Study title: Lumen apposing metal stents vs lumen apposing metal stent plus double pigtail stent for endoscopic drainage of pancreatic fluid collections: a randomized controlled trial

Principal Investigator: Patrick Yachimski, MD MPH

Background:

Pancreatic fluid collections (PFC) develop as a consequence of acute pancreatitis. Chronic PFCs can cause significant patient morbidity and need for hospitalization including: pain resulting in disability and requirement for chronic pharmacologic analgesia; gastric outlet obstruction resulting in inability to tolerate oral intake, weight loss, and nutritional compromise; obstructive jaundice; hemorrhage; and infection.

Interventional approaches for management of symptomatic PFCs include endoscopic or surgical drainage. Endoscopic drainage has emerged as the preferred first line-intervention due to the ability of endoscopic drainage to offer effective therapy in a minimally invasive fashion, with comparable efficacy, lower cost, and shorter length of hospital stay compared to surgical drainage [1].

Standard technique for endoscopic drainage has consisted of endoscopic ultrasound (EUS) for visualization of PFC, which are typically in a perigastric or periduodenal location, followed by EUS-guided transgastric or transduodenal needle access to the collection, creation of a cystotomy tract, and finally placement of a transmural stent which facilitates drainage of PFC contents into the gastrointestinal lumen.

At the time of initial development and clinical application, this technique required use of plastic or metal bile duct stents for cystgastrostomy/cystduodenostomy. More recently however, a dedicated lumen apposing metal stent (LAMS) (Axios, Boston Scientific) (Figure 1) has been granted U.S. Food and Drug Administration approval for transmural drainage of pancreatic pseudocysts (PP).

The first clinical use of an Axios stent at Vanderbilt for treatment of a PFC was in March 2015. Vanderbilt University Medical Center (VUMC) was the first and to date remains the only medical center in Tennessee where the Axios stent is in clinical use. Since March 2015, Axios stents have been placed in more than 25 patients at VUMC for management of PFCs, with a favorable efficacy and safety profile. VUMC clinical experience with the Axios stent through November 2015 was included in an international multicenter study for management of PFCs in 192 patients, which reported a 98.4% technical success rate, 92.6% clinical success rate, and a low adverse event rate [2].

In many instances, however, PFCs may contain considerable solid debris indicating the presence of walled off necrosis (WON) rather than simple PP. Such solid debris may occlude the lumen of LAMS, resulting in incomplete drainage, persistent symptoms, infection, and hospitalization. In cases of WON, passage of a flexible endoscope across the cystotomy tract may be necessary for endoscopic necrosectomy and mechanical debridement of pancreatic necrosis. Published data indicate that more than half of patients will require such additional endoscopic interventions for debridement of necrosis following LAMS placement [3, 4].

Clinical experience suggests that placement of an overlapping double pigtail plastic stent through the lumen of the LAMS will prevent stent occlusion, enable optimal drainage following LAMS placement,

and minimize the need for endoscopic reintervention (Figure 2). Controlled data to support this approach are lacking. The objective of this study is to randomize patients undergoing endoscopic drainage for PFCs containing solid debris to placement of either LAMS alone vs LAMS plus an overlapping double pigtail stent.

Study hypothesis and objectives:

The study hypothesis is that placement of LAMS plus an overlapping double pigtail stent for endoscopic transmural drainage of PFCs with solid debris will result in improved drainage and require fewer endoscopic interventions compared to placement of LAMS alone.

Study endpoints/outcome measures:

Primary endpoint:

Greater than 50% decrease in size of PFC (in mm), compared to pre-intervention size (in mm), on cross-sectional computed tomography (CT) imaging at 30 days following stent placement. This was selected as the primary outcome in order to maintain consistency with the primary outcomes of a prior multicenter study of LAMS placement for PFCs [5].

Secondary endpoints:

1) Clinical success rate for drainage of PFC, defined as complete resolution of PFC on follow-up computed tomography (CT) imaging and stent removal within 3 months;
2) Number of endoscopic interventions required for resolution of PFC prior to stent removal;
3) Need for hospital readmission following initial endoscopic intervention and prior to resolution of PFC/stent removal;
4) Need for surgical or percutaneous radiologic intervention for PFC following initial endoscopy intervention
5) Need for early (<30 days) endoscopic reintervention

Methods:

Adult patients with symptomatic pancreatic fluid collections who are scheduled to undergo EUS-guided drainage of PFCs with LAMS placement will be eligible for study participation. The initial portion of this procedure consists of diagnostic EUS for imaging and assessment of the PFC. This EUS examination is able to distinguish the relative liquid and solid components of PFCs, detail which may not be evident by CT imaging. Adult patients with PFCs consisting of >30% solid component as assessed at the time of EUS will be eligible for randomization. This threshold was selected as the enrollment criteria in order to select patients with a significant solid necrotic component to the lesion, as prior study of patients undergoing LAMS placement for drainage of PFCs have used >70% fluid content as the definition for a PFC with predominantly liquid contents [5].

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Allocation to study arm will be determined by the contents of sealed envelope. Subjects randomized to LAMS alone will undergo EUS-guided transmural placement of an Axios stent with a 15 mm luminal diameter. The choice of transgastric or transduodenal LAMS placement will be at the discretion of the endoscopist and contingent upon PFC location and window relative to the EUS transducer. Subjects randomized to LAMS plus double pigtail stent will undergo EUS-guided transmural placement of a single Axios stent with a 15 mm luminal diameter; following this, wire access across the stent lumen will be achieved using a 0.035 inch hydrophilic guidewire, and a double pigtail plastic biliary stent (6 French, 7 French, or 10 French at the discretion of the endoscopist) will be deployed over the wire. The use of fluoroscopy for stent deployment will be at the discretion of the endoscopist.

Power calculation and statistical analysis plan:

The planned study is a prospective randomized study in which subjects undergoing intervention A (LAMS alone) vs subjects undergoing intervention B (LAMS plus double pigtail stent) will be randomized in 1:1 fashion. If the failure rate (<50% decrease in size of collection on 30 day imaging) for subjects undergoing intervention A is 50% and the failure rate for subjects undergoing intervention B is 20%, then 38 subjects will need to be enrolled in each intervention arm in order to reject the null hypothesis that the failure rates for intervention A and B are equal with 80% power at an alpha (Type I error) level of 0.05. Statistical analysis of this outcome will be performed using Chi square testing.

Study timeline:

In order to accrue 76 subjects (38 in each arm), and assuming a 20% drop-out rate, 101 total subjects would need to be enrolled in this study. Given the volume of procedures performed for EUS-guided drainage of PFCs at VUMC, we anticipate that this study would be able to achieve target prospective enrollment during a period of 36 months.

Study funding:

This study will be supported by internal funding. The study will not be supported or funded by industry, and the collection, analysis, interpretation, and publication of data will be independent of industry.

Disclosures:

Dr. Yachimski has received consulting fees and speaking honoraria from Boston Scientific.

References:

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Figure 1: Fully deployed Axios stent and delivery catheter

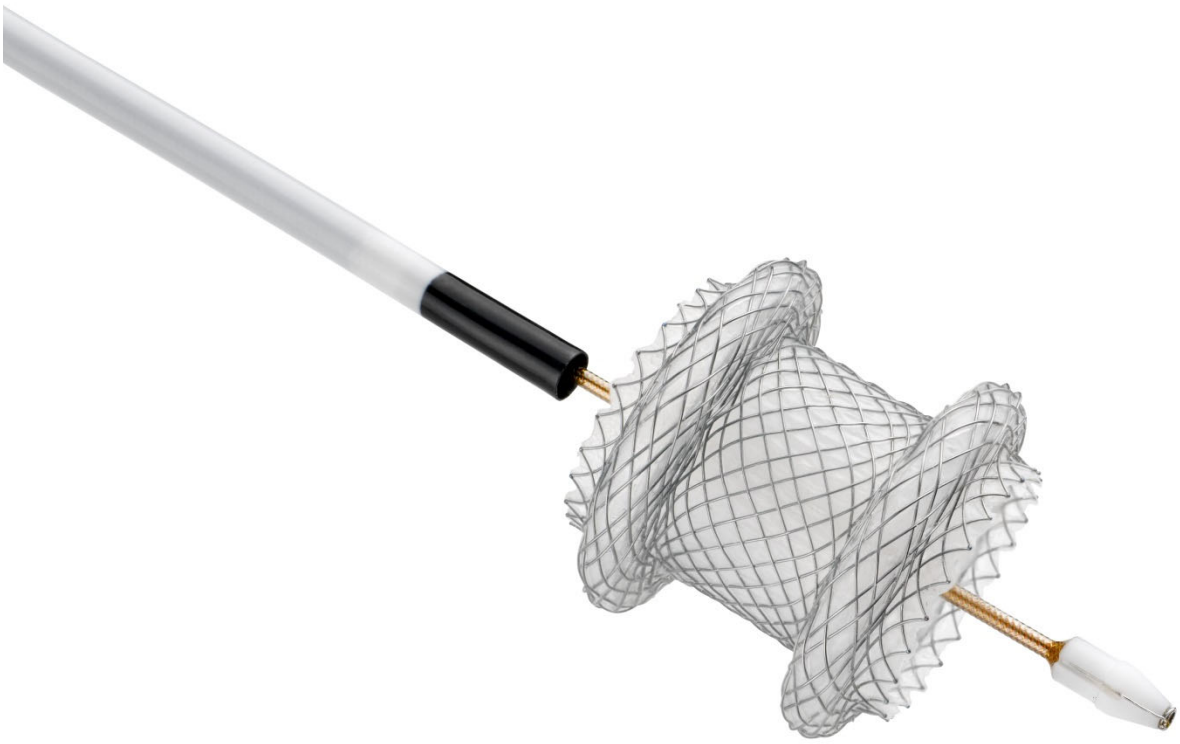

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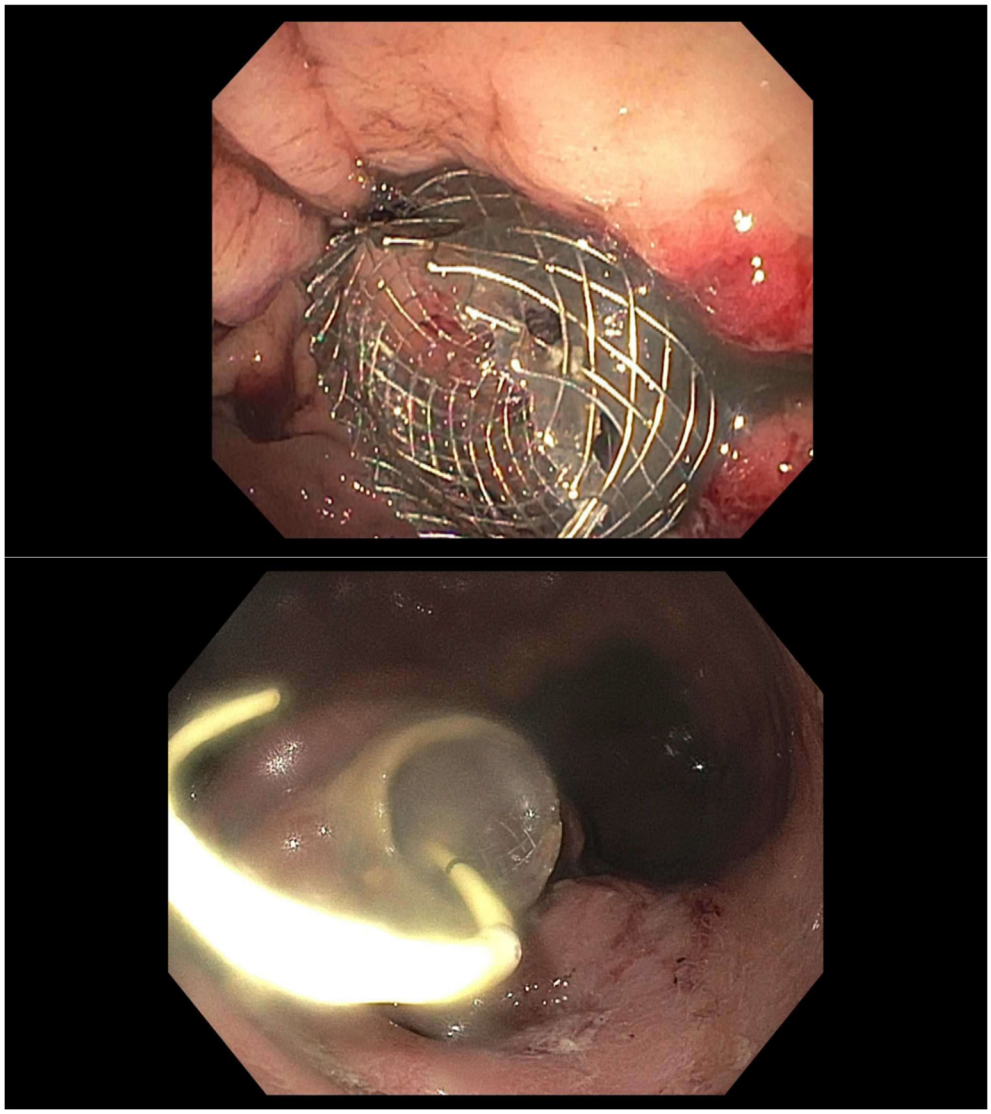
Figure 2: Endoscopic images of a LAMS alone (top image) and a LAMS plus double pigtail stent (bottom image)



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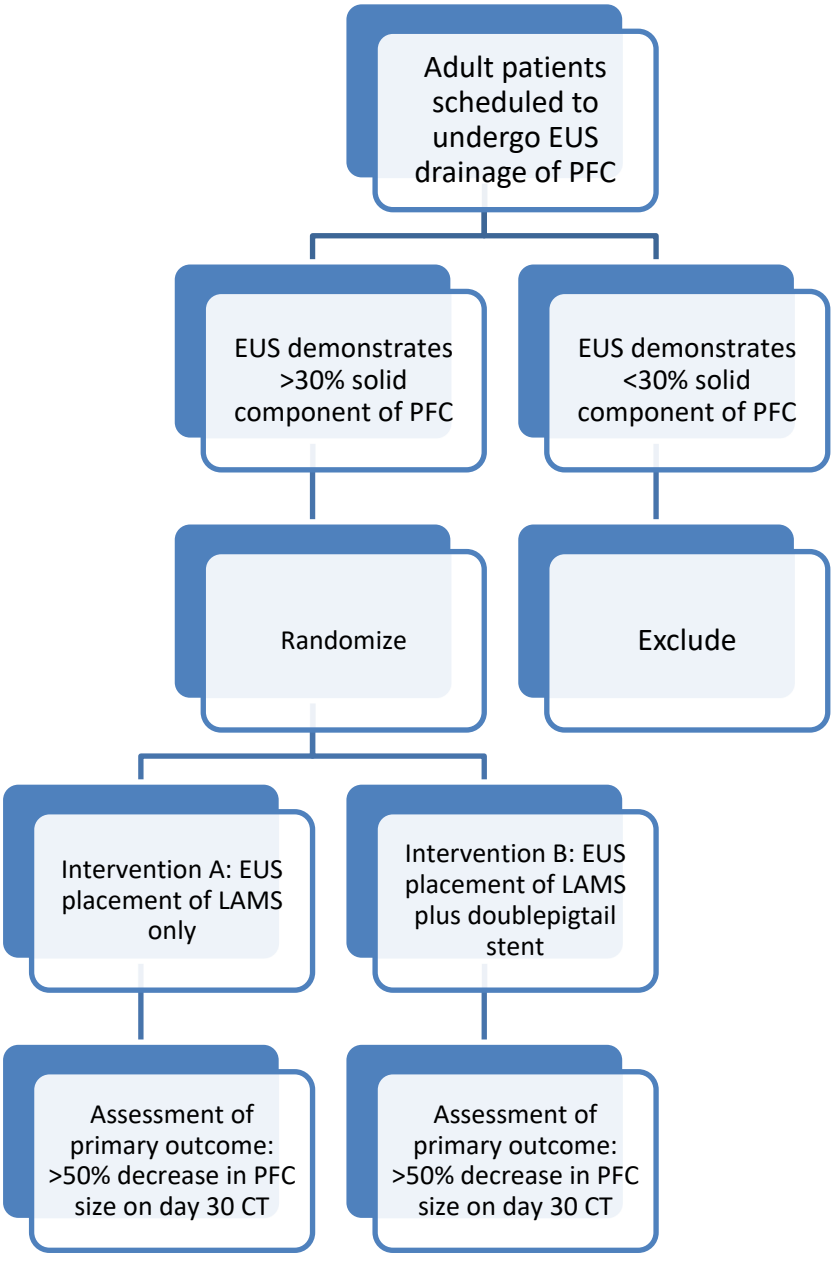
Study flow diagram



Abbreviations:

EUS (endoscopic ultrasound)
PFC (pancreatic fluid collection)
LAMS (lumen apposing metal stent)
CT (computed tomography)

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