Title of trial: Comparison of Duodenal Stenting vs Transpyloric and Duodenal Stenting for Malignant Obstruction

NCT #: NCT03125148

Date of Document: March 17, 2017

STUDY PROTOCOL

Title: Comparison of Duodenal Stenting vs Trans-pyloric and Duodenal Stenting for Malignant Obstruction

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Purpose:

Enteral self-expanding metal stents (SEMS) are routinely used to palliate malignant gastric outlet obstruction (pancreas cancer, duodenal cancer, gastric cancer and metastasis) in patients not fit for surgical bypass. The technical success in placing these stents approaches ~100% and many of these procedures can be performed in an outpatient setting. However, the functional success (patient's ability to eat after stenting) is much lower than the technical success. One of the major reasons for this discrepancy is these patients are on narcotics which are known to be associated with poor gastric motility. At the discretion of the endoscopist, FDA approved enteral stents are placed either completely within the duodenum bridging the obstruction or placed across the pyloric opening besides bridging the duodenal obstruction.

The significance of this study is to determine if trans-pyloric extension of an intra-duodenal stent facilitates better gastric emptying compared to an intra-duodenal stent without trans-pyloric extension.

Background:

No studies have shown whether duodenal stenting by itself or duodenal stenting with trans-pyloric extension is superior in patients with duodenal obstruction secondary to malignancy. In one study, refractory gastroparesis secondary to benign etiologies (idiopathic, diabetes, and post-surgical) was managed with endoscopic trans-pyloric stent placement. In this study, clinical response was observed in 75% of patients. There was a predominant response in the patient's symptoms of nausea and vomiting. Gastric emptying studies were done post-stenting which showed the mean 4-hours gastric emptying normalized in 6 patients and significantly improved in 5 patients. In light of the success of trans-pyloric stenting in the setting of refractory gastroparesis due to benign pathology, we hope to show the same level of effectiveness in the setting of malignancy for which these stents are approved by FDA.

Hypothesis:

Enteral self-expanding metal stents deployed across the malignant duodenal obstruction with trans-pyloric extension will facilitate better gastric emptying and thereby better symptom relief compared to enteral self-expanding metal stents deployed completely within the duodenum.

Aims/Objectives:

The objective of this study is to compare symptom relief and gastric emptying in the following two groups of patients with malignant gastric outlet obstruction who have enteral self-expanding metal stents deployed 1) across the malignant duodenal obstruction with trans-pyloric extension and 2) enteral self-expanding metal stents deployed completely with the duodenum without trans-pyloric extension

Recruitment Methods:

Inpatients and outpatients referred to the Gastroenterology service at Froedtert Hospital for placement of enteral stents for palliation of malignant duodenal obstruction will be recruited as per the below inclusion and exclusion criteria. These patients are generally directly referred to the advance endoscopy faculty or are referred through the GI consult service.

Inclusion Criteria

- Confirmed diagnosis of cancer
- Evidence of a single small bowel obstruction
- Considered palliative (can be on narcotics, chemotherapy, and/or radiation therapy)
- Not a surgical candidate
- >18 years of age
- Able to give consent
- Eligible for endoscopy (medically fit)
- Able to traverse past obstruction with a guidewire

Exclusion Criteria

- <18 years of age
- Unable to give consent
- Pregnant
- Have evidence of multiple sites of obstruction in the small bowel
- Have evidence of duodenal obstruction secondary to gastric cancer
- Ineligible for endoscopy (due to comorbidities or acuity of illness)
- Unable to traverse past obstruction with a guidewire

Methods/Procedures:

This is a prospective chart review study. All the procedures are being done for clinical indications. Since patients will be randomized to group A or Group B as below, a consent form will be used.

- Prospectively enroll patients based on inclusion-exclusion criteria.
- Stent deployment completely intra-duodenal vs with trans-pyloric extension based on randomization.
- Computer-generated randomization will be conducted. We expect to randomize 20 patients each to either complete intra-duodenal stenting (Group A) or with trans-pyloric extension (Group B).

- Symptoms of gastric outlet obstruction: heartburn, chest pain, regurgitation, bloating, belching, fullness after meals and epigastric pain will be collected from chart review prior to the procedure and post procedure as recorded during follow-up clinic visits.
- Medical record review of post-stent deployment (24-48 hrs post-deployment to allow for full expansion of the stent) gastric emptying studies.
- Solid and liquid T1/2 will be compared between these 2 groups using statistical analysis.
- An interim statistically analysis will be performed to determine if we need to study more patients.

Statistics:

We plan to study 40 patients prospectively (20 in each arm) and then using statistical software, conduct an interim analysis to determine if more patients are required. Solid and liquid T1/2 times will be compared between 2 groups using an unpaired T-test.

Risks to Participants

Patient will incur no additional risks associated with extending a stent trans-pyloric as opposed to leaving the stent completely intra-duodenal. Both these approaches are currently being practiced without any studies showing one approach being better or worse than the other. Also, patient's private and confidential information may be breached in case the data is accessed by an unauthorized person. In order to deal with this risk of confidentiality, the following measures will be taken:

- Personal identifying information will be available only to Dr. Dua and authorized study staff who are officially part of the study.
- Additionally, any paper forms will be kept in a locked cabinet at the gastroenterology department at MCW where the PI and research team members have access to the computer. The computer is password protected and only research members will have access to it. Any paper forms will be kept in a locked cabinet in the GI department.
- Once the data is complete from MCW, the data will be stored in an excel spread sheet that is password protected. The data will be stored for the duration of the study and analysis, and once the study is completed, all the de-identified data will be stored for no more than 10 years.
- Only Dr. Dua and other authorized personnel will have access to the study folder.

Consent Process

The study will be described in detail to the patient by the principal investigator or member of the study team who is familiar with the project. Perceived risks and benefits of the study will be described in detail. All patient question will be answered. The patient will be asked to sign a written informed consent document for the study. Consent can occur in two settings. If the patient is admitted, physical contact with the patient will occur with in person consent being obtained. If the patient is to be done as an outpatient, the patient will be consented on the day of the procedure. Patient will be given enough time (at least a minimum of 15 minutes) to read the consent form and ask any questions. Study procedures can begin as soon as the consent is signed. Each subject will have the opportunity to decline participation in the study at any time, and will be assured that declining to participate will have no effect on their future medical care. The primary language spoken by participants will be English.

References:

1. Mouen A. Khashab, Sepideh Besharati, et al. “Refractory gastroparesis can be successfully managed with endoscopic transpyloric stent placement and fixation (with video).” **Gastrointestinal Endoscopy**. 2015 Dec; 82(6): 1106-9.
2. Ahn HS, SJ Hong, et al. “Uncovered self-expandable metallic stent placement as a first-line palliative therapy in unresectable malignant duodenal obstruction.” **Journal of Digestive Disease.** 2012 Dec; 12(12): 628-33.
3. Larssen L, T Hauge, AW Medhus. “Stent treatment of malignant gastric outlet obstruction: the effect on rate of gastric emptying, symptoms, and survival.” **Surgical Endoscopy**. 2012 Oct; 26(10): 2955-2960.
4. Chandrasegaram MD, Eslick GD, et al. “Endoscopic stenting versus operative gastrojejunostomy for malignant gastric outlet obstruction.” **Surgical Endoscopy**. 2012 Feb; 26(2):323-9.
5. Kobayashi S, Ueno M, et al. “Duodenal stenting followed by systemic chemotherapy for patients with pancreatic cancer and gastric outlet obstruction.” **Pancreatology**. 2016 Nov-Dec; 16(6): 1085-1091.
6. Hamada T. Hakuta R, et al. “Covered vs uncovered metal stents for malignant gastric outlet obstruction: a systematic review and meta-analysis.” **Digestive Endoscopy**. 2016 Dec 20.

Appendix I: Data Collection Form

Data Sheet

De-Identified #: _____

A. Demographics

Gender: M F Age: _____ BMI: _____

B. Primary Diagnosis causing duodenal obstruction:

____ Pancreatic Cancer ____ Duodenal Cancer ____ Lymph Nodes

____ Metastatic Disease ____ Other

C. Diabetes:

____ Yes ____ No

D. Cancer therapy (currently/on-going):

____ Chemotherapy ____ Radiation

E. Narcotics:

____ Yes ____ No If yes: Name_____ Dose_____

Morphine Equivalent _____

F. Pre-Procedure Symptoms (circle all that apply):

Heartburn Chest Pain Regurgitation Bloating Belching

Post-prandial fullness Epigastric pain

G. Stent Placement:

Date of Procedure: _____

Attending: _____

Successful: ____ Yes ____ No

Randomization Group: ____ A ____ B

Full Expanded (within 48hrs) ____ Yes ____ No

H. Gastric Emptying

Date of Exam:_____

T 1/2 (half time for gastric emptying): _____ % retained @1hr _____

B1 (slope of 1st phase of emptying): _____ % retained @2hr _____

B2 (slope of 2nd phase of emptying): _____ % retained @3hr _____

C (time for when slope changes from B1 to B2): _____ % retained @4hr _____

Overall interpretation:

_____

I. Post Procedure Symptoms (circle all that apply)

Heartburn : Better Same Worse Chest Pain: Better Same Worse

Regurgitation: Better Same Worse Bloating: Better Same Worse

Belching: Better Same Worse Post-prandial fullness : Better/same/ Worse

Epigastric pain: Better Same Worse