EUS-guided choledochoduodenostomy for malignant distal biliary obstruction after failed ERCP: a retrospective nationwide analysis

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Background and Aims: EUS-guided choledochoduodenostomy (EUS-CDS) with a lumen-apposing metal stent (LAMS) has been proposed as an alternative procedure in patients with distal malignant biliary obstruction (DMBO) and failed ERCP.

Methods: This multicenter, retrospective analysis included all cases of EUS-CDS with LAMS performed in patients with DMBO and failed ERCP in 23 Italian centers from January 2016 to July 2020. Primary endpoints were technical and clinical success. Secondary endpoints were the assessment of the adverse event (AE) rate and variables associated with technical success.

Results: Two hundred fifty-six patients (44.9% women) with a mean age of 73.9 ± 12.6 years were included in the study. The most common etiology of DMBO was pancreatic adenocarcinoma (75%), followed by ampullary cancer (8.6%) and cholangiocarcinoma (6.6%). The common bile duct median diameter was 17.3 ± 3.9 mm. Technical and clinical success were achieved in 239 of 256 (93.3%), and 230 of 239 (96.2%) patients, respectively. The mean follow-up was 151 ± 162 days. Twenty-seven AEs occurred in 25 of 239 patients (10.5%) (3 mild, 21 moderate, and 3 severe). No fatal AEs occurred. Reinterventions to manage AEs with endoscopic or radiologic procedures occurred in 22 patients (9.2%).

Conclusions: The results of our study show that EUS-CDS with LAMSs in patients with DMBO and failed ERCP represent a viable alternative in terms of effectiveness and safety with acceptable AE rates. (Clinical trial registration number: NCT03903523.) (Gastrointest Endosc 2022;95:896-904.)

Abbreviations: AE, adverse event; ASGE, American Society for Gastrointestinal Endoscopy; CBD, common bile duct; DMBO, distal malignant biliary obstruction; EUS-BD, EUS-guided biliary drainage; EUS-CDS, EUS-guided choledochoduodenostomy; EUS-GE, EUS guided gastroenterostomy; GOO, gastric outlet obstruction; i-EUS, Interventional Endoscopy and Ultrasound Group; LAMS, lumen-apposing metal stent.

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ERCP is considered the criterion standard technique to achieve biliary drainage in cases of distal malignant biliary obstruction (DMBO).[1] However, malignant diseases involving the distal common bile duct (CBD) could be associated with infiltration and distortion of the ampulla, which could make the cannulation of the papilla very difficult.

For several years, percutaneous transhepatic biliary drainage has been considered the conventional nonsurgical option for biliary drainage in case of failed ERCP. Percutaneous transhepatic biliary drainage is a highly effective procedure, easily accessible in most facilities, but is burdened by significant morbidity and potential detriment of patient quality of life.[2]

In the last few years, EUS-guided biliary drainage (EUS-BD) has been increasingly used as an alternative technique for biliary decompression in patients with malignant biliary obstruction and failed ERCP and has shown high rates of technical and clinical success.[3] EUS-BD for DMBO can be performed as a choledochoduodenostomy (CDS) or hepaticogastrostomy depending on the drainage route, where a transduodenal extrahepatic or a transgastric intrahepatic approach can be performed, respectively.

By most experts, EUS-guided CDS (EUS-CDS) has been considered the most commonly used approach in patients with DMBO and failed ERCP. Over the years, the advent of dedicated devices such as the lumen-apposing metal stent (LAMS) has allowed a rapid spread of EUS-CDS after the dissemination of EUS-guided pancreatic fluid collections and gallbladder drainage.[4-7]

The feasibility of EUS-CDS using LAMSs after failed ERCP has been reported in several retrospective studies,[8-13] confirming its efficacy and safety. However, data reported are quite heterogeneous and mostly associated with tertiary centers referral experience.[14] To better understand the clinical implications and safety of this procedure, we conducted a multicenter nationwide study involving facilities with different geographic locations, different volume of procedures, and different levels of endoscopist expertise aimed to evaluate the feasibility and safety of EUS-CDS with LAMSs in a large cohort of patients with DMBO after failed ERCP.

METHODS

In 2019, a nationwide educational initiative was held in Italy involving gastroenterologists and GI endoscopists from 40 different centers who were performing EUS-guided drainage with LAMS. This initiative covered about 80% of the centers that were performing such procedures nationwide at the time. Thus, the i-EUS Group (Interventional Endoscopy and Ultrasound) was formed and supported an educational program aimed at improving interventional EUS procedures and optimizing the use of LAMSs in clinical practice. To collect clinical data on real-life activity on the efficacy and safety of these procedures, we planned to conduct a multicenter retrospective analysis of all procedures of EUS-guided drainage with LAMSs for the 3 major and "on-label" indications (pancreatic fluid collection, gallbladder, biliary). The study was approved by the institutional review board of each participating center (NCT03903523) and performed in accordance with the Declaration of Helsinki. The database collected 850 cases for the 3 main indications.

Our study aims to report the outcome of all consecutive patients who underwent EUS-CDS using LAMSs after failed ERCP in DMBO from January 2016 to July 2020. Data were collected across 23 centers in Italy.

Procedure

All EUS-CDS procedures were performed with a therapeutic echoendoscope, using CO_2 insufflation with the patient under deep sedation or under general anesthesia that was managed by the anesthesiologist and in accordance with local sedation policies. The procedures were performed either during the same or a different session of the failed ERCP.

We included all consecutive patients with jaundice because of DMBO after ERCP failure during the study period. Exclusion criteria were previous transpapillary stent placement, CBD diameter <10 mm, international normalized ratio >1.5, or platelet count <50,000 $10^3/mm^3$.

Under EUS guidance, the CBD was studied and drained from the proximal or medium tract through either the stomach or duodenum wall. Selection of stent type and size (electrocautery-enhanced, Hot-AXIOS system [Boston Scientific Corp, Marlborough, Mass, USA] or Nagi stent [Taewoong Medical Co Ltd, Gimpo-si, South Korea]) was based on CBD diameter at the discretion of the endoscopist. Different deployment techniques were used in function of the stent used and at the discretion of the endoscopist with or without fluoroscopic guidance.

In detail, when using a standard LAMS, puncture of the CBD with a 19-gauge needle, insertion of a .025- to .035-inch guidewire, and dilation of the tract using a cystotome and dilation balloon followed by insertion of the stent was used. When an electrocautery-enhanced LAMS was placed, the single-stage technique was used.[9] For both techniques, the deployment of the second flange was performed either endoscopically or with the intrachannel stent release technique, as previously described.[15]

Data

Data were compiled and extracted in a central database. For each procedure, patient-related data, demographics, etiology of the DMBO, reason for ERCP failure, and presence of symptoms of gastric outlet obstruction (GOO) were collected.

Procedure details were size of the CBD, type and size of the LAMS used, deployment technique, site of approach, and procedural and deployment stent time. Postprocedural data were length of hospitalization, other procedures performed such as duodenal stent placement or EUS-guided

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gastroenterostomy (EUS-GE) creation to manage GOO symptoms, starting of chemotherapy, surgical resection of the tumor, adverse events (AEs) with severity graded according to the American Society for Gastrointestinal Endoscopy (ASGE) lexicon severity grading system,[16] and their management. AEs were classified as immediate (during the procedure), early, and late (within or after 14 days from the EUS-CDS). Patients were followed with periodic laboratory analyses and clinic visits at the discretion of the responsible endoscopist at each participating hospital.

Outcomes

The primary outcomes for the study were technical and clinical success rates. Technical success was defined as the ability to complete an EUS-CDS with LAMS placement. Clinical success was defined as a decrease in the bilirubin level of at least 50% within 2 weeks after the procedure and assessed among the subgroup of patients achieving a technical success. Secondary outcomes included AE rate, analysis of factors associated with technical success, and comparison of results related to endoscopist experience.

Endoscopists were divided into 2 categories: experts and those who were less expert in EUS-CDS procedures. The latter was defined as an endoscopist with expertise in ERCP (>1000 ERCPs) and in EUS drainage with LAMSs for other indications (>10) having conducted fewer than 20 EUS-CDS. The beginner was trained by the expert for a year before dispatch.

The cutoff to discriminate endoscopist experience was set at 20 EUS-CDS procedures defining expert from nonexpert endoscopists as previously reported[13] and hence was chosen as a variable of interest. The ASGE lexicon severity grading system was used to grade AEs.[16]

Statistical analysis

Continuous variables are reported as mean ± standard deviation and categorical variables as frequency and percentage. Independent-sample t test and χ^2 test were used for comparison of continuous and categorical variables, respectively. A $P < .05$ was considered to indicate statistical significance. Logistic regression models were performed to identify variables associated with the following outcomes: technical success, clinical success, incidence of AEs, and stent occlusion. Survival analysis was carried out by the Kaplan-Meier estimator. Differences in the survival rate were assessed by log-rank testing. All statistical analyses were performed using SPSS version 25.0 for Macintosh (SPSS Inc, Chicago, Ill, USA).

RESULTS

Study population

Two hundred fifty-six consecutive patients were enrolled over the study period. Patient and clinical characteristics are outlined in Table 1.

TABLE 1. Demographic data

Characteristic	Value
Female	115 (44.9)
Age, y	73.9 ± 12.6
Etiology of biliary obstruction	
Pancreatic cancer	192 (75.0)
Ampullary cancer	22 (8.6)
Distal cholangiocarcinoma	17 (6.6)
Duodenal cancer	10 (3.9)
Metastasis from other tumors	15 (5.9)
Reason for failed ERCP	
Failed cannulation in a reachable papilla	84 (32.8)
Infiltration of the papilla	94 (36.7)
Duodenal stricture	69 (27)
Ampulla obscured by indwelling duodenal stents	9 (3.5)
Bilirubin, mg/dL	14.3 ± 7.1
Diameter of the common bile duct, mm	17.3 (3.9)

Values are n (%) or mean ± standard deviation.

Of the 256 patients, the most commonly used LAMS was the 8 × 8 mm in 132 (51.6%) followed by the 6 × 8 mm in 86 (33.6%). Characteristics of the EUS-CDS procedures are presented in Table 2 and described in Figure 1. The mean number of EUS-CDS procedures performed for each center was 24 ± 21 (Fig. 2).

Fifty-eight patients (24.3%) received a duodenal stent for GOO symptoms after EUS-CDS; in 36 of them the duodenal stent was positioned during the same procedure of EUS-CDS. In 4 of these 58 patients (6.8%) a second duodenal stent was required after a mean time of 204 ± 149 days for GOO relapse symptoms. Moreover, in 4 of 239 patients (1.7%) the GOO was managed by EUS-GE. During a mean follow-up of 151 ± 162 days, 97 patients (40.6%) received chemotherapy a mean of 27 ± 20 days after EUS-CDS, 24 patients (10.4%) underwent pylorus-preserving pancreaticoduodenectomy after a mean period of 68 ± 71 days, and 134 patients (56.1%) died from underlying disease.

Primary endpoint

Technical success was achieved in 239 of 256 patients (93.3%). Technical failure occurred in the remaining 17 patients because of LAMS misdeployment that was managed in the same session, with placement of a self-expandable metal stent into the fistulous tract in 10 patients (58.8%), deployment of a second LAMS in 4 (23.6%), and with an EUS-guided rendezvous with subsequent placement of a transpapillary stent in 3 (17.6%). Among the 239 patients with a successful LAMS placement, clinical success was obtained in 230 (96.2%). The mean percentage of decrease in bilirubin levels at 2 weeks was 72% (14.7 ± 7.11 mg/dL versus 4.11 ± 3.96 mg/dL ($P < .001$).

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TABLE 2. Characteristics of EUS-CBD procedures

Characteristic	Value
Bile duct access	
Transbulbar	250 (97.7)
Transgastric	6 (2.3)
Stent diameter	
Hot-Axios	
6 × 8 mm	86 (33.6)
8 × 8 mm	132 (51.6)
10 × 10 mm	28 (10.9)
15 × 10 mm	7 (2.7)
Nagi stent	
12 × 20 mm	1 (.4)
12 × 30 mm	1 (.4)
16 × 20 mm	1 (.4)
Step for access into the common bile duct	
Single stage	242 (94.5)
Multiple steps	14 (5.5)
Fluoroscopic control for deployment of the stent	
With	28 (10.9)
Without	228 (89.1)
Position into the common bile duct	
Proximal	63 (24.6)
Medium	193 (75.4)
Procedure time, min	34.3 ± 24.0
Stent deployment time, min	4.2 ± 4.0
EUS-CDS session of failed ERCP	
Same session	176 (68.8)
Different session	80 (31.2)
EUS-CDS procedures performed for center (range)	24 ± 21 (1-60)

Values are n (%) or mean ± standard deviation.
EUS-CDS, EUS-guided choledochoduodenostomy.

Secondary endpoints

Risk factor analysis for technical success. At univariate analysis, technical success was not statistically associated with age, gender, etiology of the DMBO, reasons for failed ERCP, stent type, and diameter (Fig. 3). A significantly higher technical success was achieved in shorter procedures, in patients with larger CBD diameter and, marginally, in patients with no symptoms of GOO, no indwelling duodenal stent, and in whom the intrachannel stent release technique was used for the deployment of the second flange of the stent. At logistic multiple regression model, shorter procedural time and the intrachannel release of the second flange were independently associated with technical success (Supplementary Table 1, available online at www.giejournal.org).

Endoscopist experience. Between nonexpert and expert endoscopists, respectively, technical success (101 [94.4%] vs 138 [92.6%]; $P = .574$), clinical success (96 [95.0%] vs 134 [97.1%]; $P = .415$), AE rate (10 [9.3%] vs 15 [10.1%]; $P = .848$), length of hospital stay (9.2 ± 8.2 vs 7.2 ± 9.0; $P = .071$), site of access (104 [97.2%] vs 146 [98%]; $P = .680$), stent dimension (42 [46.2%] vs 44 [34.6%]; $P = .086$), and intrachannel release of the second flange (95 [88.8%] vs 133 [89.3%]; $P = .904$) did not differ (Table 3). Larger CBD diameter (18.2 ± 4.7 vs 16.6 ± 3.2; $P = .002$), use of a needle with a guidewire (11 [10.3%] vs 3 [2.0%]; $P = .004$), fluoroscopy guidance (53 [49.5%] vs 38 [25.5%]; $P < .001$), and placement of the stent in the proximal CBD (35 [32.7%] vs 28 [18.8%]; $P = .011$) were more likely in the nonexpert group compared with the expert group, respectively, whereas the experts were more likely to perform the EUS-CDS in the same session of the failed ERCP (113 [75.8%] vs 63 [58.9%]; $P = .004$).

Adverse events. Twenty-seven AEs occurred in 25 (2 patients with 2 AEs) of 239 patients (10.5%) with a successful LAMS placement after a mean of 38 ± 81 days. Description of AEs are outlined in Table 4.

Stent obstruction occurred in 16 patients (6.7%) with recurrence of jaundice and symptoms of cholangitis from the stent obstruction by food impaction. This was managed with an endoscopic LAMS cleaning procedure with endoscopic extraction of impacted food in 8 patients (53.3%), through the insertion of an additional double-pigtail plastic stent within the indwelling LAMS in 6 patients (40%), and by percutaneous transhepatic biliary drainage in 2 patients (6.7%).

Four patients (1.7%) had bleeding treated by endoscopic hemostasis in 3 cases and by radiologic embolization in 1. In 2 patients (.8%) a LAMS migration occurred, managed with self-expandable metal stent placement in 1 case and double-pigtail plastic stent placement in the other case through the CDS fistula. Finally, 5 patients (2.9%) had cholangitis without jaundice treated only by antibiotics. Therefore, reinterventions to manage AEs with endoscopic or radiologic procedures occurred in 22 patients (9.2%).

According to the ASGE lexicon,[16] 3 AEs (11.1%) were classified as mild, 21 (77.7%) as moderate, and 3 (11.1%) as severe. No fatal AE occurred. Three AEs (11.1%) were classified as immediate, 7 (25.9%) as early, and 17 (62.9%) as delayed. Interestingly, when evaluating stent patency during follow-up, no significant differences between the use of a 6 × 8 mm versus 8 × 8 mm stent were observed ($P = .661$) (Supplementary Fig. 1, available online at www.giejournal.org).

DISCUSSION

The present multicenter study shows that EUS-CDS with LAMS in cases of DMBO in patients with failed ERCP represents a viable alternative for endoscopic biliary drainage with a high technical and clinical success (93.3% and

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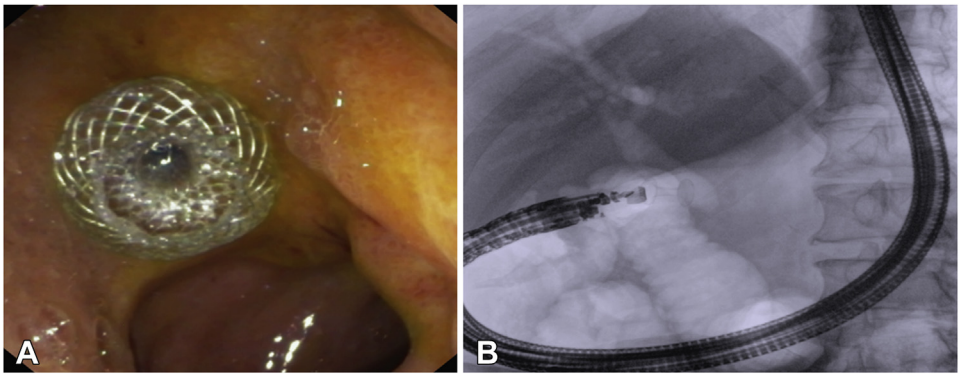

Figure 1. Final endoscopic (**A**) and radiologic (**B**) appearance of EUS-guided choledochoduodenostomy with a lumen-apposing metal stent through the duodenal bulb with a Hot-Axios stent.

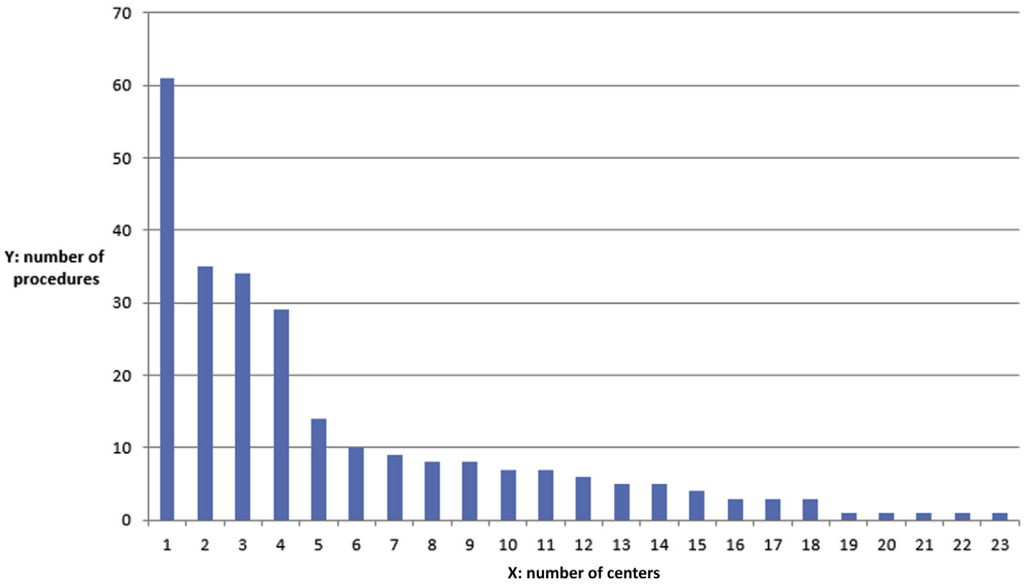

Figure 2. EUS-guided choledochoduodenostomy procedures performed per center (*x axis*) and number of procedures (*y axis*).

96.2%, respectively) and an acceptable AE rate. To the best of our knowledge, with 256 patients enrolled, this is the largest study present in the literature that focuses on this topic. Our results confirm the efficacy and safety of EUS-CDS using LAMSs in line with previously published studies.[8-11,17] Nevertheless, these studies were based on a small number of patients enrolled mainly from tertiary-level centers.

Moreover, it should be considered that the patients enrolled in our study were collected from many centers with different levels of expertise, such as tertiary-level centers with proven experience and knowledge of the technique and secondary-level centers with different rates of experience and number of procedures performed (mean of 24 ± 21 procedures). Thus, good reproducibility of the procedure was shown, confirming the efficacy of EUS-CDS also in the real-life setting with less expert endoscopists.

In recent years, EUS-BD has been more frequently chosen as an alternative for the management of biliopancreatic disease after the introduction on the market of dedicated devices. Namely for EUS-CDS, the development and constant improvement of the LAMS have ensured a simpler and safer technique for the management of patients with DMBO after ERCP failure, resulting in a rapid spread of the technique, not only in tertiary but also in secondary care centers. For these reasons, we aimed to conduct a nationwide study as a part of an education initiative involving most of our national centers performing this procedure, irrespective of the level of expertise and the number of performed procedures to evaluate not only the feasibility but also the reproducibility of the procedure. Indeed, another result of our study that should be emphasized is that technical success, clinical success, and AE rate were independent of endoscopist experience, thus confirming a possibility

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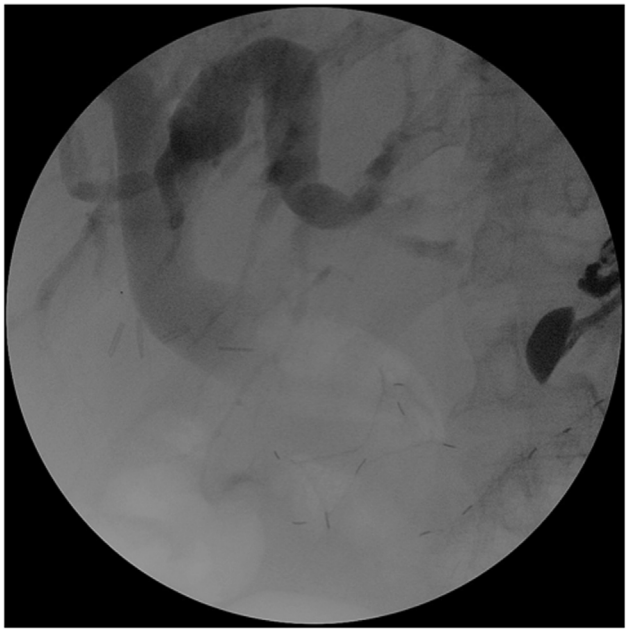

Figure 3. Final radiologic appearance of EUS-guided choledochoduodenostomy with a lumen-apposing metal stent through the duodenal bulb with a Nagi stent.

to increase, after receiving adequate training, the endoscopists able to perform the procedure.

Our results reflect the learning curve for EUS-CDS. We found that nonexpert endoscopists used the needle and guidewire more frequently to access the CBD for LAMS deployment under fluoroscopy guidance and placed the stent in the proximal part of the CBD where the diameter of the CBD could be larger. Therefore, when familiarity with the technique is increased, the endoscopist can more frequently use the freehand technique without using fluoroscopy for the stent deployment. Moreover, experts more often performed the EUS-CDS in the same session of the failed ERCP, thus managing patients with a lower CBD diameter in which the procedure could be more difficult as previously shown.[9]

Nevertheless, to date, data on the learning curve for EUS-BD are lacking, and the minimum number of EUS-CDS required to obtain competency is still not established. An Asian group of experts in interventional EUS stated that expertise in ERCP, EUS, and EUS-FNA is desirable for performing EUS-BD.[18] On the other hand, data on the learning curve for other interventional EUS procedures have been published: 25 procedures for EUS-guided gallbladder drainage, 5 to 10 for EUS-guided pancreatic fluid collection drainage, and 40 cases for EUS-GE.[18-20]

Interestingly, the number of procedures required to gain competency for EUS interventional procedures on various indications is less than the number of procedures required for the training in ERCP. Indeed, a prospective multicenter study[21] evaluating learning curves and competence among advanced endoscopy trainees showed that the average number of ERCPs for achieving competence for grade 2 ERCP procedures as per ASGE ERCP grade of difficulty[22] (including ERCP for DMBO) was 300 cases. However, even in expert hands in patients with DMBO, difficult biliary cannulation could occur in about 56.4% of ERCPs, with a cannulation failure rate up to 12.9%.[23] Considering all these data together and the efficacy, safety, and reproducibility of EUS-CDS, in the future it might be appropriate to radically change the approach to patients with jaundice because of DMBO, choosing EUS-CDS as the first treatment option. Moreover, the logistic multiple regression analysis of the study cohort identified that technical success was statistically related to the intrachannel release of the second flange; these data can be explained by an increasing familiarity with both the technique and the devices. As previously described for EUS-CDS and EUS-guided hepaticogastrostomy, the intrachannel stent release technique was a safe and effective method to release the second flange of the stent.[15,24] Another key aspect of our study worth noting is the limited mean procedural time, which may play a role in frail patients who may not be able to withstand prolonged sedation.

With regard to AEs, in our findings we account for a lower rate of AEs (10.5%) than most studies present in the literature, as also reported in a recent systematic review and meta-analysis in which 31 studies (accounting for 820 patients) were included with a pooled rate of AEs amounting to 17.1%.[25] In addition, most AEs that occurred during the follow-up period were classified as mild or moderate (89.3%) and were managed by conservative or endoscopic treatment in 75% of cases without the need to refer the patient to the surgeon or interventional radiologist. It should also be emphasized that no fatal AEs occurred.

The most common AE in our study was stent obstruction, which occurred in 6.7% of patients. This is a lower rate than previously reported,[26] although it doubled when compared with ERCP.[27] These data are particularly important because cholangitis emerged as an independent risk factor for mortality in patients who underwent endoscopic stent placement and neoadjuvant chemotherapy followed by pancreaticoduodenectomy.[28] Therefore, in these patients, it is mandatory to perform the technique of biliary drainage with the lowest rate of cholangitis and to better understand how we can reduce the risk of cholangitis in patients with LAMSs (eg, placing a double-pigtail plastic stent through the LAMS). However, a recent retrospective study comparing whether inserting a double-pigtail stent within the LAMS offers a potential benefit in EUS-CDS obstruction showed that the difference in obstruction rate was not statistically significant between the 2 groups (23.5% vs 13.6%, $P = .67$).[29] Furthermore, the authors stated that adding a double-pigtail stent through the LAMS appears not to be sufficient to prevent biliary AEs and is a time-consuming strategy.

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TABLE 3. Procedure variables and outcomes stratified by center experience

Variable	Low-experience centers (<20 procedures) (n = 107)	High-experience centers (≥20 procedures) (n = 149)	*P* value
CBD diameter, mm	18.2 ± 4.7	16.6 ± 3.2	.002
Access technique			
Single stage	96 (89.7)	146 (98.0)	.004
Needle + guidewire	11 (10.3)	3 (2.0)	
Access type			
Transgastric	3 (2.8)	3 (2.0)	.680
Transduodenal	104 (97.2)	146 (98.0)	
Under fluoroscopic control	53 (49.5)	38 (25.5)	<.001
Stent size			
6 mm	42 (46.2)	44 (34.6)	.086
8 mm	49 (53.8)	83 (65.4)	
Release of the second flange			
Intrachannel	95 (88.8)	133 (89.3)	.904
Endoscopic view	12 (11.2)	16 (10.7)	
Position			
Proximal common bile duct	35 (32.7)	28 (18.8)	.011
Medium common bile duct	72 (67.3)	121 (81.2)	
EUS procedure			
Same session of failed ERCP	63 (58.9)	113 (75.8)	.004
Different session	44 (41.1)	36 (24.2)	
Technical success	101 (94.4)	138 (92.6)	.574
Clinical success	96 (95)	134 (97.1)	.415
Adverse events	10 (9.3)	15 (10.1)	.848
Length of hospital stay, days	9.2 ± 8.2	7.2 ± 9.0	.071

Values are n (%) or mean ± standard deviation.

TABLE 4. Characteristics of main adverse events, with severity grade index and their management

Adverse event	No. of events (%)	Immediate (during the procedure)	Early (<14 days)	Late (>14 days)	Severity grade index	Management
Bleeding	4 (1.7)	3	—	1	3 moderate 1 severe	3 endoscopy 1 interventional radiology
Stent migration	2 (.8)	—	—	2	2 moderate	2 endoscopy
Infection	5 (2.1)	—	1	4	3 mild 1 moderate 1 severe	5 conservative
Stent occlusion	16 (6.7)	—	6	10	15 moderate 1 severe	14 endoscopy 2 interventional radiology

—, None.

Further randomized controlled trials are needed to assess this topic to understand how we can reduce the risk of cholangitis in patients with LAMSs. Nevertheless, regarding procedure-related AEs observed, it is worth noting that no cases of postprocedure pancreatitis were encountered, in comparison with the occurrence of biliary drainage by ERCP up to 5.5%.[23] This aspect carries significant clinical implications including shorter length of stay and faster onset of scheduled therapies.

Fifty-eight patients (24.3%) received a duodenal stent for concomitant duodenal stenosis, showing a high percentage of treated patients with advanced disease. Moreover, the GOO was treated in the same session of EUS-CDS in 36 of 58 cases with duodenal stent and in 4

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patients with EUS-GE. Having the opportunity to solve these 2 conditions in 1 session could be essential for such a critical patient.

In 4 of 58 patients (6.8%) a second duodenal stent was required for recurrence of GOO symptoms. These data, although still marginal, should encourage the possibility of seeking alternative solutions for the treatment of these patients. This may include the creation of an EUS-GE far from the original stenosis, which could prevent the onset of such a debilitating AE and improve the quality of life of these fragile patients.[30-32]

Recently, a multicenter retrospective study from a French group enrolling 70 patients recommended the use of 6 × 8 mm stents to maximize success rates.[17] Instead, in our analysis, no statistically significant difference was observed between 6 × 8 mm and 8 × 8 mm stents in terms of stent patency ($P = .661$).

Our study has several limitations related to its retrospective design and the involvement of several centers with many different operators, which could have determined some heterogeneity in the data. Nevertheless, the considerable number of involved hospitals (23 centers) with different levels of expertise could also be considered as a strength of this study, showing once again how the EUS-CDS with LAMSs can be considered safe and effective even in different centers with a range of expertise.

In conclusion, the present multicenter study for the treatment of DMBO with EUS-CDS and LAMS deployment has provided solid, secure, and efficient data with consistent evidence of its wide-scale reproducibility. Timing and a clear indication to perform this procedure still need to be addressed, but the recent evidence suggests a possible role of an "early" approach in the treatment flowchart of DMBO as in the "early precut" approach in the recent history of biliopancreatic endoscopy.

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REFERENCES

1. Dumonceau J-M, 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. 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.
3. Anderloni A, Troncone E, Fugazza A, et al. Lumen-apposing metal stents for malignant biliary obstruction: Is this the ultimate horizon of our experience? World J Gastroenterol 2019;25:3857-69.
4. Mussetto A, Fugazza A, Fuccio L, et al. Current uses and outcomes of lumen-apposing metal stents. Ann Gastroenterol 2018;31:535-40.
5. Fugazza A, Colombo M, Repici A, et al. Endoscopic ultrasound-guided gallbladder drainage: current perspectives. Clin Exp Gastroenterol 2020;13:193-201.
6. Fugazza A, Sethi A, Trindade AJ, et al. International multicenter comprehensive analysis of adverse events associated with lumen-apposing metal stent placement for pancreatic fluid collection drainage. Gastrointest Endosc 2020;91:574-83.
7. Parsa N, Nieto JM, Powers P, et al. Endoscopic ultrasound-guided drainage of pancreatic walled-off necrosis using 20-mm versus 15-mm lumen-apposing metal stents: an international, multicenter, case-matched study. Endoscopy 2020;52:211-9.
8. Kunda R, Pérez-Miranda M, Will U, et al. EUS-guided choledochoduodenostomy for malignant distal biliary obstruction using a lumen-apposing fully covered metal stent after failed ERCP. Surg Endosc 2016;30:5002-8.
9. Anderloni A, Fugazza A, Troncone E, et al. Single-stage EUS-guided choledochoduodenostomy using a lumen-apposing metal stent for malignant distal biliary obstruction. Gastrointest Endosc 2019;89:69-76.
10. Tsuchiya T, Teoh AYB, Itoi T, et al. Long-term outcomes of EUS-guided choledochoduodenostomy using a lumen-apposing metal stent for malignant distal biliary obstruction: a prospective multicenter study. Gastrointest Endosc 2018;87:1138-46.
11. Fabbri C, Fugazza A, Binda C, et al. Beyond palliation: using EUS-guided choledochoduodenostomy with a lumen-apposing metal stent as a bridge to surgery. A case series. J Gastrointest Liver Dis 2019;28:125-8.
12. Anderloni A, Buda A, Carrara S, et al. Single-session double-stent placement in concomitant malignant biliary and duodenal obstruction with a cautery-tipped lumen apposing metal stent. Endoscopy 2016;48(Suppl 01):E321-2.
13. Jacques J, Privat J, Pinard F, et al. Endoscopic ultrasound-guided choledochoduodenostomy with electrocautery-enhanced lumen-apposing stents: a retrospective analysis. Endoscopy 2019;51:540-7.
14. Auriemma F, Fugazza A, Colombo M, et al. Safety issues in endoscopy ultrasound-guided interventions using lumen apposing metal stents: a review of the literature. Min Gastroenterol 2021.
15. Anderloni A, Attili F, Carrara S, et al. Intra-channel stent release technique for fluoroless endoscopic ultrasound-guided lumen-apposing

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metal stent placement: changing the paradigm. Endosc Int Open 2017;5:E25-9.
16. Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010;71:446-54.
17. Jacques J, Privat J, Pinard F, et al. EUS-guided choledochoduodenostomy by use of electrocautery-enhanced lumen-apposing metal stents: a French multicenter study after implementation of the technique (with video). Gastrointest Endosc 2020;92:134-41.
18. Teoh AYB, Dhir V, Kida M, et al. Consensus guidelines on the optimal management in interventional EUS procedures: results from the Asian EUS group RAND/UCLA expert panel. Gut 2018;67:1209-28.
19. Teoh AY, Perez-Miranda M, Kunda R, et al. Outcomes of an international multicenter registry on EUS-guided gallbladder drainage in patients at high risk for cholecystectomy. Endosc Int Open 2019;7:E964-73.
20. Jovani M, Ichkhanian Y, Parsa N, et al. Assessment of the learning curve for EUS-guided gastroenterostomy for a single operator. Gastrointest Endosc 2021;93:1088-93.
21. Wani S, Han S, Simon V, et al. Setting minimum standards for training in EUS and ERCP: results from a prospective multicenter study evaluating learning curves and competence among advanced endoscopy trainees. Gastrointest Endosc 2019;89:1160-8.
22. Cotton PB, Eisen G, Romagnuolo J, et al. Grading the complexity of endoscopic procedures: results of an ASGE working party. Gastrointest Endosc 2011;73:868-74.
23. Fugazza A, Troncone E, Amato A, et al. Difficult biliary cannulation in patients with distal malignant biliary obstruction: an underestimated problem? Dig Liver Dis. Epub 2021 Aug 4.
24. 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;22:1312-8.
25. Amato A, Sinagra E, Celsa C, et al. Efficacy of lumen-apposing metal stents or self-expandable metal stents for endoscopic ultrasound-guided choledochoduodenostomy: a systematic review and meta-analysis. Endoscopy 2021;53:1037-47.
26. Uemura RS, Khan MA, Otoch JP, et al. EUS-guided choledochoduodenostomy versus hepaticogastrostomy: a systematic review and meta-analysis. J Clin Gastroenterol 2018;52:123-30.
27. Dumonceau J-M, Kapral C, Aabakken L, et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2020;52:127-49.
28. Darnell EP, Wang TJ, Lumish MA, et al. Preoperative cholangitis is an independent risk factor for mortality in patients after pancreatoduodenectomy for pancreatic cancer. Am J Surg 2021;221:134-40.
29. Garcia-Sumalla A, Loras C, Guarner-Argente C, et al. Is a coaxial plastic stent within a lumen-apposing metal stent useful for the management of distal malignant biliary obstruction? Surg Endosc 2021;35:4873-81.
30. Troncone E, Fugazza A, Cappello A, et al. Malignant gastric outlet obstruction: Which is the best therapeutic option? World J Gastroenterol 2020;26:1847-60.
31. Khashab MA. EUS-guided gastroenterostomy vs duodenal stenting for the palliation of malignant gastric outlet obstruction. Gastroenterol Hepatol 2019;15:323-5.
32. Khashab MA, Kumbhari V, Grimm IS, et al. EUS-guided gastroenterostomy: the first U.S. clinical experience (with video). Gastrointest Endosc 2015;82:932-8.

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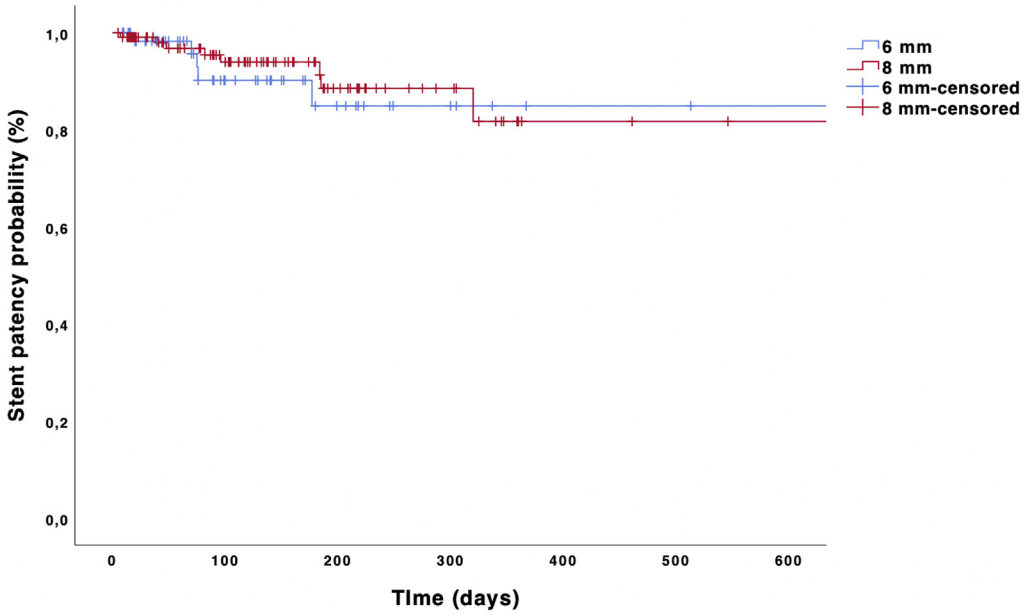

Supplementary Figure 1. Kaplan-Meier curve of stent patency probability during follow-up by stent size ($P = .661$, by log-rank test).

SUPPLEMENTARY TABLE 1. Univariate and multivariate analysis of variables associated with technical success

Variable	Univariate analysis			Multivariate analysis	
	Technical success (n = 239)	Technical failure (n = 17)	*P* value	Odds ratios (95% confidence interval)	*P* value
Symptoms of gastric outlet obstruction	66 (27.6)	8 (47.1)	.088	1.14 (.45-4.407)	.552
Indwelling duodenal stent	14 (5.9)	3 (17.6)	.058	2.60 (.53-12.5)	.23
Release of the second flange					
Intrachannel	215 (90.0)	13 (76.5)	.085	4.11 (1.06-15.9)	.04
Endoscopic view (reference)	24 (10.0)	4 (23.5)			
Procedural time	32.7 ± 23.4	55.3 ± 34.5	<.001	1.02 (1.01-1.045)	.001
Common bile duct diameter	17.4 ± 4.0	15.4 ± 3.5	.038	.88 (.74-1.049)	.16

Values are n (%) or mean ± standard deviation unless otherwise defined.

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