PROTOCOL TITLE: Comparison between endoscopic vs. suction calibration system on number of staple load firings, operative duration, cost, and gastro-esophageal reflux disease following laparoscopic sleeve gastrectomy: is there a difference?

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REVISION HISTORY

Revision #	Version Date	Summary of Changes
1	6/16/2021	Protocol revised to transfer/add study information to the latest IRB protocol template. Also added the use of DocuSign for remote consenting of patients.

Table of Contents:

1. Study Summary

Project Title	Comparison between endoscopic vs. suction calibration system on number of staple load firings, operative duration, cost, and gastro-esophageal reflux disease following laparoscopic sleeve gastrectomy: is there a difference?
Project Design	Prospective, randomized, open-label, single center, investigator-initiated study
Primary Objective	To evaluate if there is a significant difference in the number of staple load firings required for endoscopic (EGD) vs. ViSiGi® 3D suction device for calibration during sleeve gastrectomy
Secondary Objective(s)	i. To evaluate if there is a significant difference in operative duration (time) and intra-operative cost for patients undergoing EGD vs. ViSiGi® 3D suction device calibration during sleeve gastrectomy ii. To assess longer post-operative outcomes including GERD symptom severity and weight loss
Research Intervention(s)/Interactions	Screening/Consenting - In person preoperatively or electronically Docusign Electronically Operative Day- GERD baseline questionnaire / Surgical Intervention 2 months and 12 (+/- 12 months) – GERD questionnaire completion via telephone by research personnel or in person visit scheduled
Study Population	Patients requiring gastric band sleeve surgery
Sample Size	The target enrollment will be 125 subjects
Study Duration for individual participants	12 months for all participants consented prior to 05/10/2021 unless reconsented to latest version 24 months for all participants consented after 05/10/2021 or reconsented to latest version
Study Specific Abbreviations/ Definitions	BMI – Body Mass Index GERD - gastroesophageal reflux disease LSG - laparoscopic sleeve gastrectomy RB - rubber bougie

	SCD - suction calibration device SG - sleeve gastrectomy
Funding Source (if any)	This is a physician-sponsored study. Boehringer will provide the ViSiGi devices at no charge. Anticipated funding for start-up costs may also be provided by Boehringer. Internal funds will support trial implementation and analyses.

2. **Objectives**:

Primary aim:

i. Evaluate if there is a significant difference in the number of staple load firings required for endoscopic (EGD) vs. ViSiGi® 3D suction device for calibration during sleeve gastrectomy

Secondary aims:

ii. Evaluate if there is a significant difference in operative duration (time) and intra-operative cost for patients undergoing EGD vs. ViSiGi® 3D suction device calibration during sleeve gastrectomy

iii. Assess longer post-operative outcomes including GERD symptom severity and weight loss

1. GERD-HRQL questionnaire pre-op and post-op 2 (**+/- 2 months**) & 12 mo **(+/- 12 months**) (4)
2. Weight loss – mean % total body weight loss, mean % EWL, mean % change in BMI (12 mo, **+/- 12 months**)

3. **Background**

Previous studies have shown that compared to a standard weighted rubber bougie (RB), using a suction calibration device (SCD) results in a straighter staple line compared to a twisted and corkscrewed staple line (1); no studies to date have compared upper endoscopy calibration to SCD for SG. Due to the straighter, and therefore shorter, staple line, the hypothesis is the surgeon should be able to use fewer staple loads with a SCD. Bariatric staple loads are expensive, so a reduction in their use has the potential for savings to the hospital.

The study will also look at how a suction calibration system can create savings for the hospital in OR time and scope processing costs. As previously mentioned, the SCD may require fewer stapler load firings; it also eliminates the need for placing multiple tubes in to the stomach as well as an upper endoscopy leak test and therefore saves the OR staff time and may decrease operative duration. The SCD is also disposable which

eliminates the need for reprocessing. Current estimates for reprocessing an endoscope are around $200 (2) thus the SCD use may decrease operative cost.

It is also hypothesized that a misaligned smaller sleeve after a LSG procedure can increase the prevalence of post-operative GERD due to removal of the fundus and twisting of the sleeve (3). A straighter, correctly calibrated sleeve should decrease the prevalence of GERD in patients. Therefore, the study will also look at the prevalence of pre-operative vs. post-operative GERD symptoms in patients who are undergoing LSG with endoscopic calibration vs. SCD.

4. Study Intervention/Investigational Agent

	Pre-operative period & Bariatrical Surgical consult	Day of Surgery (LSG)	Immediate Post-op follow-up (3 weeks) **(+/- 2 weeks**)	2mo post op f/u **(+/- 2 months)**	12 mo post op f/u **(+/- 12 months)**
Attg Surgeon or Surgical house staff research team members	Assess candidacy of patients for enrollment in study *Patients to be randomized into either EGD vs ViSiGi calibration sleeve gastrectomy *Pre-op education on ViSiGI usage via rep and online videos, instruction sheet for surgeons involved	EGD vs ViSiGi device usage for sleeve *No SPECIMEN COLLECTED *Standardize surgeon technique *Fill out Powernote template collecting all intraop data	Assess for complication & document in **Exemplo**	*medical bariatrician f/u at 2mo *obtain cost data	Assess long-term weight loss, Compile tables, figures etc for abstract and manuscript generation
Study coordinator	Enroll, research consent process, administer	Ensure powernotes are		GERD-HRQL (in	GERD-HRQL (in person or phone)

	baseline GERD-HRQL, notify data analyst *Save hard copy of consent, paperwork in MOT7	done collection intraop data *notify data analyst		person or phone)	
Data Analyst	Enter patient as enrolled in **Exemplo** data base along with PHI, demographics, etc.	Enter OR date in **Exemplo** database along with operative duration and stapler information (HER op note, PowerNote with template for all pertinent data)	Assess for complication in EHR	EHR review for any 30-day post-op issues, GERD data entry, enter cost data as able	Query MBSAQIP for any post-op issues & weight loss data, enter GERD data entry, Assist w/ tables, figures etc for abstract and manuscript generation
Statistician	NA				TBD

5. Procedures Involved

- Pre-operative period & Bariatrical Surgical consult (usually 1-2 mo prior to surgery) period:
    - Assessing candidacy for study enrollment, research consent process, surgeon education on device, and GERD-HRQL for diagnostic and research purposes
    - Patients will be randomized to either the EGD vs. the ViSiGi device for sleeve gastrectomy calibration
    - Neither the surgeon nor patient will be blinded to the device used
    - Patients will find out if they are in the EGD vs. ViSiGi device group pre-operatively

- Day of surgery = Postop Day zero (POD0)
    - Use of EGD vs. ViSiGi calibration for sleeve intended for therapeutic and research purposes for surgeon

- Risks/discomforts of EGD and ViSiGi device are comparable. Using a ViSiGi device is similar to both a standard weighted bougie and an EGD calibration technique. The ViSiGi device is similar to a gastroscope in that they both have suction, calibration, and leak testing capabilities. The benefit of the ViSiGi device is that it obviates the need for doing an EGD during sleeve gastrectomy, is single patient use and thus does not require reprocessing, and doesn't require a scope tower to operate it. Potential benefits of using the ViSiGi device (in lieu of endoscopic calibration) in order of highest probability are as follows: 1) less staple loads, 2) shorter OR time, 3) reduced cost, 4) decreased post-op GERD rates.
- Data analyst and study coordinator to have research roles at this time

- Immediate post-op follow-up 3 weeks after surgery (+/- 2 weeks) to 12 months out (+/- 12 months)
  - Assessments made by surgeon will be for diagnostic, therapeutic and research purposes as appropriate
  - Study coordinator and data analyst will function in research roles only
  - Goal in this period is predominantly research purposes only
  - Due to constraints from COVID-19 and decreased in-person follow-up, the 12-month assessment time frame will be extended to 24 months post-surgery to help gather GERD-HRQL and weight loss data

  a. What type of information will be collected:
     i. See above table
     ii. Demographic and clinical variables will be collected at (baseline) including age, gender, race, BMI, smoking status, functional status, and medical comorbidities:
        1. EHR
        2. MBSAQIP
        3. Baseline GERD-HRQL scores (standardized questionnaire)
     iii. Intra-operative/procedure data (i.e. type of stapler used, # staple load firings, length and color stapler loads, etc.)
        1. EHR
        2. Research data sheets
     iv. Post-operative data & assessment
        1. EHR
        2. MBSAQIP (30-day outcomes and weight loss outcomes)
        3. Cost data (administrative data) from internal databases
        4. GERD-HRQL scores (standardized questionnaire)

6. Inclusion and Exclusion Criteria

Patients selected for this study will be adults, 18 years old or older, who have already agreed with their surgeon that LSG is the best choice for them. Patients will be excluded by the following criteria;

- Subjects with prior gastric surgery or bariatric surgery (including prior adjustable gastric band and/or sleeve gastrectomy).
- Concomitant hiatal surgery
- Paraesophageal hernia at time of surgery
- Any subject with prescribed immunosuppressive drugs.
- In the opinion of investigator, subject is not eligible to participate in the study.
- If patient is a female and becomes pregnant at any time during the study duration

7. Local Number of Participants

There is no additional screening for the study that the patient would already be subject to if they were not part of the study. There will be 50 patients undergoing LSG with an endoscope and 50 patients undergoing LSG with a suction calibration system. Patients will be assigned randomly to each group.

8. Recruitment Methods

9. Subjects will be identified by the 1) treating physician/surgeon and/or her clinical staff or 2) the study staff reviewing clinic and/or hospital admissions.
Risk to Participants

The risk for participating in this study is expected to be minimal and equivalent to standard peri-operative morbidity and mortality associated with sleeve gastrectomy. Moreover, patient safety and risk profiles are expected to be similar between the endoscopic vs. suction device calibration techniques. A rare complication associated with laparoscopic bariatric is tube/probe stapling during sleeve gastrectomy. Given that the ViSiGi device is a plastic tube it could potentially be stapled across during gastrectomy or cause other trauma to the stomach or esophagus with intra-operative manipulation during sleeve gastrectomy. It is also possible for a gastroscope to be stapled across during gastrectomy and to cause mucosal trauma with manipulation and suctioning during sleeve gastrectomy. Again, the overall risk directly associated with intra-operative use of either the ViSiGi or endoscopic devices during sleeve gastrectomy risk anticipated to be minimal (< 1%) and similar between groups.

10. Potential Benefits to Participants

This study, by its nature, will be focusing on bariatric surgery and therefore people with obesity who meet standard NIH criteria for weight loss procedures like LSG (5). The information from this study may help the community by giving the hospital information on ways to more effectively and efficiently perform LSG.

11. Compensation to Participants

There will be no patient reimbursement for participation in this study.

12. Data Management and Confidentiality

Data for this study will be recorded on a secure password-protected electronic database called **Exemplo**. Data entry will be done by study investigators and/or data analysts who are part of the approved IRB team. Unidentified data may be shared with the sponsor, Boehringer Laboratories LLC.

Data analysis will be done by internal or externally hired statisticians on de-identified data on spreadsheets downloaded from **Exemplo**.

Separate intra-operative data will be collected from the EHR either via the Operative Note or via standardized PowerNote templates (**if available**) to help capture data pertinent during sleeve gastrectomy including the following:

1) **Patient Full Name**: pre-populated/pull from eEMR
2) **MRN**: pre-populated/pull from eEMR
3) **Date of surgery**: pre-populated/pull from eEMR
4) **Primary Surgeon**: pre-populated/pull from eEMR
5) **Stapler used**: Echelon Flex Powered 60mm stapler, Endo GIA 60 mm Universal Stapler XL; Other (free text)
6) **Distance from pylorus for 1st stapler firing**: Free text for centimeters
7) **Calibration device**: EGD/Standard Weighted Bougie Tapered/Standard Weighted Bougie Blunt/ViSiGi device/Other (free text)
8) **Calibration device size**: free text for French
9) **Total number of stapler load firings**: free text number
10) **Length of stapler loads used** (list number): 60 mm(free text number or click n/a); 45 mm (free text number or click n/a); other (free text)
11) **Number, order & color of stapler loads** (first to last; i.e. 2 green, 2 gold, 1 blue): free text
12) **Use of Seam Guard reinforcement for stapler loads**: yes/no
    a. If yes, were all stapler loads reinforced? Yes/no; other (free text)
13) **Other procedures performed**:

a. Plication/imbricating suture to sleeve: yes/no; other (free text)
b. Pexy of omentum to sleeve: yes/no; other (free text)
c. Clipping of sleeve staple line: yes/no; other (free text)
d. Oversewing staple line: yes/no; other (free text)
e. Fibrin glue to staple line: yes/no; other (free text)
f. Any other procedures?: free text

14) **EGD done**: yes/no
a. If yes, any abnormal findings: yes/no; other (free text)
b. If abnormal findings, please list any interventions done: free text

15) **Miscellaneous Notes**: free text

13. Statistical Analysis

There will be 50 patients undergoing LSG with an endoscope and 50 patients undergoing LSG with a suction calibration system. Both methods are clinically accepted and approved methods of performing the procedure. The target enrollment will be 125 to account for attrition due to screen failures, early withdrawals, etc. For this study we use a randomized block design (RBD) to assign participants to one of two sleeve groups. In a RBD we divide participants into subgroups called blocks (e.g. gender, race, etc.), such that the variability within blocks is less than the variability between blocks. Then, subjects within each block are randomly assigned to treatment conditions (i.e. SG with EGD or SG with ViSiGi device). The purpose of the RBD is to help reduce variability within treatment conditions and potential confounding from blocking factors, producing a better estimate of treatment effects. We are adequately powered to detect a mean difference in stapler load firings of 0.4 between groups assuming a standard deviation of 0.7, which is consistent with our institutional sleeve gastrectomy experience. After all cases have been performed statistical methods will be implemented to determine any difference in outcomes. An initial approach will focus on a pairwise analysis (t-test) between the ViSiGi and EGD calibration groups for each of the primary and secondary aims. A more comprehensive multivariate analysis factoring in demographic and clinical variables will be performed to further delineate significant differences in the 2 sleeve gastrectomy methods. In the unlikely situation that an adverse event occurs, the event will be inspected to determine if an early stoppage is necessary.

14. Provisions to Monitor the Data to Ensure the Safety of Participants

All methods used in this study for performing sleeve gastrectomy are already approved and clinically accepted. Validated users of the device will be attending surgeons who have been trained using the ViSiGi device via online video-based education

(https://www.youtube.com/watch?v=zDhc-1fr32E), review of the manufacturer instructions for use (IFU) sheet below: (chromeextension://oemmndcbldboiebfnladdacbdfmadadm/https://www.boehringerlabs.com/wp-content/uploads/2018/09/5232009.pdf) as well as in-person education via representatives from Boehringer Laboratories, LLC.

All surgeons will be required to complete the video-based module and review the IFU sheet prior to using the ViSiGi device.

The PI will be responsible for ensuring participants' safety on a weekly basis as cases are performed (sleeve gastrectomies are not always done every week) and for reporting serious Adverse Events (AEs) and Unanticipated Problems (UPs) to his or her Institutional Review Board (IRB) and the monitoring body with the help of the study coordinator. The study coordinator and/or PI will prepare reports that list AEs, serious AEs, deaths, and disease-or treatment-specific events required for MB review in order to ensure good clinical care and identify any concerning trends. The Monitoring Body (MB) will act in an advisory capacity to the PI to monitor participant safety, evaluate adverse events and progress of the study. The MB will constitute two surgeons who are not directly involved in the study protocol but participate in the care of bariatric patients at Emory University Hospital Midtown and will to review the safety data annually.

The PI will be informed of serious AEs as soon as they occur by Co-Investigators (i.e., surgeons performing sleeve gastrectomy) and/or the study coordinator and notify the MB within 48 hours of becoming aware of the event. The PI will report serious AEs and UPs to his or her IRB within 5 business days of becoming aware of the event. Events constituting UPs include calibration device malfunctions such as a piece or component of the device breaking off into the stomach during manipulation, failure of the device to adequately perform a leak test, or contamination or damage to the device such that it cannot be appropriately used. Specific triggers for an ad hoc review or initiation of the process of an ad hoc review will occur if there are unforeseen deaths or if there is a serious AE including stapling across a calibration device during sleeve gastrectomy or other serious device malfunction leading to patient injury. At any point during the study time period, the study will be stopped and undergo further review if ≥ 1 deaths or a serious AE directly related to calibration device use (i.e., stapling across device while creating sleeve gastrectomy or serious device malfunction leading to patient injury) occurs.

Safety reports will be sent to the MB for review after the first 5 subjects are enrolled and within 12 months of the study start date. Safety assessment reports will provide a

detailed analysis of safety issues including the incidence of AEs, clinical severity of AEs, serious AEs, UPs, deaths and protocol deviations. The PI will also document receipt and review of these safety reports in addition to any corrective actions and/or resolutions to findings reported which will also be reported to the IRB.

The sponsor does not have any additional reporting requirement than what Emory Hospital already has in place.

15. Economic Burden to Participants

N/A

16. Informed Consent Process

Consent will be obtained in person before the patient undergoes surgery by the principal investigator, co-investigators, and/or research study coordinator. Consent will likely occur at the initial surgical consultation, but may be obtained at any point prior to randomization. Patients will be notified if they are going to be in the EGD vs. ViSiGi device arm of the sleeve gastrectomy protocol during the perioperative period; it will be explained to them that this selection is being done in a randomized fashion, similar to flipping a coin, factoring in various patient-related factors. No elements of HIPAA will be waived. The study participants are legal adults and not pregnant, prisoners, or otherwise cognitively impaired in any way.

DocuSign:

The study team will use an Emory DocuSign account that is HIPAA compliant and meets the FDA's requirement for CFR Part 11 signatures. The consent process begins when a patient is screened and identified as eligible for study participation. A member from the study team will discuss the informed consent form in its entirety with the potential participant via telephone phone and/or Zoom. The patient's identity will be verified by requesting that he/she confirm their demographical information (i.e. full name, DOB, address, etc.).

In DocuSign, potential subjects have the ability to review the consent document as freely as they would if they were consenting in person. They also have the opportunity to exit the document without signing. The patient will be offered ample time to discuss the informed consent form with family and or friends, and have questions answered.

The process for obtaining final consent is outlined below:

1. First, the IRB-approved, stamped informed consent form(s) are added to an envelope in DocuSign.

2. Secondly, recipients (subjects/coordinators) are then added to the envelope and signature and initial fields are assigned to them on the IRB approved informed consent form.
3. Finally, once the document is completed, the signed copy is forwarded to the subject electronically via email. The completed informed consent form document is also saved on our secure internal shared drive.

The signature area of the informed consent document has been updated to denote the subject's electronic signature.

17. Setting

This study will be conducted at Emory University Hospital Midtown.

18. References

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