Management of Benign Esophageal Disease

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Disclosure Slide

- Consultant for Mallincrodt and Quark Pharmaceuticals unrelated to this talk.

- Research funding from Torax for GERD treatment in lung transplant recipients.
Introduction

- Treatment of GERD
- Surgery for PEH
- Management of Achalasia
- Intervention for other benign esophageal diseases
Treatment for GERD: Medical management

PPI is the most effective management for GERD.

Symptomatic relief in
27% placebo, 60% H2RA, 83% PPI.

Esophagitis healed in
24% placebo, 50% H2RA, 78% PPI.

Some patients have relief from H2RAs.

Higher and more frequent dosing of H2RA is still inferior to PPI.

Treatment for GERD: Medical management

In an era of PPI’s, why do we need invasive therapies?

- Up to 20% of patients with breakthrough symptoms
- Economic expense of chronic medical use
- Newer evidence suggesting complications to long-term PPI use (i.e. malabsorption, CAP, bone fractures, etc.)
- Reflux material may be detrimental
Treatment for GERD: Medical management

- 144 patients with symptoms despite BID PPI therapy
- 48% were suffering from persistent acid reflux or non-acid reflux based on pH/impedance testing

PPI Side Effects Continue to Scare Us To Death

PPI side effects keep accumulating. The latest news relates to liver damage. Will these acid-suppressing drugs attract the FDA's attention any time soon?

https://www.peoplespharmacy.com/2017/10/12/ppi-side-effects-continue-to-scare-us-to-death/
Endoscopic Anti-reflux Procedures
Treatment for GERD: STRETTA

• Pioneered by Dr. David Utley, approved by FDA in 2000.
  – Curon Medical bankrupt in 2006
  – Mederi Therapeutics re-introduces in 2010…just went bankrupt last month…

• RFA (low power, 5 watts)

• LES and gastric cardia remodel and transient LES relaxations decrease

• Takes 45-60 minutes
How Stretta Works

Concentrated energy delivered to tissue  Multi-level thermal treatment remodels LES tissue  Function and GERD symptoms significantly improved

Studies show that symptoms may continually improve for six months or longer. A continuation of anti-secretory medications for two months after Stretta and a modified diet are recommended for two weeks.
Treatment for GERD: STRETTA

Recent Meta-analysis

  - 18 studies over 10 years including 1441 patients.
  - Up to 2 years mean follow-up.
  - Stretta decreased heartburn scores (3.55 to 1.19 pooled)
  - Stretta improved GERD-HRQL
  - pH exposure decreased (DeMeester 44.4 to 28.5) but didn’t normalize.

Results Summary of Meta-Analysis

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Studies (n)</th>
<th>Patients (n)</th>
<th>Mean Follow-up (mo)</th>
<th>Pre-Stretta</th>
<th>Post-Stretta</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td><strong>Subjective Measurements</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>GERD-HRQL</td>
<td>9</td>
<td>433</td>
<td>19.8</td>
<td>26.11</td>
<td>9.25</td>
<td>0.0001</td>
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<tr>
<td>QOLRAD</td>
<td>4</td>
<td>250</td>
<td>25.2</td>
<td>3.30</td>
<td>9.25</td>
<td>0.0010</td>
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<tr>
<td>SF-36 Physical</td>
<td>6</td>
<td>299</td>
<td>9.5</td>
<td>36.45</td>
<td>46.12</td>
<td>0.0001</td>
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<tr>
<td>SF-36 Mental</td>
<td>5</td>
<td>264</td>
<td>10.0</td>
<td>46.79</td>
<td>55.16</td>
<td>0.0015</td>
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<tr>
<td>Heartburn Score</td>
<td>9</td>
<td>525</td>
<td>24.1</td>
<td>3.55</td>
<td>1.19</td>
<td>0.0001</td>
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<tr>
<td>Satisfaction Score</td>
<td>5</td>
<td>366</td>
<td>21.9</td>
<td>1.43</td>
<td>4.07</td>
<td>0.0006</td>
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<tr>
<td><strong>Objective Measurements</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Esophageal Acid Exposure (%Ph&lt;4)</td>
<td>11</td>
<td>364</td>
<td>11.9</td>
<td>10.29</td>
<td>6.51</td>
<td>0.0003</td>
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<tr>
<td>DeMeester score</td>
<td>7</td>
<td>267</td>
<td>13.1</td>
<td>44.37</td>
<td>28.53</td>
<td>0.0074</td>
</tr>
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</table>
Treatment for GERD: EsophyX®

- EndoGastric Solutions Inc.
- FDA approval in 2007
- Currently available
- Provided full thickness, serosa-to-serosa plication via multiple H-fasteners (Avg 22)
- More analogous to surgical fundoplication.
- Requires general anesthesia and up to 2 hours to complete
- 200-300 degree plication
- Has been referred to as
  - Endoluminal Fundoplication (ELF)
  - Transoral Incisionless Fundoplication (TIF)
Treatment for GERD: EsophyX®

- Restores angle of His
- Large overtube advanced over video gastroscope
- “Corkscrew” grasper pulls fundus tissue down into retroflexed t-fastener device.
- H-fasteners plicate fundus to create a neo-GEJ
Treatment for GERD: EsophyX®

The TEMPO Trial at 5 Years: Transoral Fundoplication (TIF 2.0) Is Safe, Durable, and Cost-effective

https://doi.org/10.1177/1553350618755214

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline (before TIF on PPIs)</th>
<th>6 months (off PPIs)</th>
<th>12 months (off PPIs)</th>
<th>P value (6 months vs. baseline)</th>
<th>P value (12 months vs. baseline)</th>
<th>P value (6 vs. 12 months)</th>
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</thead>
<tbody>
<tr>
<td>RDQ</td>
<td>2.91 (1.32)</td>
<td>0.35 (0.53)</td>
<td>0.50 (0.73)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.772</td>
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<td>Heartburn RDQ</td>
<td>2.99 (2.55)</td>
<td>0.45 (0.86)</td>
<td>0.63 (1.01)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.776</td>
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<tr>
<td>GERD-HRQL</td>
<td>26.25 (10.51)</td>
<td>5.23 (7.14)</td>
<td>5.41 (6.80)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.995</td>
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<tr>
<td>Heartburn GERD-HRQL</td>
<td>17.69 (7.51)</td>
<td>3.74 (5.51)</td>
<td>3.76 (4.50)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&gt;0.999</td>
</tr>
</tbody>
</table>

GERD-HRQL, gastroesophageal reflux disease health-related quality of life; PPI, proton pump inhibitor; RDQ, Reflux Disease Questionnaire; TIF, transoral incisionless fundoplication.
Treatment for GERD: EsophyX®

The TEMPO Trial at 5 Years: Transoral Fundoplication (TIF 2.0) Is Safe, Durable, and Cost-effective

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Figure 6. Percentage of patients on daily proton-pump inhibitor (PPI) therapy at screening and 1-, 3-, and 5-year follow-up assessments.
Surgical Anti-reflux Procedures
Treatment for GERD: Surgical Fundoplication

- Rudolph Nissen first performed “gastroplication” in 1955.
- Large body of literature with over 500 peer reviewed publications since that time.
- Variations including partial (DOR, TOUPET) and complete wraps (NISSEN).
- Techniques include open, laparoscopic, and robotic
Treatment for GERD: Surgical Fundoplication

• Indications for surgery in patients who have:
  – Failed medical management (persistent symptoms, medication intolerance).
  – Successful medical management but opt for surgery instead of chronic medication
  – Complications of GERD (strictures, Barrett’s, non-healing esophagitis)
  – Regurgitation
  – Extra-intestinal manifestations
    • Cough, asthma, aspiration, etc.
Treatment for GERD: Surgical Fundoplication

• Medical versus Surgical Treatment
  – At least 7 randomized, controlled trials with follow-up from 1-10.6 years
  – 6 of 7 showed objective evidence of decreased acid exposure and increased LES pressure
    • Only the Spechler JAMA article did not, which was underpowered
  – Multiple studies showed comparable to improved QOL with surgery and high patient satisfaction rates
    • Only 1 randomized study did not…the Spechler JAMA article…
  – Majority of literature suggests 10-20% PPI use up to 8 years after surgery
    • One randomized study reported PPI use at 62% at 10 years…the Spechler JAMA article…

Treatment for GERD: Surgical Fundoplication

- Medical versus Surgical Treatment
Treatment for GERD: Surgical Fundoplication

• Medical versus Surgical Treatment Cost Analysis
  -- One randomized trial looked at cost-effectiveness
    -- Total Rx costs less at 5 years in 3 countries, more in 1 (Finland)
    -- Open, instead of laparoscopic nature of the procedure
    -- European cost analysis may not be applicable
  -- Cost-utility modeling suggests breakpoint in favor of surgery at 10 years.
Treatment for GERD: Surgical Fundoplication

- **LOTUS Trial**
  - Randomized, open trial in Europe between 2001-2009 with 5 year follow-up.
  - 554 patients randomized to esomeprazole (allowing for dose escalation) or surgery (standardized of technique).
  - Only PPI responders randomized for the study.
  - At 5 years, K-M estimates of treatment failure were 85% in the surgical group, compared to 92% in the PPI cohort.
Treatment for GERD: Surgical Fundoplication

• The Learning Curve and Surgical Volumes
  – High volume centers have decreased complications and conversion rates, especially for reoperative antireflux surgery.

Treatment for GERD: Linx Reflux Management System®

- Anti-reflux prosthesis approved by FDA in 2012
  - Torax Medical Inc.
  - Laparoscopically placed around GEJ.
  - Miniature string of inter-linked titanium beads with magnetic cores
  - Beads can temporarily separate to allow swallowed bolus, allow belching, etc.
  - Procedure takes less 60 minutes
Treatment for GERD: Linx Reflux Management System®

Normal Peristaltic Pressures
35-80 mm Hg

LINX® System
20-25 mm Hg

Gastric Pressures
5-10 mm Hg

CLOSED to Reflux

OPEN to Swallowing
Treatment for GERD: Linx Reflux Management System®
GERD-HRQL Score off PPI

- **Feasibility**
- **Pivotal**

N=100
N=44
N=98
N=37
N=98
N=33
N=95
N=39
N=90
N=35
N=27

BL Off PPI 3 Month 6 Month 12 Month 24 Month 36 Month
Minimally Invasive Foregut Surgery

• Why do it?
  – Laparoscopic is better than open (laparotomy or thoracotomy)\(^1\)
  – Yet many are still offered open surgeries

Minimally Invasive Foregut Surgery

• Why do it?
  – We need to do laparoscopic better.
  – PEH: 57% recurrence rate at 5 years\(^1\)

Minimally Invasive Foregut Surgery

Why do it?
- We need to do laparoscopic better.
- GPEH: 33% radiographic recurrence rate at 1 year\(^1\)
- But GERD-HRQL better in operative group

Prospective study of giant paraesophageal hernia repair with 1-year follow-up

John R. Stringham, MD,\textsuperscript{a} Jennifer V. Phillips, RN,\textsuperscript{a} Timothy L. McMurry, PhD,\textsuperscript{b} Drew L. Lambert, MD,\textsuperscript{c} David R. Jones, MD,\textsuperscript{d} James M. Isbell, MD,\textsuperscript{d} Christine L. Lau, MD,\textsuperscript{a} and Benjamin D. Kozower, MD, MPH\textsuperscript{e}

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Robotic Foregut Surgery

Why do it? The data for robotic giant PEH repair.

- Single center series: 14 patients underwent robotic giant PEH repair.¹
  - No deaths or robotic related morbidity
  - Felt to be superior for hiatal dissection
- Single center series: 40 patients with large PEH underwent robotic repair with 1 year follow-up.²
  - Subjectively, surgeons felt robotics was helpful
  - Relatively low recurrence rate

Robotic Foregut Surgery

• How do we do it? Everytime
  – Complete resection of the hernia sac from mediastinum.
  – Adequate esophageal mobilization
  – Proper hiatal closure
  – Fundoplication (?)
Robotic Foregut Surgery

• How do we do it? Sometimes
  – Anterior gastropexy
  – Crural mesh augmentation
  – Esophageal lengthening (wedge gastroplasty)


How do we do it? Set-up

Caveats

- Phase shift cephalad for mediastinal dissection (12cm subxiphoid)
- Port selection can depend upon OR staff
- 8 cm minimum between robot ports
- Narrow or thick abdomen may benefit from long robot ports
Diverticulum Dissection
Myotomy and Fundoplication
Achalasia

Laparoscopic Heller Myotomy as the Gold Standard for Treatment of Achalasia

Peter Nau · David Rattner

• Over the last 20+ years laparoscopic heller myotomy has become the gold-standard therapy for achalasia

Known, Knowns...

- Durability of symptom relief 90%+ for LHM at 2 years based on level 1 evidence.

Pneumatic Dilation versus Laparoscopic Heller's Myotomy for Idiopathic Achalasia

Guy E. Boeckxstaens, M.D., Ph.D., Vito Annese, M.D., Ph.D., Stanislas Bruley des Varannes, M.D., Ph.D., Stanislas Chaussade, M.D., Ph.D., Mario Costantini, M.D., Ph.D., Antonello Cuttiita, M.D., J. Ignasi Elizalde, M.D., Uberto Fumagalli, M.D., Ph.D., Marianne Gaudric, M.D., Ph.D., Wout O. Rohof, M.D., André J. Smout, M.D., Ph.D., Jan Tack, M.D., Ph.D., Aeilko H. Zwinderman, Ph.D., Giovanni Zaninotto, M.D., Ph.D., and Olivier R. Busch, M.D., Ph.D. for the European Achalasia Trial Investigators*

Known, Knowns…

- Even at 10-15 years success after LHM is over 80%

Four Hundred Laparoscopic Myotomies for Esophageal Achalasia

A Single Centre Experience

Giovanni Zaninotto, MD, FACS,* Mario Costantini, MD,† Christian Rizzetto, MD,‡ Lisa Zanatta, MD,† Emanuela Guirroli, MD,† Giuseppe Portale, MD,† Loredana Nicoletti,† Francesco Cavallin, PhD,‡ Giorgio Battaglia, MD,† Alberto Ruol, MD, FACS,† and Ermanno Ancona, MD, FACS‡

Known, Knowns…

- GERD after myotomy leads to worse long-term outcomes and the incidence of GERD after LHM is VERY high at nearly 50%...if you don’t do a fundoplication.

Heller Myotomy Versus Heller Myotomy With Dor Fundoplication for Achalasia

A Prospective Randomized Double-Blind Clinical Trial

William O. Richards, MD,* Alfonso Torquati, MD, MSCI,* Michael D. Holzman, MD, MPH,* Leena Khaitan, MD, MPH,* Daniel Byrne, MS, † Rami Lutfi, MD,* and Kenneth W. Sharp, MD*

Known, Knowns…

• BUT, the incidence of GERD after LHM is VERY low at 8% when a fundoplication is performed.


FIGURE 6. Distal esophageal acid exposure in the 2 groups. Data are shown as median (horizontal line), interquartile range (box), and 5th to 95th percentile (vertical line). *P = 0.001 versus Heller plus Dor.
POEM

• First procedure: Harujiru Inoue, Japan, 2008

• First publication of results in 17 patients by Dr. Inoue in 2010

Inoue et al. Endoscopy 2010
POEM: TECHNIQUE
POEM: TECHNIQUE
POEM: TECHNIQUE
POEM: TECHNIQUE
POEM: LONGER TERM OUTCOMES

Clinical outcomes five years after POEM for treatment of primary esophageal motility disorders

Ezra N. Teitelbaum¹ · Christy M. Dunst¹ ² · Kevin M. Reavis¹ ² · Ahmed M. Sharata² · Marc A. Ward¹ · Steven R. DeMeester¹ ² · Lee L. Swanström¹ ² ³

• Only 27 patients, of 36 had f/u
• Symptomatic success at 5 years: 83%, but 10% of followed patients required reintervention less than 5 years, and another 20% were being evaluated for reintervention.
• Significant continued reduction in Eckardt score (6.4 pre-POEM vs 1.7 current; p<0.001)

POEM: LONGER TERM OUTCOMES

Clinical outcomes five years after POEM for treatment of primary esophageal motility disorders

Known, Knowns…

- As you would expect, the incidence of GERD after POEM is VERY high because there is no fundoplication.
  - GERD evidenced by pH monitoring (OR 4.30, 95% CI 2.96–6.27, P<0.0001). On average (48% for POEM)
  - GERD evidenced by erosive esophagitis (OR 9.31, 95% CI 4.71–18.85, P<0.0001) (23% for POEM)

Laparoscopic Heller Myotomy Versus Peroral Endoscopic Myotomy (POEM) for Achalasia

A Systematic Review and Meta-analysis

Francisco Schlottmann, MD,* Daniel J. Luckett, BS,† Jason Fine, ScD,† Nicholas J. Shaheen, MD, MPH,‡ and Marco G. Patti, MD*
Conclusions

• KNOWN, KNOWNs
  – LHM remains the gold standard therapy for achalasia, but POEM’s short term results demonstrate equal efficacy at relieving dysphagia.
  – LHM creates minimal amounts of GERD when done concomitantly with a fundoplication
  – GERD sequelae following POEM are significant

• KNOWN, UNKNOWNs
  – POEM may be superior in subsets of achalasia
  – POEM as it evolves will likely replace current procedures