Innovations in Surgical Therapy for GERD: A tale of two therapies

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The Spectrum of GERD

Normal → NERD → Healable Esophagitis → Persistent Esophagitis → Barrett’s

Hiatal Hernia
Type I  Type II  Type III  Type IV

Stricture (Schatzki to Fibrotic) Shortened Esophagus

2 to 16 years

Adapted from Lord et al. J Gastrointest Surg 2009;13:602-610
Classic Treatments of GERD

PPIs

Circa: Olbe 1979-88

Fundoplication

Circa: Nissen 1961
Continued (12-Year) Followup of a Randomized Clinical Study Comparing Antireflux Surgery and Omeprazole in Gastroesophageal Reflux Disease

- starting dose 20 mg, but 10% started at 40 mg/d
- dose escalation to 40 mg, but could go up to 80 mg

BUT – a gradual deteriorations in the proportion of patients in remission in both groups

Continued Followup of a Randomized Clinical Study Comparing Antireflux Surgery and Omeprazole in Gastroesophageal Reflux Disease

Lundell et al. JACS 2001
Patterns of Fundoplication Failure

Type IA

Type IB

Type II

Type III

Richter, Clin Gastro Hep 2013
Effectiveness of PPIs for GERD

• AGA sponsored telephone survey
• Oct – Nov 2010
• N = 687/1004 on PPIs
• 55.3% continued to have disruptions from GERD
• felt like nothing else could be done to control GERD
• felt it difficult to get MD to understand symptom severity

Gupta and Inadomi, DDW Abstract 1154. Gastro 2012
# Risks of Chronic PPI Use

## Proposed Risks of Chronic PPI Therapy

- Increase serum gastrin levels
- Bacterial colonization of stomach
- Accelerate gastric atrophy from *H. pylori* (not substantiated)
- ↑ risk of enteric infections
- ↑ risk of pneumonia
- ↑ risk of *C. difficile* infection
- ↑ risk of SBP in cirrhosis
- Interfere with B12, Fe, Ca absorption
- ↑ risk of bone fracture
- ↑ risk of hypomagnesemia
- Decreased efficacy of clopidogrel
- Delayed metabolism of methotrexate
- ↑ risk of nephritis, chronic renal disease, colitis, food allergy, sprue, dementia, CV events

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**Effects on Vitamins/Minerals**

**Effects on Other Drugs**

**Misc.**
Therapy Gap in GERD

GERD PATIENT POPULATION

100%

PPI Therapy

Anti-reflux Surgery

60%
Satisfied with PPI Therapy

40%
Incomplete response to PPI Therapy

<1%
Reflux Surgery

Therapy Gap

“invasiveness”
durability
side effects eg flatus,
reproducibility

Opportunity for new treatments

Slide Courtesy of Dr. Tom DeMeester
Sphincter Augmentation Device (LINX™ System)

- Highest resistance when closed (0.39N)
  - Roman Arch Design assures that the device is non-compressive when closed
- Lowest resistance when expanded (0.07N)
  - Titanium wire
  - Titanium case
  - Magnetic core
Distension

A loose ligature of expanding magnetic beads

The LINX Sphincter Augmentation Device

Esophageal Sphincter Device for Gastroesophageal Reflux Disease

Robert A. Ganz, M.D., Jeffrey H. Peters, M.D., Santiago Horgan, M.D., Willem A. Bemelman, M.D., Ph.D., Christy M. Dunst, M.D., Steven A. Edmundowicz, M.D., John C. Lipham, M.D., James D. Luketich, M.D., W. Scott Melvin, M.D., Brant K. Oelschläger, M.D., Steven C. Schlack-Haerer, M.D., C. Daniel Smith, M.D., Christopher C. Smith, M.D., Dan Dunn, M.D., and Paul A. Taiganides, M.D.

ABSTRACT

BACKGROUND
Patients with gastroesophageal reflux disease who have a partial response to proton-pump inhibitors often seek alternative therapy. We evaluated the safety and effectiveness of a new magnetic device to augment the lower esophageal sphincter.

METHODS
We prospectively assessed 100 patients with gastroesophageal reflux disease before...
## Components of pH Measurements

<table>
<thead>
<tr>
<th></th>
<th>Baseline No. of Patients</th>
<th>Median Value</th>
<th>No. of Patients</th>
<th>1 Year Median Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH &lt; 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total %age of time</td>
<td>100</td>
<td>10.9</td>
<td>96</td>
<td>3.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Percentage of time upright</td>
<td>100</td>
<td>12.7</td>
<td>96</td>
<td>4.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Percentage of time supine</td>
<td>98</td>
<td>6.0</td>
<td>96</td>
<td>0.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total no. of reflux episodes</td>
<td>100</td>
<td>161.0</td>
<td>96</td>
<td>67</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No. of reflux episodes lasting &gt; 5 min</td>
<td>99</td>
<td>12.0</td>
<td>96</td>
<td>4.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Longest reflux episode (min)</td>
<td>99</td>
<td>29</td>
<td>96</td>
<td>13.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DeMeester score</td>
<td>97</td>
<td>36.6</td>
<td>96</td>
<td>13.5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Secondary Outcomes after LINX

A  Proton-Pump-Inhibitor Use

B  Regurgitation Symptoms

C  Dysphagia

D  Esophagitis Severity

BACKGROUND & AIMS: Based on results from year 2 of a 5-year trial, in 2012 the US Food and Drug Administration approved the use of a magnetic device to augment lower esophageal sphincter function in patients with gastroesophageal reflux disease (GERD). We report the final results of 5 years of follow-up evaluation of patients who received this device.

METHODS: We performed a prospective study of the safety and efficacy of a magnetic device in 100 adults with GERD for 6 months or more, who were partially responsive to daily proton pump inhibitors (PPIs) and had evidence of pathologic esophageal acid exposure, at 14 centers in the
Multi-institutional outcomes using magnetic sphincter augmentation versus Nissen fundoplication for chronic gastroesophageal reflux disease

Heather F. Warren¹ · Jessica L. Reynolds¹ · John C. Lipham¹ · Joerg Zehetner² · Nikolai A. Bildzukiewicz² · Paul A. Taligandés² · Jody Mickley³ · Ralph W. Aye³ · Alexander S. Farivar⁴ · Brian E. Louie⁴

Received: 23 April 2015 / Accepted: 28 October 2015 / Published online: 5 November 2015 © Springer Science+Business Media New York 2015

Abstract
Background Magnetic sphincter augmentation (MSA) has emerged as an alternative surgical treatment of gastroesophageal reflux disease (GERD). The safety and efficacy of MSA has been previously demonstrated, although adequate comparison to Nissen fundoplication (NF) is lacking, and required to validate the role of MSA in GERD management.

Methods Retrospective and prospective case-control studies were performed of consecutive patients undergoing each procedure with chronic gastroesophageal reflux disease (GERD) and a hiatal hernia of less than 3 cm.

Results Sixty-six patients underwent operations (34 MSA and 32 LFN). The groups were similar in reflux symptom (95 vs. 43 %) with less gas bloating (47 vs. 59 %). Propensity-matched cases showed similar GERD-HRQL scores and the differences in ability to belch or vomit, gas and bloating persisted in favor of MSA. Mild dysphagia for MSA (44 vs. 32 %). Resumption of daily PPIs higher for MSA (24 vs. 12, p = 0.02) with similar patient-reported satisfaction rates.

Conclusions MSA for uncomplicated GERD achieves improved 20.6 to 5.0 for MSA vs 22.8 to 5.1 for LNF. Postoperative DeMeester scores (14.2 vs 5.1, p = 0.0016) and the percentage of time pH was less than 4 (64 vs 1.1) (p = 0.0001) were normalized in both groups but statistically different. MSA resulted in improved gas and bloated feelings (3.2 vs 2.36, p = 0.59) and enabled belching in 67% compared with none of the LNFs. MSA results in similar objective control of GERD, symptom resolution, and improved quality of life compared with LNF. MSA seems to restore a more physiologic sphincter that allows physiologic reflux, facilitates belching, and creates less bloating and flatulence.

Factors influencing the outcome of magnetic sphincter augmentation for chronic gastroesophageal reflux disease

Heather F. Warren¹ · Lisa M. Brown² · Mathias Mihura³ · Alexander S. Farivar⁴ · Ralph W. Aye³ · Brian E. Louie³

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Abstract
Objectives Magnetic sphincter augmentation (MSA) is a surgical treatment option for patients with gastroesophageal reflux disease (GERD). MSA consistently improves quality of life, maintains freedom from PPIs, and objectively controls GERD. However, up to 34% of patients did not achieve these outcomes. We sought to identify factors predicting outcomes after MSA placement.

Methods Retrospective case-control study of consecutive patients undergoing laparoscopic Toupet fundoplication versus magnetic sphincter augmentation.

Observational cohort study with propensity score analysis
Emanuele Asti, MD, Gianluca Bognita, MSc, Andrea Lovece, MD, Veronica Lazzari, MD, Luigi Bonavita, MD, PhD, FACS

Received: 23 April 2015 / Accepted: 28 October 2015 / Published online: 5 November 2015 © Springer Science+Business Media New York 2015

Abstract
Longitudinal comparison of quality of life in patients undergoing laparoscopic Toupet fundoplication versus magnetic sphincter augmentation

Emanuele Asti, MD, Gianluca Bognita, MSc, Andrea Lovece, MD, Veronica Lazzari, MD, Luigi Bonavita, MD, PhD, FACS

Only a minority of patients with gastro-esophageal reflux disease (GERD) are offered a surgical option. This is mostly due to the fear of potential side effects, the variable success rate, and the extreme alteration of gastric anatomy with the current gold standard, the laparoscopic Nissen fundoplication. It has been reported that laparoscopic Toupet fundoplication (LTF) and laparoscopic sphincter augmentation using a magnetic device (LINX) can treat reflux more physiologically and with a lower incidence of side-effects and reoperation rate. We present the first comparing quality of life in patients undergoing LTF versus LINX.

Observational cohort study. Consecutive patients undergoing LTF or LINX over the same time period were compared by using the propensity score matching method and generalised estimating equation. Criteria of exclusion were >3 cm hiatal hernia, grade C-D esophagitis, ineffective esophageal motility, body mass index >35, and previous upper abdominal surgery. The primary study outcome was quality of life measured with the Gastro-Esophageal Reflux Disease Health-Related Quality of Life (GERD-HRQL) questionnaire. Secondary outcomes were proton pump inhibitors (PPI) use, presence of gas-related symptoms or dysphagia, and reoperation-free probability.

Results From March 2007 and July 2014, 238 patients with GERD met the criteria of inclusion in the study. Of these, 103 underwent an LTF and 135 a LINX procedure. All patients had a minimum 1-year follow-up. Over time, patients in both groups had similar GERD-HRQL scores (odds ratio [OR] 1.04, confidence interval [CI] 0.99–1.17; P = 0.578). PPI use (OR 1.18, CI 0.81–1.70; P = 0.389), gas-related symptoms (OR 0.69, CI 0.21–2.29; P = 0.5429), dysphagia (OR 0.82, CI 0.29–2.38; P = 0.241), and reoperation-free probability (unstratified log-rank test; P = 0.558).
The Nissen-Hill Hybrid
The Problem – Paresophageal Hernia

- PEH - Nissen
- Oelschlager – 55-59% recurrence @ 5 years
- Dallemagne – 66% recurrence @ 10 years

- PEH – Hill
- Jobe – 57% recurrence @ 5 - 7 years

Jobe: J Gastrointest surg 2002 Mar-Apr;6(2):181-8
Hill failures:
Loosening (2/56)

Nissen failures:
Herniation (2/46)
1. Hiatal Dissection
2. Resection of Hernia Sac
3. Posterior Cruroplasty
4. Hill Suture Placement
   - Anterior Bundle
   - Posterior Bundle
   - Pre-aortic Fascia
   \[ x2 \]
5. Nissen Fundoplication
A Combined Nissen Plus Hill Hybrid Repair for Paraesophageal Hernia Improves Clinical Outcomes and Reduces Long-Term Recurrences Compared with Laparoscopic Nissen Alone

Gal Levy • Ralph W. Aye • Alexander S. Farivar • Brian E. Louie

Abstract

Introduction We compared clinical and objective outcomes of combined Nissen-Hill hybrid (HYB) to Nissen fundoplication (LNF) for repair of paraesophageal hernia (PEH).

Methods This study is a single-institution retrospective chart review of prospectively collected data for consecutive patients undergoing PEH repair from 2006 to 2015 with at least 6 months of follow-up. Quality of life metrics (QOLRAD, HRQL, and dysphagia), manometry, radiographic imaging, and pH testing were administered pre- and postoperatively.

Results With 319 repairs (HYB = 141, LNF = 178), the groups were comparable in age and gender, but HYB had a higher BMI (30.95 vs 29.27, p < 0.05), larger hernia (6 vs 5 cm, p < 0.05), and more Barrett’s esophagus (42 vs 29, p < 0.05). At a median
POST OP QUALITY OF LIFE

<table>
<thead>
<tr>
<th></th>
<th>Hybrid</th>
<th>Nissen</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>90</td>
<td>89</td>
</tr>
<tr>
<td>Median f/u</td>
<td>28 months</td>
<td>20.5 months</td>
</tr>
</tbody>
</table>

**Hybrid Nissen**

- GERD HRQL
  - N=90: 3.75
  - N=89: 7.49
  - P=0.01

- Swallow Function
  - N=90: 40.71
  - N=89: 36.47
  - P=0.01

- QOLRAD
  - N=90: 6.59
  - N=89: 6.23
  - P=0.04

# POST OPERATIVE pH AND PPI USE

<table>
<thead>
<tr>
<th></th>
<th>Hybrid N= 70</th>
<th>Nissen N= 63</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median f/u</td>
<td>28 mo</td>
<td>20.5 mo</td>
<td></td>
</tr>
<tr>
<td>DeMeester</td>
<td>9.6</td>
<td>14.99</td>
<td>0.13</td>
</tr>
<tr>
<td>PPI</td>
<td>2 (2%)</td>
<td>15 (16%)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

LONG TERM FOLLOW UP (>24 mo)

Recurrence

<table>
<thead>
<tr>
<th></th>
<th>Hybrid N=39 (%)</th>
<th>Nissen N=31 (%)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median f/u</td>
<td>61mo</td>
<td>62mo</td>
<td></td>
</tr>
<tr>
<td>Anatomic Recurrence</td>
<td>2 (5%)</td>
<td>14 (45%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Surgical revision</td>
<td>1 (2.6%)</td>
<td>3 (9.7%)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Individualized and Tailored GERD Treatment

- Normal
- NERD
- Acid Suppression
  - Healable Esophagitis
  - Persistent Esophagitis
  - Nissen-Hill Fundoplication
- Barrett’s
  - PEH Repair
    - Short Esophagus – Collis/Nissen Hill
- LINX
  - Nissen

Adapted from Lord et al. J Gastrointest Surg 2009;13:602-610
Conclusions

• Therapy for GERD has more 100% more options than in the past 30 years

• These innovations are surgical

• Innovation based on surgical inquiry provides a framework for future GERD therapies

• A tailored approach to GERD is now feasible
Innovations in Surgical Therapy for GERD: A tale of two therapies

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