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Original Article

Classification, risk factors, and management of lumen apposing metal stent dysfunction during follow-up of endoscopic ultrasound-guided choledochoduodenostomy: Multicenter evaluation from the Leuven-Amsterdam-Milan Study Group

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Objectives: Long-term outcomes of endoscopic ultrasound-guided choledochoduodenostomy (EUS-CDS) performed with lumen apposing metal stents (LAMS) have been poorly evaluated in small or retrospective series, leading to an underestimation of LAMS dysfunction.

Methods: All consecutive EUS-CDS performed in three academic referral centers were included in prospectively maintained databases. Technical/clinical success, adverse events (AEs), and dysfunction during follow-up were retrospectively analyzed. Kaplan–Meier analysis was used to estimate dysfunction-free survival (DFS), with Cox proportional hazard regression to evaluate independent predictors of dysfunction.

Results: Ninety-three patients were included (male 56%; mean age, 70 years [95% confidence interval (CI) 68–72]; pancreatic cancer 81%, metastatic disease 47%). In 67% of procedures, 6 mm LAMS were used. Technical and clinical success were achieved in 97.8% and 93.4% of patients, respectively, with AEs occurring in 9.7% (78% mild/moderate). Dysfunction occurred in 31.8% of patients after a mean of 166 days (95% CI 91–241), with an estimated 6 month and 12 month DFS of 75% and 52%, respectively; mean DFS of 394 (95% CI 307–482) days. Almost all dysfunctions (96%) were successfully managed by endoscopic reintervention. Duodenal invasion (hazard ratio 2.7 [95% CI 1.1–6.8]) was the only independent predictor of dysfunction.

Conclusions: Endoscopic ultrasound-guided choledochoduodenostomy shows excellent initial efficacy and safety, although stent dysfunctions occurs frequently during long-term follow-up. Almost all stent dysfunctions can be managed successfully by endoscopic reinterventions. We propose a comprehensive classification of the different types of dysfunction that may be encountered and rescue procedures that may be employed under these circumstances. Duodenal invasion seems to increase the risk of developing EUS-CDS dysfunction, potentially representing a relative contraindication for this technique.

Key words: biliary drainage, choledochostomy, pancreatic neoplasm, stent, therapeutic endoscopic ultrasound

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INTRODUCTION

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) with placement of a self-expandable metal stent (SEMS) is the gold standard for distal malignant biliary obstruction (MBO).[1] However,

despite technical proficiency and the use of advanced techniques, ERCP fails in 3.4–16% of cases.[2–4]

Endoscopic ultrasound (EUS)-guided choledochoduodenostomy (EUS-CDS) is a more recent alternative that, in the hands of experts, has shown high technical (93.3%) and clinical (94.8%) success.[5] In this procedure a biliodigestive anastomosis is created through normal tissue without the need of traversing the tumor. EUS-CDS precludes the need to reach the papilla and is technically feasible in patients with duodenal obstruction with spared duodenal bulb. All-in-one electrocautery-enhanced lumen apposing metal stents (LAMS) have further simplified the procedure by obviating the need for device exchanges, potentially leading to fewer adverse events (AEs)[6] (6.2% in one study[5]). Comparative studies have revealed that EUS-CDS is superior to the percutaneous approach,[7] and as such EUS-CDS has been recommended by international guidelines as the preferred drainage strategy after failed ERCP in distal MBO.[8]

Despite these promising results, the long-term outcomes of EUS-CDS have only been reported in a limited number of studies.[9,10] Long-term patency data are crucial, as this may improve understanding of this technique and patient selection.

We conducted an international, multicenter, retrospective study of prospectively maintained databases to: (i) evaluate the frequency of EUS-CDS dysfunction, (ii) identify predictors of stent dysfunction, and (iii) report outcomes of different management strategies for dysfunction. Occurring events were used to create a classification with the aim of improving the reporting on EUS-CDS dysfunction, creating more precise insight into the underlying pathogenesis of dysfunction, and tailoring rescue strategies to specific cases. For each item in the classification, a clinical algorithm with suggested management strategy is provided.

METHODS

THE PROSPECTIVELY MAINTAINED registries of therapeutic EUS procedures in three tertiary, academic, referral centers were retrospectively queried for all consecutive patients undergoing EUS-CDS for distal MBO.

Procedures performed between January 2017 and January 2022 were included. For the purpose of this study, a minimum follow-up of >30 days was required, unless death or surgery occurred earlier.

In our centers, EUS-CDS is performed by free-hand placement of a LAMS (Hot-Axios; Boston Scientific, Marlborough, MA, USA) in a long-route position from the duodenal bulb, with the tip of the catheter pointing towards the hilum; the proximal flange is released under EUS control, with intrachannel opening of the distal flange and release under endoscopic view. In case of failed ERCP, EUS-CDS is performed in the same session.

Demographic and procedural variables were registered, among which underlying disease, disease stage, reason for EUS-CDS, LAMS size, and placement of coaxial double pigtail plastic stent (DPPS).

This research was conducted in compliance with the Declaration of Helsinki and Good Clinical Practice, and approved by the Ethics Committee at the coordinating center (ID: 178/INT/2020) and at each location.

Patients were followed-up by scheduled visits per standard of care in our centers, by accessing electronic health databases from referral network hospitals, or conducting telephonic follow-up when no follow-up visit was available, especially due to the COVID-19 pandemic. Moreover, a relevant quota of patients was included in a standardized prospective monthly follow-up under the PROTECT Registry (NCT04813055) or ongoing clinical trials.

Outcomes

The primary outcome was LAMS dysfunction during follow-up of technically/clinically successful EUS-CDS, both as rate (proportion) and time-to-event (dysfunction-free survival [DFS]).

Secondary outcomes were evaluation of: (i) technical success, clinical success (CS), and AEs of the cohort, (ii) management of dysfunction, and (iii) predictors of dysfunction.

Definitions

Technical success was defined as the successful placement of the LAMS between the common bile duct (CBD) and the duodenum. Clinical success was defined as a ≥50% bilirubin decrease during follow-up.

Adverse events were scored through the American Society for Gastrointestinal Endoscopy lexicon.[11]

"Duodenal invasion" was defined as the endoscopic appearance for tumoral invasion, even without overt stenosis and regardless of whether the papilla could be endoscopically reached. In case the papilla could not be reached, this was defined as "inaccessible papilla." All other unsuccessful ERCPs were recorded as "failed ERCP."

Dysfunction was defined as a new onset/increase of bilirubin values and/or occurrence of cholangitis after former CS. DFS was calculated from the date of the procedure to the time of dysfunction, death, or surgical removal of the EUS-CDS, whichever presented first. Rescue procedures and the number of reinterventions were analyzed.

The Leuven-Amsterdam-Milan Study Group classification of EUS-CDS dysfunction

A comprehensive classification was developed based on the dysfunction events reported in this series. After revision of all available preprocedural (computed tomography, magnetic resonance imaging) and intraprocedural (endoscopic, fluoroscopic) imaging, events were first extensively described in the database. Three investigators (G.V., R.v.W., M.B.) independently grouped all events into a classification proposal. The three proposals were then compared, critically revised, and simplified by discussion, with disagreements resolved by a senior investigator (S.v.d.M.). Schematic images were prepared for each item in the classification. The same methodology was used to classify management strategies, and to link each event to a rescue strategy into a proposed clinical algorithm.

Statistics

Descriptive statistics are reported as frequencies (proportions) and mean (95% confidence interval [CI]) or medians (interquartile range) as appropriate.

Comparisons between patients with or without dysfunction were performed through the χ^2-test or Fisher's test for qualitative data and the *t*-test or Mann–Whitney test for quantitative data, as appropriate.

Dysfunction-free survival was analyzed by Kaplan–Meier statistics. Patients were censored at dysfunction, death, last telephonic follow-up, or surgical removal of the LAMS, whichever came first. Predictors of dysfunction were analyzed through Cox proportional hazards regression and results expressed as hazard ratios (HR) and 95% CI. Variables significant at univariable analysis were included in the multivariate model.

All analyses were performed using Medcalc (Ostende, Belgium).

RESULTS

NINETY-THREE PATIENTS WERE finally included (Table 1); the inclusion process is depicted in Figure S1. The mean age was 70 (95% CI 68–72) years, 56% were male. Primary disease was pancreatic cancer in 75 (81%) and duodenal/ampullary cancer in 10 (11%). Duodenal invasion was identified in 44 (48%) cases. Reasons for EUS-CDS were: inaccessible papilla in 21% of cases, failed ERCP in 69%, and primary EUS-CDS (within trial context) in 11% of cases.

Procedural characteristics are reported in Table 2. Two-thirds of procedures were performed with 6 × 8 mm LAMS, whereas one-third underwent 8 × 8 mm LAMS placement. A coaxial DPPS was placed in only six (6.5%) cases. In one case, the LAMS was released over-the-wire due to a small-caliber CBD.

Table 1 Characteristics of included patients

Variable	Total *N* = 93
Mean age, years (95% CI)	70 (68–72)
Male, *n* (%)	52 (55.9)
Primary disease, *n* (%)	
Pancreatic cancer	75 (80.6)
Ampullary/duodenal cancer	10 (10.8)
Metastatic lesion	3 (3.2)
Distal cholangiocarcinoma	3 (3.2)
Other malignancies	2 (2.2)
Oncological staging, *n* (%)	
Metastatic	43 (46.2)
Locally advanced	30 (32.3)
Borderline resectable	7 (7.5)
Resectable	13 (14)
Reason for EUS-CDS, *n* (%)	
ERCP failure	64 (68.8)
Inaccessible papilla (duodenal stenosis)	19 (20.4)
Primary EUS-CDS (trials)	10 (10.8)
Duodenal invasion, *n* (%)	44 (47.3)
Duodenal stent in place, *n* (%)	9 (9.7)

CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; EUS-CDS, endoscopic ultrasound-guided choledochoduodenostomy.

Technical success was attained in 91/93 (97.8%) patients; among four initial misdeployments, two regarding the distal flange alone were immediately endoscopically salvaged, whereas two misdeployments after both flanges were released required percutaneous transhepatic biliary drainage (PTBD).

Clinical success was reached in 85 out of 91 technically successful procedures (93.4%; representing 91.4% of the total population). Among six clinical failures, two underwent PTBD, one required EUS-guided gallbladder drainage after early LAMS migration, whereas three did not reach CS due to short survival (n = 2) or diffuse metastatic liver invasion (n = 1).

Adverse events occurred in 9/93 (9.7%) cases, which were mild/moderate in seven (7.5%) and severe in two (2.2%) cases (Table 2).

Nine patients underwent a pancreaticoduodenectomy after a mean of 45 (95% CI 24–65) days after EUS-CDS. Four patients experienced an AE (three pancreatic fistulas and one chyle leak), whereas no technical issue or AEs potentially related to the presence of the LAMS were reported.

Table 2 Characteristics of endoscopic ultrasound-guided choledochoduodenostomy procedures

Variable	Total $N = 93$
EC-LAMS diameter (mm), *n* (%)	
6	62 (66.7)
8	30 (32.3)
15	1 (1.1)
Over-the-guidewire LAMS placement, *n* (%)	1 (1.1)
Coaxial DPPS, *n* (%)	6 (6.5)
Outcomes	
Technical success, *n* (%)	91 (97.9)
Initial misdeployments	4 (4.3)
Solved intraprocedurally[†]/failed placement	2/2
Clinical success, *n* (%)[‡]	85/91 (93.4)[‡]
Adverse events, *n* (%)[§]	9 (9.7)
Mild	2 (2.2)
• 2 cholangitis ➔ antibiotics	
Moderate	5 (5.4)
• 2 cholangitis ➔ antibiotics	
• 1 bile leak (incomplete deployment) ➔ PTBD	
• 1 acute cholecystitis ➔ EUS-GBD	
• 1 retroperitoneal collection ➔ antibiotics	
Severe	2 (2.2)
• 1 perforation ➔ surgical biliodigestive anastomosis	
• 1 bile leak (misdeployment) ➔ PTBD	
Mean postprocedural overall survival, days (95% CI)	184 (143–225)
Deaths, *n* (%)	37 (41.24)

[†]One by repeating de novo the procedure and one by inserting a guidewire through the lumen apposing metal stent (LAMS) catheter and deploying a second LAMS over-the-wire.
[‡]Among the 91 patients with technical success.
[§]Classified according to the American Society for Gastrointestinal Endoscopy lexicon.
CI, confidence interval; DPPS, double pigtail plastic stent; EC-LAMS, electrocautery enhanced LAMS; EU-GBD, endoscopic ultrasound-guided gallbladder drainage; PTBD, percutaneous transhepatic biliary drainage.

Dysfunction

Excluding failures, 85 clinically successful procedures were available for follow-up (mean 138 [95% CI 104–173] days).

Twenty-seven patients (31.8%) experienced dysfunction after a mean of 166 (95% CI 91–241) days, with a similar rate between the participating centers (Table 3). The most frequent dysfunction (Fig. 1) was related to stone impaction (Type 2a, 9 [33.3%]), followed by food impaction (Type 2b, 5 [18.5%]) and LAMS invasion/compression on the duodenal side (Type 3b, 3 [11.1%]). Notably, a concomitant gastric outlet obstruction (GOO) was found to be the only explanation for dysfunction in seven (25.9%) patients (Type 5). The most frequent rescue strategy (Fig. 2 and Table S1) was the placement of a coaxial DPPS (Type A, 12 [44%]), followed by balloon swipes (Type B, 3 [11%]) and the treatment of the GOO without further intervention on EUS-CDS (Type F, 3 [11%]).

Overall, dysfunctions were endoscopically managed in 26 (96%) cases, while one patient underwent PTBD. Seven (7.1%) patients required a second reintervention after a mean of 49 (95% CI 17–81) days, for a different circumstance in four cases (Table S2). In four cases a previously placed coaxial DPPS required a more definitive solution, such as a transpapillary SEMS ($n = 2$), resolution of GOO ($n = 1$), and EUS-hepaticogastrostomy (HGS; $n = 1$).

Dysfunction-free survival analyzed through Kaplan–Meier analysis is shown in Figure 3. Mean estimated DFS was 394 (95% CI 307–482) days, with a DFS probability at 3, 6, and 12 months of 81%, 75%, and 51%, respectively.

Characteristics of patients who did and did not experience dysfunction are reported in Table 4. No difference was detected in demographics or primary disease. However, patients experiencing dysfunction exhibited duodenal invasion more frequently, while having lower rates of resectable disease. The presence of duodenal invasion (HR 2.7 [95% CI 1.1–6.8]) was found to be the only independent predictor of dysfunction, in a model correcting for disease stage and the presence of an enteral stent.

DISCUSSION

ENDOSCOPIC ULTRASOUND-GUIDED CHOLEDOCHODUODENOSTOMY is recommended as the preferred salvage strategy in distal MBO when ERCP fails. Despite high short-term clinical efficacy, a paucity of information exists regarding long-term patency. In our multicenter evaluation, EUS-CDS dysfunction occurred in one-third of patients. We identified five distinct clinically relevant patterns of stent dysfunction. Duodenal neoplastic invasion was the only independent predictor of EUS-CDS dysfunction. Depending on dysfunction subtype, nine endoscopic rescue strategies were performed, which were successful in 96% of patients. A clinically oriented algorithm linking each event to a possible management strategy is proposed in Table S1.

Two prospective and 10 retrospective studies on EUS-CDS using LAMS have previously reported dysfunction rates of EUS-CDS using LAMS between 2.7% and 26% (Table 5),[9,10,12–21] with a pooled rate of 103/803 (12.9%). Reasons for the higher dysfunction rate in our study are

Table 3 Characteristics and classifications of endoscopic ultrasound-guided choledochoduodenostomy (EUS-CDS) dysfunction

Variable	Total *N* = 93
Excluded from follow-up	*n* = 8
Technical/clinical failure	2/6
Available follow-up	Total *N* = 85
Mean follow-up, days (95% CI)	138 (104–173)
Dysfunctions, *n* (%)	27/85 (31.8)
Mean time-to-dysfunction, days (95% CI)	166 (91–241)
Dysfunction classification, *n* (%)	*N* = 27
1: Sump syndrome	1 (3.7)
2a: Stone/sludge impaction	9 (33.3)
2b: Food impaction	5 (18.5)
3a: LAMS invasion/compression on biliary side	1 (3.7)
3b: LAMS invasion/compression on duodenal side	3 (11.1)
4: LAMS migration	1 (3.7)
5: GOO	7 (25.9)
Rescue procedure classification, *n* (%)	*N* = 27
A: Coaxial DPPS	12 (44.4)
B: Balloon/basket swipes	3 (11.1)
C: Through-the-LAMS biliary SEMS	2 (7.4)
D1: Transpapillary SEMS (retrograde by standard cannulation)	1 (3.7)
D2: Transpapillary SEMS (entry through the LAMS for rendezvous)	2 (7.4)
D3: Transpapillary SEMS (entry through the LAMS for antegrade stenting)	0[†]
E: Over-the-wire LAMS exchange	1 (3.7)
F: Resolution of GOO	3 (11.1)
G1: Redo EUS-CDS	1 (3.7)
G2: EUS-HGS	1 (3.7)
G3: PTBD	1 (3.7)
Endoscopic/percutaneous/surgical management	96%/4%/0
Number of reinterventions, *n* (%)	*N* = 85
0	58 (68.2)
1	21 (24.7)
2	5 (5.9)
3	1 (1.2)
Dysfunctions per location, *n* (%)	*P* = 0.9
Milan	14/43 (32.6)
Amsterdam	7/24 (29.2)
Leuven	6/18 (33.3)

[†]Used as rescue procedure after a second dysfunction, see Table S2.

DPPS, double pigtail plastic stent; EUS-HGS, endoscopic ultrasound-guided hepaticogastrostomy; GOO, gastric outlet obstruction; LAMS, lumen apposing metal stent; PTBD, percutaneous transhepatic biliary drainage; SEMS, self-expandable metal stent.

unclear but may be related to the prospectively maintained and updated databases, patient selection, the exclusion of lost-to-follow-up patients, and a low threshold for endoscopic reintervention in case of recurring symptoms; however, the identical dysfunction rates among the three centers of different nationalities underline that these rates are generalizable and realistic. In contrast to previous series, we mostly (98.9%) used the smallest caliber LAMS (6 and 8 mm diameter), theoretically reducing the risk of food impaction and ascending cholangitis, but potentially increasing stent occlusion. While two previous studies found no increased risk for the 6 mm vs. larger LAMS,[17,18] a recent study did so; interestingly, stent dysfunction could be prevented by prophylactic DPPS placement.[21] In our study, no influence of LAMS size was detected, whereas only a minority of patients received prophylactic DPPS placement. Whether prophylactic coaxial DPPS placement significantly influences outcomes remains unclear[16,18] until a randomized controlled study will provide the final answer.[22]

Stent dysfunction in our cohort was caused by five different types of obstruction (Fig. 1). Differentiating between specific underlying causes seems clinically relevant, as each type of dysfunction may be best resolved by specific interventions (Fig. 2, Tables 5, S1).

Sump syndrome is a well-known adverse event of surgical choledochoduodenostomy, where the distal bile serves as a reservoir for static bile and debris leading to cholangitis.[23] However, in EUS-CDS, CBD distal to the LAMS is occupied by a malignant stricture and the reservoir is limited, unlike surgical derivations performed for benign indications. In our series, one case was detected due to an almost complete response to chemotherapy. In these cases, transpapillary stent placement may be the ideal rescue therapy.

In the majority of cases, dysfunction was caused by impaction of biliary sludge (Type 2a) or food (Type 2b). LAMS are considerably shorter than tubular stents, and the shorter barrier as well as an unintentional oral orientation after stent expansion may direct partially digested food particles towards the bile ducts. Indeed, EUS-CDS performed with tubular stents directed towards the oral side vs. downwards have been associated with dysfunction.[24] Cleaning the stent and bile duct using balloon or basket swipes is considered essential, and generally followed by placement of the DPPS, aimed at maintaining stent patency.[25,26] This strategy, however, may fail in some cases and the LAMS may be used as entry to place a wire across the papilla, followed by antegrade stenting or ERCP rendezvous.[27]

Lumen apposing metal stents morphology may lead to occlusion at either flange. At the duodenal flange (Type

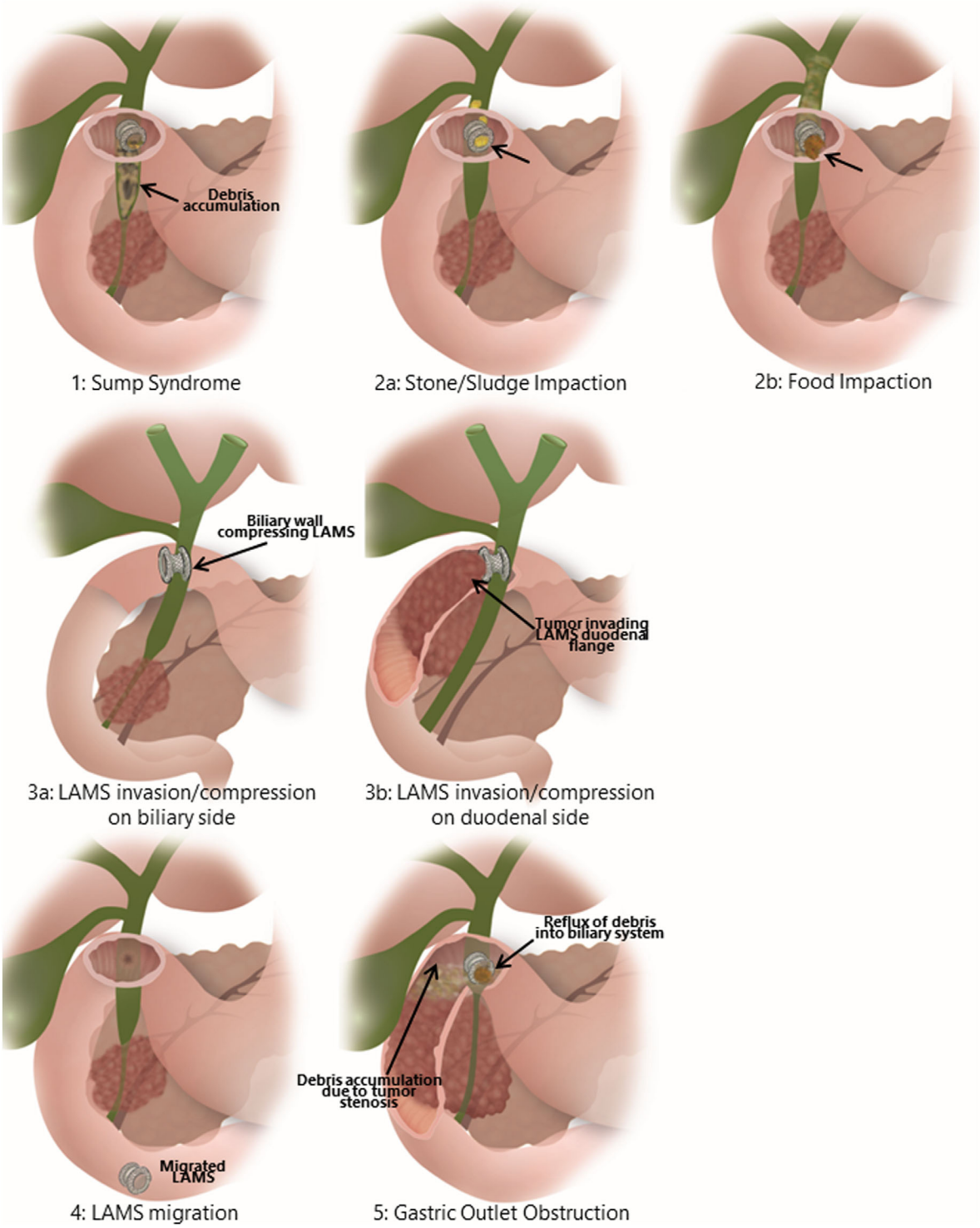

Figure 1 Lumen apposing metal stent (LAMS) classification of dysfunctions following endoscopic ultrasound-guided choledochoduodenostomy. Illustrations of the most frequent events according to the classification (left-to-right and top-to-bottom). 1: Sump syndrome; 2a: stone/sludge impaction; 2b: food impaction; 3a: LAMS invasion/compression on biliary side; 3b: LAMS invasion/compression on duodenal side; 4: LAMS migration; 5: gastric outlet obstruction.

3b), neoplastic progression may lead to overgrowth and/or compression of the LAMS. Less frequently, the contralateral wall of the CBD may occlude the biliary flange (Type 3a) as soon as the bile duct diameter decreases. Whether a small CBD diameter is associated with a higher risk for this to occur is yet unknown. In both scenarios, DPPS or SEMS through the LAMS could be useful strategies.

Even though the dumbbell shape of LAMS should prevent stent migration, spontaneous LAMS dislodgement has been described in fluid collection,[28] gallbladder,[29] and EUS-guided gastroenterostomy.[30] In these cases, a new LAMS release using the same fistula,[31] a new EUS-CDS, or other (EUS-guided) biliary drainage strategies are viable options.

When distal MBO occurs together with GOO, EUS-CDS patency may be severely affected. Food remnants and gastric fluid unable to pass through the duodenal stenosis may induce LAMS obstruction and ascending cholangitis. The priority in these cases (Type 5 dysfunction) is to resolve GOO. This is preferably done at a distance from the EUS-CDS by EUS-guided gastroenterostomy.[8] Even after re-establishing efficient gastroduodenal transit, some accumulation of food remnants and gastric juices in the prestenotic duodenal bulb may intermittently obstruct the LAMS. In line with recent data, patients with a combination of GOO and EUS-CDS seem at higher risk for LAMS dysfunction, especially in those treated with enteral stents.[32] Alternatives

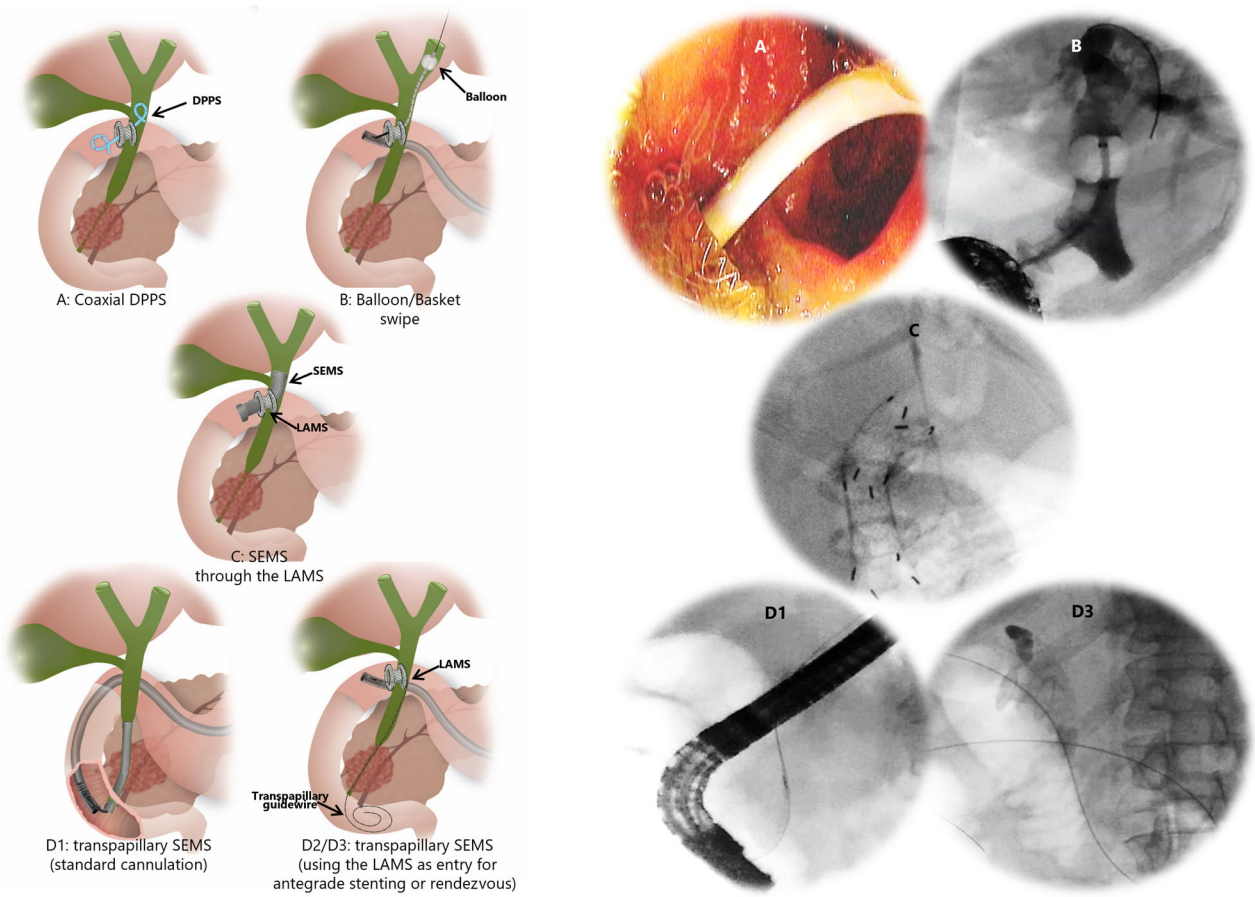

Figure 2 Lumen apposing metal stent (LAMS) classification of rescue procedures for management of endoscopic ultrasound-guided choledochoduodenostomy dysfunctions. Illustrations of the most frequent procedures according to the classification (left-to-right and top-to-bottom). (A) Coaxial double pigtail plastic stent (DPPS) placement. (B) Balloon/basket swipes. (C) Through-the-LAMS biliary self-expandable metal stent (SEMS) placement. (D1) Transpapillary SEMS (retrograde by standard cannulation). (D2/D3) Transpapillary SEMS (the LAMS is used as entry to place a transpapillary guidewire for antegrade stenting or endoscopic retrograde cholangiopancreatography rendezvous). On the right side of the figure, the corresponding endoscopic or radiological images are included.

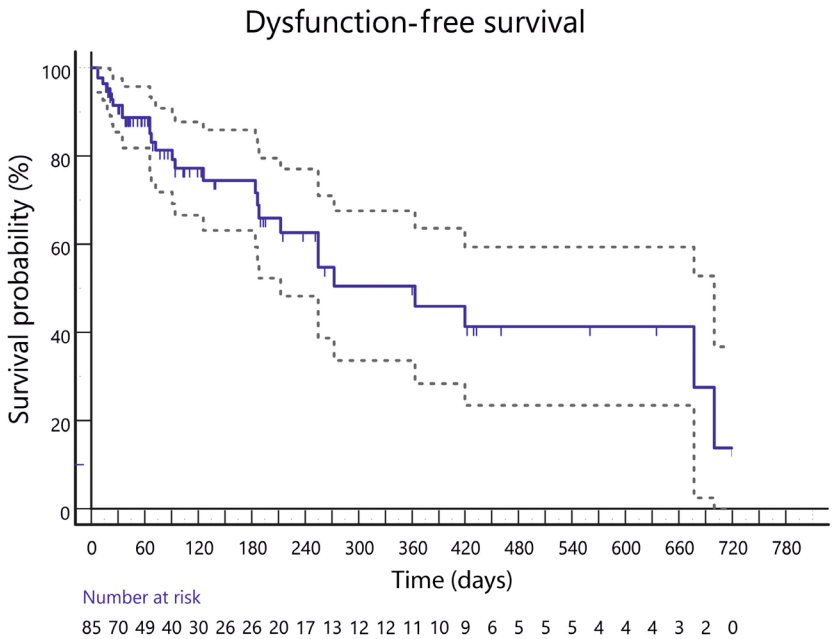

Figure 3 Kaplan–Meier curve of dysfunction-free survival (DFS) following endoscopic ultrasound-guided choledochoduodenostomy placement (blue line; dotted lines represent 95% confidence intervals [CI]). Mean estimated DFS was 394 (95% CI 307–482) days, with a probability of DFS at 1, 3, 6, and 12 months of 92%, 81%, 75%, and 51%, respectively.

Table 4 Characteristics of patients/procedures experiencing dysfunction

Variable	Recurrence (*N* = 27)	No recurrence (*N* = 58)	*P*-value	Cox proportional hazards regression analysis			
				Univariate analysis, HR (95% CI)	*P*-value	Multivariate analysis, HR (95% CI)	*P*-value
Median age, years (IQR)	71 (64–79)	70 (62–75)	0.50	1.0 (0.96–1.04)	1.00	–	–
Male sex, *n* (%)	14 (51.9)	13 (48.1)	0.90	1.0 (0.5–2.2)	1.00	–	–
Primary disease, *n* (%)							
Pancreatic cancer	20 (74)	48 (82.7)	0.30	1.0	–	–	–
Duodenal/ampullary cancer	5 (18.5)	5 (8.6)		1.2 (0.4–3.3)	0.70	–	–
Distal cholangiocarcinoma	2 (7.4)	1 (1.7)		3.0 (0.7–13.1)	0.20	–	–
Metastatic lesions	0	3 (5.2)		0.0 (0.0–∞)	1.00	–	–
Others	0 (0.0)	1 (1.7)		0.0 (0.0–∞)	1.00	–	–
Oncological staging, *n* (%)							
Resectable	2 (7.4)	10 (17.2)	0.04	1.0	–	–	–
Borderline resectable	0 (0.0)	7 (12.1)		0.0 (0.0–∞)	1.00	–	–
Locally advanced	14 (51.9)	15 (25.9)		1.7 (0.4–7.8)	0.50	–	–
Metastatic	11 (40.7)	26 (44.8)		1.4 (0.3–6.6)	0.70	–	–
LAMS diameter, *n* (%)							
6 mm	17 (63)	40 (69)	0.60	1.0	–	–	–
8 mm	10 (37)	17 (29.3)		0.6 (0.3–1.4)	0.20	–	–
15 mm	0 (0.0)	1 (1.7)		0.0 (0.0–∞)	1.00	–	–
Coaxial DPPS, *n* (%)	3 (11.1)	3 (5.2)	0.30	2.4 (0.7–8.1)	0.20	–	–
Duodenal invasion, *n* (%)	16 (59.3)	23 (39.7)	0.09	2.4 (1.1–5.4)	0.03	2.7 (1.1–6.8)[†]	0.04
Enteral stent in place, *n* (%)	4 (14.8)	3 (5.2)	0.10	2.4 (0.8–7.2)	0.10	–	–

[†]Adjusted for previous placement of duodenal stent and oncological staging.
CI, confidence interval; DPPS, double pigtail plastic stent; HR, hazard ratio; IQR, interquartile range; LAMS, lumen apposing metal stents.

Table 5 Literature review of studies reporting dysfunction of endoscopic ultrasound-guided choledochoduodenostomies with lumen apposing metal stents (LAMS)

First author	Design, geographic area	Study dates	Patients	Follow-up (days)	Clinical success, *n* (%)	Stent dysfunction, *n* (%)	LAMS diameter	Prophylactic DPPS placement
Anderloni *et al.*[12]	Retrospective, single center (Europe)	2015–2018	46	Mean 114 (95% CI 73–155)	42 (91.3)	4 (9.5)	6 mm: 46% 8 mm: 41% 10 mm: 13%	None
de Benito Sanz *et al.*[14]	Retrospective, single center (Europe)	2011–2019	37	Mean 376 ± 145[†]	36 (95.0)	1 (2.8)	6 mm: 11% 8 mm: 73% 10 mm: 14%	60%
Chin *et al.*[13]	Retrospective evaluation of prospective collection, single center (New Zealand)	2016–2020	60	230	55 (91.7)	10 (18.2)	8 mm: 72% 10 mm: 28%	None
Di Mitri *et al.*[15]	Retrospective, single center (Europe)	2015–2019	36	Median 160 (102–205)	29 (80.6)	2 (6.9)	6 mm: 3% 8 mm: 67% 10 mm: 25% 15 mm: 6%	None
El Chafic *et al.*[16]	Retrospective, multicenter (North America)	2015–2018	67	Median 184 (12–819)	40 (100)[‡]	7 (17.5)	10 mm: 100%	69%
Fugazza *et al.*[17]	Retrospective, multicenter (Europe)	2016–2020	256	Mean 151 ± 162	230 (89.8)	16 (7.0)	6 mm: 34% 8 mm: 52% 10 mm: 11% 15 mm: 3%	None
Garcia-Sumalla *et al.*[18]	Retrospective, multicenter (Europe)	2015–2020	41	Mean 80 ± 80.2	32 (78.0)	7 (21.9)	6 mm: 49% 8 mm: 51%	44%
Jacques *et al.*[19]	Retrospective evaluation of prospective collection, multicenter (Europe)	2017–2018	70	Median 153	69 (98.6)	7 (10.1)	6 mm: 86% 8 mm: 13%	None
Kunda *et al.*[20]	Retrospective, multicenter (Europe)	2012–2014	57	Mean 151 ± 145	54 (94.7)	5 (9.3)	6 mm: 64% 8 mm: 4% 10 mm: 29% 15 mm: 3%	None
On *et al.*[21]	Retrospective, multicenter (Europe)	2016–2020	120	Median 70 (3–869)	92 (94.8)[§]	9 (8.3)[§]	6 mm: 38% 8 mm: 57% 10 mm: 4%	29%
Tarantino *et al.*[9]	Prospective, single center (Europe)	2015–2018	21	Median 188 (8–554)	21 (100)	3 (14.3)	6 mm: 5% 8 mm: 76% 10 mm: 14% 15 mm: 5%	None

Table 5 (*Continued*)

First author	Design, geographic area	Study dates	Patients	Follow-up (days)	Clinical success, *n* (%)	Stent dysfunction, *n* (%)	LAMS diameter	Prophylactic DPPS placement
Tsuchiya *et al.*[10]	Prospective, multicenter study (Asia)	2013–2015	19	Median 184 (12–819)	18 (95)	5 (26.3)	6 mm: 53% 8 mm: 47%	None
Current study	Retrospective evaluation of prospective collection, multicenter (Europe)	2019–2022	97	Mean 138 (95% CI 104–173)	85 (91.4)	27 (31.8)	6 mm: 67% 8 mm: 32% 15 mm: 1%	None

†Follow-up time reported for the whole cohort including tubular stents.
‡Follow-up was available in 40/67 patients.
§Follow-up was available in 97/120 patients. Stent dysfunction was only reported as a total of those with technical success (9/109).
Percentage of stent dysfunction is reported as a percentage of patients with clinical success; therefore, the percentages may vary from those reported in the original studies.
CI, confidence interval; DPPS, double pigtail plastic stent.

such as EUS-guided or percutaneous transpapillary stenting or EUS-HGS may be preferred in these patients.[33]

Despite stent dysfunction, EUS-CDS remains an invaluable technique in case of failed/impossible ERCP in distal MBO. This technique is less invasive compared to PTBD and less challenging compared to EUS-HGS or antegrade stenting. Most importantly, similar dysfunction rates have been reported in randomized trials of ERCPs with SEMS.[34–36] Stone extraction, stent exchange, or stent-in-stent treatment are accepted solutions for SEMS dysfunction and endoscopists should become familiar with LAMS revisions given the large-scale implementation of EUS-CDS in clinical practice.

This study had several limitations. First, the retrospective evaluation of outcomes might lead to an underestimation of dysfunction; however, we believe that the prospectively maintained databases and a fraction of patients being included in a predefined prospective follow-up significantly contributed to this cohort presenting the highest dysfunction rate reported so far. Second, the mean follow-up may appear limited; however, no lost-to-follow-up patient was included by definition, and the limited follow-up likely reflects the natural disease course, as well as some patients undergoing curative surgery shortly after biliary drainage; moreover, the use of Kaplan–Meier statistics reassures that the estimated dysfunction probability takes into account the contribution of single cases according to the time spent under observation. Third, generalizability of these outcomes outside tertiary referral centers with advanced experience in therapeutic EUS and ERCP cannot be assured. Finally, the proposed classification is based on a limited number of events and requires validation in separate and prospective EUS-CDS cohorts.

Although larger cohorts of EUS-CDS procedures are available, to our knowledge no earlier work has concentrated specifically on LAMS dysfunction and rescue strategies. The strict inclusion criteria, the multicentric design, as well as detailed long-term follow-up are clear strengths of the current study.

In conclusion, our study confirms the high immediate efficacy and safety of EUS-CDS using LAMS mentioned in previous publications. Our study also documented a considerably higher incidence of stent dysfunction during follow-up when compared to previous series. After EUS-CDS placement, almost one-third of patients experienced stent dysfunction, although endoscopic reintervention was effective in almost all cases. We furthermore propose a new classification, dividing EUS-CDS dysfunction into five distinct subtypes, aimed at standardizing future research, providing deeper insight into the pathogenesis of EUS-CDS dysfunction, improving patient selection, identifying

procedure-specific relative contraindications, as well as subsequent rescue strategies.

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CONFLICT OF INTEREST

AUTHOR M.B. HAS consultancy agreements with Taewoong and Prion Medical, receives travel grants from Taewoong, Norgine, and Prion Medical, and receives medical device support from Taewoong and Prion Medical. W.L. co-chairs the Boston Chair in Interventional Endoscopy and has consultancy agreements with Boston Scientific and Cook Medical. H.v.M. has consultancy agreement with Boston Scientific. P.F. has consultancy agreements with Olympus and Cook Medical. S.v.d.M. co-chairs the Boston Chair in Interventional Endoscopy, holds the Cook Chair in the study of portal hypertension, has consultancy agreements with Boston Scientific, Cook Medical, and Pentax, and reports participation in the Board of Boston Scientific and Cook Medical. R.P.V. has consultancy agreement with Boston Scientific and receives research grants from Boston Scientific. R.L.J.v.W. has consultancy agreement with Boston Scientific. G.V. and G.D. report travel grants from Pentax Medical. The other authors declare no conflict of interest for this article.

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NONE.

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SUPPORTING INFORMATION

ADDITIONAL SUPPORTING INFORMATION may be found in the online version of this article at the publisher's web site.

Figure S1 Flowchart of inclusion/exclusion of patients.

Table S1 Rescue strategies for managing stent dysfunctions.

Table S2 Need for second reinterventions.