Gastroesophageal Reflux

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Gastroesophageal Reflux Disease (GERD)

GERD: Symptoms or mucosa damage produced by the abnormal reflux of gastric contents into the esophagus

Reflux esophagitis: A subset of GERD patients who also have endoscopic or histopathologic evidence of esophageal inflammation
### Gastroesophageal Reflux Disease (GERD)

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<table>
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<tbody>
<tr>
<td><strong>Population Prevalence of GERD</strong> 10-20%</td>
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### Diagnostic Evaluation of GERD

- "Endoscopy at presentation should be considered in patients who have symptoms suggesting complicated disease, those at risk for Barrett's esophagus, or when the patient and physician feel early endoscopy to be appropriate."

*ACG Practice Guideline 2005*

### Clinical Manifestations of GERD

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<tr>
<td><strong>Heartburn</strong></td>
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<td><strong>Regurgitation</strong></td>
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<tr>
<td><strong>Dysphagia</strong></td>
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<tr>
<td><strong>“Water brash”</strong></td>
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<td><strong>Globus sensation</strong></td>
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<td><strong>Odynophagia – Atypical</strong></td>
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### Diagnostic Evaluation of GERD: Useful

- Endoscopy
- Pillcam ESO
- Ambulatory esophageal pH monitoring

### Diagnostic Evaluation of GERD: Limited Use

- Esophageal manometry
- Bernstein test
- Double contrast barium swallow
- Symptomatic response to antisecretory therapy

### Endoscopy in GERD

- Allows mucosal examination and biopsy
- Useful to exclude alternate diagnoses
- Evaluates for complications (strictures, Barrett’s)
### Endoscopy in GERD

Grading Schemes:
- Savary-Miller Classification
- Los Angeles Classification

### Savary-Miller Grade II

![Image of Savary-Miller Grade II]

### Savary-Miller Grade I

![Image of Savary-Miller Grade I]

### Savary-Miller Grade III

![Image of Savary-Miller Grade III]
### Savary-Miller Grade IV

<table>
<thead>
<tr>
<th>Histologic Findings of GERD</th>
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<tr>
<td>• Hyperplasia of basal layer</td>
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<td>• Elongation of papillae of epithelium</td>
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<tr>
<td>• Neutrophils and eosinophils</td>
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<td>• Dilated vascular channels</td>
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### Complications of GERD

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<tr>
<td>• Esophagitis</td>
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<td>• Peptic stricture</td>
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<td>• Barrett’s metaplasia</td>
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<tr>
<td>• Esophageal adenocarcinoma</td>
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<td>• Pulmonary and laryngeal complications</td>
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Barrett’s Esophagus

- Columnar epithelium must line the distal esophagus
- Biopsy of the columnar epithelium must reveal specialized intestinal metaplasia

Barrett’s Esophagus

- 3-5% of chronic GERD patients have long segment (> 3 cm) Barrett’s esophagus
- 10-15% of chronic GERD patients have short segment Barrett’s esophagus
Barrett’s Esophagus Risk Factors

- Mean age at diagnosis 55 years
- Male to female ratio 2:1
- More common in Caucasians

Pillcam ESO/ESO2

- Wireless capsule
- Approved by FDA for detection of mucosal disease of the esophagus
- Detection of esophagitis, Barrett’s, esophageal varices
- Cost effectiveness?
Ambulatory Esophageal pH Monitoring

- Confirm GERD in endoscopy negative patients
- Confirm GERD in ppi failures

Bravo

Ambulatory Esophageal pH Monitoring

- Performed ON or OFF antisecretory therapy
- 24 hour study, unrestricted diet
- Symptom log/correlation
### Treatment of GERD

- Disorder of both motility and esophageal acid exposure
- Acid suppression is the predominant target for pharmacologic therapy
- Proton pump inhibitors dominate the classical GERD treatment algorithm

### Treatment of GERD

- Self-care
- Primary care
- Secondary (GI) care

### Treatment of GERD

- Antacids
- H2 blockers
- Proton pump inhibitors
### PPI Site of Action

**Parietal Cell**

<table>
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<tr>
<th>Histamine</th>
<th>Gastrin</th>
<th>Acetylcholine</th>
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### Treatment of GERD

#### Lifestyle Modification
- Dietary moderation
- Reduce meal size and fat content
- Limit alcohol, caffeine
- Refrain from smoking
- Move evening meal earlier
- Elevate head of bed
- Sleep in left lateral position

#### Antacids
- Postprandial “acid pocket”
- Intermittent/rapid symptom relief
- Weak acid neutralizers

#### H2 Blockers
- Cimetidine (Tagamet HB)
- Ranitidine (Zantac 75)
- Famotidine (Pepcid AC)
- Nizatidine (Axid)
### Treatment of GERD

#### Proton Pump Inhibitors

- Omeprazole (Prilosec OTC, Prilosec, generic omeprazole)
- Lansoprazole (Prevacid)
- Rabeprazole (Aciphex)

#### Treatment of GERD

- Intermittent “on demand” ppi
- “Half dose” ppi
- “Full dose” ppi
- Twice daily dose of ppi
- PPI plus additional drug
- Anti-reflux surgery

### Treatment of GERD

#### Proton Pump Inhibitors

- Pantoprazole (Protonix)
- Esomeprazole (Nexium)
- Omeprazole/sodium bicarbonate (Zegerid)

### GERD Summary

- Endoscopy
- Evaluate promptly when “warning signs” are present
- Role of Pillcam ESO yet to be defined
- Limited indications for ambulatory pH monitoring
GERD Summary

• GERD is extremely common and important because of QOL and complications
• Incidence of esophageal adenocarcinoma is rising and heartburn is a risk factor
• GERD is readily diagnosed and effectively treated

Severe Esophagitis

Interventional Therapy for Gastroesophageal Reflux

W. Scott Melvin, M.D.
The Ohio State University

GERD Treatment Goals

• Prevent acid exposure to distal esophagus
• Stop refluxate exposure to airway
• Reinforce sphincter mechanism
• Repair associated hiatal hernia
• Allow normal transit
• Potential regression and or stop progression of Barrett’s epithelium
• Prevent esophageal cancer?
### Therapeutic Interventions for GERD

- **Endoluminal Interventions**
  - Stretta (Radiofrequency Energy Application)
  - Bulking agents (Enteryx, PMMA)
  - Transoral Plication or Fundoplication
    - Endocinch, NDO, Esophyx
- **Surgical Options**
  - Laparoscopic Nissen Fundoplication

### “Injectable” Anti-Reflux Devices

- Theory was to “Augment” the LES
- Gatekeeper (Endonetics)
- Enteryx (Boston Scientific)
- PMMA (Rofi Medical)

### Stretta

- Approved by the FDA in 2000
- Reasonable Clinical results
- CPT code assigned in 2004 (43257)
- Not widely reimbursed
- Insurers issued policy against payment
- Curon bankrupt in December 2006
- Long Term efficacy published in December 2007

### Enteryx™

(Ethylene Vinyl alcohol with DMSO)

- Approved by the FDA after clinical trials showed efficacy:
  - Recall October 2005
  - Deviere J et al 2001
Transoral Plication

- **Endocinch**
  - FDA approved endoscopic suturing device
  - Utilized for GERD and perforations of the upper GI tract.

- **NDO**
  - Stapling device designed and preliminary studies completed, FDA Approved 5/2003
Endocinch: Long Term Data

- 38 pts with 12 month follow up
- 5 had treatment more than once
- None had all the sutures intact
- 10% had persistent fundoplication
- 20% off PPI
- Conclude: Not effective long term


Endocinch: Sham Controlled Trial

- 60 total pts, randomized to three arms
- Outcomes: PPIs, symptoms and pH
- PPI usage, symptoms significantly decreased
- pH moderately improved, no significance
- Results persisted from 3 to 12 months

### NDO Plicator

- Approved in May 2003
- Published results limited
- 64 pts multicenter trial
- 41 had 6month follow up
- GERD-HRQL mean improved
- 34/41 off PPI's

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### NDO Plicator: Video

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### NDO Plicator: Multi Center Long Term

- 29 patients at five centers
- 12 and 36 month minimum follow up
- 57% off PPI's
- GERD HRQoL improved
- >50% improvement
  - 59% @12mos vs. 55% @36mos.

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### NDO Plicator: Sham Trial

- 78 pts treated vs. 81 pts sham (3months f/u)
- Outcome: >50% better on GERD-HRQL
  - 56% NDO vs 18.5% Sham (p<.001)
- Off PPI 50% vs. 24%, (p=.002)
- Median pH<4, decreased 7 to 10 (p<.001)
- Acid Exposure normal
  - 23% with NDO vs 15% Sham

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**Transoral Fundoplication**

- Fundus of stomach supports GE valve
- Full thickness fasteners on distal esophagus
- Esophyx approved by the FDA in Sept 2007
- Requires endoscopy and general anasthesia
- Early clinical results from Europe promising
- Acquiring long term results worldwide now

**Esophyx Video**

**Esophyx: Data**

- 38 pts in Maastricht
- 49 y.o., 2:1 male to female
- 81 min (35-142 min), All pts < 24 hour stay
- 1 pt with bleeding, one unit transfusion
- Hiatal hernia of 1-5 cm in 95% of pts
- NO other adverse events
- pH study at 3 months
  - 85% improved
  - 60% normal
### Esophyx Follow Up

- 10 month median follow up
- GERD HRQL improved by 87% (.001)
- PPI daily use stopped in 82% of pts
- Hiatal hernia reduced in 75%
- pH study at 3 months
  - 85% improved
  - NORMAL in 42% of pts
- Stratified subgroups did even better (60%)

Bouvy, et al., *GI Endoscopy*, 2008

### Esophyx: Phase 2

- 86 pts with long term follow up in 81(6mos)
- 77 minutes (28-208)
- 2 neck esoph perf, 1 post op bleeding
- GERD-HRQL improved by 80%
- 83% off Daily PPIs
- pH normalized in 40%
- Tight valves did better (ph Normal in 50%)


### Nissen Fundoplication

- First described in 1956
- Includes repair of hiatal hernia
- Most common surgical treatment “Gold”
- 85-95% Good results
- Low morbidity
- Majority with GERD treated medically
### Laparoscopic Nissen

- 1991, Dallemagne on 12 patients
- Quickly adapted to worldwide use
- Safe, Apparently effective
- Multiple studies confirmed early successes
- Long term Follow now being added

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### Outcomes of Laparoscopic Nissen

- 199 pts with sx and pos pH probe
- 30 paraesophageal hernia, 4 conv to open
- **Post op Symptom Score:**
  - 87% (173) excellent or good
  - 13% (26) fair or poor

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### Laparoscopic Nissen Long Term Follow Up

- 503 Patients, minimum of 1 year
- 0% mortality
- 3.5% complication
- 100% early dysphagia
- 4% “failure” rate
- 90.2% Visick I or II

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### Predictors of Success

- Symptomatic response to acid suppression therapy.
- Typical symptoms at presentation.
- Abnormal 24-hr pH score***
- Esophageal exposure to pH < 4, greater than 4.4% on 24-hour pH monitoring.

- Non Predictors
  - age, sex, BMI, Mucosal injury, Hernia
### Surgical Outcomes: Laparoscopic Fundoplication

- 10,489 pts with primary LS Surgery
- 41 centers
- Reported from 1993-2000
- 76% Total Fundoplication
- 24% partial Fundoplication
- Mean Follow up of 10-20 months

Carlson MA, Frantzides CT, JACS 193,4,2001

### Surgical Outcomes: Laparoscopic Fundoplication

- Conversion to open 3.1%
- Complications ~5%
- Mortality 0.08%
- Reoperation 2.8%
- Dysphagia* 2.5%
- n=10,489

### Surgical Outcomes: Laparoscopic Fundoplication

- Symptom Scoring (Visick Scores)
  - n=10,489
  - Visick I or II 91%
  - Visick III 6.5%
  - Visick IV 3.5%

### Surgery versus PPI’s

- 155 pts randomized to 2 arms (multi center)
- Multiple changes in treatment strategy
- During 5 years of follow-up, surgery more effective than omeprazole 20 mg/d (for sxs)
- If omeprazole increased to 40 mg/d or 60 mg/d, efficacy similar to surgical therapy

Lundell et al., J Am Coll Surg 2001; 192: 172-179
### Surgery versus PPI’s

- 239 original pts followed (160 survivors)
- 129 pts (91 MED, 38 SURG)
- 62% SURG vs 92% MED were regular users of anti-acid medications
- Long term mortality greater with surgery
- Widely cited but much to criticize
  - VA study, open surgery, poor interim care

Surgery versus PPI’s

*Spechler et al., JAMA 2001; 285: 2331-2338*

### Reflux and Esophageal Cancer

- Swedish health Registry
- 529 AdenoCA, 167 SquamCA, 820 Controls
- Odds ratio of developing Cancer was 7.7 for Ca of the Esophagus, and 2.0 for CA of the Cardia
- For pts with severe GERD Odds ratio 43.5 for developing Esophageal Cancer

Reflux and Esophageal Cancer

*NEJM, 1999*

### Long term Outcomes of Nissen for Barrett’s

- 85 pts followed up at 5 years
- 67 (79%) were asymptomatic
- 18 (20%) symptoms
- 7 had redo surgery and were asymptomatic
- Repeat pH probe was normal in 81%
- No Hi Grade Dysplasia or CA (410 pt/yr)

Long term Outcomes of Nissen for Barrett’s


### Long term Outcomes of Nissen for Barrett’s

- 58 pts with Nissen and Barretts randomized to APC ablation or surveillance
- 40 pts with 65 month follow up
- 14 of 20 pts with ablation: no Barretts
- 5 of 20 pts with Nissen alone: No Barretts
- Antireflux surgery effective in barretts regression and makes ablation durable

Long term Outcomes of Nissen for Barrett’s

*Bright et al. Ann Surg, 2007*
**The Effect of Antireflux surgery on Barrett’s Esophagus**

- Systemic Review, 25 articles met criteria
- Included 700 surgical and 996 medical
- Esophageal Ca incidence per 1000pt/years
  - 2.8 surgery vs 6.3 medical (p=.034)
- Progression of IM decreased in surgical
- Regression increased with Surgery
  - 15.4% vs 1.9% (p=.0004)

**GERD Treatment: The Bottom Line**

- PPI’s for most pts
- Mechanical reconstruction of the GE jxn offers the best acid and bile reflux control
- LS Nissen is very good with ~90% good success, 80-90% off meds
- Transoral fundoplication is promising and emerging as option for pts with normal anatomy
- Barrett's ablation and reflux control may decreasing the risk of esophageal cancer.

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**Barrett's Ablation**

- Guidelines recommend surveillance only
- Increased rates of Progression to Cancer
- Traditional Methods for Ablation
  - PDT, APC, Laser not used widely
- New Methods for ablation
- Data now clear that RFA ablation of IM can result in durable Complete Response at two years, acid suppression plays a role