PROTOCOL TITLE:

Hiatal Hernia Repair Using Surgimend Mesh: A Pilot Study

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REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
1	03/31/2020	Added time windows to visits	No
2	08/07/2020	Added language for remote consenting and remote visits	No
3	09/11/2020	Adjusted time windows for visits	No

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1.0 Study Summary

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<tr><td>Study Title</td><td>Hiatal Hernia Repair Using SurgiMend Mesh at the hiatus: A Pilot Study</td></tr>
<tr><td>Study Design</td><td>Prospective, single-arm, open-label study to evaluate re-occurrence and quality of life in subjects undergoing primary Hiatal hernia repair using SurgiMend biological mesh. Up to 15, with a target of 10, subjects are planned to be enrolled at one site. All subjects will receive the SurgiMend mesh during surgery. Data collected will be compared to historical data.
Subjects will complete a pre-operative visit. After surgery, in addition to any standard of care visits, subjects will complete 3- and 6-month follow-ups involving a phone QOL survey and will have an upper GI series at 6 months.</td></tr>
<tr><td>Primary Objective</td><td>Recurrence rates of hiatal hernia as compared to historical rates</td></tr>
<tr><td>Secondary Objective(s)</td><td>To evaluate quality of life of patients in which SurgiMend mesh was used during Hiatal hernia surgery using the GERD-HRQL, compared to historical data.</td></tr>
<tr><td>Research Intervention(s)/ Investigational Agent(s)</td><td>Assessment of recurrence rates of hiatal hernias following use of SurgiMend mesh compared to historical rates</td></tr>
<tr><td>IND/IDE #</td><td>N/A</td></tr>
<tr><td>Study Population</td><td>Patients having a planned hiatal hernia repair</td></tr>
<tr><td>Sample Size</td><td>Up to 15, target of 10</td></tr>
<tr><td>Study Duration for individual participants</td><td>7 to 8 months (6 months post-surgery, plus up to 45 days prior to surgery)</td></tr>
<tr><td>Schedule of Assessments</td><td>
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<tr><td>Visit</td><td>Pre-op/ baseline (w/in 45 days pre-op)</td><td>1-2 Week SOC follow-up (±2 weeks)</td><td>3 Month Follow-up (±2 weeks)</td><td>6 Month Follow-up (±2 weeks)</td></tr>
<tr><td>Informed Consent</td><td>X</td><td></td><td></td><td></td></tr>
<tr><td>Verify Eligibility Criteria</td><td>X</td><td></td><td></td><td></td></tr>
<tr><td>Quality of Life (QoL)* Questionnaire</td><td>X</td><td></td><td>X</td><td>X</td></tr>
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	*QoL and AE assessment can be done via phone call. Questionnaire used is the GERD Health-Related Quality of Life Questionnaire (GERD-HRQL)
Study Specific Abbreviations/ Definitions	Quality of Life: (QOL); Gastroesophageal reflux disease (GERD); Upper gastrointestinal tract radiography (UGI); Gastroesophageal Reflux Disease-Health Related Quality of Life (GERD-HRQL), Adverse Event (AE); Standard of Care (SOC)

2. Objectives*

2.1. Study recurrence rates of hiatal hernias after use of SurgiMend mesh compared to historical rates. As available, recurrence rates will be compared to historical rates with and without using mesh for hernia repair.

2.2. Assess the quality of life status post laparoscopic hiatal hernia repair with SurgiMend Mesh compared with historical rates as available

3. Background

3.1. Hiatal hernia repair is a surgical procedure with a well-recognized high recurrence rate of 25.5 % up to 50% and low post-op satisfaction and quality of life (1-3). Literature suggests that follow up imaging for evaluation of repair does not generally occur until 1 year post operatively with little data on when the recurrence actually occurred (1-3). Biologic mesh has been studied as a possible adjunct in these surgeries to decrease recurrence and increase QOL. However, there are very few studies that have examined the actual recurrence rate following the use of mesh to reinforce the hiatal hernia repair. We wish to study the efficacy of surgical mesh (Surgimend) for use in hiatal hernia repair to decrease recurrence and increase QOL

3.2. Currently, there is conflict in the literature as to the best type of surgical procedure to be performed and there is little overall literature about the use of bovine dermis product used in hernia repair to reduce recurrence rate and QOL improve with the addition of mesh for a laparoscopic hiatal hernia repair. There is some evidence that bovine dermis has the ability to adjust to the pressure points and is less likely to pull apart and tear under pressure. This results in a decrease in mesh erosion ultimately resulting in less complications, including fewer recurrences. (4)

4. Study Endpoints

4.1. Primary Endpoint: Recurrence of hiatal hernia as assessed by upper GI and clinical evaluation.

4.2. Secondary Endpoint: Quality of life as marked by GERD symptoms on GERD-HSQL (5)

5. Study Intervention/Investigational Agent

5.1. Description: SurgiMend Mesh -FDA approved noncross-linked bovine dermis biologic mesh

5.2. SurgiMend Mesh will be used according to FDA approved recommendations for the use of abdominal wall hernia reinforcement

5.3. SurgiMend is intended for implantation to reinforce soft tissue where weakness exists and for surgical repair of damaged or ruptured soft tissue membranes. SurgiMend is specifically indicated for:

5.3.1. Hernia repair including abdominal, inguinal, femoral, diaphragmatic, scrotal, umbilical, and incisional hernias.

6. Procedures Involved

6.1. Intervention: Following placement of SurgiMend mesh during laparoscopic hiatal hernia repair, patient will be scheduled for follow up using an upper GI series to check for recurrence of the hiatal hernia. Follow up upper GIs will be performed at 6 months post-surgery. Subjects will also complete a QOL survey to assess other GI associated symptoms before and after surgical repair. The QOL survey and AE assessment can be administered by phone by study team members

6.2. Study Calendar:

Visit	Pre-op/ baseline (within 45 days of procedure)	1-2 Week SOC follow-up (±2 weeks)	3 Month Follow-up (±2 weeks)	6 Month Follow-up (±2 weeks)	Medical Records review throughout 6 month follow up
Informed Consent	X				
Verify Eligibility Criteria	X				
Quality of Life (QoL) Questionnaire	X		X	X	
Upper GI				X	
AE Assessment	X	X	X	X	X
Vitals, Labs, EKG	X	X			X

6.3. Patients having hiatal hernia repair performed by Dr. Levy, who is the PI for the study, will have Surgimend mesh placed as per the SurgiMend approved use.

6.4. Dr. Levy and/or surgical residents who are named as study team members will introduce and explain the study to the patient. If the patient is interested, they will be provided with a copy of the complete informed consent form and one-page summary of the study. A research coordinator will follow up with the patient by phone. If a patient decides to participate, informed consent will be obtained by a member of the

study team in the office prior to surgery or a coordinator will call the patient to ensure patient understanding and desire to proceed with enrollment in study prior to the day of surgery by completing telephone consent. For remote consent, telephone consent will be utilized, with two team members verifying consent and documenting on the ICF. A copy of the ICF will also be emailed or mailed to the subject to sign as well. The subject will then return the sign copy, via scan, fax, picture, or return hard copy via mail or next in-person visit and will be filed with the consent completed by 2-person verification. A research coordinator will confirm eligibility prior to the patient being enrolled in the study.

6.5. After informed consent is obtained and eligibility is confirmed, the patient will answer the GERD-HRQL survey (please see 6.8.2 for details on the survey) prior to the day of surgery.

6.6. The patient will then undergo the planned elective procedure for hiatal hernia repair. Following the procedure, they will be admitted and observed in the hospital per standard of care. After discharge, the patient will be seen in the office for a standard of care follow up visit 1 to 2 weeks after discharge. The patient will complete the same QOL survey at 3 and 6 months as well as have a fluoroscopic Upper GI with contrast at 6 months to check for radiographic recurrence as outlined below. The research coordinator may administer the survey by telephone

6.7. The research procedures for this study include UGI and QOL survey

6.7.1. UGI is a procedure that uses a fluoroscopic x-ray examination with the use of an orally ingested barium-based or other contrast material (as determined by the radiologist performing the test) to visualize the esophagus, stomach, and duodenum. This is a non-invasive test to identify abnormalities in the digestive tracts, including hiatal hernias (6).

6.7.2. UGI Risks –

6.7.2.1. Exposure to radiation (6mSv) is comparable to 2 years of background radiation (https://www.radiologyinfo.org/en/info.cfm?pg=safety-xray)

6.7.2.2. Approximately ¼ the exposure of a CT

6.7.2.3. allergic reaction to contrast material

6.7.2.4. constipation/obstruction from incomplete passage of the contrast agen

6.7.3. QOL survey: GERD-HRQL

6.7.3.1. The GERD-HRQL was initially developed to measure the typical symptoms of GERD and their effect on a patient's quality of life. It was initially determined to have face validity and subsequent studies assessed its content validity and criterion validity. Reliability was determined by the test-retest

method. This instrument is practical, with little administrative burden and has been validated for use via the telephone call (5).

6.7.3.2. Because this QOL survey is directly tied to how a patient's gastrointestinal (GI) symptoms impact their quality of life, there is little risk for undue psychological harm or emotional distress experienced by the patient.

6.8. Recurrence rate will be analyzed by a UGI done 6 months postoperatively in conjunction with patient's reported physiological assessment per the GERD-HRQL. As indicated, the physician reviewing this information will follow up with patient to ensure proper care and future treatment.

6.8.1. Patients will have an UGI x-ray at 6 months postoperatively

6.8.1.1. The UGI will be scheduled by a study team member through central scheduling at KHN.

6.8.1.2. The patient will be instructed to not eat, drink, smoke or chew gum for four hours prior to the exam.

6.8.1.3. As determined by the radiologist, a pregnancy test may be required and will be paid for by the study.

6.9. Data to be collected includes Standard-of-Care data, normally collected pre- and post-surgery. Such data includes pre-operative and post-operative lab tests, and EKG (if applicable), vitals, age, gender, BMI. While the patient is on the study, their medical will be reviewed to capture any unscheduled visits.

6.9.1. The patient will be instructed to not eat, drink, smoke or chew gum for four hours prior to the exam.

6.9.2. UGI x-ray uses a very small dose of ionizing radiation to produce pictures of the inside of the abdominal cavity.

7. Data and Specimen Banking*

7.1. N/A - no specimen Banking. Data banking for future use is not planned.

8. Sharing of Results with Subjects*

8.1. Results of study will not be formally shared with the subjects, however individual subjects will be informed of their progress per usual care

9. Study Timelines*

9.1.1. Enrollment time period: up to 1.5 years or up to 15 patients

9.1.2. Follow-up/completion of all study related activities – 2 years

10. Inclusion and Exclusion Criteria*

10.1.1. Inclusion

10.1.1.1. Diagnosis of type 3 or 4 hiatal hernia (8)

10.1.1.2. Subject is able to give informed consent
10.1.1.3. Adults at least 18 years of age

10.1.2. Exclusion

10.1.2.1. Currently pregnant
10.1.2.2. Prior hiatal hernia repair
10.1.2.3. Prior gastric surgery
10.1.2.4. Prior foregut surgery
10.1.2.5. Known esophageal dysfunction or dysmotility
10.1.2.6. Cirrhosis or ascites
10.1.2.7. Known malignancy
10.1.2.8. Known allergy to biologic mesh
10.1.2.9. Known allergy to barium or other contrast material used in UGI
10.1.2.10. Religious objection to animal implant
10.1.2.11. Cognitive impairment

11. Vulnerable Populations*

11.1. Prisoners will excluded from study due to the increased difficulty to follow patients and schedule non-medically necessary testing.

12. Local Number of Subjects

12.1. Enrollment up to 15 patients with a target of 10 patients.

13. Recruitment Methods

13.1. Patients screened at First Surgical Care (Dr. Levy's main office) after referral. These patients will be approached by the surgeon regarding the study. A member of the study team will explain the study to them in detail and give them an opportunity to ask questions.

13.2. Patients will take consent and brief study overview home to review and given time to ask questions

13.3. Consent will then be obtained at subsequent encounter or via telephone. If consent is to be obtained on the day of surgery, a phone call conversation will be documented stating the consent document was reviewed in full and all questions were answered.

13.4. Patients will be compensated for time and travel.

13.4.1. At completion of the 3 month visit, patients will complete the quality of life questionnaire and will receive $25. At the 6 month visit, patients will receive $50 at per visit. Patients will need to complete both the UGI and the GERD-HRQL to receive stipend. Patient will receive a check from Kettering once all activities are completed for that timepoint.

14. Withdrawal of Subjects*

14.1. Patients may withdraw consent at any time and cease to participate in additional research activities. All previously collected data will be used in the analysis. Further data will not be collected after subject withdraws

15.Risks to Subjects*

15.1. Breach of confidentiality is major risk for patients.

15.1.1. See section 17.1 for mitigation of privacy risks

15.2. Risk of UGI includes the use of a small amount of ionizing radiation and the ingestion of barium or other contrast material.

15.2.1.1. Exposure to radiation (6mSv) is comparable to 2 years of background radiation (https://www.radiologyinfo.org/en/info.cfm?pg=safety-xray)

15.2.1.2. Approximately ¼ the exposure of a CT

15.2.1.3. Reaction to the barium or other contrast material include allergic reaction, constipation/obstruction from incomplete passage of the contrast agent. Patients will be instructed to drink plenty of fluids following the procedure to mitigate risk of constipation and obstruction

15.3. Risk of allergic reaction to bovine mesh is approximately 3% in the general population (6,7).

15.4. The overall risk of psychological impact of QOL survey is minimal. This survey was designed to specifically assess the impact of GI symptoms on a patient's quality of life. Therefore, there is a minimal psychological impact as patients have already been enduring GI side effects from the hiatal hernia, including heartburn, pain, and reflux.

16.Potential Benefits to Subjects*

16.1.1. Subjects may or may not benefit. Subjects may experience reduction in recurrence of hiatal hernia as well as improved QOL.

17.Data Management* and Confidentiality

17.1. Due to the low number of patients expected to be enrolled, statistical analysis will be descriptive in nature. Recurrence rates and QOL means may be compared to historical controls.

17.1.1. Data to be collected: Demographics, vitals, surgical history, medications, recurrence of hernia, comorbidities, dysphagia and reflux symptoms, results of UGI for presence/absence of recurrence of hiatal hernia and labs including a complete blood count (CBC), complete metabolic panel (CMP), and an EKG, which are all standard of care for this procedure.

18. Provisions to Monitor the Data to Ensure the Safety of Subjects*

18.1. Standard of care monitoring and follow-up; 24 hour patient accessibility to a physician; hospital follow-up phone call week of surgery per hospital protocol; phone interview by a member of the study team at 3 and 6 months. Surgeon will be informed of and handle any potentially adverse events related to the study or surgical procedure.

19. Provisions to Protect the Privacy Interests of Subjects

19.1. Data will be encrypted and stored in a password protected shared drive accessible to study personal listed. Only de-identified information will be shared with sponsor and statistician.

20. Compensation for Research-Related Injury

20.1. While the surgical procedure is considered greater than minimal risk, there is not an increase in risk using the SurgiMend mesh compared to other types of surgical mesh. The patient will receive the usual perioperative care and SurgiMesh regardless of whether participating in the study. There is no compensation set aside for injury while on study.

21. Economic Burden to Subjects

21.1. No anticipated additional economic burden will be placed on the participants as they will receive standard of care for surgery. They will be compensated as described in section 13.4.

22. Consent Process

22.1. See above – section 13; patient will receive education about the study during their doctor visit and given a consent and study summary to take home and read. When the patient returns, study questions will be answered and if willing to participate, patient will sign the consent. Alternatively, a member of the study team will call the patient to review the study and obtain informed consent over the phone. In such cases, the patient will sign consent documents on the day of surgery or the consent will be signed and documented by two study coordinators.

23. Setting

23.1. See section 13 for more detail. Patients will be introduced to study at physicians office. They will have surgery per standard of care at a KHN facility, followed by an SOC follow up office visit with the surgeon 1 to 2 weeks post-surgery. They will receive a phone call at 3 months and 6 months to fill out the GERD-HRQL and will travel to a KHN facility of their choice to have an abdominal X-Ray performed at the 6 month time points.

24. Resources Available

24.1. Physician has allocated time for research; residents are required to have research done prior to graduation.

25.Multi-Site Research*

25.1.1. N/A

26.References

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