# Randomized controlled trial comparing covered metal stents versus uncovered metal stents for palliative biliary decompression in inoperable malignant distal bile duct obstruction

Participating centers:

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Version Date: September 23, 2019

**Background:**

Endoscopic retrograde cholangiopancreatography (ERCP) with transpapillary placement of an endoprosthesis is an established intervention for palliation of malignant distal extrahepatic bile duct obstruction. Such intervention may provide relief of jaundice and pruritus, reduce the risk of ascending cholangitis, and permit administration of systemic chemotherapy. Plastic biliary stents are prone to stent occlusion and malfunction, with median stent patency duration of 12 weeks for 8 French gauge stents and 32 weeks for 10 French gauge stents[1], and therefore require repeat intervention via ERCP for stent removal and exchange every several months. The need for repeat intervention may require interruption of ongoing chemotherapy, may be otherwise undesirable from a patient perspective, and may have cost implications. Indeed, the goal of endoscopic biliary decompression should be to provide durable biliary drainage—ideally extending for the duration of the patient's overall survival—in a single intervention.

Self-expanding metal biliary stents (SEMS) offer an internal diameter up to 10 mm, offer more durable biliary drainage compared to plastic stents[2,3], and have therefore become the endoprosthetic of choice for palliation of inoperable malignant distal bile duct obstruction. Variations in SEMS design exist, however, and the choice of ideal SEMS is uncertain—uncovered SEMS (U-SEMS) consist of a bare metal scaffold which may be prone to hyperplastic tissue ingrowth and stent occlusion; alternatively, covered SEMS (C-SEMS) feature a polyurethane coating which may prevent tissue ingrowth but which may increase the likelihood of inadvertent stent migration. A prior randomized controlled trial of a stainless steel U-SEMS versus a stainless steel partially covered C-SEMS revealed no difference in time to recurrent biliary obstruction[4]; and a recent meta-analysis demonstrated no clear advantage of C-SEMS vs U-SEMS[5].

Due to variations in stent material, design, and manufacture, however, such data may not be generalizable to current generation metal stents, which feature a nickel titanium alloy scaffold and which, in C-SEMS version, offer a full rather than partial polyurethane coating.

**Hypothesis:**

We hypothesize that current generation C-SEMS offer more durable biliary drainage and will decrease the need for biliary reintervention compared to U-SEMS in patients with inoperable malignant distal bile duct obstruction.

**Objectives**:

Primary objective: Compare the rate of long-term stent failure, defined as need for repeat biliary intervention (endoscopic, percutaneous, or surgical) following placement of C-SEMS vs U-SEMS for palliation of inoperable malignant distal bile duct obstruction.

Secondary objective: Compare the rate of adverse stent-related or intervention-related outcomes (pancreatitis, cholangitis, cholecystitis, perforation) following placement of C-SEMS vs U-SEMS for palliation of inoperable malignant distal bile duct obstruction.

**Design**:

Single-center prospective randomized controlled trial.

**Inclusion criteria**:

- Patients with distal bile duct obstruction due to pancreatic cancer, cholangiocarcinoma, or metastatic malignancy with a confirmed tissue diagnosis referred for ERCP with intended palliative metal stent placement for palliation of jaundice
- Patients 18 years of age and older
- Serum bilirubin > 2 mg/dL

**Exclusion criteria**:

- Prior endoscopic or percutaneous biliary drainage
- Post-surgical anatomy (ie pancreaticoduodenectomy, Billroth-type gastrectomy, Roux-en Y hepaticojejunostomy)
- Primary site of biliary obstruction involving the common hepatic duct or hilum
- Tumor involving gastric outlet, duodenum, or ampulla either precluding endoscopic access to the papilla or otherwise preventing endoscopic biliary cannulation
- Inability to provide written informed consent

**Procedure**:

- Patients will undergo ERCP under either MAC/general anesthesia or conscious sedation per institutional standard of care.
- Following endoscopic biliary cannulation and diagnostic cholangiography, performed per standard of care, a sealed envelope will be opened to determine patient randomization to either a 10 mm diameter C-SEMS (Wallflex, Boston Scientific) or a 10 mm diameter U-SEMS (Wallflex, Boston Scientific). Due to the nature of the intervention, the proceduralist will not be blinded to study allocation. The choice of a 40 mm or 60 mm stent length will be at the discretion of the proceduralist.
- Post-procedure monitoring and discharge will be performed per institutional standard of care.

**Follow-up**:

- Day 1 follow-up for assessment of post-procedural adverse events will be performed by telephone call by an endoscopy post-assessment nurse (for outpatients) or by physician assessment at the patient's bedside (for inpatients), as per current institutional standard of care
- Follow-up will occur every 60 days by review of the electronic medical record or patient self-report to assess for primary and secondary study outcomes

**Major treatment outcomes**:

- Primary outcome: Performance of repeat ERCP, percutaneous biliary drainage, or surgical biliary bypass for palliation of persistent or recurrent biliary obstruction.
- Secondary outcomes: pancreatitis requiring hospital admission; cholangitis requiring hospital admission and intravenous antibiotics; cholecystitis requiring percutaneous, surgical, or endoscopic intervention; perforation.

**Sample size and planned statistical analysis**:

Retrospective data from VUMC has identified a long-term 25% failure rate of U-SEMS and 0% failure rate of C-SEMS when placed for palliation of malignant distal bile duct obstruction[6]. Assuming a somewhat more conservative estimate of durability rates, a sample size of 96 patients (48 per treatment arm) would be required to detect a 20% difference in stent failure rates at 80% power with an alpha level of 0.05. Also anticipating a 20% rate of dropout/loss to follow-up, the goal would be to enroll and randomize 116 total patients in the study.

Fisher's exact test will be used to assess the statistical significance in proportion of primary and secondary study outcomes, respectively. Additional univariate and multiple variable logistic regression analysis will be used to identify potential predictors of stent failure, to be reported including odds ratio and 95% confidence intervals. A two-sided P value of $<0.05$ will be the threshold for statistical significance in all cases.

**Role of industry**:

This is an investigator-initiated study. The stent manufacturer (Boston Scientific) has no role in the design, conduct, data collection or data analysis, reporting, monitoring, or funding of this study.

References:


1) Speer AG, Cotton PB, MacRae KD. Endoscopic management of malignant biliary obstruction: stents of 10 French gauge are preferable to stents of 8 French gauge. Gastrointest Endosc 1988; 34: 412-7.
2) Davids PH, Groen AK, Rauws EA et al. Randomised trial of self-expanding metal stents versus polyethylene stents for distal malignant biliary obstruction. Lancet 1992; 340: 1488-92.
3) Kaassis M, Boyer J, Dumas R et al. Plastic or metal stents for malignant stricture of the common bile duct? Results of a randomized prospective study. Gastrointest Endosc 2003; 57: 178-82.
4) Telford JJ, Carr-Locke DL, Baron TH et al. A randomized trial comparing uncovered and partially covered self-expandable metal stents in the palliation of distal malignant biliary obstruction. Gastrointest Endosc 2010; 72: 907-14.
5) Almadi MA, Barkun AN, Martel M. No benefit of covered vs uncovered self-expandable metal stents in patients with malignant distal biliary obstruction: a meta-analysis. Clin Gastroenterol Hepatol 2013; 11: 27-37.
6) Trawick E, Slaughter J, Yachimski P. Endoscopic biliary stent placement for palliation of jaundice due to pancreatic cancer: self-expanding metal stents offer more durable biliary drainage compared to plastic stents, and minimize need for biliary reintervention. Am J Gastroenterol 2012; 107: S111.

**Appendix A—Data Instrument**

**Study ID**: _____

**Demographics**:

Age_____ Gender: M F

**Underlying diagnosis**:

Pancreatic CA Cholangio CA Other (specify)_____

**Additional clinic data**:

Serum bilirubin (mg/dL) _____

Serum WBC_____

Prior cholecystectomy Y N

**Cholangiographic and technical procedure data**:

Stricture length at ERCP: _____cm

Stricture extending to ampulla: Y N

Endoscopic ampullary mass present: Y N

Stricture involving cystic duct takeoff Y N indeterminate

Randomization: C-SEMS U-SEMS

**Follow-up**:

Day 1 adverse events: pancreatitis cholangitis cholecystitis perforation none

Day 30 (and at each 30 day interval thereafter):

Patient alive: Y N If deceased, days from stent placement until death: ___

Repeat ERCP since stent placement: Y N

Percutaneous biliary drainage since stent placement: Y N

Surgical biliary bypass since stent placement: Y N

Surgical, endoscopic, or percutaneous gallbladder interventi