Options for Gastroesophageal Reflux: Endoluminal

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Montefiore Medical System and the Albert Einstein School of Medicine
The patient with GERD
Prescribe the power of PREVACID™
LANSOPRAZOLE 15 mg and 30 mg capsules 20
PROVEN PROTON PUMP INHIBITOR
✓ Power to relieve the pain of erosive esophagitis
Median percentage of nights patients were free from heartburn:

<table>
<thead>
<tr>
<th>Week 2</th>
<th>Week 3</th>
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✓ Power to heal erosive esophagitis effectively
PREVACID 20 mg once a day healed 93% of patients with erosive esophagitis in 8 weeks.

✓ Now PREVACID can be sprinkled!
Patients who have difficulty swallowing capsules can open the capsule, sprinkle the granules on a tablespoon of applesauce, and swallow it immediately. The granules should not be chewed or crushed.

In short-term clinical trials, adverse events reported were similar among patients who received PREVACID and placebo, including diarrhea, abdominal pain, and nausea.

PREVACID should not be used as a maintenance therapy for patients with erosive esophagitis and hiatal hernia. If symptoms persist, treatment with a proton pump inhibitor may be necessary. PREVACID is not recommended in patients with known hypersensitivity to any component of the formulation. For further information, consult the prescribing information, available at 1-800-HELP-247.

Place the intended number of granules in the desired volume of capsules on the following pages.
The Therapy Gap

Effectively Treated with PPI

Not Effectively Treated With PPI

- Long-term PPI use
- Continued Heartburn
- Regurgitation
- Nocturnal Breakthrough

Treatment Gap

Nissen Impact

Severity of Symptoms and Dissatisfaction

Low

High
New Options for Gastroesophageal Reflux

• Old Options (lifestyle, diet and medical Rx)
• Radio Frequency Energy Application to the Gastroesophageal Junction (Stretta)
• Transoral Endoscopic Plication
  – Endocinch, NDO
• Transoral Incisionless Fundoplication:
• Mechanical Barriers
• Injection of Biomaterials (Enteryx)
• Laparoscopic Magnetic Augmentation
• Nissen Fundoplication
stretta™
A new, minimally invasive treatment for GERD

www.curonmedical.com
Stretta: Procedure

- Outpatient Endoscopy Procedure
- Placement of catheter at GE junction
- Rfe Application, 45 degree rotation
- 8 applications, 2cm below, 6 above GE jxn
- Repeat endoscopy
- Total time about one hour
- Few complications reported
Long Term data

• 50 pts referred for surgery, Stretta
• 32 pts with long term f/u (53 months)
• 19 of 32 underwent ARF surgery for sxs
• 13 responders had improved GERD QoL and Symptom score

Long Term data

- 108pts 4 year f/u
- 96 pts at 48 months
- Heartburn Scores 3.6 to 1.8*
- GERD QoL 27.8 to 7.1*
- Medication usage 100% to 75%
  Noar, et al. GIE, March, 2007

- 83 pts at 48 months follow up
- GERD symptom score 24 to 4.3*
- GERD QoL 2.7 to 0.6*
- Medication 100% to 13.6%*
Stretta New Data

- 48 month followup, multi center, Europe
- 56 pts evaluated (69 pts treated)
- GERD and HRQL improved significantly
- 41 of 56 were off PPIx
- Appears that Stretta is effective and durable

- Dughera, etal., 2011
<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>
</tr>
</thead>
<tbody>
<tr>
<td>GERD-HRQL score</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 score</td>
<td>4</td>
<td>250</td>
<td>25.2</td>
<td>3.30</td>
<td>4.97</td>
<td>0.0010</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>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>
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<tr>
<td>LES pressure</td>
<td>7</td>
<td>263</td>
<td>8.7</td>
<td>16.54</td>
<td>20.24</td>
<td>0.0302</td>
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</table>

Table 1: Comparison of Pre-Operative and Latest Post-Operative Observations of the Study Parameters

Banarjee, Perry, Melvin, Surg Lap Endo Perc Tech, 2012
No Evidence for Efficacy of Radiofrequency Ablation for Treatment of Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis.

- Evaluated 4 trials and evaluated 153 pts
- No improvement compared to sham or ppi
- No change in pH or HRQL

- Clin Gastro Hepatol, 2014
- Lipka S, Kumar A, Richter J.
Economics

- Approved by the FDA in 2000
- CPT code assigned in 2004 (43257)
- Curon bankrupt in December 2006
- Technology Acquired
- Currently Available, Mederi Therapeutics
- Available worldwide for clinical use
Esophyx:
Transoral Incisionless Fundoplication

• Approved for US in Sept 2007
• Over the scope fundoplication device
• Under direct vision
• Full thickness anchoring devices
• Reduce small Hiatal Hernias
• General anesthesia, short stay
• Gaining long term experience
Esophyx at Ohio State

• Single institution prospective study all pts undergoing EsophyX Sept 07 - March 09

• Demographics, procedure related complications

• Outcomes:
  – safety
  – symptomatic improvement: symptom scores (Anvari) and HRQL (Velanovich) and PPI use
Results: Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Preop</th>
<th>Postop</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRQL (Velanovich)</td>
<td>22 (13)</td>
<td>8 (7)</td>
<td>0.002</td>
</tr>
<tr>
<td>Symptom Score (Anvari)</td>
<td>34 (14)</td>
<td>16 (15)</td>
<td>0.004</td>
</tr>
<tr>
<td>Medication use</td>
<td>100%</td>
<td>65%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>41% preop 24% half dose</td>
<td></td>
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</table>
Esophyx Data

- 37 consecutive pts with GERD
- 68% respiratory symptoms
- All underwent TIF, endoscopically
- 2 complications
- 6 month follow up:
  - 82% no drugs, 54% no symptoms, 21% better
  - 5 (13.5%) had LS nissen for failure
Esophyx : Long Term

- 38 pts with three year follow up (56% pts had hiatal hernia)
- One peri op bleeding
- 14 pts (36%) underwent ARF surgery
- Remaining pts QOL scores improved
- 76% off meds
- In subset results were satisfactory
Esophyx: Multicenter Registry

• Prospective data collection: 100 patients
• No procedural complications.
• 6-month f/u:
  • GERD HRQL normalized 73%
  • Reflux Symptom Score Median 24 to 7
  • pH normalized in 54% (15 out of 28)
• Safe, good symptom control
  – Bell RW, et al, JACS 2012
# Meta Analysis

<table>
<thead>
<tr>
<th>Measurement</th>
<th>No. Studies</th>
<th>Total Patients</th>
<th>Average Decrease</th>
<th>Mean Follow-up (Months)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>GERD-HRQL score</td>
<td>9</td>
<td>325</td>
<td>20.6</td>
<td>8.2</td>
<td>0.0001*</td>
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<tr>
<td>RSI Score</td>
<td>2</td>
<td>133</td>
<td>23.3</td>
<td>6.8</td>
<td>0.1026</td>
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<tr>
<td>Continued PPI use</td>
<td>9</td>
<td>320</td>
<td>25.0%</td>
<td>9.2</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Hiatal hernia incidence</td>
<td>3</td>
<td>63</td>
<td>36.0%</td>
<td>7.5</td>
<td>0.2423</td>
</tr>
<tr>
<td>Mean LES pressure</td>
<td>3</td>
<td>103</td>
<td>-5.0 mmHg</td>
<td>10.1</td>
<td>0.0762</td>
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<tr>
<td>Esophageal Acid Exposure Time (% time ph &lt;4)</td>
<td>3</td>
<td>99</td>
<td>2.8%</td>
<td>10.0</td>
<td>0.2027</td>
</tr>
<tr>
<td>DeMeester Score</td>
<td>3</td>
<td>107</td>
<td>7.7</td>
<td>10.0</td>
<td>0.2008</td>
</tr>
<tr>
<td>Number of acid refluxes</td>
<td>4</td>
<td>61</td>
<td>22.1</td>
<td>6.7</td>
<td>0.3066</td>
</tr>
</tbody>
</table>
TIF for Regurgitation

- Multicenter trial, randomized blinded sham controlled vs, BID Prilosec
- Symptoms scores, pH studies and evaluations at 2, 12 and 26 weeks
- Reduced regurgitation (67 vs 45% p=.023)
- pH improved with TF more than sham
- GERD symptoms were reduced in both

New Data Collection

- AGA sponsored STAR Registry
- Comparing TIF to Nissen in patients with troublesome GERD
- Case control data registry
- First pt enrolled in 2014, three year plan
Medigus/ MUSE

- 11SRS vs 16 Lap Nissen
- Safe efficient use
- Shorter OR time
- No diff in PPI
- No difference in HRQL

SRS/MUSE, Multicenter

- 69 pts, 6 sites, 6 month follow up
- GERD HRQL, > 50% Improvement in 73%
- Off PPIs: 42% none
- Total time pH < 4.0, mean decreased (p.001)
  - pH upright, supine, and total episode #, n.s.
- 1 post op bleed, 1 perf (Chest tube)

SRS/MUSE Medigus

- FDA approved, Q1 2014
- International registry underway
- Available in select centers currently
- Data will accumulate
- Reimbursement and finances are important
Endoluminal Fundoplication

- Finances are important
- 2014: Not widely funded, considered “experimental”
- February 2015 CPT assigned
- RUC evaluation is ongoing
- Will become active January 2016
LINX™ ANTI-REFLUX SYSTEM

Magnetic Sphincter Augmentation
Lynx Economics

- About 7000 sold and installed
- A few explantations, no late erosions
- Appears Safe
- CPT 2015 is a Category 3
- Not widely reimbursed
- Difficult to use clinically right now
Clinical Spotlight Review: Endoluminal GERD

2/2013
by the Society of American Gastrointestinal and Endoscopic Surgeons

• **EsophyX**
  - Long term data is not yet available for EsophyX. In short term follow-up, from 6 months to 2 years, EsophyX may be effective in patients with typical and atypical GERD. Further studies are required to define optimal techniques and most appropriate patient selection criteria…
  - Quality of Evidence: (++). GRADE Recommendation: Weak

• **Stretta**
  - Stretta is considered appropriate therapy for patients being treated for GERD who are 18 years of age or older, who have had symptoms of heartburn, regurgitation, or both for 6 months or more, who have been partially or completely responsive to anti-secretory pharmacologic therapy, and who have declined laparoscopic fundoplication.
  - Quality of Evidence: (++++) . GRADE Recommendation: Strong
Surgical therapy is a treatment option for long-term therapy in GERD patients. (Strong recommendation, high level of evidence)

Surgical therapy is generally not recommended in patients who do not respond to PPI therapy. (Strong recommendation, high level of evidence)

Preoperative ambulatory pH monitoring is mandatory in patients without evidence of erosive esophagitis. All patients should undergo preoperative manometry to rule out achalasia or scleroderma-like esophagus. (Strong recommendation, moderate level of evidence)

Surgical therapy is as effective as medical therapy for carefully selected patients with chronic GERD when performed by an experienced surgeon. (Strong recommendation, high level of evidence)

Obese patients contemplating surgical therapy for GERD should be considered for bariatric surgery. Gastric bypass would be the preferred operation in these patients. (Conditional recommendation, moderate level of evidence)

The usage of current endoscopic therapy or transoral incisionless fundoplication cannot be recommended as an alternative to medical or traditional surgical therapy. (Conditional recommendation, moderate level of evidence)
GERD Treatment: The Bottom Line

- PPI’s for most pts
- Mechanical reconstruction of the GE jxn offers the best acid and bile reflux control
- Transoral fundoplication is promising and emerging as option for pts with normal anatomy
- Stretta is now available and data suggests good symptom control in many patients
- Magnetic Augmentation provides excellent early results
- LS Nissen is very good with ~90% good success, 80-90% off meds.
- Barretts ablation and reflux control may decreasing the risk of esophageal cancer.
- Evaluation of objective data including costs is important