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Endoscopic ultrasound-guided placement of AXIOS stent for drainage of pancreatic fluid collections

Rashmee Patil[a], Mel A. Ona[b], Charilaos Papafragkakis[c], Sury Anand[b], Sushil Duddempudi[b]

Mount Sinai Health System, NY; The Brooklyn Hospital Center, Academic Affiliate of The Icahn School of Medicine at Mount Sinai Clinical Affiliate of The Mount Sinai Hospital, Brooklyn, NY; MD Anderson Cancer Center, Academic and Clinical Affiliate of the University of Texas, Houston, USA

Abstract

Pancreatic fluid collections (PFCs) have conventionally been treated with surgery, percutaneous drainage, or with the more recently established endoscopic ultrasound (EUS)-guided drainage modality. Currently, endoscopic plastic or metallic stents are used for PFC drainage. Plastic stents present issues with stent migration and premature occlusion requiring frequent stent exchanges or placement of additional stents. Metallic stents are tubular and may migrate, resulting in inefficient drainage, content leakage, retrieval and replacement, and possible mucosal injury. The aim of this review was to summarize and evaluate the clinical and technical effectiveness of EUS-guided placement of the recently developed AXIOS stent, a lumen-apposing self-expandable metallic stent (LASEMS)for PFC drainage. A literature review was performed to identify the studies describing this technique. In this review article we have summarized case series or reports describing EUS-guided LASEMS placement. The indications, techniques, limitations and complications reported are discussed. A total of 298 patients were included across all studies described thus far in the literature. Overall, a 97% technical success rate and a 96% clinical success rate have been reported. Early and late complications related to the placement or removal of LASEMS have been reported, however few cases have presented life-threatening results. EUS-guided PFC drainage and LASEMS placement can be a safe and effective alternative approach in the management of selected patients.

Keywords Endoscopic ultrasound, pancreatic fluid collection, drainage, lumen-apposing stent, AXIOS

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Introduction

Pancreatic fluid collections (PFCs) can be categorized as acute peripancreatic fluid collections, pancreatic pseudocysts, acute necrotic collections, and walled-off pancreatic necrosis (WOPN). Symptomatic PFCs can be treated surgically, percutaneously, or endoscopically [1,2]. Though surgery and percutaneous treatment are more traditional forms of management of PFCs, both modalities have their drawbacks. Surgery is associated with higher rates of morbidity (5-35%) and mortality (6%), whereas the external catheter in percutaneous treatment increases the risk of infection or fistula formation (14%) [3,4]. The endoscopic management of peripancreatic fluid collections has also been technically challenging and associated with significant shortcomings, however the recent development of the lumen-apposing self-expandable metallic stent (LASEMS) attempts to overcome the limitations of current endoscopic accessories used in the treatment of PFCs [5].

Traditional endoscopic management of PFCs has included the use of a variety of accessories. Plastic stents were conventionally used for drainage, and although the pigtail feature of the plastic stents prevents migration, their narrow lumen may cause premature occlusion in up to 18% of cases, resulting in frequent stent exchanges or placement of additional stents [21,22]. After the development of plastic stents, fully covered, self-expanding metal stents offered a larger diameter lumen for more efficient drainage and less likelihood of stent occlusion. However, these stents were tubular and could migrate, resulting in inefficient

Departments of [a]Internal Medicine, Mount Sinai Health Systems, New York (Rashmee Patil); [b]Gastroenterology and Hepatology, The Brooklyn Hospital Center, Academic Affiliate of The Icahn School of Medicine at Mount Sinai, Clinical Affiliate of The Mount Sinai Hospital, Brooklyn, New York (Mel A. Ona, Sury Anand, Sushil Duddempudi); [c]Advanced Therapeutic Endoscopy, MD Anderson Cancer Center, Academic and Clinical Affiliate of the University of Texas, Houston (Charilaos Papafragkakis), USA

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Correspondence to: Rashmee Patil, MD, 1000 10th Ave, New York, NY 10019, USA, Tel.: +1 409 656 6475, e-mail: rashmee84@gmail.com

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drainage, leakage, and a more frequent need for retrieval and replacement of the stent if it migrated. Currently, it is very difficult to predict which WOPN collections can be efficiently and safely managed without necrosectomy. In large PFCs with considerable necrosis, necrosectomy is usually required and is commonly performed when the initial endoscopic drainage has not been effective [6,7].

The AXIOS lumen-apposing stent (Xlumena Inc., Mountain View, California, USA) attempts to overcome the limitations of current endoscopic accessories with a removable fully covered, nitinol, braided stent deployed under endoscopic ultrasound (EUS) guidance. A "dumbbell" configuration with two large flanges aims to avoid stent migration. When fully expanded the stent has a flange diameter twice that of the "saddle" section allowing apposition of the tissue layers. The large diameter capacity of the stent also allows necrosectomy in repeated sessions without the need for stent replacement [8,9]. The stent is available in two diameter sizes, 10 or 15 mm.

A few authors have recently summarized the clinical and technical success of using the LASEMS in PFC drainage. In the present review, the indications, techniques, success rates, limitations, and complications reported thus far with EUS-guided PFC drainage using the LASEMS are described.

Materials and methods

An extensive English language literature search was conducted using PubMed, Medline, and Google to identify peer-reviewed original and review articles using the keywords 'endoscopic ultrasound', 'lumen-apposing self-expandable metal stent', 'pancreatic fluid collection', 'AXIOS' and 'drainage'. Only human articles were selected. The references of pertinent studies were manually searched to identify additional relevant studies. The indications, procedural details, technical and clinical success rates, complications, and limitations were considered as part of the inclusion criteria. Search results yielded mostly small sample sized prospective studies and case reports, which limited statistical analysis in the form of meta-analysis. None of the authors have any conflicts of interest or financial relationships with the company that produces or distributes the device described in the review article.

Results

Eleven original articles published were considered appropriate to be included in the review article. Of these, five were case reports from Italy [10,14], New York, USA [17,19], and Spain [11]. Six articles were case series from Italy [13], Colorado, USA [15], Netherlands [12], Spain [18], Utah, USA [20] and Japan [9]. All studies have been summarized in Table(s)1 and 2.

Demographics

As mentioned in Table 1, most of the cases were reported from European countries. A total of 298 patients were included across all studies. 99 patients were female while 199 were male. Mean age calculated from all reported cases was 56 years.

Indications

Indications for EUS-guided pancreatic fluid drainage included the following symptomatic lesions: pancreatic pseudocyst, walled off pancreatic necrosis, infected pancreatic necrosis, and acute peripancreatic fluid collection. All patients who underwent EUS-guided placement of LASEMS were symptomatic at the time of diagnosis. PFC diameter ranged from 50 to 200 mm.

Table 1 Patient characteristics in lumen-apposing self-expandable metallic stent cases

Study, location	Patients (number)	Age (years)	M/F (number)	Type of study
Anderloni *et al* (2015) Italy [10]	1	70	0/1	Case report
Boumitri *et al* (2015) USA [17]	1	52	1/0	Case report
Fabbri *et al* (2015) Italy [14]	1	70	1/0	Case report
Parra *et al* (2015) USA [19]	1	56	1/0	Case report
Rinninella *et al* (2015) Italy [13]	93	60*	71/22	Case series
Shah *et al* (2015) USA [15]	33	53*	18/15	Case series
Siddiqui *et al* (2015) USA [20]	82	53*	49/33	Case series
Walter *et al* (2015) Netherlands [12]	61	55*	38/23	Case series
Gornals *et al* (2013) Spain [16]	9	55*	7/2	Case series
Gornals *et al* (2012) Spain [11]	1	37*	1/0	Case report
Itoi *et al* (2012) Japan [9]	15	54*	12/3	Case series

Age listed as mean of cohort (*)

Table 2 Summary of procedure and outcomes describing endoscopic ultrasound-guided pancreatic fluid collection drainage with lumen-apposing self-expandable metallic stent cases

Study, location	Type of PFC	Dimensions of PFC (mm)	Stent name	Stent size (mm) length×diameter	Approach	Tract dilator	Early complications	Clinical success rate (%)	(%)	Follow up for stent removal
Anderloni *et al* (2015) Italy [10]	Pancreatic pseudocyst	80×60	Hot-AXIOS	10×15	TG	NM	None	1/1 (100)	1/1 (100)	6 months, no complications
Boumitri *et al* (2015) USA [17]	WOPN	140×200	AXIOS	10×15	TG	NM	None	1/1 (100)	1/1 (100)	Removed on admission
Fabbri *et al* (2015) Italy [14]	Symptomatic PFC	NM	AXIOS	10x15	TG	Balloon dilation	None (late complication, gastric mucosa stent burial)	1/1 (100)	1/1 (100)	1 month, late complication
Parra *et al* (2015) USA [19]	Infected pancreatic necrosis	67×168	AXIOS	10×15	TG	NM	None	1/1 (100)	1/1 (100)	Removed on admission
Rinninella *et al* (2015) Italy [13]	Pseudocyst=18 WON=52 Acute peripancreatic fluid collection, 4 Pancreatic abscess, 19	100 (38-240)	Hot-AXIOS	10×15 (n =53) 10×10 (n=37) 6×8 (n=2) 10×15 and 10×10 (n=1)	TG=83 TD=10	NM	Massive bleeding, 1/92 (1%) Perforation, 1/92 (1%) Pneumoperitoneum, 1/92 (1%) Stent migration, 1/92 (1%) Infection, 1/92 (1%)	86/93 (92.5)	92/93 (98.9)	320 days, no complications
Shah *et al* (2015) USA [15]	Pancreatic pseudocyst and WOPN	NM	AXIOS	10×10 (n=18) 10×15 (n=12)	TG=30 TD=3	Dilating bougie or balloon dilation	Access-site infection, 1/33 (3%) Stent migration 1/33 (3%) Back pain, 1/33 (3%) Fever with prolonged hospitalization, 1/33 (3%) Abdominal pain requiring endoscopy, 1/33 (3%)	30/33 (91)	30/33 (91)	30 and 60 days, stent removed successfully in 29/30 (96.7%)
Siddiqui *et al* (2015) USA [20]	WOPN=68 Pancreatic pseudocyst=14	118	AXIOS	10×10 or 10×15	TG=77 TD=5	8-10 F Soehendra dilator or 6-8mm balloon dilation	Stent maldeployment in pseudocyst group, 2/14 (14%) Self limited bleeding in WOPN group, 5/68 (7%)	12/12 (100) in pseudocyst group 60/68 (88) in WOPN group	80/82 (97.5)	All stents were removed
Walter *et al* (2015) Netherlands [12]	Pancreatic pseudocyst=15 WOPN = 46	90 (40-200)	AXIOS	10×10 (n=22) 10×15 (n=39)	TG=58 TD=3	NAVIX device or cystosome	PFC infection, 4/57 (7.0%) Perforation, 1/57 (1.8%)	13/14 (93) pseudocyst 35/43 (81) WON	60/61 (98)	32 days, 47/57 (82%) removed
Gornals *et al* (2013) Spain [16]	Simple pseudocyst=4 WOPN = 5	105 (70-150)	AXIOS	10×10 (n=7) 10×15 (n = 2)	TG=7 TD=1 TE=1	NAVIX device, balloon dilation	Pneumothorax, 1/9 (11%)	9/9 (100)	8/9 (88.8)	33 days, no complications
Gornals *et al* (2012) Spain [11]	Pancreatic pseudocyst	80×50	AXIOS	10×10	TE	NAVIX device, balloon dilation	Tension pneumothorax	1/1 (100)	1/1 (100)	21 days, no complications
Itoi *et al* (2012) Japan [9]	Pancreatic pseudocyst	98.3 (55-200)	AXIOS	10×10	TG=12 TD=3	Dilating bougie (6F-10F), balloon dilation (4-mm), or electrocautery catheter (10F)	Stent migration, 1/15 (6.0%) Self-limited oozing, 3/15 (20.0%)	15/15 (100)	14/15 (93)	33 days, no complications

PFC, pancreatic fluid collection; WOPN, walled-off pancreatic necrosis; D, diameter; L, length; TD, transduodenal; TG, transgastric; TE, transesophageal; G, gauge; NM, no mention; DEN, direct endoscopic necrosectomy

Technique

An oblique/forward-viewing therapeutic linear array echoendoscope was used in all cases. A transgastric approach via the antral wall was performed in 259/298 (87%) patients while a transduodenal approach was performed in 22/298 (7%) cases. A rarer transesophageal approach was only used in two patients across all studies. The remaining 15 patients were not included in the transgastric, transduodenal, or transesophageal approach because the authors did not describe a specific approach in the study. A 0.035-inch guidewire was passed and the tract dilated by using of one of the following: dilating bougie, dilating balloon, NAVIX device, cystosome, or electrocautery catheter. The NAVIX device (Xlumena Inc., Mountain View, California, USA)is a multi-function system that enables exchange-free access, tract dilation and delivery of two guidewires during endoscopic pancreatic pseudocyst drainage [10]. The LASEMS was inserted under direct fluoroscopic and EUS control. Most endoscopists prefer performing the procedure with added radiographic imaging that allows for more efficient stent insertion, however the procedure can be performed without fluoroscopic guidance. In most cases, the selection of a 10-mm or 15-mm stent diameter was based on the contents of the PFC and the presence of solid debris identified on EUS. A larger 15-mm diameter was preferred for PFCs containing solids or necrotic material in order to allow for subsequent debridement, irrigation, and cystoscopy. The AXIOS stent was used in 100% of patients who underwent placement of LASEMS. Two patients underwent stent placement with the novel Hot-AXIOS stent delivery system. The Hot AXIOS System (Xlumena Inc., Mountain View, California, USA)combines a cautery-enabled access catheter with the therapeutic AXIOS Stent for a streamlined, exchange-free procedure [11-14]. It is important to note that Hot-AXIOS is not available in the United States at this time but is used in Europe.

Technical and clinical success rate

The combined clinical success rate was 96% in all case reports and case series with most studies measuring success as clinical improvement and alleviation of pain symptoms. The combined technical success rate was 97% across all studies. Technical success was measured as complete drainage of the PFC. Studies that reported lower technical success rates were Gornals *et al* 2013 [16] and Shah *et al* [15]. In Gornals *et al* 2013 [16], the stent was successfully positioned in all patients except one, due to a failure of the delivery system. In this failure case, PFC drainage was completed by placing two plastic double-pigtail stents. The clinical success rate was 100% in that study however, and patients experienced immediate symptom relief after the interventions. In Shah *et al* [15], the three unsuccessful LASEMS placements were possibly related to limited operator experience as well as one case of device malfunction. As stated in this study, it is likely that technical success increased based on operator experience. Finally, in Siddiqui *et al* [20], the two cases of technical failure were due to stent maldeployment in the pancreatic pseudocyst group.

Complications and adverse outcomes

Four studies had no early adverse outcomes. Minor early complications were reported in seven studies and are summarized in Table 2. The AXIOS stent, with its "dumbbell" configuration and two large flanges, aims to avoid stent migration. In our review, Rinninella, Shah and Itoi each reported only one case of stent migration, totaling three cases of stent migration in all [9,13,15]. Rinninella *et al* reported major complications of massive bleeding and perforation in two patients [13]. Gornals *et al* 2011 reported two cases of pneumothorax that were both presumably caused by a trans-esophageal approach to LASEMS placement [11]. Other early complications reported included pneumoperitoneum, access-site infection, self-limited oozing, abdominal pain, back pain, and PFC infection. There were no mortalities directly related to the procedure.

Follow up and stent removal

In 8 of 11 studies, there were no complications during removal of the LASEMS. The majority of stents were removed using a snare or rat-tooth forceps. In Walter *et al*, endoscopic stent removal was performed in 47 of 57 patients (82%). In the 10 patients in whom endoscopic stent removal was not performed, the reasons included: migration of the stent, stent dislodgement during necrosectomy, removal during surgery, and refusal by the patient [12]. In Fabbri *et al*, attempts at removal of the LASEMS showed the stent embedded in the gastric wall. It was removed using rat-tooth forceps [14]. This case represented a late complication of LASEMS placement and was the first case describing the "buried stent". Though the majority of AXIOS stents were removed in the studies included in our review, there is little data regarding recurrence after removal or outcomes for stents left in permanently. In Siddiqui *et al* follow up of patients after LASEMS removal was 9 months for the walled-off pancreatic necrosis group [20]. Of the 68 patients, there was 1 recurrence that occurred 4 months after removal of the AXIOS stent that was retreated successfully by placement of a new stent through the previous cyst-gastrostomy tract [20]. As more prospective studies following patients long-term after AXIOS stent insertion and removal are reported, more data will be available regarding the pros and cons of stent removal versus permanent stent insertion.

Limitations

Thus far, clinically successful cases have been published with few complications reported, but this may be due to a publication bias as the procedure is fairly new. As more cases that are technically and clinically relevant are published,

further data may be assessed regarding the potential efficacy and safety of LASEMS in the treatment of PFCs.

Summary and future directions

Our current literature review suggests that LASEMS is an innovative therapeutic approach for PFC drainage with excellent efficacy, safety, and relatively few adverse outcomes. Conventionally, multiple plastic stents are placed to drain PFCs. However, the migration rates, smaller diameter, and the need for multiple stent placements has necessitated alternative options such as placing metal stents to permit efficient drainage. Because of the "dumbbell" shape of the LASEMS and its large diameter, apposition and a reduced risk of migration are possible. A distinct advantage of the anchoring design and large lumen diameter of this device is the ability to perform direct endoscopic necrosectomy through the stent while maintaining stent integrity, especially if the 15-mm diameter stent is used. The large diameter enables endoscope advancement into the PFC for debris removal while the flanges keep the stent in place [15-19]. LASEMS placement for PFC drainage showed a technical success rate as defined by PFC resolution of 97%. It is likely that technical success will increase with additional experience and use. Clinical success was measured at 96% across all studies.

This is the first review article reporting clinical and technical results of the LASEMS stent selectively designed for PFC drainage. It shows that the LASEMS may be, in the future, a feasible and safe alternative to surgery or percutaneous drainage in patients with PFCs. In the cases described in the literature, the majority of patients progressed adequately in a short period of time without significant complications related to the procedure. Preliminary reports appear promising and large multicenter prospective studies are needed in the future to further determine its safety and efficacy. With further experience and the development of more sophisticated accessories, the arena of EUS-guided drainage and stent placement is likely to expand. In conclusion, our study showed that the LASEMS is safe and efficient for PFC drainage. Advantages of LASEMS compared with other stents include single-step deployment and the ability to perform direct endoscopic debridement with minimal stent migration. Whether the safety and efficacy of LASEMS is superior to conventional double-pigtail plastic stents for PFC drainage would require a prospective, randomized, controlled trial.

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