of time, EUS-BD has demonstrated advantages over other drainage options in this group of patients [5–9, 11, 12]. Some studies even suggest that EUS-BD can be an equivalent to ERCP as the first option for biliary drainage in patients with malignant distal obstruction [7, 8, 12], with the advantage of providing a precise diagnosis and palliative therapy in one session using only one endoscope. In the present study, we found that there were no differences in the rates of technical success among the studied options; however, we observed that the EUS-BD may have advantages with respect to a smaller number of reinterventions and lower costs. Other studies have found similar results [7, 8]. In the present study, the technical success of ERCP is within the previously reported range, but was high; this was probably due to the fact that patients with duodenal invasion that prevented the passage of the duodenoscope were not included in any of the groups (although these patients were not deliberately excluded). Duodenal invasion was observed in 21.3% (25 patients) of the total group, but it did not represent a problem to reaching the major papilla in any patients. We have to mention that, according to our results, clinical success with ERCP-PS is the worst compared to ERCP-MS and EUS-BD. This is very important to consider because there are many centers where ERCP-PS is used as first-line therapeutic option because the false impression that is the cheapest and clinically effective, but according with our results this could not be real.

According to our results, performing EUS-BD requires fewer interventions compared with ERCP biliary drainage.

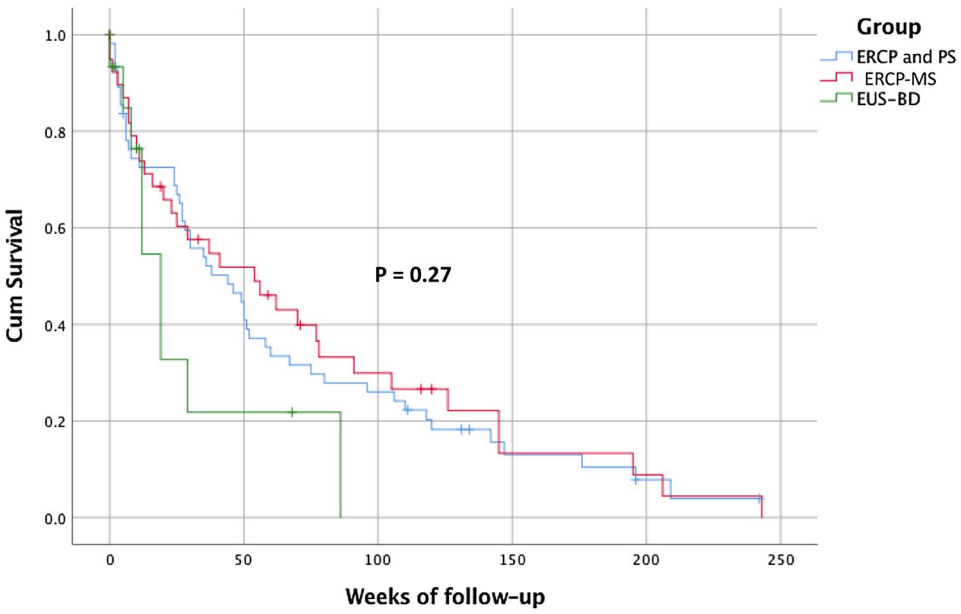

Fig. 1 Survival time after drainage procedure according to different groups

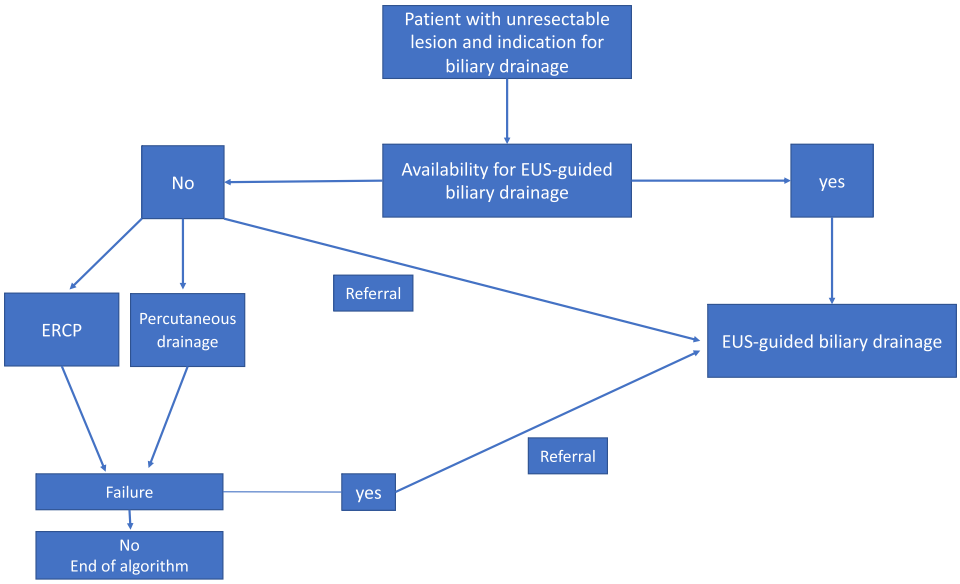

Fig. 2 Proposal for technique selection in patients with need for biliary drainage

Most of the reinterventions in the ERCP groups were caused by occlusion of the stent by a tumor or detritus. Due to this, we think that the smaller number of reinterventions in the EUS-BD group can be related to the fact that, with drainage guided by EUS, the created anastomosis does not come into contact with the tumor. Conversely, in patients treated with ERCP, both the metal and plastic stents pass through the tumor, which may lead to contact if the tumor grows, in which case it can occlude the stent. Regarding costs, EUS-BD represents a lower cost compared to ERCP drainage. According to our results, the difference was related to the smaller number of procedures in this group of patients. When we analyzed the need for hospital stays or complications, there were no differences between groups. Thus, we consider that the differences in cost are related to the number of procedures only. In relationship to survival, we could observe that was not difference among groups (Fig. 1). We must consider that patients with EUS-BD were patients with at least one previous failed ERCP, with consequent delay in biliary drainage, higher levels of basal bilirubin, and is reasonable to think that these patients could have worst basal status in this aspect. All these points could impact against the EUS-BD results because patients were often more complicated with manipulated biliary tract.

This study has some limitations, such as the retrospective design and the sample size. EUS-BD is a relative recent procedure limited to some third level centers and, until now, it has been mainly accepted in cases in which ERCP previously failed. Three studies have reported the possibility of proceeding to directly performing EUS-BD in patients with malignant distal biliary obstruction [7, 8, 12]. All these studies focused on the success and complication rates, whereas our results mainly focused on the number of reinterventions and the costs; two of these studies were randomized control trial [7, 8]. Our results support the idea that in third level centers where technical expertise is available, EUS-BD could be considered a primary option in patients with distal malignant biliary obstruction. In Fig. 2 we show a proposal for technique selection in patients with need for biliary drainage. Another limitation is that we only evaluated choledochoduodenostomy and not the other variations of EUS-based approaches. However, this is the most frequently used approach, compared to the hepatogastrostomy, rendezvous, or antegrade techniques. Moreover, we considered that selecting only one technique (the most commonly practiced EUS-based technique) enabled the best possible comparison with the reference standard (ERCP).

In conclusion, EUS-BD requires a smaller number of reinterventions and has a lower cost, compared to drainage by ERCP-PS or ERCP-MS.

Author contributions FIT and MAF designed the report; FIT, MAF, EM, JFR, and JR were the attending doctors for the patients; FIT, MR, and FV performed the endoscopies; FIT and EM organized the report; and FIT wrote the paper. All authors read the draft and made important intellectual contributions to the final manuscript.

Compliance with ethical standards

Disclosures Félix I. Téllez-Ávila, Mónica Auxiliadora Figueredo-Zacarías, Everardo Muñoz-Anaya, José Froylan Rodríguez-Sánchez, Jesús Ramírez-García, Miguel Ramírez-Luna, and Francisco Valdovinos-Andraca have no conflicts of interest or financial ties to disclose.

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