Definition of a hospital volume threshold to optimize outcomes after drainage of pancreatic fluid collections with lumen-apposing metal stents: a nationwide cohort study

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Background and Aims: There is increasing interest in expanding the use of lumen-apposing metal stents (LAMSs) in patients with pancreatic fluid collections (PFCs). The aim of this study was to determine whether there is a hospital volume threshold for which patient outcomes could be optimized.

Methods: Data from a large multicenter series of patients with PFCs treated with LAMSs were retrieved. Rate of adverse events (AEs) was the primary outcome. Multivariable models with restricted cubic splines were used to identify a hospital volume threshold by plotting hospital volume against the log odds ratio (OR) of AE rate. Propensity score matching was applied to obtain 2 well-balanced groups according to hospital volume, and univariate/multivariate logistic regression analysis was performed to identify significant predictors of AEs.

Results: Overall, 516 patients were included. Increasing hospital volume was associated with a reduced AE rate ($P = .03$), and the likelihood of experiencing an AE declined as hospital volume increased up to 15 cases. After propensity score matching, 175 patients in the high-volume (>15 cases) and 132 in the low-volume hospital group were compared. Overall, 41 AEs were observed (13.3%), of which 14 (8%) and 27 (20.4%) occurred at high-volume and low-volume centers, respectively ($P = .001$). Severe and fatal events were observed more frequently in low-volume centers (6% vs 1.7% and 2.2% vs 0%, respectively; $P = .05$). In multivariate analysis, main pancreatic duct injury (OR, 2.62; 95% confidence interval [CI], 1.26-4.67; $P = .02$), presence of abnormal vessels (OR, 2.93; 95% CI, 1.41-5.02; $P = .006$), and institutional experience (OR, 2.95; 95% CI, 1.48-5.90; $P = .002$) were significant predictors of AEs.

Conclusions: With 15 procedures representing the minimum number of cases associated with the lowest risk for postprocedural AEs, hospital volume is associated with improved outcomes. (Clinical trial registration number: NCT03903523.) (Gastrointest Endosc 2022;95:1158-72.)

Abbreviations: AE, adverse event; CI, confidence interval; DEN, direct endoscopic necrosectomy; LAMS, lumen-apposing metal stent; MPD, main pancreatic duct; OR, odds ratio; PFC, pancreatic fluid collection; RCS, restricted cubic spline; WON, walled-off necrosis.

DISCLOSURE: *The following author disclosed financial relationships: S. F. Crinò: Speaker for Steris Endoscopy. A. Anderloni: Consultant for Boston Scientific. A. Fugazza: Consultant for Boston Scientific. All other authors disclosed no financial relationships.*

*See Acknowledgements for other members of the i-EUS Group.

0016-5107/$36.00
https://doi.org/10.1016/j.gie.2021.12.006

Received October 1, 2021. Accepted December 11, 2021.

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Drainage through lumen-apposing metal stents (LAMSs) or double-pigtail plastic stents plays a pivotal role in the therapeutic management of pancreatic fluid collections (PFCs). Specifically, LAMSs allow effective drainage of pancreatic pseudocysts and walled-off necrosis (WON) because of their wide lumen that enables quick and effective drainage of the collection (including direct endoscopic necrosectomy [DEN] in patients with WON[1,2]). LAMSs are also associated with reduced risk of occlusion with necrotic tissue, which represents a common pitfall of double-pigtail plastic stents. Furthermore, their biflanged design decreases the risk of stent migration.[3,4]

The high success rate observed with LAMS placement[5,6] has culminated in their widespread use in clinical practice, suggesting that a step-up approach with endoscopic transluminal drainage by DEN through the LAMS represents the best therapeutic option for WON.[7-9] However, non-negligible rates of adverse events (AEs) such as bleeding, infection, and buried stent syndrome have been reported after LAMS placement.[10] The AE rate has been reported to be as high as 6.4%, with stent removal after 4 weeks and PFC size $\leq$7 cm as significant predictors of delayed AEs in an American prospective study.[11] A slightly higher AE rate was observed in patients with WON (13.1%) as compared with pancreatic pseudocyst patients (7.1%) in a meta-analysis.[6]

However, most published literature is based on the experience of high-volume centers. The generalizability of these outcomes to hospitals that perform a small number of these procedures has recently been questioned, hence the need for nationwide studies that include low- and high-volume hospitals.

As already demonstrated in complex surgical procedures, such as pancreatic or cardiovascular surgery,[12,13] 2 studies observed a linear relationship between the number of procedures performed and treatment outcomes in EUS drainage of patients with PFCs.[14,15] However, both studies were reported before LAMSs were developed. An Asian consensus group suggested that performance of 5 to 10 procedures under supervision might represent the minimum requirement to obtain competency in interventional EUS procedures and acknowledged the urgent need of studies focused on LAMS placement.[16]

Therefore, determining a minimum number of procedures that potentially defines a high-volume hospital is essential. The aim of this study was to determine whether a minimum number of LAMS placements by a hospital was associated with a reduced likelihood of postoperative AEs. We also investigated whether there was a correlation between hospital volume and efficacy outcomes.

METHODS

Patients

To collect clinical data on real-life activity on the efficacy and safety of LAMS placement, a nationwide initiative from the Interventional Endoscopy and Ultrasound (i-EUS) group was held in Italy involving gastroenterologists and endoscopists from centers throughout the national territory who were performing EUS-guided drainage with LAMSs. Retrospective data collection was approved by the institutional review board of each participating center and performed in accordance with the Declaration of Helsinki. The protocol was registered on clinicaltrials.gov (NCT03903523). Overall, the database collected 850 cases for the 3 main indications (PFC, gallbladder, and biliary drainage).

Procedures

EUS-guided PFC drainage procedures were performed by endoscopists with different experience in PFC management. Details on the training of the endoscopists in the i-EUS group were described in a recent survey, reporting that 38.8% attended a training course, 27.7% were supported by an expert, 22.2% had both opportunities, and 8.3% had none.[17] Moreover, 1 main manufacturer of the device chose to distribute it to centers only after endoscopists completed a predefined standardized 2-day hands-on training.

Procedures occurred with patients under deep sedation or general anesthesia using a therapeutic echoendoscope with CO_2 insufflation. Patients were given broad-spectrum antibiotic prophylaxis. The type, dosage, and course of antibiotic therapy were at the discretion of the endoscopist or in accordance with local hospital policies.

Doppler flow was used to avoid interposed blood vessels within puncture trajectory. PFCs were drained through either the stomach or duodenum wall according to the location of the collection. Different stent types (Hot-Axios [Boston Scientific, Marlborough, Mass, USA], Spaxus [Taewoong, Busan, South Korea], or Nagi [Taewoong, Busan, South Korea]) and sizes were used according to center availability and/or endoscopist preference. LAMS deployment technique and use of fluoroscopic guidance were at the discretion of the endoscopist.

When a cautery-enhanced LAMS was placed, puncture of the PFC was performed directly using the same device with pure-cut settings (single-stage technique). For standard LAMS placement, puncture of the cavity with a 19-gauge needle, insertion of a .025-/.035-inch guidewire, and dilation of the tract using a cystotome and dilation balloon followed by insertion of the delivery system and deployment of the stent were performed. For both techniques, the deployment of the second flange was

performed either endoscopically or with the intrachannel stent release technique. DEN was performed using several standard devices (snares, standard biopsy forceps, rat-tooth forceps, Roth nets, and biliary basket), at the endoscopists' discretion. The timing and frequency of DEN were based on several factors, such as symptoms, imaging data, and center policy, and were performed until emptying of the cavity was achieved.

Data collection

Data were compiled and extracted from a web-based central database. Demographics, collection-related features (etiology, type, percentage of necrosis, location, size, extension, site of access, injury appearance of the main pancreatic duct [MPD] at CT/magnetic resonance imaging or EUS, presence of abnormal vessels including portal vein thrombosis, perigastric varices, pseudoaneurysm, etc), LAMS-related data (eg, type and size, placement technique), and procedural data (complementary maneuvers during the procedure) were collected. Postprocedural data were resumption of an enteral diet classified as before or after 48 hours, length of hospitalization, other procedures performed such as further LAMS placement, need for percutaneous drainage, successful stent removal after resolution of PFCs, recurrence during follow-up, onset of AEs, and AE management.

Outcomes

AEs were defined, classified, and graded according to the American Society for Gastrointestinal Endoscopy lexicon.[18] All symptomatic events related to the use of LAMSs, such as bleeding, infection, stent occlusion, and migration, and resulting in prolongation of hospital stay, requiring medical therapy, or further procedure or action to resolve the event were considered.[18]

Technical success was defined as correct LAMS placement. Clinical success was defined as WON or pancreatic pseudocyst resolution (ie, <2 cm on axial imaging 1-6 months after LAMS insertion) without the need for further interventional radiologic or surgical procedures.

Statistical analysis

Patient characteristics are expressed as median and interquartile range for continuous variables and absolute frequencies and percentages for categorical data. A multivariable logistic regression model with restricted cubic splines (RCSs) was used to specify and estimate the functional form of hospital volume with respect to the incidence of AEs.[19] The RCS statistical method provides a flexible model to examine the adjusted effect of a continuous predictor on an outcome and allows visualization of the relationship without prior knowledge of the functional form of the association.[20] This model is used, and the knots are placed at the quintiles of the uncensored data. The knot of the piecewise linear spline representing a break point in the log odds function was interpreted as a threshold value.[20]

Based on the identified hospital volume threshold, the cohort was dichotomized into 2 groups: high-volume centers (more than threshold hospital volume) and low-volume hospitals (less than or equal to threshold hospital volume). To overcome biases because of the different distribution of covariates among these 2 groups, a propensity score–matching analysis was performed. The propensity score represents the probability of each individual patient being assigned to a particular condition in a study given a set of known covariates.[21]

A multivariate logistic regression was built to predict the probability of each individual patient being submitted to the 2 groups on those covariates that were significantly different at baseline, namely percentage of necrosis, appearance of the collection (whether single or multiloculated), extension to the paracolic gutter, indication to treatment, etiology of pancreatitis, type of stent used, stent diameter, endoscopic appearance of the cavity, and use of the nasocystic tube drainage. The predictive values were then used to obtain a match by using nearest-neighbor matching within a specified caliper distance. Nearest-neighbor matching within a specified caliper distance selects for matching a control subject whose propensity score is closest to that of the treated subject ("nearest-neighbor matching" approach) with the further restriction that the absolute difference in the propensity scores of matched subjects must be below some prespecified threshold (the caliper distance) settled, as suggested by Austin,[22] to a width equal to .2 of the standard deviation of the logit of the propensity score.[23]

Comparison between groups was performed using the χ^2 test and McNemar analysis before and after matching, respectively, in the case of categorical variables, whereas the Mann-Whitney and Wilcoxon rank test before and after matching, respectively, were used for continuous variables. Correlation between baseline factors and AE occurrence was then analyzed by means of univariate/multivariate logistic regression, and significant predictors in the univariate analysis were entered in the multivariate model. Results were expressed in terms of odds ratio (OR) and 95% confidence interval (CI).

All analyses were 2-tailed, and differences were considered significant at $P < .05$. Statistical analyses were performed using the splines and MatchIt packages in R Statistical Software 3.0.2 (Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patients and hospital volume

Data of 516 patients with PFCs who underwent LAMS placement were collected across 30 secondary and tertiary care centers in Italy from January 2016 to July 2020. The

TABLE 1. Baseline patient characteristics and outcomes before propensity score matching

Variable	Total patients (n = 516)	High-volume centers (n = 384)	Low-volume centers (n = 132)	*P* value
Age, y	62 (52.1-74)	62 (49.5-73)	63 (50-74)	.42
Gender				.30
Male	351 (68)	256 (67)	95 (72)	
Female	165 (32)	128 (33)	37 (28)	
Pancreatic fluid collection type				.73
Pseudocyst	247 (48)	186 (48)	61 (46)	
Walled-off necrosis	269 (52)	198 (52)	71 (54)	
Percentage of necrosis	45 (30-60)	50 (38-60)	32 (28-52)	**.04**
Location				.06
Body	348 (67)	269 (70)	79 (60)	
Head	87 (17)	62 (16)	25 (19)	
Tail	81 (16)	53 (14)	28 (21)	
Collection width, mm	90 (60-120)	95 (62-115)	88 (56-110)	.21
Collection length, mm	75 (52-100)	80 (59-100)	74 (52-96)	.35
Collection				**<.001**
Multiloculated	112 (22)	69 (18)	43 (33)	
Single	404 (78)	315 (82)	89 (67)	
Extension to paracolic gutter				**.03**
Not reported	15 (3)	15 (4)	0 (0)	
No	367 (71)	268 (70)	99 (75)	
Yes	134 (26)	101 (26)	373 (25)	
Injury of main pancreatic duct				.85
Leak	36 (7)	23 (8)	10 (4)	
No leak	324 (63)	247 (64)	80 (58)	
Complete disruption	16 (3)	12 (1)	4 (9)	
Unknown	140 (27)	102 (27)	38 (29)	
Vessel appearance				.22
No alterations	415 (80)	308 (80)	107 (81)	
Perigastric varices	34 (7)	30 (8)	4 (3)	
Pseudoaneurysm	10 (2)	6 (2)	4 (3)	
Portal vein thrombosis	21 (4)	14 (4)	7 (5)	
Splenic vein thrombosis	36 (7)	26 (7)	10 (8)	
Indication				**.01**
Abdominal pain	165 (32)	126 (33)	39 (30)	
Early satiety	38 (7)	35 (9)	3 (2)	
Infection	207 (40)	155 (40)	52 (39)	
Outlet obstruction	60 (12)	35 (9)	25 (19)	
Vessels thrombosis	8 (2)	6 (2)	2 (2)	
Vomiting	20 (4)	14 (4)	6 (5)	
Other	18 (3)	13 (3)	5 (4)	
Etiology of pancreatitis				**.005**
Alcohol	92 (18)	57 (15)	35 (27)	
Autoimmune	1 (.2)	1 (.2)	0 (0)	
Biliary	254 (49)	192 (50)	62 (47)	

(*continued on the next page*)

TABLE 1. Continued

Variable	Total patients (n = 516)	High-volume centers (n = 384)	Low-volume centers (n = 132)	*P* value
Idiopathic	68 (13)	46 (12)	22 (17)	
Post-ERCP	23 (4)	21 (5)	2 (2)	
Postoperative	14 (3)	12 (3)	2 (2)	
Trauma	46 (9)	41 (11)	5 (4)	
Other	18 (3)	14 (4)	4 (3)	
Type of stent				**<.001**
Axios	386 (75)	259 (67)	127 (96)	
NAGI	90 (17)	88 (23)	2 (2)	
Spaxus	7 (1)	7 (2)	0 (0)	
Other	33 (6)	30 (8)	3 (2)	
Access				66
Needle + guidewire	180 (35.5)	136 (35)	44 (33.3)	
Single stage	336 (64.5)	248 (65)	88 (66.7)	
Fluoroscopic guide				0.67
Yes	180 (35.5)	137 (35)	43 (33.3)	
No	336 (64.5)	247 (65)	89 (66.7)	
Stent diameter				**<.001**
10 × 10	58 (11)	32 (8)	26 (20)	
15 × 10	270 (52)	183 (48)	87 (66)	
20 × 10	52 (10)	38 (10)	14 (11)	
8 × 8	3 (1)	3 (1)	0 (0)	
Other	133 (26)	128 (33)	5 (4)	
No. of stents				.312
1	504 (98)	373 (97)	131 (99)	
2	12 (2)	11 (3)	1 (1)	
Second flange deployment				.26
Endoscopic view	175 (34)	136 (35)	39 (30)	
Intrachannel	341 (66)	248 (65)	93 (70)	
Approach				.38
Transduodenal	38 (7)	29 (8)	9 (7)	
Transgastric	466 (90)	343 (89)	123 (93)	
Both	1 (.2)	1 (.2)	0 (0)	
Other	9 (1.4)	9 (1.4)	0 (0)	
Not reported	2 (.4)	2 (.4)	0 (0)	
Stent dilation				.91
No	414 (80)	309 (80)	105 (80)	
Yes	102 (20)	75 (20)	27 (20)	
Necrosectomy				.60
No	307 (59.6)	232 (59.6)	75 (57)	
Yes	208 (40)	151 (39)	57 (43)	
Not reported	1 (.4)	1 (.4)	0 (0)	
Endoscopic appearance of cavity				**.009**
Purulent fluid	224 (43)	173 (45)	51 (39)	
Solid debris	169 (33)	115 (30)	54 (41)	

(*continued on the next page*)

TABLE 1. Continued

Variable	Total patients (n = 516)	High-volume centers (n = 384)	Low-volume centers (n = 132)	*P* value
Vessels	11 (2)	11 (3)	0 (0)	
Other	103 (20)	81 (21)	22 (17)	
Not reported	9 (2)	4 (1)	5 (4)	
Hydrogen peroxide irrigation				.14
No	362 (70)	273 (71)	89 (67)	
Yes	143 (28)	100 (26)	43 (33)	
Not reported	11 (2)	11 (3)	0 (0)	
Antibiotic irrigation				.62
No	492 (95.3)	368 (95.8)	126 (95.4)	
Yes	19 (3.6)	14 (3.6)	5 (3.7)	
Not reported	3 (1.1)	2 (.6)	1 (.9)	
Nasocystic tube drainage				**.01**
No	432 (84)	312 (81)	120 (91)	
Yes	73 (14)	61 (16)	12 (9)	
Not reported	11 (2)	11 (3)	0 (0)	
Pigtail use through stent				.62
No	450 (87)	337 (88)	113 (86)	
Yes	66 (13)	47 (12)	19 (14)	
Need of percutaneous drainage				.10
No	497 (96)	373 (97)	124 (94)	
Yes	19 (4)	11 (3)	8 (6)	
Days to stent removal	50 (35-61)	58 (35-72)	48 (30-60)	.09
Technical success	504 (98)	378 (98)	126 (96)	.35
Clinical success	473 (92)	351 (91)	122 (92)	.85
Collection recurrence	35 (7)	27 (7)	8 (6)	.47
Adverse event rate	76 (15)	49 (12.7)	27 (20.4)	**.03**

Values are median (interquartile range) or n (%). Comparisons were performed with Mann-Whitney U test for continuous variables and Fisher exact test for categorical ones. Significant values are shown in bold.

baseline characteristics of the entire study population were reported in Table 1.

Median follow-up was 311 days (95% CI, 248-375). Pancreatic collection was predominantly WON (269 patients [52.1%]) followed by pseudocysts (247 patients [47.9%]), which were drained. In the case of WON, the median percentage of necrosis at imaging was 45% (95% CI, 30-60). Median collection width was 90 mm (95% CI, 60-120), and median length was 75 mm (95% CI, 52-100).

The number of procedures performed by a hospital ranged from 1 to 55 cases per year, with a median of 12 cases per year (interquartile range, 5-20). Hospital procedural volume was significantly associated with decreasing odds of experiencing a postprocedural AE ($P = .03$). The adjusted RCS plot demonstrated a nonlinear association between hospital procedural volume and AE rate. This confirmed the existence of a possible hospital volume threshold corresponding to the lowest risk of experiencing a postprocedural AE. Further, the plot showed that increasing hospital procedural volume was significantly associated with decreasing odds of patients experiencing an AE for up to 15 procedures. The curve reached a plateau with an increasing number of cases, which did not significantly impact patient outcomes (Fig. 1).

Hospital volume status was then defined based on the threshold identified by the RCS model: low-volume hospitals (≤15 cases) and high-volume hospitals (>15 cases). As reported in Table 1, 384 patients underwent LAMS placement at high-volume centers and 132 patients at low-volume hospitals.

Compared with patients treated at low-volume hospitals, patients with WON treated at high-volume hospitals had a higher percentage of necrosis (50% [interquartile range, 38-60] vs 32% [interquartile range, 28-52], $P = .04$). PFC location was frequently in the body of the pancreas (269 patients [70%]), whereas morphology was frequently

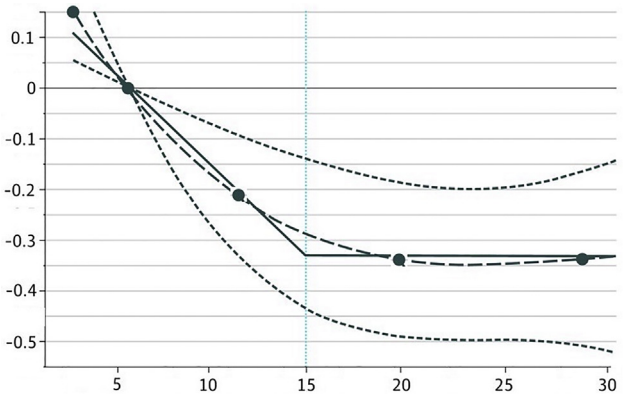

Figure 1. Smoothed restricted cubic spline plot of the adjusted log odds ratio of experiencing an adverse event in correlation with the number of lumen-apposing metal stent placement procedures for drainage of pancreatic fluid collection performed per hospital. The *curved line with long dashes* represents the regression line in the change point estimation. The 2 *small-dashed curves* represent the 95% confidence intervals. The *black dots* correspond to the location of the knots used in the model. The intersection at the value of 15 cases (*dotted blue vertical line*) is the cutoff identified by the model.

multiloculated (33% vs 18%) in patients treated at high-volume centers. A higher use of the Hot-Axios stent was registered at low-volume centers (96% vs 67%, $P < .001$). Overall, 49 (12.7%) and 27 (20.4%) AEs were registered in patients treated at high- and low-volume centers, respectively ($P = .03$).

Propensity score–matching analysis

After propensity score matching, 307 patients were selected for comparison: 175 in the high-volume group and 132 in the low-volume group. Details of propensity score matching are shown in Figure 2A and B. Characteristics of the 307 propensity score-matched patients are reported in Table 2.

Median patient age was 62 years (range, 51-73) with no difference between the 2 groups ($P = .51$). One hundred twenty-six (72%) and 95 (72%) male patients were treated at high- and low-volume centers, respectively ($P = .30$).

Nearly half of all cases were pseudocysts ($P = .73$) with no difference in any of the aforementioned parameters. Specifically, collections were multiloculated in 53 patients (30%) treated at high-volume centers and in 43 patients (33%) treated at low-volume centers ($P = .62$) with no difference regarding extension to the paracolic gutter ($P = .13$). The main indication to treatment was collection infection (37.1% and 39% in the 2 groups, respectively; $P = .32$), and the etiology of pancreatitis was predominantly biliary (50% vs 47%, $P = .5$).

No difference in terms of type and diameter of the stent used was observed between the 2 groups ($P = .81$ and .43, respectively), with most patients in both groups (94% and 96%, respectively) treated with the Hot-Axios stent. A similar use of hydrogen peroxide irrigation ($P = .4$), nasocystic tube drainage ($P = .15$), and pigtail through the stent ($P = .67$) was observed after propensity matching between the 2 groups. The median time to LAMS removal was 52 days (95% CI, 37-69) in the high-volume group and 48 days (95% CI, 25-60) in the low-volume group ($P = .17$).

Outcomes

A detailed list of study outcomes is reported in Table 3. Technical success was 99% at high-volume centers and 96% at low-volume centers ($P = .06$), whereas clinical success was registered in 168 patients (96%) treated at high-volume centers and 122 patients (92%) treated at low volume centers ($P = .17$).

Overall, 41 AEs (13.3%) were observed, of which 14 (8%) occurred in patients treated at high-volume centers and 27 (20.4%) in patients treated at low-volume centers ($P = .001$). No difference in terms of the type of AE observed was registered ($P = .18$), with bleeding (4.5%) and infection (3.5%) the most frequent AEs. Moreover, 3 patients (1%) experienced stent occlusion and 3 patients (1%) stent migration. Perforation and capnoperitoneum were experienced by 3 patients (1%), whereas other AEs were less frequent (Table 3). These events were managed conservatively in 15 patients (4.8%), with interventional radiology embolization in 6 patients (1.9%) and with endoscopic treatments in 18 patients (5.8%). Surgery was needed in only 2 patients (.6%).

AEs were classified as mild in 14 patients (4.5%), of which 8 (4.5%) occurred in high-volume centers and 6 (4.4%) in low-volume centers. Moderate AEs were registered in 14 patients (4.5%), of which 4 (2.3%) occurred in high-volume centers and 10 (7.5%) in low-volume centers. Severe and fatal events were observed more frequently in low-volume centers (6% vs 1.7% and 2.2% vs 0%, respectively; $P = .05$). The recurrence rate of the collection was 15 of 307 patients (4.8%), with 7 patients (4%) at high-volume centers and 8 (6%) at low-volume centers ($P = .40$).

In the subgroup of patients who did not undergo endoscopic necrosectomy, the AE rate was 6 of 103 (5.8%) in high-volume centers and 14 of 75 (18.6%) in low-volume centers ($P = .007$). In high-volume centers, 4 mild, 1 moderate, and 1 severe AE were registered, whereas 2 mild, 8 moderate, and 4 severe AEs were observed in low-volume centers ($P = .05$).

When univariate logistic regression modeling was used, the appearance of the MPD at preprocedural imaging/EUS (OR in the case of leak/disruption, 2.62; 95% CI, 1.26-4.67; $P = .02$), presence of abnormal vessels (OR in the case of perigastric varices, 2.93; 95% CI, 1.41-5.02; $P = .006$; OR in the case of pseudoaneurysm, 1.98; 95% CI, 1.65-4.91; $P = .003$), and experience of the center (OR, 2.95; 95% CI, 1.48-5.90; $P = .002$) were significant predictors of AE occurrence (Table 4). All these variables were confirmed as

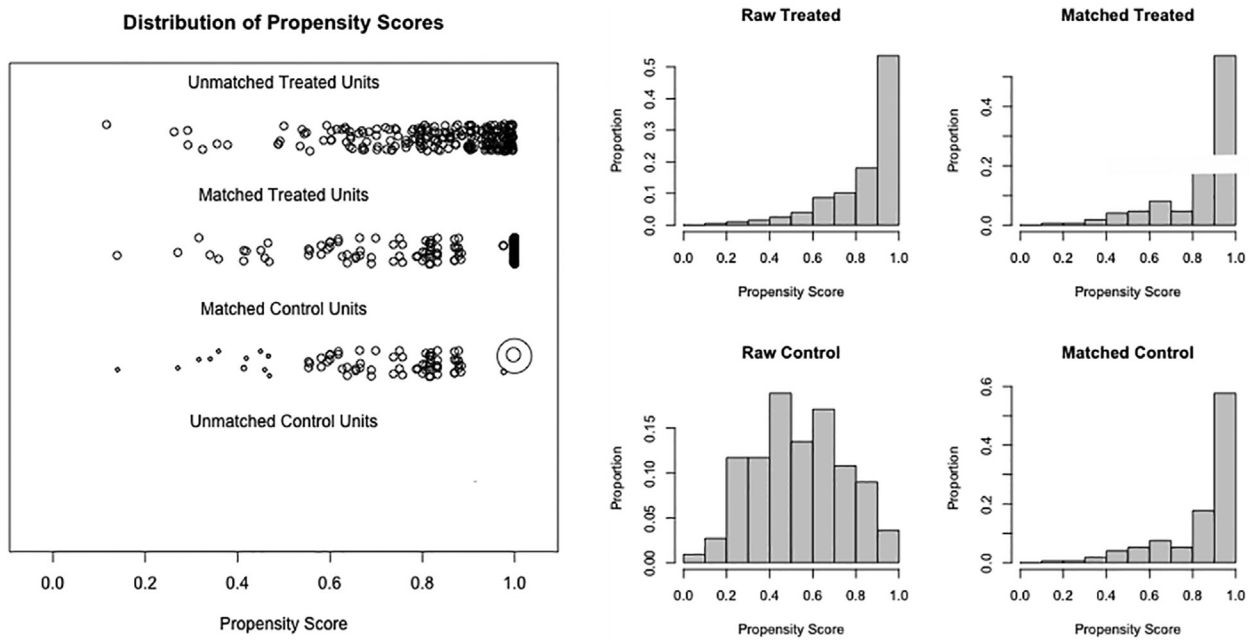

Figure 2. Propensity score matching. Of the initial 516 patients, after propensity score caliper matching 307 patients were selected for comparison: 175 treated at high-volume centers and 132 at low-volume centers. **A,** Propensity score–matching jitter plot. **B,** Propensity score–matching histogram.

significant predictors of AEs in multivariate analysis (Table 4).

DISCUSSION

Endoscopic drainage represents the first-line therapy for PFC drainage because it is associated with lower cost, shorter hospital length of stay, and better quality of life as compared with surgery.[24-26] However, like in other surgical and endoscopically complex procedures,[12,13,27] evidence suggesting an association between lower hospital procedural volume and compromised outcomes has prompted debate about the safety of LAMS placement and a call for potentially restricting the procedure to high-volume hospitals.

Higher hospital procedural volume was significantly associated with decreasing odds of patients experiencing a postprocedural AE. Our RCS analysis identified a hospital procedural volume threshold of 15 cases to be associated with the lowest risk for experiencing an AE. RCSs, which are a transformation of a continuous predictor, provide a simple and accurate way to create, test, and model nonlinear relationships in regression models.[20]

Patients were grouped into 2 cohorts, with most patients treated at high-volume centers (384 subjects) versus 132 at low-volume centers. As reported in Table 1, high-volume centers advocated the use of this procedure in more difficult cases (higher percentage of necrosis, more frequent extension to paracolic gutter, multiloculated collections, or worse endoscopic appearance of the cavity); however, in spite of these differences, the AE rate was higher in patients treated at low-volume centers (20.4% vs 12.7%, $P = .03$).

To overcome the potential biases related to the retrospective nature of the study and to consider any confounding variables, we performed a propensity score–matching analysis on the basis of several demographic and PFC-related features. Thus, 2 perfectly balanced treatment groups were obtained. Overall, no difference in terms of treatment effectiveness was observed, although technical success showed a nonsignificant trend in favor of high-volume centers ($P = .06$). The dichotomy between center-related AEs became more evident after propensity score matching (20.4% vs 8%, $P = .001$). Moreover, more severe AEs were observed in patients treated at low-volume centers. The severe AE rate was 6% at low-volume centers and only 1.7% at high-volume centers, whereas the 3 fatal events registered in our series were all observed in patients treated at low-volume centers ($P = .05$). Consequently, in addition to certain imaging characteristics of the collection, the volume of the center was found to be a significant predictor of AEs both in univariate and in multivariate regression analyses.

These results are of particular interest because the definition of the proficiency of a center represents a paramount quality index in several surgical and interventional endoscopy procedures. In several countries, the shift of the healthcare system from a fee-for-service to a value-based model that links hospitals' reimbursement to the quality of care provided has made this debate even more revelant.[28] Favorable outcomes published from large-

TABLE 2. Baseline patient characteristics after propensity score matching

Variable	Total patients (n = 307)	High-volume centers (n = 175)	Low-volume centers (n = 132)	*P* value
Age, y	62 (51-73)	62 (53-72)	63 (50-74)	.51
Gender				.30
Male	221 (71.9)	126 (72)	95 (72)	
Female	86 (28.1)	49 (28)	37 (28)	
Pancreatic fluid collection type				.73
Pseudocyst	145 (47.2)	84 (48)	61 (46)	
Walled-off necrosis	162 (52.8)	91 (52)	71 (54)	
Percentage of necrosis	45 (30-60)	50 (38-60)	45 (28-58)	.23
Location				.26
Body	191 (62.2)	112 (64)	79 (60)	
Head	56 (18.2)	31 (17.5)	25 (19)	
Tail	60 (19.6)	32 (18.5)	28 (21)	
Collection width, mm	90 (60-120)	92 (64-113)	88 (56-110)	.21
Collection length, mm	75 (52-100)	78 (58-100)	74 (52-96)	.45
Collection				.62
Multiloculated	96 (31.2)	53 (30)	43 (33)	
Single	211 (68.8)	122 (70)	89 (67)	
Extension to paracolic gutter				.13
Not reported	7 (2.2)	7 (4)	0 (0)	
No	221 (71.9)	122 (70)	99 (75)	
Yes	79 (25.9)	46 (26)	33 (25)	
Injury of main pancreatic duct				.85
Leak	19 (6.1)	9 (5)	10 (4)	
No leak	183 (59.6)	103 (59)	80 (58)	
Complete disruption	11 (3.5)	7 (4)	4 (9)	
Unknown	94 (30.8)	56 (32)	38 (29)	
Vessel appearance				.22
No alterations	247 (80)	140 (80)	107 (81)	
Perigastric varices	18 (6)	14 (8)	4 (3)	
Pseudoaneurysm	7 (2)	3 (2)	4 (3)	
Portal vein thrombosis	13 (4)	6 (4)	7 (5)	
Splenic vein thrombosis	22 (8)	12 (6)	10 (8)	
Indication				.32
Abdominal pain	94 (30)	55 (31.4)	39 (30)	
Early satiety	9 (3)	6 (4)	3 (2)	
Infection	117 (38)	65 (37.1)	52 (39)	
Outlet obstruction	57 (18)	32 (18.5)	25 (19)	
Vessel thrombosis	5 (2)	3 (2)	2 (2)	
Vomiting	12 (4)	6 (4)	6 (5)	
Other	15 (5)	10 (3)	5 (4)	
Etiology of pancreatitis				.5
Alcohol	91 (29)	56 (32)	35 (27)	
Autoimmune	0 (0)	0 (0)	0 (0)	
Biliary	150 (49)	88 (50)	62 (47)	

(*continued on the next page*)

TABLE 2. Continued

Variable	Total patients (n = 307)	High-volume centers (n = 175)	Low-volume centers (n = 132)	*P* value
Idiopathic	48 (16)	26 (15)	22 (17)	
Post-ERCP	3 (1)	1 (2)	2 (2)	
Postoperative	3 (1)	1 (2)	2 (2)	
Trauma	6 (2)	1 (2)	5 (4)	
Other	6 (2)	2 (3)	4 (3)	
Type of stent				.81
Axios	298 (96.2)	171 (94)	127 (96)	
NAGI	4 (1.8)	2 (3)	2 (2)	
Spaxus	0 (0)	0 (0)	0 (0)	
Other	5 (2)	2 (3)	3 (2)	
Access				.71
Needle + guidewire	105 (35.5)	61 (35)	44 (33.3)	
Single stage	202 (64.5)	114 (65)	88 (66.7)	
Fluoroscopic guide				.71
Yes	104 (35)	61 (35)	43 (33.3)	
No	203 (65)	114 (65)	89 (66.7)	
Stent diameter				.43
10 × 10	58 (19)	32 (18)	26 (20)	
15 × 10	206 (67)	119 (68)	87 (66)	
20 × 10	32 (10)	18 (10)	14 (11)	
8 × 8	0 (0)	0 (0)	0 (0)	
Other	11 (4)	6 (4)	5 (4)	
No. of stents				.54
1	301 (98)	170 (97)	131 (99)	
2	6 (2)	5 (3)	1 (1)	
Second flange deployment				.36
Endoscopic view	100 (32.5)	61 (35)	39 (30)	
Intrachannel	207 (67.5)	114 (65)	93 (70)	
Approach				.82
Transduodenal	23 (7)	14 (8)	9 (7)	
Transgastric	284 (93)	161 (91)	123 (93)	
Both	0 (0)	0 (0)	0 (0)	
Other	0 (0)	0 (0)	0 (0)	
Not reported	0 (0)	0 (0)	0 (0)	
Stent dilation				.98
No	245 (80)	140 (80)	105 (80)	
Yes	62 (20)	35 (20)	27 (20)	
Necrosectomy				.73
No	178 (58)	103 (59)	75 (57)	
Yes	129 (42)	72 (41)	57 (43)	
Not reported	0 (0)	0 (0)	0 (0)	
Endoscopic appearance of cavity				.39
Purulent fluid	123 (40)	72 (41)	51 (39)	
Solid debris	124 (41)	70 (40)	54 (41)	

(*continued on the next page*)

TABLE 2. Continued

Variable	Total patients (n = 307)	High-volume centers (n = 175)	Low-volume centers (n = 132)	*P* value
Vessels	0 (0)	0 (0)	0 (0)	
Other	48 (15)	26 (16)	22 (17)	
Not reported	10 (4)	5 (3)	5 (4)	
Hydrogen peroxide irrigation				.4
No	209 (68)	120 (69)	89 (67)	
Yes	98 (32)	55 (26)	43 (33)	
Not reported	0 (0)	0 (0)	0 (0)	
Antibiotic irrigation				.52
No	296 (95.7)	170 (97)	126 (95.4)	
Yes	10 (4)	5 (3)	5 (3.7)	
Not reported	1 (.3)	0 (0)	1 (.9)	
Nasocystic tube drainage				.15
No	282 (91.8)	162 (93)	120 (91)	
Yes	25 (8.2)	13 (7)	12 (9)	
Not reported	0 (0)	0 (0)	0 (0)	
Pigtail use through stent				.67
No	267 (87)	154 (88)	113 (86)	
Yes	40 (13)	21 (12)	19 (14)	
Need of percutaneous drainage				.18
No	390 (94.5)	166 (97)	124 (94)	
Yes	17 (5.5)	9 (5)	8 (6)	
Days to stent removal	48 (26-60)	52 (37-69)	48 (25-60)	.17

Values are median (interquartile range) or n (%). Comparisons were performed with the McNemar test for continuous variables and Fisher exact test for categorical ones. The following demographic, technical, and collection-related variables were selected for propensity score calculation: percentage of necrosis, appearance of the collection, extension to paracolic gutter, indication for treatment, etiology of pancreatitis, type of stent used, stent diameter, endoscopic appearance of the cavity, and use of the nasocystic tube drainage.

volume hospitals are not easily generalized to hospitals performing a fewer number of cases. Hence, there is an urgent need for large nationwide analyses to capture "real-world" descriptions of state-of-the-art advances in this setting.

Our study is aligned with other reports regarding the rate of AEs observed[29,30] but demonstrates a significant association between hospital volume and improved outcomes in patients with PFCs treated with LAMSs. In fact, although a correlation between hospital volume and outcomes has been previously postulated,[16] a specific analysis could not be performed because it required a large sample size collected evenly in high- and low-volume centers, a characteristic that can be observed only in large nationwide studies.

Although the underlying mechanisms behind the hospital volume–outcomes association have not been fully determined, this association seems to be clinically intuitive. High-volume hospitals potentially have more experienced pancreatic endoscopists and surgeons, developed intensive care units, structured processes for postprocedural care, and accurate algorithms discussed in multidisciplinary meetings. These factors would likely facilitate better patient selection for the procedure, a lower likelihood of technical errors, and an enhanced ability to recognize postprocedural AEs and treat patients experiencing major AEs, as already observed in other settings of pancreatic endoscopy and surgery.[31,32]

Our study found that MPD disruption/leak can be considered a significant predictor of AEs after LAMS drainage, thus pointing out the importance of ascertaining the integrity of the MPD. In fact, besides being an expression of the severity of the injury, MPD damage leads to continuous pouring of pancreatic juice into the collection, thus increasing the risk of vessel erosion and/or recurrence after early LAMS removal. On the other hand, PFC size and timing of LAMS removal were not confirmed as significant predictors of AEs, unlike the previous study by Bang et al.[11] Evidently, the size of the PFC does not always represent a risk factor for difficult management. This probably depends on other factors such as the shape, content, and location of the collection. Moreover, the alarming

TABLE 3. Outcomes

	Total patients (n = 307)	High-volume centers (n = 175)	Low-volume centers (n = 132)	*P* value
Technical success	299 (97.3)	173 (99)	126 (96)	.06
Clinical success	290 (94.4)	168 (96)	122 (92)	.17
Adverse event rate	41 (13.3)	14 (8)	27 (20.4)	**.001**
Type of adverse event				.18
Bleeding	14 (4.5)	5 (2.8)	9 (6.8)	
Infection	11 (3.5)	2 (1.1)	9 (6.8)	
Stent occlusion	3 (1)	1 (.6)	2 (1.5)	
Stent migration	3 (1)	1 (.6)	2 (1.5)	
Stent dislodgement	2 (.6)	1 (.6)	1 (.7)	
Perforation	3 (1)	1 (.6)	2 (1.5)	
Capnoperitoneum	3 (1)	1 (.6)	2 (1.5)	
Other	2 (.6)	2 (1.1)	0 (0)	
Severity adverse event				**.05**
Mild	14 (4.5)	8 (4.5)	6 (4.4)	
Moderate	14 (4.5)	4 (2.3)	10 (7.5)	
Severe	10 (4.2)	2 (1.7)	8 (6)	
Fatal	3 (1.2)	0 (0)	3 (2.2)	
Collection recurrence	15 (4.8)	7 (4)	8 (6)	.40

Values are n (%). Significant values are reported in bold.

data from Bang et al's study[11] about potentially worse outcomes after late removal of the stent were not confirmed in our study.

There are several limitations to our study. First, the retrospective nature of the study, although it allowed the inclusion of different centers with variable experience, could raise some concerns about different technical approaches used for performing the procedure. However, the propensity score analysis enabled the comparison of 2 nearly perfectly matched groups, thus partially obviating this bias.

Second, this study was based on data mostly representing the earliest experiences with LAMS drainage of PFCs in Italy, which could affect interpretation of the results. In fact, determination of a hospital volume threshold should be considered a dynamic concept and may evolve as an increasing number of endoscopists gain more experience with the procedure.

Third, data about single-endoscopist volume were not complete; thus, the independent effect of a specific endoscopist versus hospital volume could not be examined. However, in most centers, particularly low-volume centers, these procedures were performed by a single endoscopist, and thus our findings could be considered related not only to the hospital volume but also to the individual endoscopist experience. Finally, although high-volume centers may have started to perform these procedures before 2016 (starting point of our study), the results of our series suggest that the learning curve shows a plateau once the threshold of 15 procedures is reached and supports the notion that previous experience did not influence the primary outcome.

In conclusion, this large study provides valuable information about the importance of hospital volume and implementation of LAMS drainage of PFCs. Our study suggested that 15 procedures might represent the minimum number of cases associated with the lowest risk for postprocedural AEs. This finding is timely and relevant, given the ongoing debate regarding safe implementation of this complex procedure and the current shift toward value-based healthcare reimbursement models.

ACKNOWLEDGMENTS

Members of the i-EUS Group are as follows: Daryl Ramai, Massimiliano Mutignani, Gastroenterology & Hepatology, University of Utah Health, Salt Lake City, Utah, USA; Edoardo Forti, Paolo Giorgio Arcidiacono, Digestive and Interventional Endoscopy Unit, Ospedale Ca' Granda Niguarda, Milan, Italy; Maria Chiara Petrone, Elisabetta Conte, PancreatoBiliary Endoscopy and EUS Division, Pancreas Translational and Clinical Research Center, San Raffaele Scientific Institute IRCCS, Milan, Italy; Roberto Di Mitri,

TABLE 4. Univariate/multivariate logistic regression analysis for prediction of adverse events

Variables	Univariate analysis Odds ratio (95% confidence interval)	*P* value	Multivariate analysis Odds ratio (95% confidence interval)	*P* value
Age	1.42 (.87-1.92)	.21		
Gender (reference female)	1.04 (.75-2.1)	.58		
Collection type (reference walled-off necrosis)	.88 (.51-1.25)	.45		
Percentage of necrosis	1.05 (.79-1.33)	.24		
Location (reference body)	Head: 1.26 (.71-2.2)	.58		
	Tail: .72 (.39-1.50)	.42		
Collection width (<70 mm)	1.18 (.83-2.02)	.58		
Collection length (<70 mm)	1.26 (.58-1.94)	.28		
Collection appearance (reference single)	1.18 (.68-1.95)	.68		
Extension to paracolic gutter (reference no)	1.04 (.62-1.81)	.32		
Main pancreatic duct injury on imaging/EUS (reference normal)	Leak/disruption: 2.62 (1.26-4.67) Unknown: 1.09 (.68-1.38)	**.02** .24	Leak: 2.21 (1.08-4.5)	**.05**
Abnormal vessels (reference no alterations)	Perigastric varices: 2.93 (1.41-5.02) Pseudoaneurysm: 1.98 (1.65-4.91) Portal vein thrombosis: 1.68 (.63-4.07) Splenic vein thrombosis: 1.53 (.75-3.14)	**.006** **.003** .31 .28	Perigastric varices: 2.18 (1.06-3.15) Pseudoaneurysm: 2.11 (1.54-4.22)	**.05** **.005**
Indication (reference infection)	Abdominal pain: .87 (.55-1.84)	.43		
	Early satiety: 1.52 (.68-3.41)	.35		
	Other: 1.05 (.51-4.21)	.28		
	Outlet obstruction: 1.48 (.89-4.14)	.15		
	Vessels thrombosis: 2.28 (.41-3.54)	.35		
	Vomiting: .76 (.34-4.12)	.71		
Etiology of pancreatitis (reference biliary)	1.98 (.79-2.21)	.16		
Type of stent (reference Hot Axios)	1.15 (.61-2.44)	.68		
Access (reference single stage)	1.18 (.62-2.04)	.45		
Use of fluoroscopy (reference yes)	.83 (.58-1.43)	.69		
Stent diameter (reference 15 × 10)	10 × 10: 1.17 (.51-2.48)	.89		
	20 × 10: 1.49 (.73-3.14)	.48		
Second flange release (reference intrachannel)	1.09 (.72-1.88)	.72		
Approach (reference transgastric)	.72 (.28-2.13)	.40		
Stent dilation (reference no)	1.61 (.82-2.74)	.23		
Necrosectomy (reference no)	1.62 (.95-3.03)	.09		
Endoscopic appearance of cavity (reference purulent fluid)	Solid debris: 1.62 (.90-2.46)	.45		
	Other: 1.21 (.65-2.44)	.62		
Hydrogen peroxide irrigation (reference no)	.74 (.43-1.31)	.29		

(*continued on the next page*)

TABLE 4. Continued

Variables	Univariate analysis Odds ratio (95% confidence interval)	*P* value	Multivariate analysis Odds ratio (95% confidence interval)	*P* value
Nasocystic drainage (reference no)	.68 (.35-1.51)	.38		
Pigtail use through the stent (reference no)	.96 (.48-1.82)	.14		
Need of percutaneous drainage (reference no)	2.02 (.98-5.65)	.06		
Days to removal (reference <30)	1.36 (.72-3.28)	.12		
Experience of the center (reference high)	2.95 (1.48-5.90)	**.002**	3.04 (1.67-7.02)	**.001**

Significant values are reported in bold.

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