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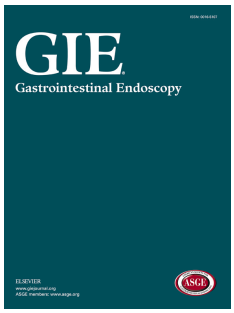

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International multicenter comprehensive analysis of adverse events associated with lumen-apposing metal stent placement for pancreatic fluid collection drainage

Alessandro Fugazza[1], Amrita Sethi[2], Arvind J Trindade[3], Edoardo Troncone[4], John Devlin[5], Mouen A. Khashab[6], Frank P Vleggaar[7], Auke Bogte[7], Ilaria Tarantino[8], Pierre H. Deprez[9] , Carlo Fabbri[10], , José Ramón Aparicio[11], Paul Fockens[12], Rogier P. Voermans[12], Will Uwe[13] , Geoffroy Vanbiervliet[14], Antoine Charachon[15], Christopher D. Packey[2] , Petros C Benias[3],Yasser El-sherif[5], Christopher Paiji[6], Dario Ligresti[8], Cecilia Binda[10], Belén Martínez[11], Loredana Correale[1], Douglas G Adler [16], Alessandro Repici[1,17], Andrea Anderloni[1]

Affiliation:

[1] Digestive Endoscopy Unit, Departement of Gastroenterology, Humanitas Research Hospital, Rozzano(MI), Italy

[2] Division of Digestive and Liver Disease, Columbia University Medical Center-NYPH, USA

[3] Long Island Jewish Medical Center, Zucker School of Medicine at Hofstra/Northwell, Northwell Health System, New Hyde Park, NY, USA

[4] Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy

[5] Kings College Hospital, London, UK

[6] Therapeutic Endoscopy, Johns Hopkins Hospital, Division of Gastroenterology and Hepatology Baltimore, USA

[7] Department of Gastroenterology and Hepatology, University Medical Center, Utrecht, Netherlands

[8] Endoscopy Service, Department of Diagnostic and Therapeutic Services, IRCCS-ISMETT, Palermo, Italy.

[9] Department of Hepatogastroenterology, Cliniques universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium.

[10] Unit of Gastroenterology and Digestive Endoscopy, Forlì-Cesena Hospitals, AUSL Romagna, Italy.

[11] Endoscopy Unit, Digestive Service, Alicante University General Hospital, Alicante, Spain

[12] Department of Gastroenterology & Hepatology, Amsterdam University Medical Centers- location AMC, Amsterdam, Netherlands.

[13]Department of Gastroenterology, Municipal Hospital, Gera, Germany.

[14] Digestive Endoscopy Unit, l'Archet University Hospital, Nice, France.

[15] Service d'Hépato-gastro-entérologie, CH Princesse Grace, Monaco.

[16] University of Utah School of Medicine, Division of Gastroenterology and Hepatology, Salt Lake City, USA.

[17] Humanitas University, Rozzano(MI), Italy

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Affiliation:

[1] Digestive Endoscopy Unit, Department of Gastroenterology, Humanitas Research Hospital, Rozzano(MI), Italy

[2] Division of Digestive and Liver Disease, Columbia University Medical Center-NYPH, USA

[3] Long Island Jewish Medical Center, Zucker School of Medicine at Hofstra/Northwell, Northwell Health System, New Hyde Park, NY, USA

[4] Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy

[5] Kings College Hospital, London, UK

[6] Therapeutic Endoscopy, Johns Hopkins Hospital, Division of Gastroenterology and Hepatology Baltimore, USA

[7] Department of Gastroenterology and Hepatology, University Medical Center, Utrecht, Netherlands

[8] Endoscopy Service, Department of Diagnostic and Therapeutic Services, IRCCS-ISMETT, Palermo, Italy.

[9] Department of Hepatogastroenterology, Cliniques universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium.

[10] Unit of Gastroenterology and Digestive Endoscopy, Forlì-Cesena Hospitals, AUSL Romagna, Italy.

[11] Endoscopy Unit, Digestive Service, Alicante University General Hospital, Alicante, Spain

[12] Department of Gastroenterology & Hepatology, Amsterdam University Medical Centers-location AMC, Amsterdam, Netherlands.

[13]Department of Gastroenterology, Municipal Hospital, Gera, Germany.

[14] Digestive Endoscopy Unit, l'Archet University Hospital, Nice, France.

[15] Service d'Hépato-gastro-entérologie, CH Princesse Grace, Monaco.

[16] University of Utah School of Medicine, Division of Gastroenterology and Hepatology, Salt Lake City,
USA.

[17] Humanitas University, Rozzano(MI), Italy

Abstract

Background and Aims:

High rates of technical and clinical success were reported of lumen-apposing metal stent (LAMS) placement for peripancreatic fluid collection (PFC) drainage. However, data on the adverse event (AE) rates are heterogeneous. The aim of this study was to evaluate the incidence, severity, management, and risk factors of AEs related to the use of LAMSs for drainage of PFCs in a large cohort of patients.

Methods:

This is a multicenter, international, retrospective review from 15 centers of all patients who underwent placement of LAMSs for the management of PFCs. A nested case-control study was conducted in patients with (case) or without (control) AEs.

Results:

A total of 333 procedures in 328 patients were performed (5 patients treated with 2 LAMS). Technical success was achieved in 321 (97.9%) patients. Three hundred four patients were finally included in the study (7 excluded for lost to follow-up information; 10 excluded for deaths unrelated to LAMSs). The rate of clinical success was 89.5%. Seventy-nine LAMS-related AEs occurred in 74 out of 304 patients (24.3%), after a mean time of 25.3 days (median, 18 days, IQR, 6-30 days) classified as 20 (25.3%) mild, 54 (68.4%) moderate, or 5 (6.3%) severe. On multivariable analysis, compared with controls, cases were more likely to have walled-off necrosis

(WON) versus pancreatic pseudocysts (PP) (ORs, 2.18; 95% CI, 1.09-4.46; P=0.028), whereas cases were less likely to have undergone tract (balloon) dilation (yes vs no, OR, 0.47; 95% CI, 0.22-0.93; P=0.034).

Conclusions:

Data from this large international retrospective study confirm that the use of LAMSs for management of PFC has excellent technical and good clinical success rates. The rate of AEs, however, is not negligible and should be carefully considered before using these stents for drainage of PFCs, and in particular for WON. Further prospective studies are needed to confirm these findings.

Introduction

Pancreatic pseudocyst (PP) and walled-off necrosis (WON) are peripancreatic fluid collections (PFCs) resulting from acute or chronic pancreatitis, which substantially differ in the amount of necrotic content, with more abundant debris in WON and mostly absent in PP (1). In many cases, in particular when necrotic material is absent, such collections may resolve spontaneously (2, 3). In other cases, they can become symptomatic causing gastric outlet obstruction, biliary obstruction, pain, or infection, thereby causing significant morbidity and mortality and requiring prompt intervention (4). Surgical debridement or percutaneous drainage are associated with a significant risk of adverse events (AEs) and mortality, so less-invasive approaches, such as endoscopic drainage, are preferred when the expertise is available (5-7). In the past 2 decades, EUS-guided drainage of peripancreatic fluid and necrotic collections has significantly advanced, using relatively small plastic stents and also larger self-expanding metallic stents (SEMSs). With both methods, drainage of the necrotic collection was feasible and allowed access into the collection to perform endoscopic transmural necrosectomy (ETN) when needed (8). However, endoscopic drainage has been limited by the absence of dedicated devices, as the stents initially used had been created for biliary drainage. Because they were not specifically designed for internal drainage of extraluminal

collections, plastic stents and SEMSs are limited by shortcomings and possible AEs, such as obstruction, migration, peritoneal leakage, bleeding and the need of multiple endoscopic reinterventions (8). In recent years, a new type of fully covered SEMS has become available, namely lumen-apposing metal stent (LAMS), with a specific biflanged design that facilitates the creation of a stable and sealed fistula between the gastric or the duodenal wall and the target cavity (9). The use of LAMSs for PFC drainage, and for WON drainage in particular, has brought good results, with a high rate of technical and clinical success, and potentially lower risk of fistula occlusion and perforation compared with plastic stents, although high-quality evidence is still missing (9-13). The same studies have also highlighted the risks associated with the use of LAMSs, such as bleeding, stent obstruction by necrotic tissue, buried stents, or biliary duct compression, thus raising questions regarding the proper indication for these stents and the correct timing for removal (14, 15). Data on AEs with LAMSs in the setting of PFC drainage are heterogeneous and only a few prospective studies are available. In order to better understand how to avoid serious AEs and maximize the benefits from the use of LAMSs, we conducted a retrospective multicenter study aimed to evaluate the incidence, severity, management, and risk factors of AEs related to the use of LAMSs for the drainage of PFCs in a large cohort of patients.

Methods

The present study is a multicenter, international, retrospective review from 15 secondary and tertiary care centers (11 in Europe, 4 in the United States) of all patients treated in these institutions with LAMS [AXIOS or Electrocautery-enhanced (EC)-AXIOS System, Boston Scientific Corp, Marlborough, Mass, USA] for the management of PPs or WON between March 2013 and October 2017. Intraprocedural and postprocedural AEs were recorded, classified, and graded according to the ASGE lexicon (16). The institutional review board of each hospital approved the observational study (NCT03544008) and the protocol was performed in accordance with the Helsinki Declaration.

Study device

The AXIOS stent is a SEMS made up of braided nitinol that is fully covered with silicone, with wide flanges on both ends in order to provide anchoring between the gastrointestinal and cyst lumens.

The stent is preloaded in a 9F or a 10.8F catheter, with a through-the-scope delivery system compatible with therapeutic echoendoscopes having a working channel of 3.7-mm diameter or larger. The delivery system allows for endoscopic control and uses a locked 2-step release system to prevent unintended deployment of the second flange.

The novel EC-LAMS stent incorporated an electrocautery wire into the distal tip of the delivery catheter allowing for the lumen-to-lumen passage of the device followed by immediate deployment of the stent, thus allowing for drainage to be performed in as a single-maneuver procedure.

These stents are available in different diameters and lengths: 6x8 mm, 8x8 mm, 10x10 mm, 15x10 mm and the novel 20x10 mm. The 10-mm, 15-mm and 20-mm diameter stents are felt to be more appropriate for PFC.

Procedure

All EUS procedures were performed by experienced endoscopists in the endoscopy suite with a therapeutic echoendoscope. Only mature PFC (ie, after at least 4 weeks from the index pancreatitis, as defined in Atlanta classification (1)) were included in the study. Under EUS guidance, the PFC was studied and drained from either the stomach or duodenum. Two different deployment techniques were used in function of the stent used at the discretion of the endoscopist.

When a standard LAMS (AXIOS) was used, an initial puncture with a 19-gauge needle through the gastrointestinal (GI) wall into PFC followed by insertion of a 0.025-inch or a 0.035-inch guidewire was performed. After that, the tract was dilated using a cystotome and dilation balloon, followed by insertion of the delivery system and deployment of the stent.

When the cautery-enhanced LAMS (EC-AXIOS) was used, a freehand technique was employed, with direct access into the PFC by puncture with the device using pure cut setting, followed

immediately by deployment of the stent without any exchange of devices. For both systems, the deployment of the second flange was released either endoscopically or with the intrascope channel stent release technique (17).

Complementary maneuvers performed during the same or further procedures were at the discretion of the endoscopist and included the following: balloon dilation of the LAMS, hydrogen peroxide irrigation of the PFC, placement of nasocystic drainage tube or double-pigtail stent through the LAMS, and/or extraction of necrotic debris. Placement of a concomitant percutaneous drainage was added in some cases. All patients were under broad-spectrum antibiotic therapy at the moment of the LAMS placement. The type, the dosage and the course of the antibiotic therapy were at the discretion of the endoscopist and/or of the medical team (eg, Gastroenterology Unit, Intensive Care Unit) that was taking care of the patient at each institution.

All data were extracted and compiled into a central database.

Patient-related data included patient demographics, type of PFC, size and location of the collection, presence of disruption of pancreatic duct, previous imaging (CT scan, magnetic resonance imaging [MRI], magnetic resonance cholangiopancreatography [MRCP]), presence of abnormal vessels on imaging (including portal vein thrombosis, splenic vein thrombosis, perigastric varices, pseudoaneurysm, or others), etiology of pancreatitis and indication for drainage.

Procedural data included type and size of the LAMS used, approach, endoscopic appearance of the cavity, complementary maneuvers during the procedure and/or subsequent placement of a concomitant percutaneous drainage.

Postprocedural data included length of hospitalization, successful stent removal after resolution of PFC, recurrence of PFC during follow-up, AEs with severity graded according to the ASGE lexicon's severity grading system (16), and their management.

AEs were classified as early, when presenting within 14 days, and late, when presenting after 14 days from LAMS placement.

Patients were followed up with periodic laboratory analyses, clinic visits, and imaging (CT and/or MRI) at the discretion of the responsible endoscopist at each of the participating hospitals in an ambulatory setting.

Definitions

AEs were defined as all symptomatic events related to the use of LAMSs such as bleeding, infection, stent occlusion and stent migration resulting in prolongation of hospital stay, requiring medical therapy or further procedure or action to resolve the event or to treat the symptoms.

The ASGE lexicon's severity grading system was used to grade the AEs (16).

Technical success was defined as successful LAMS placement into the PFC across the gastric or duodenal wall.

Clinical success was defined as WON or PP <2 cm on axial imaging 1 to 6 months after stent insertion without need for further interventional radiologic, endoscopic, or surgical procedures. A nested case–control analysis was conducted in patients with (case) or without (control) AEs, looking for factors associated with occurrence of AEs. Cases and their controls were recruited from each institution.

Statistical analysis

Descriptive analysis was carried out by calculating mean and standard deviation (SD) for continuous variables and proportions for categorical variables. We used univariate and multivariable logistic regression analysis to identify risk factors for AEs from possible variables. For the purpose of this analysis, patients were separated according to a binary variable: those with any AE (mild/moderate/severe) and those without AEs. Lack of individual matching for all centers permitted the use of unconditional logistic modelling (18). The univariate model used independent variables related to characteristics of patients and characteristics of procedures. Crude ORs and their 95% CIs were calculated. Any factors associated with AEs with a p-value ≤0.100 on the univariate

analysis was entered into a multivariable logistic regression analysis to determine any independent predictors of AEs. Adjusted ORs (AORs) and their 95% CIs were obtained from multiple logistic regression model. In our study, there was a possible source of nonindependence of data. Patients treated in a particular center may be more alike compared with patients treated in another center due to differences in treatment policies. As a result, patients treated in the same center are dependent (clustered), rather than independent. Therefore, an adjustment by using clustered standard error was required for this hospital effect in estimating regression parameters.

Secondary outcome measures included cumulative frequencies and times (from stent insertion to occurrence) of different types of AEs (ie, stent migration, bleeding, infection and stent occlusion). Times were summarized using descriptive statistics with mean and variability. A linear regression model was used to estimate time with type of AEs. For additional verification, frequencies of different types of AEs among early (≤14 days) and late (>14 days) events were determined; differences between the 2 groups were assessed using the Chi square test.

All analyses were done using R software, version 3.3.2 (2016-10-31 (R Core Team (2016). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/). The significance level was set at less than or equal to 0.05.

It is recognized that there was multiple testing of outcome data arising from individual patients. The p-values for the univariate statistical tests are not corrected for multiple testing, because those tests were taken as exploratory. The subsequent multivariable logistic regression analysis was considered the main definitive result as it determined those variables independently associated with the occurrence of AEs after adjusting for the contributions of the other variables in the model. Other statistical results including those comparing times from stent insertion with occurrence of AEs are secondary, to be taken as descriptive only, and not requiring correction of their p-values for multiple comparisons.

Results

During the study period, a total of 333 procedures in 328 patients, (116 women, 35.4%; mean age, 56.0; SD, 16.0, range, 4-86) were performed. Five patients (1.5%) have been treated with 2 LAMSs in different sessions. Overall, technical success was obtained in 321 (97.9%) patients.

Among the 7 (7/328, 2.1%) patients with technical failure, 4 patients subsequently underwent a new LAMS placement with or without concomitant coaxial plastic stents. The remaining 3 patients underwent successful plastic stents placement. No LAMS-related AEs were seen among the 7 patients with technical failure.

The median follow-up (FU) length was 153 days (mean, 258 days; IQR, 92-365).

After exclusions for technical failure (7 patients, 2.1%), lost to follow-up information (7 patients, 2.1%), and deaths unrelated to LAMSs (2 patients (0.6%) for cardiac arrest and 8 patients (2.4%), who presented with sepsis and multiorgan failure (MOF) before any intervention, received intensive care support and finally died), 304 patients were included in the analysis, constituting our study population. The rate of clinical success was 89.5% (272/304).

One or more LAMS-related AE were noted in 74 out of 304 (24.3%) patients. The 74 cases included 79 AEs (5 patients with 2 AE) consisting of: 22 (27.8%) bleeding (Figure 1), 20 (25.3%) stent migration (Figure 2), 19 (24.1%) infection, 14 (17.7%) stent occlusion, 3 (3.8%) buried stent syndrome (Figure 3), and 1 (1.3%) occlusion of the pylorus (Table 1). The control group consisted of 230 patients without any of these conditions. Baseline characteristics for cases and controls are given in Table 2.

For the 74 patients who experienced AEs, the mean age was 56 years (SD, 17) and 25 (33.8%) were females. Forty-four (59%) patients underwent drainage for WON. Pancreatic pseudocysts were drained in the remaining 30 (41%) patients. Most common etiologies of pancreatitis were gallstone (35.1%), alcohol (33.8%), and idiopathic (17.6%). Major indications for drainage were abdominal pain (33.8%), gastric outlet obstruction (28.4%), and symptoms suggestive of infection (27%). Fluid collection extension into the paracolic gutter was observed in 6.8% of the cases. In the majority of cases (91.9%), EUS-guided drainage were performed with the EC-LAMSs. Twenty-

eight patients (37.8%) required endoscopic necrosectomy. Concomitant percutaneous drainage was used in 12.2% of cases.

According to ASGE lexicon (16) 20 (25.3%) AEs were classified as mild, 54 (68.4%) as moderate, and 5 (6.3%) as severe.

Regarding all 79 included AEs, 46 (58.2%) were managed endoscopically, 27 AEs (34.2%) were managed conservatively, and 6 (7.6 %) were managed through interventional radiology. No AE required surgical management.

All results of the univariate analysis are shown in Table 2. On univariate analysis, case and control groups did not differ statistically in terms of age, gender, indication for collection drainage, etiology of pancreatitis, fluid location and fluid mean size, stent type and diameter, and endoscopic necrosectomy. There were, however, some differences. Compared with controls, cases were more likely (at p<=0.100) to have performed drainage of WON vs. pancreatic pseudocyst (OR, 1.66; 95% CI, 0.98-2.86; p=0.062) and to need for concomitant percutaneous drainage (OR, 2.13; 95% CI, 0.85-5.01, p=0.098), whereas they were less likely to have PFC extending up to the paracolic gutter (OR, 0.44; 95% CI, 0.14-1.10; P=0.100), to undergo nasocystic tube (OR, 0.40; 95% CI, 0.16-1.01; P=0.046) and to undergo pneumatic tract dilation (OR, 0.61; 95% CI, 0.33-1.08; p=0.092). On multivariable analysis (Table 3), PFC classification (WON vs pseudocyst, OR, 2.18; 95% CI, 1.09-4.46; P=0.028) and pneumatic tract dilation (yes vs no, OR, 0.47; 95% CI, 0.22-0.93; P=0.034) remained statistically significant.

Among cases, AEs were diagnosed after a mean time of 25.3 days (median, 18 days, IQR, 6-30 days) from the time of stent placement. The mean days of diagnosis (and interquartile range) for each AE was as follows: bleeding (16.0, 0.0-75), stent migration (45.0, 2-146), and stent occlusion (23.8, 1-60). Stent migration was significantly associated with longer time from stent insertion as compared with other events (p=0.026). The cumulative incidence of AE during the study period is shown in Figure 4. Early AEs, within 14 days from LAMS placement, were observed in 34 out of 79 (43.0%) cases. Among early AEs, bleeding (13/34, 39.4%) and infection (11/34, 32.3%) were

the most commonly diagnosed. Stent migration and stent occlusions represented the 17.6% (6/34) and 8.8% (3/34) of early AEs, respectively. Severe/moderate AEs had (not significantly) shorter time (22.0 days; 95% CI, 14.5-50.3) to diagnosis as compared with mild AE (36.5 days; 95% CI, 22.6-50.4; P= 0.071).

Discussion

In the last 2 decades, endoscopic drainage of PFC has become widespread. Additionally, the availability of devices specifically designed for transmural drainage, such as LAMS, has substantially contributed to the diffusion of these procedures. As the use of LAMS has increased, more safety data regarding clinically relevant AEs at unexpectedly high rates, have raised concerns about LAMS safety, highlighting the need of further and focused studies. In this work, we reported data from a wide cohort of patients treated with LAMS for symptomatic mature PFC (ie, pseudocyst or WON), and factors related to AEs were investigated through a nested case-control study. In our cohort, the overall rate of AE is 24.3%, whereas data from published series report rates from 3% to 53% (9-12) (13-15, 19-23). Most of these studies are not prospective, and the definitions of AEs are not uniform, preventing generalizability of LAMS-related AEs. For instance, some published series did not report nor analyze the stent occlusion rate or buried stent syndrome as an AE (10, 19).

It is known that the clinical outcomes of collections containing solid debris are worse than drainage of pseudocysts (24, 25). In fact, the solid necrotic material may not drain spontaneously through the stent, requiring additional procedures, such as endoscopic necrosectomy in around 60% of patients (20). Although a lower clinical success rate for WON compared with PP has been already described, it is not clear whether WON drainage procedures are burdened by an increased risk of AEs.

In our study, drainage of WON compared with PP is associated with an increased risk of AEs in both univariate and multivariate analysis, whereas none of the others additional procedures usually performed to facilitate drainage of collections (ie, endoscopic necrosectomy, plastic stent through the LAMS) increased such risk.

Consistently, nasocystic tube drainage and pneumatic dilation of the stent reduce the risk of AEs, even if only the latter has been confirmed in multivariate analysis (OR, 0.47; 95% CI, 0.22-0.93; P=0.034). As reported above, this could be attributed to the presence of necrotic material that can obstruct the stent, impairing the drainage of the collection and increasing the risk of AEs such as infection and stent occlusion. Larger and well-designed studies are needed to address this critical point. Bleeding is one of the most feared AEs related to SEMSs and LAMSs in the setting of PFC drainage. Bleeding can originate from the gastric wall, which is easier to manage endoscopically, or from the cavity, where the retroperitoneal vessels are usually larger and the possibilities of successful endoscopic hemostasis are significantly reduced. In these cases, radiological embolization is often required. It has been hypothesized that the LAMSs could result in a rapid collapse of the cavity, resulting in the risk of contact between the retroperitoneal vessels and the distal flange of the stent (26). The prolonged contact and movement relative to the stent could result in erosion and rupture of the vessels, thus causing acute severe bleeding. Considering this hypothesis, the bleeding may be associated with the stent indwell time, with greater risk in case of late removal. This point has been recently stressed in many studies, and early removal of the LAMS after 4 weeks is emerging as a proposed strategy in clinical practice (14, 23, 27). In our study, bleeding represents 27.8% of all AEs (22/79), with an overall risk of 22 of 304 (7.2%), and 3 cases (3/304, 0.98%) classified as severe. Published series and randomized trials report a bleeding risk ranging from 0% to 21% (9-12) (14, 15, 19-23). Interestingly, 13 (59%) of 22 cases of bleeding were reported in the first 14 days from the positioning of the stent. Although early removal of the stent after the resolution of the collection could be a reasonable strategy, these data highlight that bleeding caused by LAMS cannot be considered exclusively as a late AE. Recently, Dhir and colleagues (27) described a protocol of early removal of the metal stent after 3.5 weeks, and reported a bleeding risk of 3.5%, thus confirming the presence of residual risk. Of note, one case of bleeding from our cohort was reported at the time of LAMS removal; therefore, endoscopists should be aware of such an AE in every step of the PFC management.

LAMSs were conceived with a specific antimigratory design, in order to overcome the high risk of migration reported for SEMSs. However, several studies reported risk of migration up to 20% (14, 21, 22). In this study, we reported an overall risk of migration of 6.6% (20/304), which is in line with most published series (9-12) (13-15, 19-23). The LAMS can migrate into the gastrointestinal lumen, where it can be easily retrieved, or into the cavity. In the latter case, it is necessary to enter the cavity to retrieve the stent, such as during necrosectomy, with possible further risks and AEs. No cases of migration into the cavity were reported in our cohort, and in most cases, migration was a minor AE, treated conservatively in 12 out of 20 (60%) because the collection had resolved. Of note, stent migration occurred most commonly as a late AE, with a mean time of diagnosis of 45 days (2-146), and was significantly associated with longer time from stent insertion as compared with other events.

Traditionally, endoscopic transmural drainage of PFC has been a complex multistep procedure that requires access to the cavity, over-the-wire dilation of the tract, and finally stent positioning through the dilated tract. In case of the need for necrosectomy, removal of most stents and hydraulic dilation of the tract to 12 mm or more are required. These procedures involve multiple steps with an inherent small risk of fluid leakage between the gut wall and the collection. In our study population, 276 out of 304 (90.8%) of the procedures were performed with the enhanced-cautery delivery system, which allows the catheter to enter the cavity with a “free-hand” technique, and subsequently to deliver the stent without the need for device exchange. It is interesting to note that, despite the significant number of procedures reported in this study, no cases of procedure-related perforation or peritonitis were described, which have occasionally been reported during the multistep drainage procedure. Overall, no AEs required surgical management.

In our cohort, we reported a not-negligible mortality rate (12 events: 2 cardiac arrest; 10 multiorgan failure) none of which was related to LAMSs. The main indication of the drainage in these patients was the infection of the collection, complicated by MOF, which finally lead to death. As mentioned, infected pancreatic necrosis is a severe clinical condition. It has been reported to have an overall

mortality of 15% in patients with infected necrosis, which reached 35% in patients with MOF (28). In a recent study, the overall mortality in patients with infected necrosis who underwent endoscopic drainage was about 18% (20). Focusing on PFC drainage with LAMS, published cohorts reported a lower risk of mortality, which ranges from 0%, in most studies, to 5% (9-12) (13-15, 19-23). In our study, the overall mortality risk was 3.7%. Of note, these cases were mostly complicated patients who necessitated intensive care unit (ICU) before the endoscopic procedure, or with advanced cancer, and in whom the events leading to MOF and death was not related to the procedure and/or to the stent. The best approach to drain these high-risk patients is not yet defined, but it has been hypothesized that a shorter procedure, without the need of general anesthesia, could limit the postoperative stress and could be beneficial for the prognosis (20, 29, 30). In this setting, the delivery of an LAMS with an enhanced-cautery system provides expedited drainage, with an even faster procedure. Our study did not report a protective effect of the use of EC-LAMSs compared with “cold” LAMSs, even if the total number of procedures with “cold” LAMSs was probably too small to make this comparison.

The present study has some limitations, mainly related to the retrospective design. It should also be noted that only one type of commercially available LAMSs has been included in this analysis. Moreover, the involvement of several centers with many different operators and clinical settings could have determined some heterogeneity in the data. At the same time, the involvement of several centers could make the results more generalizable. On the other hand, the strengths of this work include the relevant number of patients involved, the standardized definition of AEs and the design allowing for evaluation of AE-associated risk factors. In conclusion, the findings discussed in this work expand our knowledge about PFC management with LAMSs, and could guide further prospective studies aimed to maximize clinical success and to minimize the risk of AEs for patients with PFC.

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Figure Legend

Figure 1. Esophagogastroduodenoscopy revealed correct placement of the lumen-apposing metal stents (LAMSs), fully opened, crossable by standard gastroscope. In the fluid collection cavity, an oozing bleeding from a large arterial vessel was visible.

Figure 2. CT scan shows migration of the LAMS in the sigmoid colon.

Figure 3. Esophagogastroduodenoscopy revealed a buried stent syndrome with gastric mucosa partially covering the LAMS.

Figure 4. Cumulative proportion of AEs after LAMS placement

Table 1. Characteristics of main AE, with severity grade index and their management

Adverse event	**No. of events (%)**	**Early (< 14 days)**	**Late (>14 days)**	**Severity Grade Index**	**Management**
Bleeding	22 (27.8%)	13	9	3 Severe 17 moderate 2 mild	12 Endoscopy 5 Interventional radiology 5 Conservative
Stent Migration	20 (25.3%)	6	14	8 moderate 12 mild	8 Endoscopy 12 Conservative
Infection	19 (24.1%)	11	8	2 severe 12 moderate 5 mild	10 Endoscopy 8 Conservative 1 Interventional radiology
Stent Occlusion	14 (17.7%)	3	11	13 moderate 1 mild	13 Endoscopy 1 Conservative

Table 2. Demographic Data and Analyzed Variables of Case and Control Groups

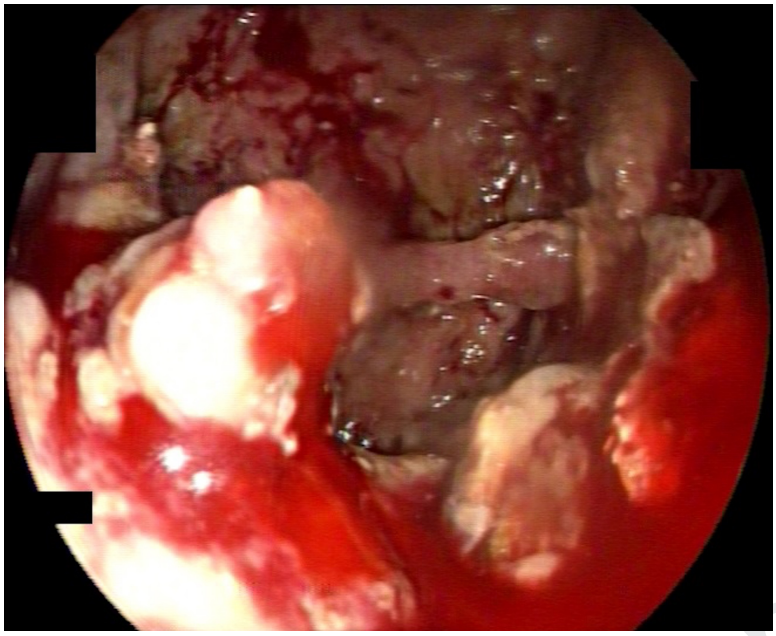
			Univariable analysis		
Variable	Case (n=74)	Control (230)	OR	95% CI	*P* value
Age (years)					
mean (SD)	56 (17)	56 (16)	1.00	(0.99;1.02)	0.787
Gender, % (n)					
Male,	49 (66.2)	150 (65.2)	1		
Female	25 (33.8)	80 (34.8)	0.99	(0.54;1.77)	0.969
Indication for PFC drainage, n (%)					
Abdominal pain	25 (33.8)	74 (32.2)	1		
Gastric outlet obstruction	21 (28.4)	46 (20.0)	1.35	(0.68;2.64)	0.425
Symptoms suggestive of infected collection	20 (27)	88 (38.2)	0.65	(0.32;1.26)	0.280
Early satiety	5 (6.8)	16 (7.0)	0.93	(0.28;2.64)	0.946
Jaundice	2 (2.7)	2 (0.9)	2.96	(034; 25.7)	0.273
rapid increase in size	1 (1.4)	4 (1.7)	0.74	(0.04;5.29_	0.819
PFC Location, n (%)					
Head	16 (21.6)	37 (16.1)	1		
Tail	17 (23.0)	49 (21.3)	0.80	(0.36;180)	0.592
Body	41 (55.4)	144 (62.6)	0.66	(0.34;1.32)	0.229
PFC Classification					
PP	30 (41.0)	123 (53.5)	1		
WON	44 (59.0)	107 (46.5)	1.66	(0.98;2.86)	0.062
PFC Size mean (SD)	113.5 (44.2)	113.6 (64.0)	1	(0.99;1.00)	0.799
Length of hospitalization (days), mean (SD)	8.3 (14.1)	9.2 (18.3)	1	(0.99;1.02)	0.797
Procedure time (min), mean (SD)	31.6 (20.3)	32.1 (21.1)	1	(0.99;1.02)	0.795
Recurrent WON or pseudocyst					
No	63 (85)	214 (93.0)	1		
Yes	11 (15)	16 (7.00)	2.15	(0.90-4.93)	0.073
Stent Type, n (%)					
EC-LAMS(Hot- Axios)	68 (91.9)	208 (90.4)	1	-	-

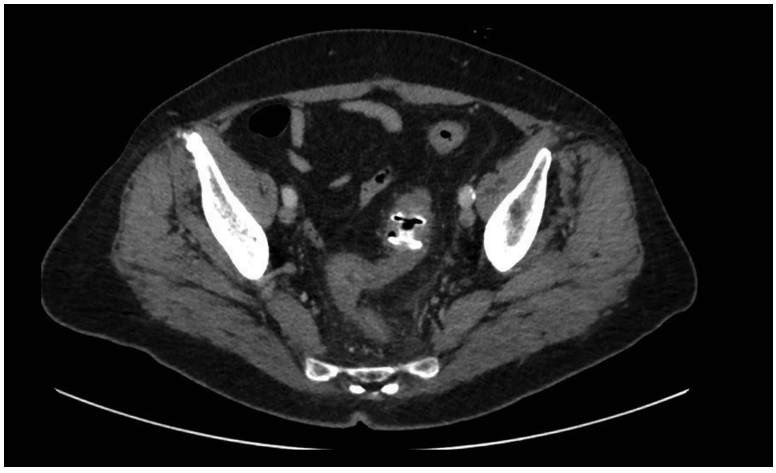
LAMS (Cold - Axios)	6 (8.1)	22 (9.6)	0.83	(9.30;2.03)	0.706
Stent diameter, n (%)					
<=10 mm	25 (33.8)	62 (27.0)	1		
>10 mm	49 (66.2)	168 (73.0)	0.72	(0.41;1.28)	0.259
Drainage approach, n (%)					
Transgastric	70 (94.6)	217 (94.3)	1		
Transduodenal	4 (5.4)	13 (5.7)	0.83	(0.30;2.65)	0.726
Tract dilation, n (%)					
No	54 (73.0)	147 (64.0)	1		
Yes	20 (27.0)	83 (36.0)	0.61	(0.33;1.08)	0.092
Necrosectomy, n (%)					
Yes	28 (37.8)	78 (33.9)	1		
No	46 (62.2)	152(66.1)	0.9	(0.53;1.54)	0.691
Hydrogen peroxide irrigation, n (%)					
Yes	16 (21.6)	59 (25.7)	1		
No	58 (78.4)	171(74.3)	1.02	(0.57;2.07)	0.950
Nasocystic Tube					
Yes	9 (12.2)	12 (5.2)	1		
No	65 (87.8)	218 (94.8)	0.40	(0.16;1.01)	0.046
Pigtail stents placed through the LAMS, n (%)					
Yes	9 (12.2)	25 (10.9)	1		
No	65 (87.8)	205 (89.1)	0.87	(0.40;2.07)	0.748
Concomitant Percutaneous Drainage, n (%)					
No	65 (87.8)	216 (94.0)	1		
Yes	9 (12.2)	14 (6.0)	2.13	(0.85;5.01)	0.098
Extension of fluid collection to paracolic gutter, n (%)					
No	59 (79.7)	167 (72.6)	1		
Yes	5 (6.8)	32 (13.9)	0.44	(0.14;1.10)	0.100
Not reported	10 (13.5)	31 (13.5)	0.91	(0.42;1.96)	0.420

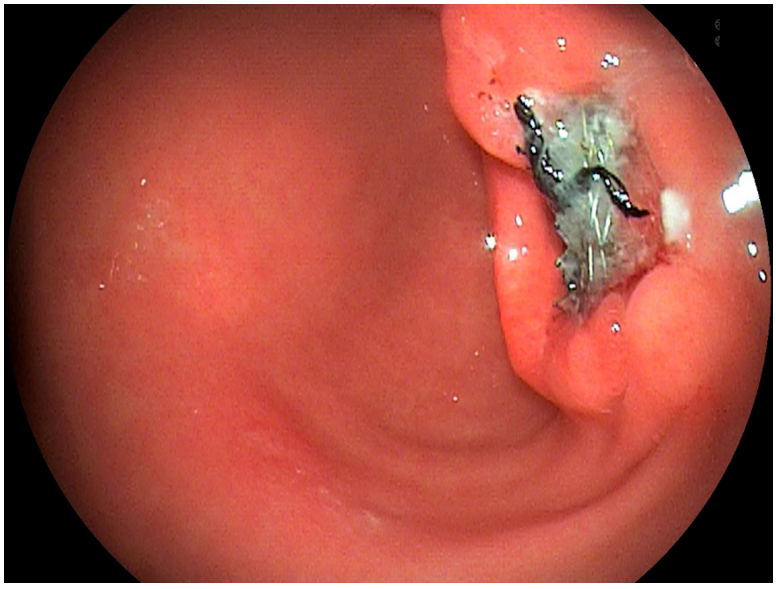
SD: standard deviation, PFC: pancreatic fluid collection, PP: pseudocyst, WON: walled-off necrosis, EC-LAMS: Electrocautery enhanced lumen-apposing metal stent, LAMS: lumen-apposing metal stent

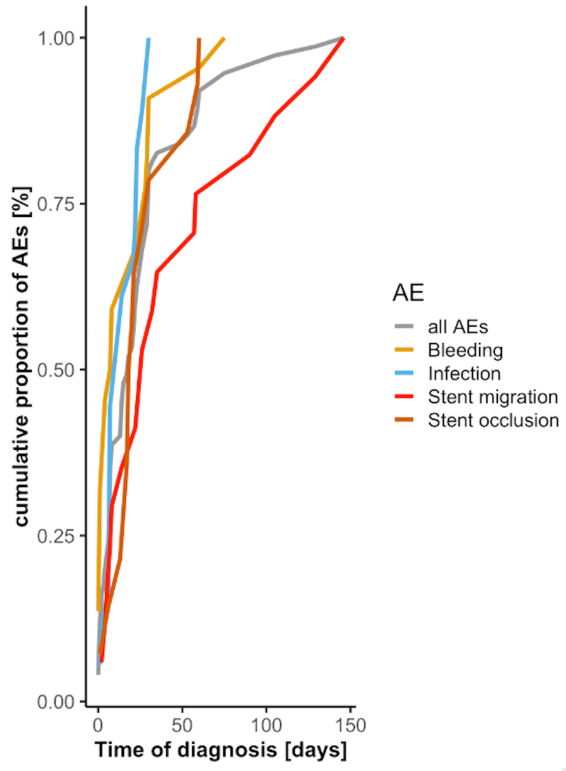
Table 3. Results from the multivariable analysis.

	Multivariable analysis		
Variable	**OR**	**95% CI**	***P* value**
PFC Classification			
Pseudocyst	1		
WON	2.18	(1.09;4.46)	0.028
Recurrent WON or PP			
No	1		
Yes	1.79	(0.62-4.80)	0.259
Tract dilation, n (%)			
No	1		
Yes	0.47	(0.22;0.93)	0.034
Nasocystic Tube			
Yes	1		
No	0.72	(0.26;2.09)	0.522
Concomitant Percutaneous Drainage, n (%)			
No	1		
Yes	1.51	(0.49;4.38)	0.456
Extension of fluid collection to paracolic gutter, n (%)			
No	1		
Yes	0.43	(0.14;2.10)	0.097
Not reported	0.94	(0.43;1.07)	0.975
PFC: Pancreatic fluid collection, WON: walled-off necrosis, PP: pseudocyst			









List of Acronyms

PP Pancreatic pseudocyst

WON Walled-off necrosis

PFC Peripancreatic fluid collections

AEs adverse events

EUS endoscopic ultrasonography

SEMS self-expanding metallic stent

ETN endoscopic transmural necrosectomy

LAMS Lumen apposing metal stent

CT Computer Tomography

MRI Magnetic Resonance Imaging

MRCP Magnetic Resonance Cholangiopancreatography

SD standard deviation

AOR Adjusted ORs

FU follow-up

MOF Multi-Organ Failure