

Fusion radiology in interventional endoscopy (FRlend): a new approach for pancreatic fluid collections



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ABSTRACT

Background and study aims Fusion imaging consists of overlaying preoperative imaging over live fluoroscopy, providing an augmented live guidance. Since 2017, we have been using a new hybrid operating room (Discovery IGS 740 OR, GE Healthcare) for biliopancreatic endoscopy, combining fusion imaging with traditional endoscopic ultrasound (EUS). This study aimed to assess the advantages that fusion imaging could bring to EUS-guided drainage of post-pancreatitis fluid collections.

Patients and methods Thirty-five drainage procedures performed between 2012 and 2019 with traditional guidance and fusion imaging were retrospectively compared, assessing the overall treatment success rate – i. e. symptom improvement with complete PFC emptying – as a primary outcome.

Secondary outcomes included technical success rate, time to resolution, hospital stay length, adverse events, recurrence rate, and procedure time.

Results Patients treated with standard EUS (n=17) and with fusion imaging (n=18) were homogeneous in age, gender, pancreatitis etiology, and indication for drainage; the second group had larger PFCs, more frequently walled-off necrosis than pseudocysts, and were treated more emergently, indicating higher case complexity in this group. During the period when fusion imaging was adopted, procedures had a higher overall treatment success rate than during the period when standard EUS was adopted (83.3% vs. 52.9%, $P=0.075$), and complete emptying was reached in less time (61.1% vs. 23.6% complete emptying within 90 days, $P=0.154$), differences compatible with random fluctuations.

Conclusions This study suggests that fusion imaging in combination with EUS might improve clinical and procedural outcomes of PFC drainage.

Introduction

Acute pancreatitis (AP) incidence ranges from 4.6 to 100 per 100,000 across European countries with increasing trends [1].

The rate of hospital mortality associated with the condition is approximately 1% [2].

Clinical management of AP still represents a difficult challenge, as patients with severe disease have a high probability of systemic inflammatory response syndrome and multiorgan

failure (MOF) with or without infection and sepsis, leading to a mortality rate of 10% to 15% [3]. The mortality rate associated with MOF has significantly decreased due to improvement in Intensive Care Unit technology, so that up to 80% of residual deaths are linked to late complications of sepsis [4]. Notably, 10% to 20% of AP cases are associated with necrosis of the pancreatic gland, the peripancreatic tissue, or both: this subset of patients may face a complex, prolonged clinical course, with associated mortality of up to 20% to 30% when infection develops in fluid collections [5].

In 2012, an international consensus revised AP classification and new definitions of local complications were released. The new classification supported more specific recommendations about use of drainage: walled-off necrosis (WON) and pseudocysts were the two pancreatic fluid collections eligible for this treatment [6,7]. Both have a well-defined wall, but pseudocysts only contain liquid, whereas WON holds infected necrotic material.

Recently endoscopic drainage has evolved from use of surgical to percutaneous drainage, which has equal efficacy with fewer complications and shorter hospital length of stay [8, 9]. The classical approach exploits endoscopic ultrasound (EUS) guidance to identify the collection to drain. This technique is limited by the narrow field of view offered by EUS imaging. Thus, once the collection is identified, it is difficult to single out the best position to place the device, hypothetically allowing for the most efficient drainage. Given that endoscopic drainage also accounts for a non-negligible complication rate [10], reducing drainage time and the rate of post-drainage complications is an unmet health care need in patients with pancreatitis. Increasing the accuracy of anatomic knowledge about PFC might be a way to reduce the risk of complications and to improve drainage.

Radiology provides fundamental support for operative procedures in digestive endoscopy. In recent years, technologies in this field have evolved considerably with the development of hybrid operating rooms (HORs). Among advanced technologies available in modern HORs, fusion imaging consists of overlaying clinical information from preoperative computed tomography (CT)/magnetic resonance imaging (MRI) work-up, or per-operative Cone Beam CT to augment live fluoroscopy, providing a continuous 3D/2D overlay for augmented live guidance [11–13].

These technologies have widely been applied in vascular surgery [13, 14]: during complex intravascular and percutaneous procedures, fusion imaging has demonstrated a significant reduction in radiation exposure, duration of procedures, dosage of injected contrast medium, and provided benefits in clinical outcomes [16–18].

Initial experiences in gastroenterology have also been described integrating preoperative MRI and CT with ultrasound (US) [19,20] – one of these just for PFC drainage – but also with EUS [21], improving the accuracy in defining the anatomical field of intervention and allowing for more precise maneuvers.

In this paper, we describe a new original fusion imaging and augmented fluoroscopy technique that we have been using for-

our biliopancreatic endoscopy procedures following the installation of a new HOR at our institution in 2017 (Discovery IGS 740 OR, GE Healthcare).

This retrospective study aimed to assess the potential benefits of this new technique in terms of clinical and procedural outcomes of EUS-guided drainage of PFC.

Patients and methods

Patients

Among the patients admitted to our hospital from January 2012 to December 2019 for moderate and severe AP, those who had one or more PFCs eligible for endoscopic drainage according to the existing guidelines were included in the study. Diagnosis of moderate and severe AP, PFC, and WON was based on the revised standards from Atlanta [6]. The first set of consecutive patients (17 patients, over the period 2012–2017) received the standard EUS approach whereas the last set of consecutive patients (18 patients, over the period 2017–2019) were treated with the “fusion imaging” approach. Informed consent for the interventional procedures was obtained from each patient. Data were collected and analyzed retrospectively. This study was approved by the Ethics Committee of Area Vasta Emilia Nord of the Emilia Romagna Regional Health System (protocol number 2020/0089372). Patients were asked to sign written informed consent. For patients who were not reachable at the time of the retrospective study, the Ethics Committee authorized the use of patient data without their informed consent if all reasonable efforts had been made to contact them to them and acquire their consent.

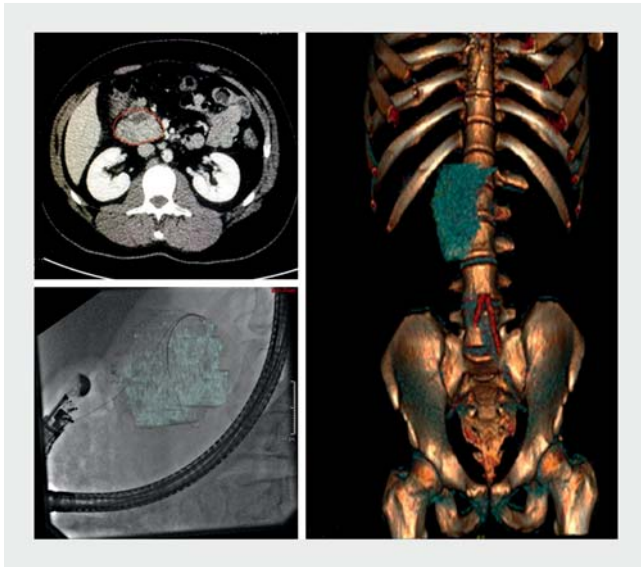
Patient characteristics including age, pancreatitis etiology, collection site, type of collection, baseline size on work-up imaging, indication for drainage, time to drainage from pancreatitis onset, and maximum follow-up time after the procedure are reported for both groups.

Treatment

Equipment and materials: “fusion imaging” technique

Patients arriving at the Reggio Emilia hospital from February 2012 to April 2017 and needing a PFC drainage received standard EUS guidance combined with a traditional surgical mobile C-arm (OEC 9800 Plus, GE Healthcare, Chicago, Illinois, United States). Patients arriving from June 2017 to December 2019 were treated in a modern HOR suite equipped with advanced fusion imaging, using Discovery IGS 740 OR. In the fusion imaging group, the following operative sequence was adopted (► **Fig. 1**):

1. Manual segmentation of the PFC was performed based on the pre-procedural CT.
2. The resultant region of interest was placed on the volume rendering, a volumetric reconstruction algorithm that allows three-dimensional visualization of the skeleton [22];
3. The volume including PFC and bone was superimposed onto live fluoroscopy (ASSIST software, GE Healthcare). Registration between the preoperative volume and the live fluoroscopy was performed on two orthogonal fluoroscopy pro-



► **Fig. 1** The three steps in the fusion imaging procedure before draining pancreatic fluid collections.

jections using anatomical landmarks (such as vertebrae and iliac crest) or “proxy” landmarks (clips, stents, etc.). Once registered in these two views, PFC volume from the preoperative CT remained fused to intraprocedural fluoroscopy for every image acquisition, showing the real-time scope tip relative to the whole PFC shape, thus supporting the choice of puncture site. Fusion imaging remained automatically registered with Gantry and Table motion, allowing for augmented fluoroscopy with flexible system setup.

Equipment and materials: endoscopic drainage

All procedures were performed under general anesthesia by endoscopists with over 5 years of experience in interventional endosonography (R.S., L.C., P.C., V.I.). A linear therapeutic echo-endoscope was used in combination with fluoroscopy.

The presence and location of vessels were assessed by means of color Doppler ultrasonography to determine the optimal transmural puncture (gastric or duodenal) site on the cyst. Under real-time EUS and fluoroscopy guidance, a 19-gauge access needle (Cook Medical, Limerick, Ireland) was used to puncture the PFC, whose shape was subsequently outlined – especially in patients treated with standard EUS – by contrast medium. After a 400-cm, 0.035-inch guidewire (Visiglide, Olympus) had been introduced and coiled into the cyst cavity, the needle was removed.

Subsequently, a cysto-gastrostomy was made using a 10F cystogastrotome (Cook medical, Limerick, Ireland) and dilated as needed using a balloon dilator (QBD-6×3, Cook Medical) in order to make the insertion of double pigtail plastic stents (PS) (7F or 10F, Cook Medical) or fully covered self-expandable metal stents (FCSEMS) (Taewoongh Niti-S) easier. In the case of lumen-apposing metal stents (LAMS) (Hot Axios, Boston Scientific), the stent was directly positioned after the guidewire placement. Moreover, a nasocystic tube (7F or 10F, ENBD-7-LIGU-

ORY-C, Cook Medical) was inserted into the cavity for lavage. Endoscopic retrograde cholangiopancreatography was not routinely performed before transmural drainage.

Necrosectomy

After the initial procedure, the endoscopist determined whether an endoscopic necrosectomy – direct (DEN) or to be performed in a subsequent endoscopic session – was required depending on the patient’s condition and whether the pre-procedural imaging showed remarkable solid debris. When performed, it was usually carried out using snares, retrieval nets or Dormia baskets as appropriate and hydrogen peroxide 3% (1:10 saline solution) infusions.

Baseline and follow-up radiologic imaging

For each patient with PFC, radiological work-up was performed by following the same method (CT or MRI, according to clinical indication) at baseline (before the endoscopic procedure) and at follow-up. PFC evolution was assessed according to clinical indication either in an outpatient clinic or in local hospitals, at 2 weeks and 6 to 8 weeks after first stent placement on average, and until complete resolution or at the last available follow-up.

All patients, except those who died or were lost of follow-up, were monitored for at least 3 months up to a maximum of 43 months.

CT scans were performed by means of a 64- or a 128-multi-detector scanner, while MRI exams were performed with a 1.5T scanner. PFC volume identified by both methods was retrospectively calculated at baseline and during follow-up examinations by a single radiologist blinded to baseline clinical condition and type of endoscopic procedure, by using a manual segmentation method similar to that described for fusion imaging. Examples of baseline and follow-up radiological images of PFC patients are reported in ► **Fig. 2** and ► **Fig. 3**.

Endoscopic follow-Up

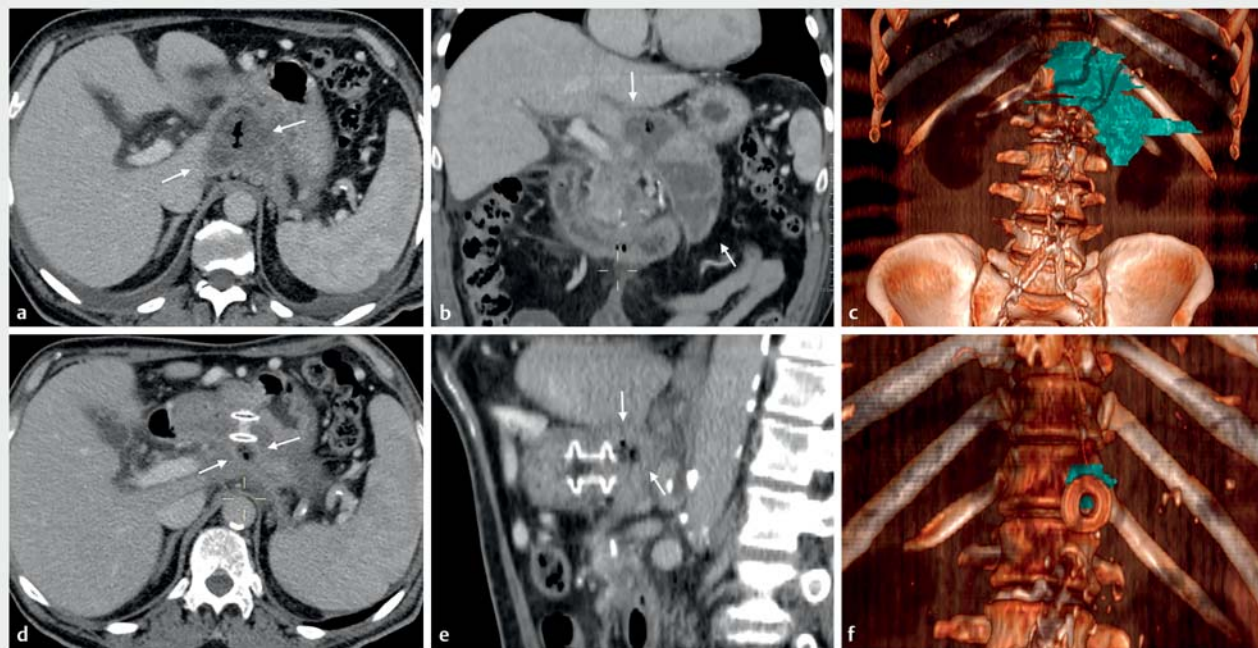
Stents were removed using standard endoscopic snares or rat-tooth forceps based on the type of stent, FCSEMS or LAMS (for the latter a stricter indication for early removal exists). When drainage was not complete subsequent plastic stents were placed.

Study outcomes

We aimed to assess the differences in procedural and clinical outcomes between the traditional EUS approach and the fusion imaging advanced guidance.

Our primary outcome was overall treatment success rate, defined as both clinically significant improvement in patient symptoms and complete resolution (complete emptying) of PFC. Complete resolution of PFC was considered on follow-up imaging for non-measurable residual collections < 10 mL in volume (e.g. adipose tissue stranding with fibrotic strands and possibly minimal free fluid, without walls).

Secondary outcomes included technical success rate, time to resolution, hospital stay length, adverse events (AEs), and recurrence rate. Technical success was defined as successful



► **Fig. 2** **a** Axial and **b** coronal portal venous phase CT scan showed a fluid collection containing gas and demonstrating enhancing walls (arrows). **c** This walled-off necrosis was manually segmented for our analysis, resulting in a volume of 147 mL. Three months after drainage performed using traditional guidance (Group 1), a small residual collection was still visible in **d** axial and sagittal **e** portal venous phase CT scan (arrows), it had a volume of 12 mL.

transmural stent placement. Time to resolution was determined as the time needed to reach complete emptying, from endoscopic drainage. AEs were classified according to the American Society of Gastrointestinal Endoscopy (ASGE) guidelines [22]. Major AEs included events that required surgery, interventional treatments (such as endoscopic, percutaneous and vascular treatment) or transfusion, or those inducing death.

Length of hospital stay was defined as the time from initial stent placement to hospital discharge. Recurrence was defined as the presence of a PFC >3 cm³ in size discovered after its initial complete resolution, by assessing the imaging obtained up to the last available follow-up date.

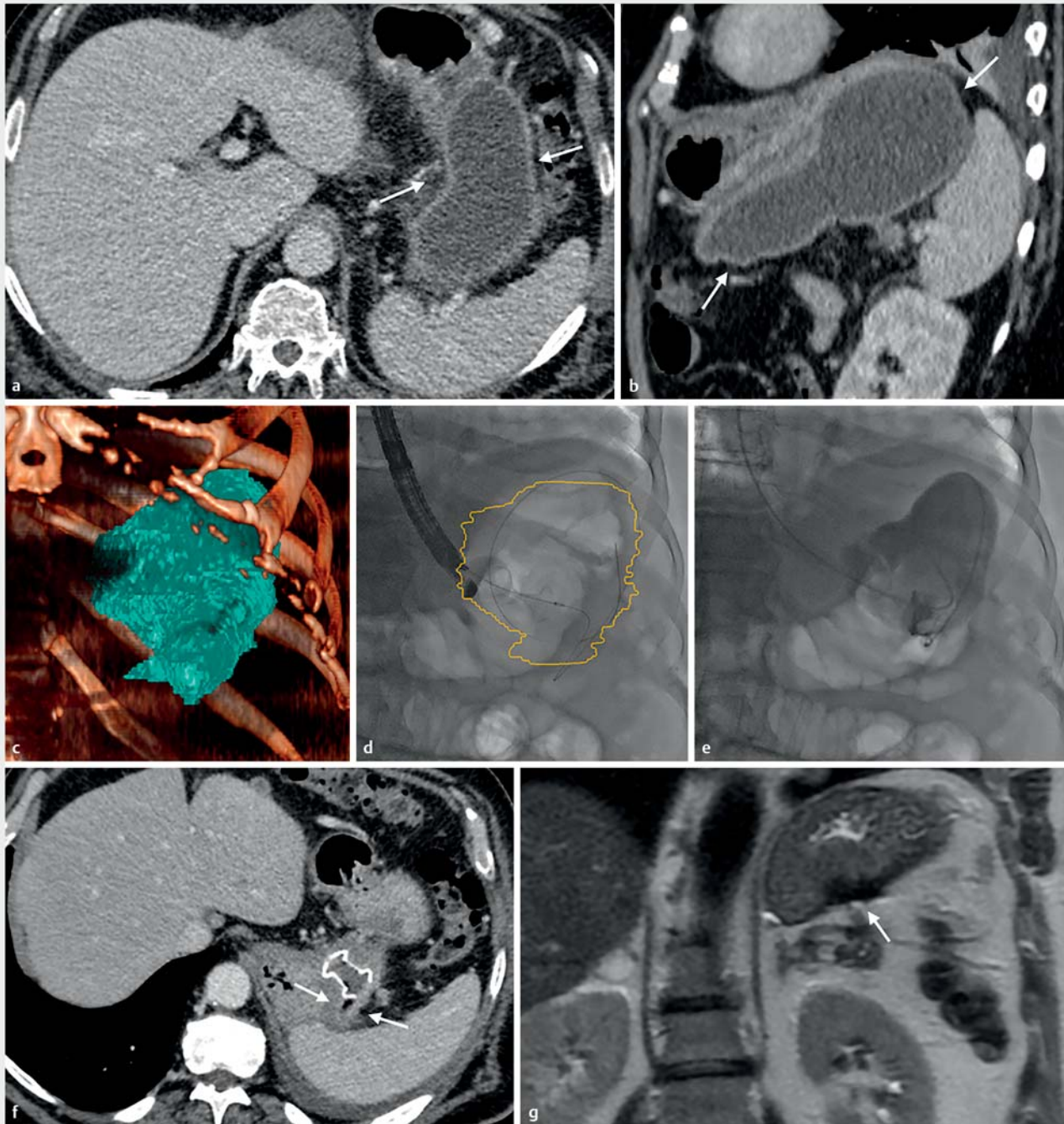
We reported procedural differences as well, including use of a nasocystic tube, the type of stent used, access site, use of iodate contrast medium, presence of stent obstruction, procedure time, time to stent removal, and need for reintervention or necrosectomy. Procedure time was determined as duration of the intervention from insertion to withdrawal of the endoscope. Reintervention was defined as need to repeat an endoscopic intervention for AEs or insufficient drainage (including endoscopic necrosectomies). Notably, planned stent changes and stent removals were not counted as reintervention

Statistical analyses

Continuous variables (age, baseline size, follow-up times, procedure time, hospital stay length) are reported as median (IQR) and mean (SD). Categorical variables are reported as proportions.

To compare variables between two groups, as well as to assess the impact of the stents used, the Fisher exact test was used for categorical variables, and the median test was used for continuous variables.

Analyses were conducted on a per-PFCs basis while taking into account the intra-individual correlation to obtain robust variance estimates with SVY command on STATA/IC version 16. Odds ratios (OR) with 95% confidence intervals (95% CI) for overall treatment success were estimated using a multivariable model, adjusted for known prognostic factors that were upstream the procedure in the causal pathway, i. e. age (<45, 45–65, >65), baseline size (cm³) and type of collection (pseudocyst, WON). We did not include in the model variables that could be linked to the procedure itself to avoid adjusting for potential mediators, i. e. type of stent, site of stent placement, necrosectomy. To exclude that, the association between outcome and fusion imaging was exclusively due to introduction of the Axios stent or to the presence of necrosectomy – two characteristics that were almost exclusively present in the period when fusion imaging was introduced – we present the association between the type of stent and necrosectomy and outcome in the supplementary materials. No significance threshold was fixed; *P* values were interpreted as continuous variables.



► **Fig. 3** **a** Axial and **b** sagittal portal venous phase CT scan showed a fluid collection with a volume of 523 mL and with enhancing walls strictly adherent to the gastric wall (arrows). **c** This collection was manually segmented and **d** overlaid to augment live fluoroscopy. **e** During this procedure, contrast media was also injected in the collection to verify its consistency. One month after stent positioning, a very small residual collection was visible in **f** axial portal venous phase CT scan (arrows), with a residual volume <2 mL. **g** Three months after, a coronal T2-weighted MR scan showed only fibrosis without residual fluid collection (arrow).

Results

General data

From 2012 to 2019, 437 patients were admitted to our center for severe and moderately severe AP. Among them, 38 patients had PFCs amenable to endoscopic drainage, but three of them

were excluded from our analysis: two patients had mucinous cystadenoma and serous cystadenoma at subsequent diagnostic investigations; one was a postsurgical collection in a patient with pancreatitis. Of 34 patients with 35 PFCs ultimately included in the study, the first 17 consecutive were treated with the

traditional approach while the latter 18 were offered the fusion imaging guidance technology.

Patient characteristics and comparison of the prognostic factors

Patient characteristics are listed in ► **Table 1**. The two groups had very similar age and sex distribution and the pathogenesis of pancreatitis was similarly distributed. The groups differed in terms of baseline size and typology of pancreatic fluid collections: patients treated with fusion imaging had larger PFCs (570.0 vs 263.9 cm³, n.s.) mostly WON ($P=0.041$) than those treated drainage with EUS. Moreover, obstructive symptoms (gastric outlet obstructive syndrome, pain, jaundice) were the prevalent indication for drainage in those treated with standard EUS, while patients treated with fusion imaging required earlier treatment (40 vs. 115 days from pancreatitis onset, $P=0.007$) for PFC infection and its systemic implications. One patient treated with fusion imaging had previously been treated with percutaneous US-guided drainage as well, and the poor result led to attempting the endoscopic route.

Effectiveness outcomes

Clinical and procedural outcomes are reported in ► **Table 2**. There was no difference in terms of technical success between the two groups: the stent was placed in all cases. Symptom improvement was 88.9% with fusion imaging and 76.5% with standard EUS ($P=0.539$) and complete emptying rates were 83.3% and 64.7%, respectively ($P=0.264$). When combining the two outcomes in the overall treatment success rate, the difference was more evident (83.3% vs. 52.9%, $P=0.075$), corresponding to a failure rate that was three times lower. Regarding time to complete emptying, 11 PFCs treated under fusion imaging guidance achieved resolution within 90 days (61.1%), while four PFCs did (23.6%) among those treated with EUS.

The logistic regression model adjusted for age, baseline PFC volume, and kind of collection confirmed the direction of the association with a higher overall treatment success rate with fusion imaging (OR=5.28; 95% CI=0.79–35.51), even if this association may be due to random fluctuations (► **Table 3**).

Among those treated with standard EUS, the following AEs were observed: three sepsis (fever+ positive hemoculture), one intraprocedural bleeding, one spleno-mesenteric thrombosis, and one stent buried in the gastric wall. Among those treated under fusion imaging guidance, two gastric perforations by plastic stents and two massive bleedings of the splenic artery were reported. Overall, six were major AEs requiring endoscopic management (with hemostatic maneuvers or stent removal) or radiological embolization, with equal distribution between the two groups; four were treated conservatively with medical therapy (antibiotics and anticoagulants). Although these complications are connected with the endoscopic procedure, some of them could be considered stent-related complications (bleeding, incystment and perforation).

Hospital stay was longer for those treated under fusion imaging guidance compared with those who received standard EUS (median 26 vs 7 days, $P=0.006$).

One patient per group had recurrence after resolution: as both were asymptomatic, they are still being followed radiologically and clinically.

Procedural differences

Procedural differences are reported in ► **Table 4**. Iodate contrast medium was used in 82.4% of standard EUS cases versus 33.3% in cases treated with fusion imaging ($P=0.006$). In particular, contrast injected after puncture was used in most standard EUS procedures to confirm the puncture site and outline the collection shape. However, this post-contrast X-ray acquisition is late and operatively useless because it is only available after the puncture site has already been chosen and the cysto-gastric tract has consequently been created. Conversely, fusion imaging allowed PFC visualization before puncture, so contrast was rarely used in cases treated under fusion imaging guidance. In the few cases contrast was used, it was to assess alignment between the virtual PFC volume and the real PFC during the first drainages performed with the new technology.

PFCs treated under fusion imaging guidance were drained predominantly with Axios stents (83.3%), introduced in our center in 2015, whereas FCSEMS were the most used stents in standard EUS (64.7%). Procedure time was reduced with fusion imaging compared with standard EUS (69.4 vs. 99.7 minutes, $P=0.033$).

On average, first stent removal was scheduled and performed earlier in patients treated under fusion imaging guidance compared to standard EUS (32.8 vs 106.7 days, $P=0.0001$). This is most likely because of the higher use of Axios stents. In four of 16 subjects treated with standard EUS and eight of 18 subjects with fusion imaging ($P=0.15$), the first stent was substituted with another to carry on with the drainage.

Reintervention was necessary in 41% and 67% of patients treated with standard EUS and fusion imaging, respectively ($P=0.18$), due not to controlled ongoing sepsis or persistency of the pancreatic fluid collection volume or failure to improve symptoms. Among reinterventions, endoscopic necrosectomy was performed exclusively over the second period of time, i.e. when fusion imaging was adopted, in seven of 18 patients; only one was DEN whereas the other cases were executed in subsequent sessions after stent placement.

To evaluate whether the aforementioned difference in treatment success in favor of fusion imaging could be due to the impact of Axios stents and necrosectomies, we compared the results obtained with Axios stents and non-Axios stents stratified for standard EUS and fusion imaging (**Supplementary Table 1**), and with necrosectomy and without necrosectomy in patients treated with fusion imaging, because there is no necrosectomy in the standard EUS (**Supplementary Table 2**). Success rates were almost identical in the results with Axios and non-Axios stents, while a longer median time to removal in the non-Axios group was only observed (120 vs. 50 days, $P=0.45$) for standard EUS – this is likely due to the strict indication to remove Axios stents within 3–4 weeks – in fusion imaging patients, the median time to removal between Axios and not-Axios stents was the same. Only seven patients underwent a necrosectomy and they

► **Table 1** Clinical characteristics of the included patients as a whole population, and subdivided in to two groups.

Baseline characteristics				
	Total	Standard EUS	Fusion imaging	
	N	N (% col)	N (% col)	p ¹
Total no. patients	35	17	18	
Male sex	27 (77.7)	13 (76.5)	14 (77.7)	0.57
Age (years)				
median (IQR)	57 (47–68)	49 (44–67)	60 (52–78)	0.39 ²
Pancreatitis				0.43
▪ Alcohol	11 (31.4)	6 (35.3)	5 (27.8)	
▪ Lithiasis	11 (31.4)	4 (23.5)	7 (38.9)	
▪ Dyslipidemia	1 (2.9)	1 (5.9)	0 (0)	
▪ Idiopathic	6 (17.1)	2 (11.8)	4 (22.2)	
▪ Post-ERCP	1 (2.9)	0 (0)	1 (5.6)	
▪ Missing	5 (14.3)	4 (23.5)	1 (5.6)	
Kind of collection				0.04
▪ Pseudocyst	20 (57.1)	13 (76.5)	7 (38.9)	
▪ WON	15 (42.9)	4 (23.5)	11 (61.1)	
Collection site				
▪ Pancreatic region	32	14	18	
▪ Left pararenal region	8	6	2	
▪ Right pararenal region	3	0	3	
▪ Subhepatic region	6	3	3	
Baseline size (cm ³)				
median (IQR)	417.8 (153.9–785.4)	263.9 (130.9–586.4)	570.0 (257–857.7)	0.13 ²
Baseline size (cm ³)				0.16
▪ (30–125)	4 (11.4)	4 (23.5)	0 (0)	
▪ (126–420)	14 (40)	7 (41.2)	7 (38.9)	
▪ (421–1000)	12 (34.3)	4 (23.5)	8 (44.4)	
▪ (1001–1910)	5 (14.3)	2 (11.8)	3 (16.7)	
Reason for drainage				0.08
▪ GOOS	12 (34.3)	8 (47.1)	4 (22.2)	
▪ Abdominal pain	6 (17.1)	2 (11.8)	4 (22.2)	
▪ Infected pseudocyst	7 (20.0)	5 (29.3)	2 (11.1)	
▪ Infected necrosis	10 (28.6)	2 (11.8)	8 (44.4)	
Drainage after (days)				
▪ median (IQR)	45 (30–96)	115 (62–315)	40 (25–60)	0.007
Maximum follow-up (days)				
▪ median (IQR)	76 (50–240)	170 (43.5–240)	55.5 (50–72)	0.03

Clinical characteristics of the included patients as a whole population, and subdivided into two groups.

EUS, endoscopic ultrasound; ERCP, endoscopic retrograde cholangiopancreatography; WON, walled-off necrosis; GOOS, gastric outlet obstruction syndrome; IQR, interquartile range.

¹ Fisher's exact test.

² Median test. Values are reported as number (%) unless otherwise indicated.

► **Table 2** Procedural results for the included patients as a whole population, and subdivided into two groups.

Effectiveness outcomes	Tot	Standard EUS	Fusion imaging	
	N	N (% col)	N (% col)	p ¹
Total number of patients	35	17	18	
Symptom improvement				0.54
▪ Yes	29 (82.9)	13 (76.4)	16 (88.8)	
▪ No	3 (8.6)	2 (11.8)	1 (5.6)	
▪ Partial	3 (8.6)	2 (11.8)	1 (5.6)	
Complete emptying				0.26
▪ No	9 (25.7)	6 (35.3)	3 (16.7)	
▪ Yes	26 (74.3)	11 (64.7)	15 (83.3)	
Overall treatment success				0.075
▪ No	11 (31.4)	8 (47.1)	3 (16.7)	
▪ Yes	24 (68.6)	9 (52.9)	15 (83.3)	
Time for complete emptying (days)				0.15
▪ <39	9 (25.7)	3 (17.7)	6 (33.3)	
▪ 40–90	6 (17.2)	1 (5.9)	5 (27.8)	
▪ >91	11 (31.4)	7 (41.2)	4 (22.2)	
▪ Never	9 (25.7)	6 (35.3)	3 (16.7)	
Complications				0.29
▪ No	24 (68.6)	11 (64.7)	14 (73.8)	
▪ Yes	11 (31.4)	6 (35.3)	4 (22.2)	
Death				0.60
▪ No	32 (91.4)	15 (88.2)	17 (94.4)	
▪ Yes	3 (8.6)	2 (11.8)	1 (5.6)	
Hospital stay (days)				0.006 ²
▪ Median (IQR)	10 (7–28)	7 (6–10)	26 (9–30)	
▪ Mean ± SD	19.7 ± 27.3	8.2 ± 4.3	29.1 ± 34.4	

EUS, endoscopic ultrasound; SD, standard deviation; IQR, interquartile range.

¹ Fisher's exact test.

² Median test. Values are reported as number (%) unless otherwise indicated.

were all during the period when fusion imaging was adopted. Overall success rate was almost identical in patients with and without necrosectomy, while time to complete emptying and hospital stay were longer in patients with necrosectomy.

Discussion

In the present case series, introduction of a new original approach combining augmented fluoroscopy with EUS in a HOR was associated with a simultaneous improvement in clinical success rate and shorter time to complete emptying of the PFC. The study design did not permit us to assess whether these

associations were causal or if other changes that occurred concomitantly in the case mix or in the procedures confounded our results. Nevertheless, it is worth noting that although patients treated during the second period of time, when fusion imaging guidance was adopted, required earlier intervention for larger, more complex and often infected collections compared to patients treated with standard EUS, the clinical treatment failure rate was about three times lower and complete emptying within 90 days almost doubled. These estimates are rather imprecise and differences may be due to chance, but if they were confirmed, it would be a clinically relevant improvement. On the other hand, it must be considered that in the period of

► **Table 3** Logistic regression model for overall treatment success, defined as significant improvement in patient symptoms and complete resolution (complete emptying) of PFC.

	OR	95% CI	P value
Age			
▪ 20–44 years	1		
▪ 45–64 years	0.64	0.06–6.96	0.704
▪ 65–89 years	0.25	0.02–2.91	0.260
Baseline PFC Volume (for 1 cm ³ increase)	1.00	1.00–1.00	0.342
Kind of collection			
▪ Pseudocyst	1		
▪ WON	0.99	0.16–6.15	0.995
Group			
▪ Standard EUS	1		
▪ Fusion imaging	5.28	0.79–35.51	0.085

Covariates selected as clinically relevant were: age, baseline PFC volume, kind of collection and patient group, odds ratio, confidence interval, pancreatic fluid collection, and wall-off necrosis. PFC, pancreatic fluid collection; OR, odds ratio; CI, confidence interval; WON, walled-off necrosis; EUS, endoscopic ultrasound.

time when fusion imaging was adopted, hospital length of stay was longer, particularly in cases undergoing necrosectomy, and this was only the case over this time period and it was not true when standard EUS was used.

In our experience, endoscopists perceived that augmenting live fluoroscopy guidance with the PFC anatomy volume from preoperative CT was helpful in identifying the optimal drainage point relative to the anatomy of the PFC, particularly for complex and multiloculated collections. Augmentation of the operating field with a virtual model of the collection compensated for EUS's limited field of view in the choice of this drainage point. In our center, we used to inject contrast medium to obtain better control of site puncture and to identify the collection's shape, before placing FCSEMS, LAMS, and plastic stents. Fusion imaging helped us to avoid use of contrast. In fact, in the few cases in which we decided to inject contrast medium to assess the technology, the virtual volume observed with fusion imaging showed excellent consistency and alignment accuracy with the real collection (► **Fig. 4**). Minimal distortion was observed due to endoscope introduction and insufflation. In addition, it is known that injection of iodinated contrast medium within closed cavities like a PFC increases the risk of infection [23], which has been the prevalent complication in patients treated with traditional guidance. Therefore, less use of contrast media after the introduction of fusion imaging might be responsible for the reduction in AEs in patients treated under fusion imaging guidance.

In addition to reducing contrast utilization, procedure time was about 20 minutes shorter with fusion imaging than with standard EUS. Fusion imaging required additional preparation

time for CT segmentation and alignment on fluoroscopy, which was not measured in this study. However, in our experience, this time was of about 10 minutes, with the total procedure time thus still decreasing with use of the new approach. Despite the fact that this difference was possibly due to chance, it is also consistent with an increase in endoscopist confidence in the puncture maneuver. Furthermore, although not quantified in this study, associated benefits in terms of patient and operator radiation exposure are foreseen and warrant further investigation.

The evident limitations of the study include limited sample size and the heterogeneity of the two groups in terms of size and typology of lesions and clinical indication for drainage. However, while prognostic factors should have worked in favor of the standard EUS guidance group, a better clinical success rate was observed in the fusion imaging group. The increased complexity in the treated cases is the consequence of the progressive increase in indications for PFC drainage applied in our center, in accordance with changes in international guidelines [24]. Furthermore, other procedural features of the intervention changed during the study period. In particular, in the fusion group, the use of LAMS Axios was more systematic, but our analysis suggests that this change had little or no impact on outcomes and cannot explain the differences observed between the two groups. Also, the execution of necrosectomy only occurred in cases treated in the second study period, because it was actually feasible only after positioning LAMS, and it was deemed necessary because of patient critical clinical situations, linked to the infection of WON, which was also more prevalent in the second study period. In addition, this difference cannot explain the higher success rate in the second study period, because necrosectomy was not associated with the success rate, while it was inversely associated with time to complete emptying and hospital length of stay. In particular for this latter outcome, the median time in patients without necrosectomy was very similar in the two study periods (**Supplementary Table 2**), suggesting that the observed negative association between hospital length of stay and fusion imaging was partially due to the difference in the proportion of patients needing necrosectomy. Finally, drainage was assessed exclusively with CT and MRI scans, with the usual (and variable) timing of clinical follow-up in these patients and not according to fixed timing for follow-up. Also, the clinical outcome assessment was not blinded to the intervention group, thus, assessment bias could be present. To reduce this bias, assessment of drainage through imaging was conducted retrospectively by a radiologist who was blinded to the group.

Conclusions

Use of radiology to support endoscopic treatment is constantly evolving, with the goal of more effective and safer therapies with a limited number of treatments. The new technique we propose is not so difficult to implement in clinical practice. However, it requires use of a modern HOR equipped with fusion imaging, which is certainly not widespread in gastroenterology

► **Table 4** Procedural characteristics of the included patients as a whole population, and subdivided in to two groups, to underscore potential procedural differences among groups.

	Total	Standard EUS	Fusion imaging	
	N	N (% col)	N (% col)	p [†]
Total no. patients	35	17	18	
Endoscopic sessions				0.31
▪ 1	13 (37.1)	8 (47.1)	5 (27.8)	
▪ >1	22 (62.9)	9 (52.9)	13 (72.2)	
Nasocystic tube				1.000
▪ No	7 (20.0)	3 (17.7)	4 (22.2)	
▪ Yes	28 (80.0)	14 (82.4)	14 (77.8)	
Type of stent (first)				0.001
▪ No	1 (2.9)	1 (5.9)	0 (0)	
▪ FCSEMS	14 (40)	11 (64.7)	3 (16.7)	
▪ Axios	19 (54.2)	4 (23.5)	15 (83.3)	
▪ Plastic	1 (2.9)	1 (5.9)	0 (0)	
Type of stent (second)				0.15
▪ No	23 (65.7)	13 (76.4)	10 (55.6)	
▪ Plastic	11 (31.4)	3 (17.7)	8 (44.4)	
▪ FCSEMS	1 (2.9)	1 (5.9)	0 (0)	
Access				0.48
▪ Stomach	27 (79.4)	15 (88.2)	13 (72.2)	
▪ Duodenum, preexisting fistula	2 (5.9)	0 (0)	2 (11.1)	
▪ Duodenum	5 (14.7)	2 (11.8)	3 (16.7)	
Contrast medium				0.006
▪ No	15 (42.9)	3 (17.7)	12 (66.7)	
▪ Yes	20 (57.1)	14 (82.4)	6 (33.3)	
Stent obstruction				0.40
▪ No	28 (80)	15 (88.2)	13 (72.2)	
▪ Yes	7 (20)	2 (11.8)	5 (27.8)	
Stent removal after (days)				0.0001 ²
▪ median (IQR)	35.5 (27–60)	120 (50–170)	30 (26–37)	
▪ Mean ± SD	58.3 ± 50.7	106.7 ± 60.4	32.8 ± 13.5	
Necrosectomy				0.008
▪ No	28 (80.0)	17 (100)	11 (61.1)	
▪ Yes	7 (20.0)	0 (0)	7 (38.9)	
▪ Direct	1		1 (14.3)	
▪ Indirect	6		6 (85.7)	
▪ With H ₂ O ₂	5		5 (71.5)	
▪ Without H ₂ O ₂	2		2 (28.5)	

► **Table 4** (Continuation)

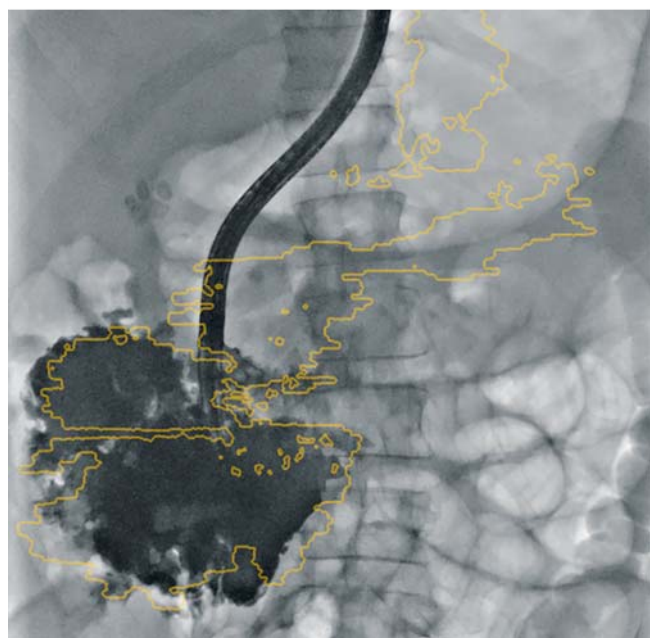
	Total	Standard EUS	Fusion imaging	
	N	N (% col)	N (% col)	P ¹
Reintervention				0.18
▪ 0	16 (45.7)	10 (58.8)	6 (33.3)	
▪ 1	10 (28.6)	5 (29.4)	5 (27.8)	
▪ > 1	9 (25.7)	2 (11.8)	7 (38.9)	
Reintervention rate	54%	41%	67%	
Procedure time (minutes)				0.39 ²
▪ Median (IQR)	80 (55–100)	95 (60–145)	73 (45–92)	
▪ Mean ± SD	84.1 ± 39.1	99.7 ± 43.9	69.4 ± 27.8	

Values are reported as number (%) unless otherwise indicated.

EUS, endoscopic ultrasound; FCSEMS, fully covered self-expandable metal stents; IQR, interquartile range; SD, standard deviation.

¹ Fisher's exact test.

² Median test.



► **Fig. 4** Augmented fluoroscopy overlaying a virtual PFC volume from the pre-operative CT to the live fluoroscopy. The iodinated contrast infused in the PFC reveals great alignment of the virtual PFC volume with live fluoroscopy.

facilities, but often may be available in hospitals for use by physicians in other specialties.

Despite the study's limitations, the results suggest that use of fusion imaging and augmented fluoroscopy in HORs might reduce the time necessary for PFC drainage and improve clinical success rates. It must be noted that some other outcomes, such as hospital length of stay and reintervention rate, went in the opposite direction. Future research should be conducted to explore use of this advanced guidance in larger and more homogeneous patient series.

Competing interests

The authors declare that they have no conflict of interest.

Clinical trial

Clinical.Trials.gov

NCT04698668

TRIAL REGISTRATION: Single-Center, observational, retrospective study at clinicaltrials.gov

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