Chronic GERD: Opportunities for Collaborative Shared Decision-Making and Health Services Research

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Goals

• Introduce JH Heartburn Center
• Provide brief overview of treatment choices for chronic GERD and treatment of its complications (Barrett’s esophagus)
• Discuss opportunities for developing a shared decision-making process and health services research
GERD is the most common chronic GI disease

- GERD prevalence 8%-33% of adults in worldwide
- Definition: heartburn and/or regurgitation at least weekly
- LPR = laryngopharyngeal reflux (throat clearing, excess mucus, lump, sore throat, chronic cough, mild hoarseness)

El-Serag HB, Gut 2014;63:871-80
Gastroesophageal Reflux Disease (GERD)

- Affects 20% of the U. S. population
- Increasing incidence: obesity epidemic
- High cost: hospitalizations, medications (billions)
- Complications: esophagitis, stricture, Barrett’s esophagus (precancerous), esophageal cancer, asthma, hoarseness, laryngitis, pneumonia, chronic lung disease
- Impacts quality of life
Heartburn Center of Excellence
Mission Statement

• To provide efficient, high quality multidisciplinary *patient-centered* care for patients with GERD and its complications

• To conduct clinical trials, outcomes/comparative effectiveness studies, and translational research related to patients
Our Team

- **Gastroenterology**: 13 providers
  - Columbia (Knoll North): Canto, Gupta, Abdi, Badurdeen, Chowdhury
  - Baltimore (Green Spring Station): Mathews, Khashab
  - Baltimore (Bayview Medical Center): Ngamrhuengphong, Brewer
  - Baltimore (Johns Hopkins Outpatient Center): Shin
  - White Marsh: Veloso, Gonzalez
  - Washington DC: Kumbhari

- **Surgery** – 7 providers
  - Baltimore (Green Spring Station): Adrales
  - Baltimore (Johns Hopkins Outpatient Center): Coker, Marohn, Akst (ENT)
  - Howard County (Columbia): Schwartz
  - Washington DC: Broderick, Lamond

- **Radiology**: Fynes

- **Pathology**: Voltaggio, Montgomery

- **Nursing/NP**: (4) Baumann, Dunlap, Koller, Carpino
Types of Patients
GERD and LPRD

• Symptomatic typical and atypical GERD
  – PPI-averse or intolerant
  – Refractory GERD
  – Atypical chest pain syndromes
  – Postoperative (fundoplication)

• Extra-esophageal syndromes (LPRD)
  – Globus, throat pain, cough, asthma
  – Chronic laryngitis, dental erosion
GERD in Special Populations

- Barrett’s esophagus
- Bariatric patients
- Pulmonary
  - Chronic interstitial lung disease (CILD)
  - Asthma
  - Post lung transplant
Types of Patients Swallowing Problems

- Esophageal strictures due to reflux, radiation, surgical resection, endoscopic BE therapy, esophageal lichen planus
- Eosinophilic esophagitis
- Zenker’s diverticulum
- Primary achalasia
SDM in Gastroenterology

• No study involving GERD patients
• 2010-2019: 25 papers
• IBD: therapeutic agents
• Colorectal cancer screening
• Hepatitis C treatment
GERD Medical Management

• Diet and lifestyle changes
  – Avoid meals before bedtime
  – Weight loss
  – Elevate head of bed (Medcline pillow (5 clinical trials: 85% more effective than standard wedge or raising head of bed))

Kaltenbach T, Arch Intern Med 2006;166:965-71
GERD Medical Therapy

• Take anti-acid medications daily for symptoms > 2-3x/week
• PPI’s are 3rd most commonly prescribed drug (after statins and anti-psychotics)
  ->100 M prescriptions, but OTC use cannot be estimated accurately
• < 50% of GERD pts. satisfied with Tx
• Increasing concern about chronic PPI AEs
Concerns with PPIs
Few good studies for causal relationship

- *Bacterial astroenteritis (2-6x) or C. difficile colitis (up to 3x) – moderate evidence*
- Small intestinal bacterial overgrowth - weak
- Decreased absorption of iron, calcium, B12 - weak
- Bone fractures of hip, wrist, and spine - weak
- Chronic kidney disease - weak
- Dementia – weak
- Pneumonia – no evidence
GERD Medical Therapy: PPIs

• Empiric trial if no alarm symptoms

• “Refractory GERD”: incomplete or lack of a response to once daily PPI (about 40%)
  – 25% of cough and LPR symptoms
  – 26-44% of regurgitation
  – Atypical symptoms

Wilder-Smith C, Aliment Pharmacol Ther 2010;32:1249-56
Patient Anatomy Influences Potential Treatment Options

Hansdotter, Endosc Int Open 2016
Surgical Fundoplication

Surgery is effective in 90% for symptom resolution

Nissen fundoplication provides a 360° posterior wrap

Toupet fundoplication provides a 270° posterior wrap

Surgery – excellent alternative to medications, not perfect

- Patient satisfaction 15 years – 85%
- Durability = 80-90% at 15 years, 75% at 20 years
- Medication use in up to 40% 5 yrs post op
- Problems:
  - gas-bloat 5-34%
  - dysphagia 3-17%
- Prolonged recovery
LNF failures may be difficult

• 20% of primary LNF fail
• Operative re-do Nissen are difficult, tedious, place vagus nerve at risk due to adhesiolysis
• Intra-op esophageal/gastric injury in 13%
• Overall Cx rate = 14% (0-55%)
• Success of re-do in 78% (< than primary LNF)
• Average life span 8-10 years
Transoral Incisionless Fundoplication
How does TIF work?

EsophyX device reconfigures GEV through series of plications

EsophyX device delivers SerosaFuse “H” fasteners to fixate plications

End result is 2 to 3 cm by ~270° valve, similar to anterior Toupet LNF

Gastroenterology March 2015
Transoral Incisionless Fundoplication (TIF) – Esophyx

Reconstruct LES via full thickness plication and ligation to create a 2-3 cm long 270 deg *anterior* wrap under complete endoscopic guidance.
TIF versus LNF
Endo View of GEJ and Valve

TIF

Lap Nissen

Bell, Surg Endosc, 2012
Indications for TIF

• Candidates
  – Refractory GERD/LPRD
  – PPI responsive but averse

• Exclusions:
  – Morbidly obese BMI > 35
  – HH > 2 cm
  – Hill grade 3 and 4
  – Grade D esophagitis
  – Motility disorder
Patient Selection

• PPI-responsive but refractory (to daily PPI)
  – Heartburn versus regurgitation
  – Extra-esophageal symptoms (LPRD) – globus, sore throat, hoarseness, cough

• PPI-intolerant: adverse effects (diarrhea)

• PPI-averse
Transoral Incisionless Fundoplication (TIF) – Esophyx

- **Two operator endoscopic procedure (20 studies)**
- 6-month RESPECT trial: RCT TIF + placebo vs. sham + PPI (crossover); 100 patients
  - TIF superior for eliminating *regurgitation*
  - (+) decreased esophageal pH (9.3% to 6.3%)
- 6-year follow-up: durable results, no PPI in 85%
- TIF vs LNF: equal, but shorter hospital stay (2.9 vs. 6.4 days, p < 0.0001)

Hunter, Kahrilas, Bell, Gastroenterology 2016
Testoni, Surg Endosc 2015
Transoral Incisionless Fundoplication (TIF) – Esophyx

- 6-month TEMPO RCT: TIF vs. PPI in 7 community hospitals
- 63 patients (40 TIF, 23 PPI)
- Regurgitation eliminated in 97% TIF (50% PPI)
- Regurg + extra-eso Sx 62% TIF vs. 5% PPI
- 90% of TIF off PPIs

Trad, Surg Innov 2015
TIF Economic Analysis
Overall Health Care Utilization

• CPT 43210 – Medicare reimbursement + major
  – Esophagogastric fundoplasty
  – May be combined with lap hiatal hernia repair same session

• TEMPO trial: using Optimum Healthcare data

• At 2 years after TIF:
  – Lower expenditure for TIF ($66,000) vs. LNF ($124,000)
Advantages of Endoscopic TIF

- High HRQL, improved GERD symptoms
- Like LNF, excellent results for high volume reflux
- Outpatient procedure under GA (endo unit)
- Short procedure time 35-45 minutes
- Learning curve short, about 10 procedures
- Fewer adverse effects, early return to work
- Re-intervention rate low, but repeat TIF easy
- Does not impede rescue LNF
- Can be combined with large HH repair in O.R.
Cons of Endoscopic TIF

• Not as readily available as LNF (therapeutic GI or surgeons who perform endoscopy) – about 100 centers in U.S.
• 7 RCTs, relatively small numbers (40-100)
• Limited long-term data, durability uncertain
Laparoscopic Linx Procedure
Magnetic LES Augmentation

- FDA approved 2012 (Torax Medical)
- Augment LES with ring of magnets (*no MRI*)
- Increase LES pressure
- *Removable*
- *No MRI > 1.5T*
Laparoscopic Magnetic Sphincter Augmentation (LINX)

- 5 year outcomes in 100 patients
- Main outcome (normal pH/ 50% reduction): 64%
- Secondary outcomes:
  - 93% with reduction of PPI >=50%
  - 93% improved GERD HRQL
  - 12% mod-severe HB, 1% regurg (improved)
- AE: 8% gas bloat, dysphagia; erosions
- LINX surgically removed in 3-4% (dysphagia)
- Less gas bloat & dysphagia than LNF
Laparoscopic Magnetic Sphincter Augmentation (LINX)

- Only RCT sponsored by Torax Medical - LINX (47) vs BID PPI (101) for refractory mod-severe regurgitation (foregut symptom questionnaire)
- Inclusion/Exclusion: BMI < 35, HH ≤ 3cm, (+) acid pH, no abnormal motility, BE or Grade C/D esophagitis

Bell, GIE 2019
Laparoscopic Magnetic Sphincter Augmentation (LINX)

- Short-term outcomes (6 months)
- Adverse events: dysphagia in 32%, 4% ongoing and severe

Bell, GIE 2019
Patient Selection for GERD Therapy

PPI
Stretta

Normal, no HH
TLESR
Upright refluxer
NERD

PPI
TIF

Upright + supine reflux
↓LES pressure
Hill grade 1-2
HH< 2cm

PPI
TIF
LNF

Regurgitation
LPRD

TIF: HH< 2cm
Hill 1-2

LNF: HH≥2cm
Hill > 2

PPI
LNF, crural repair

Para-esoph Hernia
## Efficacy Comparisons (No RCT)

<table>
<thead>
<tr>
<th></th>
<th>LNF (Surgery)</th>
<th>Endoscopy</th>
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</thead>
<tbody>
<tr>
<td>GERD symptom/HQRL improvement</td>
<td>90%</td>
<td>86%</td>
</tr>
<tr>
<td>6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off PPI 6 months</td>
<td>80%</td>
<td>80%-90%</td>
</tr>
<tr>
<td>Objective testing – 24 hr acid</td>
<td>N or imp</td>
<td>N or imp</td>
</tr>
<tr>
<td>exp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GERD symptom/HQRL improvement</td>
<td>87%</td>
<td>73%</td>
</tr>
<tr>
<td>5 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off PPI 5 years</td>
<td>34-91%</td>
<td>86%</td>
</tr>
<tr>
<td>Patient satisfaction at 5 years</td>
<td>80-96%</td>
<td>70-80%</td>
</tr>
<tr>
<td>Durability at 15-20 years</td>
<td>64-80%</td>
<td>NA</td>
</tr>
<tr>
<td>Off PPI at 17 years</td>
<td>60%</td>
<td>?</td>
</tr>
<tr>
<td>Need for re-intervention</td>
<td>16% for GERD</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>or dysphagia</td>
<td></td>
</tr>
</tbody>
</table>
### Non-Medical Treatment Options for GERD
#### Review of Factors Influencing Patient Choice

<table>
<thead>
<tr>
<th>Risks</th>
<th>LNF (Surgery)</th>
<th>Endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incision (pain)</td>
<td>Laparoscopic; conversion in 3%</td>
<td>None</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>0.2%</td>
<td>None</td>
</tr>
<tr>
<td>Morbidity</td>
<td>4.7-11% (early wrap herniation, pneumothorax, bowel perforation, wound infection, splenectomy, diarrhea)</td>
<td>Mild sore throat, chest pain, shoulder pain x 3-7 days</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>Post op 50%, may last 2-3 months; 3-17% dilation</td>
<td>None</td>
</tr>
<tr>
<td>Gas-bloat; excess flatus</td>
<td>5-34%</td>
<td>None</td>
</tr>
<tr>
<td>Inability to vomit</td>
<td>25%</td>
<td>None</td>
</tr>
</tbody>
</table>
## Non-Medical Treatment Options for GERD
### Review of Factors Influencing Patient Choice

<table>
<thead>
<tr>
<th>Recovery</th>
<th>Surgery</th>
<th>Endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital stay</td>
<td>6.4 days</td>
<td>None-2 days</td>
</tr>
<tr>
<td>Recovery: diet to minimize dysphagia</td>
<td>6-12 weeks: liquids, pureed, soft; 5-6 “meals” per day, prolonged chewing</td>
<td>2 weeks: liquids, soft</td>
</tr>
<tr>
<td>Return to work</td>
<td>1-2 weeks</td>
<td>1-3 days</td>
</tr>
<tr>
<td>Activity: exercise, weight lifting</td>
<td>None &gt; 10 lbs first 3 weeks, &gt; 25 pounds for 3 months, &gt; 50 pounds for life</td>
<td>Same</td>
</tr>
</tbody>
</table>
Challenges in Endo GERD Tx Research

• No direct comparisons between surgery or endoscopy (Level 1 evidence); meta-analyses (flawed)

• AGA-sponsored RCT LNF vs. TIF unsuccessful (poor enrollment, patients declined randomization)

• Evolving endoscopic device platform with optimization – differences in outcomes over 10 years
Summary - GERD

• PPIs are most cost-effective Tx for GERD symptom reduction but increased interest in alternative less invasive options
• LNF has highest efficacy for GERD Qol, longest durability – gold standard
• TIF is a safe and effective “middle” primary alternative to LNF and PPI; may rescue
• More research to enable best selection of Tx for appropriate patient – ideal for SDM!
Thank you!