Registry of Outcomes from AntiReflux Surgery (ROARS)

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Study Purpose and Background:

Purpose:
The purpose of the study is to compare patient outcomes after certain laparoscopic antireflux procedures utilizing a prospective registry.

Background:
Treatment of GastroEsophageal Reflux Disease (GERD) by surgical or endoscopic methods is a reconstructive procedure aimed at restoring competency of the gastroesophageal junction and reduction/repair of a hiatal hernia when present. As with other surgical fields, minimally invasive procedures are now employed in various manners to perform this reconstruction, including laparoscopic antireflux surgery (e.g. Nissen), magnetic sphincter augmentation (LINX), and transoral fundoplication (Esophyx, MUSE). Comparative data between these procedures is lacking especially in regard to long-term efficacy and side effects. This study is designed as a prospective registry of outcomes of laparoscopic procedures that are considered standard care and (if the case) will use only FDA-approved devices for the procedures. Patients to be enrolled in the Registry will have standard indications for an antireflux procedure and/or hiatal hernia repair (e.g. symptoms refractory to medication, ongoing esophageal injury despite medication, side effects from or desire not to take antireflux medication). Patients undergoing hiatal hernia repair because of the hernia primarily have an antireflux procedure performed regardless of preoperative reflux symptoms. This is due to the significant prevalence of pathologic reflux after surgery and the increased risk of a second surgery, and these patients are also appropriate subjects for this Registry. Initially the Registry will be limited to patients undergoing laparoscopic antireflux procedures without any transoral component. This may be expanded at a later date.

Design
- A prospective, multi-center, observational database of laparoscopic antireflux and hiatal hernia repair surgical patients
- Patients meeting Registry qualification will be tracked over a 5-year period
- Up to 40 sites will participate in the Registry
  Registry will enroll up to 1000 patients (of which, at least 500 are LINX patients).

Objective:
The Registry has been established to:
- Collect data about antireflux surgical treatment options (LINX and LNF) in everyday clinical practice
- Track the clinical course of patients from pre-operative assessment to 5-years post-surgery to evaluate reflux symptoms, use of medication and side effects
Subgroup analyses will be conducted across multiple criteria to determine best future patient selection.
Criteria for Subject Selection

Number of Subjects:
The study will be conducted in the United States. This clinical evaluation will be conducted at multiple sites. It is anticipated that enrollment will enroll up to 1000 patients within the first 2 years. The target is to enroll at least 500 LINX patients. Study duration will be approximately 7 years (includes time for enrollment and continued follow-up).

Gender of Subjects:
This is a prospective registry that does not restrict or allocate enrollment based on gender. Pregnant women will be excluded.

Age of Subjects:
Subject must be at least 21 years of age and at least the minimum Age of Majority according to applicable State Law.

Racial and Ethnic Origin.
This is a prospective registry that does not restrict or allocate enrollment based on race or ethnic origin.

Inclusion Criteria:
• Subject must be at least 21 years of age and at least the minimum Age of Majority according to applicable state law.
• Subject is a suitable surgical candidate, i.e. is able to undergo appropriate anesthesia and endoscopic procedure or laparoscopic surgery.
• Appropriate indications for and documentation of disease process requiring surgery. (Documented gastroesophageal reflux disease by accepted endoscopic or ambulatory reflux monitoring criteria, or have a hiatal hernia that meets accepted criteria for repair (e.g. large paraesophageal hernia with chest pain)).
• Subject is willing and able to cooperate with follow-up examinations
• Subject has been informed of the study procedures and treatment and has signed an informed consent for the study.

Exclusion Criteria (General)
• Suspected or confirmed esophageal or gastric cancer.
• Cannot understand trial requirements or is unable to comply with follow-up schedule
• Pregnant or nursing, or plans to become pregnant during the course of the study
• Medical illness (i.e. congestive heart failure) that may cause the subject to be non-compliant with or able to meet the protocol requirements or is associated with limited life expectancy (i.e. less than 3 years)
• Diagnosed psychiatric disorder (e.g. bipolar, schizophrenia, etc.), subjects that exhibit depression that are on appropriate medication(s) are allowable.

Exclusion Criteria (Specific)
• As the study will involve various procedures and devices, patients will not undergo a procedure for which there is an FDA-specified contraindication to that specific device.
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**Vulnerable Subjects:**
No vulnerable subjects will be included in the study.

**Methods and Procedures**
The study design is a prospective registry. The procedures used in the study would all occur regardless of research and are standard of care. The following schedule will be used for the subjects.

**Table 1: Data to be recorded. X=Expected; 0=Optional, based on standard care at site.**

<table>
<thead>
<tr>
<th>Screening (Per standard of care)</th>
<th>Surgical procedure</th>
<th>48 hour/Discharge</th>
<th>1 Week</th>
<th>6 months (Office Visit preferred)</th>
<th>12 months (Office Visit preferred)</th>
<th>Years 2-5</th>
<th>Type of Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td>Health History</td>
</tr>
<tr>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>SOARS QOL Questionnaire</td>
<td></td>
<td>On PPI</td>
</tr>
<tr>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>SOARS QOL Questionnaire</td>
<td></td>
<td>OFF PPI</td>
</tr>
<tr>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>PPI, H2, Antacid and other</td>
<td></td>
<td>Medication Use</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>Medication Use</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>Esophageal pH</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>Esophageal Manometry</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>Endoscopy (EGD or TNE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>X</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Barium Esophagram (Fluoroscopy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Adverse Events Reporting</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Definitions:

*Health History*: Standardized medical health history

*GERD-HRQL*: A validated 10-question evaluation of GERD-related quality of life (6 heartburn, 2 dysphagia, 1 medication, scored 0-5 and 1 question on satisfaction with current health) along with a standardized set of 6 questions regarding regurgitation symptoms scored 0-5. Attached.

*Foregut Symptom Questionnaire*: A validated 16 question evaluation of foregut symptoms (Attached).

*PPI, H2, Antacid and other Medication Use*: Recording of utilization of acid-suppressive medication, including type, dose, and frequency of use.

*Esophageal pH*: Ambulatory recording of esophageal acid exposure 5 cm above the lower esophageal sphincter for a minimum of 16 hours using a catheter or wireless capsule system.

*Esophageal Manometry*: Evaluation of esophageal swallowing pressures using a transnasal catheter.
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*Endoscopy:* Visual evaluation of the esophagus and upper stomach using a flexible scope. This may be performed either under sedation (Esophagogastroduodenoscopy; EGD) or unsedated (4 mm diameter TransNasal Endoscopy; TNE).

*Barium Esophagram:* A study performed by having the subject swallow a radiopaque slurry while X-rays are taken of the esophagus.

*Abdominal/Chest X-ray:* A simple X-ray to determine location of the LINX device.

*Adverse Event Reporting:* Evaluation of any complications or other adverse events related to the device or the procedure.

Antireflux Surgical Procedure
Treatment is determined by the patient and the treating physician based on the clinical situation and local practices. When implanting the LINX System, the considerations provided in the IFU for surgical access, sizing of the esophagus, and placement of the implant device should be followed. Patients undergoing surgery for Fundoplication will be treated per standard of care at the participating institution.

*Data Analysis and Data Monitoring:*
Data analysis will be performed using standard statistical analyses of summary data at different time points. For example the GERD-HRQL results in a composite score (range 0-50); analysis will be performed of differences between the composite scores obtained at the various time points noted above, across the entire cohort, using Kruskal-Wallis or other appropriate non-parametric tests. Sub-analysis may be performed based upon the aggregate results.

The intervention of placing the LINX device does involve potential serious risk to the subject as does performing a laparoscopic fundoplication. However the risk of LINX implantation has previously been assessed as part of the FDA approval process and is quite low. Adverse events related to LINX implantation will be reported to the manufacturer (Torax Medical) per standard of care protocol. It is not anticipated that a data monitoring committee will be required.

*Data Storage and Confidentiality:*
Data will be stored in a front-end/back-end database format. The back-end database will contain anonymous data (i.e. stripped of all personal identifiers and containing only a subject code) and is stored off site using an encrypted, password protected database (FileMaker) that is the sole provenance of the Principal Investigator(s) (PI). Any data exported from this back-end database for analysis is therefore stripped of all personal identifiers and contains only a subject code.

In order to be able to contact patients for follow-up some personal identifier information is required (e.g. name, phone number or email address). A separate front-end database will be available to each site and will also be encrypted and password protected. As every investigator will be the Subject’s Health Care Provider (HCP), this data will be accessible to the HCP and as determined by that HCP any authorized co-investigators /research coordinators to the extent needed to obtain patient consent, assist with data entry or follow-up. Any non-HCP monitoring of data that might contain subject identifiers will require a signed HIPAA compliance agreement.

The link between the subject code and personal identifier is maintained solely within the front-end database. With this front-end/back-end model personal identifiers will not be protected from other investigators.
The security of this database design is greater than web-based data-entry systems as entry into the system requires not only a URL and password, but also the appropriate front-end database with appropriate database-specific form. This front-end database can be scrubbed of any personal identifiers for sites that prefer a 3rd layer of protection.

![Diagram](image)

**Figure 1: Schema of where identified and de-identified data will be stored.**

**Transition from Research Participation:**
Subjects are followed by the research team as part of the routine follow-up performed in the role of HCP. Should a subject terminate participation in the study he or she will still be offered follow-up and care as that HCP's patient. Any transition to another HCP would follow protocol for transitioning of patient care.

**Risk Category:**
Participation in the research carries minimal risk.

**Risks**
The Registry involves the use and disclosure of health information. Only information relevant to the Registry's objectives will be collected. The risk of providing this health information is believed to be minimal as information directly identifying the patient will not be part of the dataset for analysis (back-end). Specifically, the identifiers listed below will NOT be available in the back-end portion of registry database:

- Name
- Postal address information including city, state and zip code
- Telephone or fax numbers
- Email addresses
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The following PHI will not be stored at all in the database:
- Medical health record numbers
- Health plan beneficiary numbers
- Account numbers
- Certificate or license numbers
- Vehicle identification and serial numbers
- URLs and IP addresses
- Biometric identifiers (fingerprints, retinal scans, etc.)
- Full face photos and comparable images

Data will be tracked in the Registry database using only Patient Research IDs.

Any potential procedural risks are not changed by a patient’s participation in the Registry. The treating physician, as with any gastroesophageal surgery, is expected to counsel the patient on the risks and benefits specific to the planned treatment and obtain the appropriate procedure-related informed consent per institutional policy and procedure.

The Registry does not increase a patient’s exposure to physical harm because no additional invasive or radiologic assessments are required by participation in the Registry. Patients are expected to undergo the same routine pre-operative and post-surgical evaluations as would be performed regardless of participation in the Registry.

**Protection Against Risks:**
Patients are thoroughly counseled regarding the potential risks of the tests and surgery prior to offering them enrollment as subjects in the study. The registry itself does not entail any known additional risk.

**Potential Benefits to the Subjects:**
The Registry provides no direct benefit to patients and does not require any additional invasive tests or procedures not already planned as part of the patient’s individualized treatment plan. It is hoped that sharing of information through the Registry will lead to a better understanding of anti-reflux surgical options in everyday clinical practice.

**Alternatives to Participation:**
Patients will be counseled that participation in the registry is not mandatory for having an antireflux procedure.

**Subject Identification, Recruitment, and Consent:**

**Method of Subject Identification and Recruitment:**
Subjects will be identified from the pool of patients presenting to the HCP seeking surgical treatment of the GERD / HH. Patients who then qualify for surgery and meet the study inclusion/exclusion criteria will be considered for participation in the registry and will be approached during the course of preoperative care at the clinic.
Process of Consent:
Consent will be obtained by the site.

Subject Capacity:
Subject capacity will be assessed during the evaluation process for antireflux surgery. Consent for participation in the registry will require consent for the surgery and the associated assessment of subject/patient capacity to provide informed consent are appropriate to providing consent for the registry.

Subject Comprehension:
See Subject Capacity above.

Consent Form:
Consent form is attached. Original of study consent form is stored in a locked location in the PIs office.

Costs to Subject:
The subject will entail costs related to being a patient treated for gastroesophageal reflux disease, including any costs related to standard of care follow-up and/or complications from the treatment. The study is a registry that will not entail any additional costs to the patient.

Payment for Participation:
The subject will not receive any payment for participation in the study.

Quality Assurance of Data
The Principal Investigator is responsible for assuring that accurate and complete data are collected and entered into the Registry. Data will be reviewed periodically for missing data points, incomplete information, and discrepancies. When necessary, issues will be resolved by electronic mail, telephone, facsimile, or site visit. All data management and analysis will occur in a validated computing environment.

Each site will maintain retrievable source documents for all patients enrolled in the Registry until notified in writing that record retention is no longer necessary.

Registry Enrollment Compliance
Sites are expected to enroll consecutive eligible patients into the Registry. When a patient declines authorization to disclose health information, the patient will be denoted as declined. This will allow for tracking of how many anti-reflux surgical patients qualified versus how many disqualified for the Registry. This information will be helpful in assessing if the collected data is a representative sample.