What’s New in GERD Therapy?

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4th Annual Kaiser-Permanente National Surgical Symposium
Ojai, California

No financial conflicts
Gastroesophageal Reflux
GERD-Rx

- 40% of population affected ≥ 1/week
- 10% affected daily
- $$$ $pent on GERD treatments
  - > $8 Billion per year in USA
- Competing options:
  - Medical
  - Surgical
    - open options
    - laparoscopic
    - endoscopic
New Therapies
Natural History

Example: Lap Appendectomy
Barrett’s Metaplasia?
GERD-Rx

Esophagus treatment gaining in use

Bad-tissue zapper shows promise as disorders climb

-3 million at risk in USA
-50X increased risk of cancer
-Hospitalizations double 1998 → 2005
-Cancer rates up 600% in 20 yrs
->14,000 will die this year
-RFA for ablation of Barrett’s (???)

ASSOCIATED PRESS

SD Union Tribune, 4/1/08
New Therapies
Natural History

Example: Lap Nissen Fundoplication

NEW!
Topics to Cover
GERD-Rx

- The Current Standard
- New possible therapies
  - Endoluminal augmentation
  - Endoluminal suturing
- Obesity & GERD?
- Miscellaneous topics
- Refreshments …
Nissen Fundoplication
Lap-Rx GERD

- Proven methods
- Same as open procedure
- Less trauma of access
- Less painful recovery
Long-Term Outcomes
GERD-Rx

• 441 patients, database 1993-1999
  – Laparoscopic anti-reflux surgery (LARS)
  – 65% follow-up by questionnaire
  – Median follow-up 69 months

• Results:
<table>
<thead>
<tr>
<th></th>
<th>Improved</th>
<th>Resolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td>90%</td>
<td>67%</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>92%</td>
<td>70%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>78%</td>
<td>62%</td>
</tr>
<tr>
<td>Cough</td>
<td>69%</td>
<td>40%</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>69%</td>
<td>47%</td>
</tr>
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• 10% on PPIs, 41% on antacids, 3% reoperations
• Young men with dysphagia did best

Oelschlager… Pellegrini, Am J Gastro 2/2008
Lap Fundo vs PPIs
GERD Rx

• n = 217 pts, randomized
  – 109 laparoscopic fundoplication
  – 108 PPIs +/- escalation
  – Endoscopy, pH, manometry, QoL @ 3 & 12 month followup

• **LESP** mmHg @ 3-months
  – 6 → 17 LNF vs 8 → 8 PPIs

• **DeMeester acid exposure** score:
  – 42 → 8 LNF vs 37 → 17 PPIs

• **GI Symptom** Rating Scale @ 12 months:
  – 31 → 37 LNF vs 34 → 35 PPIs

• General **well-being** scores @ 12 months
  – 95 → 106 LNF vs 98 → 100 PPIs

*LNF ➔ less GERD and better QoL than PPIs*

Mahon, Rhodes, … Br J Surg 92:695, 2005
Lap-Fundo Costs
GERD Rx

- n = 100 pts, randomized
  - Lap Nissen fundoplication vs PPIs
  - 12-month follow-up
- Costs & Score improvement calculated
  - Extrapolated using published data
- 1-yr costs: Lap Fundo = PPIs + £2250

Lap-Fundo favored after 8 years
Cookson/Rhodes, Br J Surg 92:700, 2005

→ Who Pays???
Costs of Treatment
GERD Options

Crossover @ 6 years- USA

Cost

Time

Medical Rx

Surgical Rx
Atypical Reflux Symptoms
GERD-Rx

- Atypical symptoms
  - Globus sensation, hoarseness or cough
  - Equivocal pH testing

- Combined pH and multichannel impedance
  - Diagnosis Rates, 41 patients:
    - 24-hr pH + Impedance $\rightarrow$ 61% increase in Dx
    - Impedance alone $\rightarrow$ 49% more Dx
    - pH alone $\rightarrow$ 29% more Dx
    - Endoscopy only $\rightarrow$ 23% more Dx

- New Gold Standard for Dx-GERD???

Bajbouj, Digestion 3/2007
New Diagnostic Options?
GERD-Rx

- Capsule Endoscopy
  - 20 patients with known Barrett’s
  - Two blinded observers

- Results:
  - Barrett’s changes identified or suspected
  - Observer #1: 8 patients (44%)
  - Observer #2: 3 patients (16%)

- Conclusions: forgetaboutit!

Qureshi  Am J Gastroenterol  3/08
Robotic Fundoplication?
GERD-Rx

- Pediatric patients
  - 1st 50 patients
  - Teaching institution
- 4-port technique
- Operating time (not set-up)
  - Plateau at 5 cases
  - 90 minutes
- “Acceptable method”
- “Learning curve short and steep”

Pre-Fundoplication Checklist

GERD-Rx

• Esophagitis? → biopsies required
• Do symptoms match acid exposure?
  – pH monitoring useful in all
  – Impedance measurements of LES?
• Is there enough esophageal motility?
  – Manometry useful in all
• Does stomach empty normally?
• Is weight loss needed? … >30 BMI?
Improving LES Function
Transient LES Relaxations

GERD-Rx

- 22 GERD pts, 10 with hiatal hernia
  - 24-hr pH and manometry
- More acid exposure in pts with HH
  - TLESR’s no difference
    - Number & association with GERD unchanged
- HH patients had more reflux
  - Swallow-associated reflux
  - Lower LES pressures
  - Straining-associated GERD

Van Hewaarden  Gastroenterology  12/2000
Stretta™ Lesions @ LES
GERD Options

• Sequential RFA lesions
• Results:
  • compliance change?
  • sensory change?
  • tightening of LES?
  • fewer TLESR’s?
Stretta™ Results
GERD Options

Sham-Controlled Trial

Source: Internet review
RFA vs Sham
GERD Endo-Rx

- n = 64 patients, randomized, Kaiser Healthcare
  - 35 Stretta™ vs 29 Sham …
  - 6-month crossover allowed, 12-month f/u
- Heartburn free: 61% RFA vs 33% Sham
- ≥50% improved HB-Scores: 61% vs 30%
- At 6-months: no difference PPI usage
- No difference in acid exposure

RFA ➔ moderate and transient

Corley … Gastroenterology 125:668, 2003
LES Augmentation?
GERD-Rx

- Stretta procedure …. as good as placebo
- Collagen injections….. don’t last
- Silicone injections…. get absorbed
- Polymer injections ..... puncture aortas
- Hydrogel prostheses …. slough and pass

- How about magnets ????
Magnetic Augmentation LES?
GERD-Rx

- Porcine model
- Magnets in appliance
- Acute and 44-week survivals
  - Gastric yield & LES pressures can be improved
    - Correlate with magnet strength
  - No device migration
  - “Normal” animal behavior

Ganz, .. DeMeester. Gastrointest Endosc 2/2008
Durable Augmentation?

Endoscopic GERD Rx

Cost

Time

Medical Rx

Surgical Rx

Crossover @ 6 years- USA

Endo-GERD Treatments
Endoscopic Gastroplasty
Plication Sequence
GERD Endo-Rx

- Scope-in-scope view
- Sequential steps
  - puncture
  - pass
  - tie knot
  - repeat…

Source: Internet review
**Endoluminal Plication**  
*GERD-Rx*

- **NDO Plicator device**
  - 33 pts with GERD
  - Prospective
  - Multi-site study
  - Full-thickness plication
  - 1cm below GEJ

- **Early results**
  - 30/33 off PPIs

- **Results @ 5-yr**
  - 20/30 off PPIs
  - HRQL improved
    - 10 vs 19, p < 0.001
    - GERD-HRQL ≥50% better in 16/32 pts
  - No adverse events

- **Conclusion**
  - EndoPlication can last 5-yr

Report 3/2008
Endoluminal Fundoplication
GERD-Rx

- EsophyX™ device
- Feasibility study
  - 17 patients with GERD
  - Endo-luminal fundoplication (ELF)
  - Valve created at GEJ
    - 4 cm long
    - 210 degree wrap
  - 13 patients’ small hiatal hernias reduced
- Results @ 12 months:
  - 81% retained wrap tightness
  - 82% remained off PPIs
  - 63% normal pH studies
  - 82% satisfied
- Conclusion:
  - Feasible
  - More studies needed

Cadieri  Surg Endosc 2/2008
Hybrid Endo-Pursestring
GERD-Rx

- 5 pigs, up to 6 months follow-up
- **Methods:**
  - Trocar through abdomen into stomach
    - Similar to PEG
  - Pursestring at GEJ
  - 24-hr pH monitoring
- **Results:**
  - Improved number, lengths and total time of reflux
- **Conclusion:**
  - Who knows? It could work…

Fedenko & Evdoshenko, Obes Surg 6/07
Endoluminal Suturing
GERD-Rx

Full Thickness Suturing

Source: UCSD Research Lab
Obesity & GERD
• BMI >30 predicts complications
  • As high as 40% recurrence rates
• Barrett’s correlates with abd girth, not BMI
  • Corley, Gastroenterology 7/07
• CPAP improves LES pressures
  • +/- Sleep apnea
  • Shepherd, Am J Physiol Gastro Liver Physiol, 5/07
• Gastric electrical stimulation- pacemaker
  • Improves reflux symptoms in obese pts
  • Increases LES pressure in dogs
Miscellaneous Topics
GERD-Rx
Right or Left Lateral ???

GERD-Rx

- 15 pts with documented GERD
  - pH and manometry after meal
  - R- and L-lateral positions studied
- Results:
  - TLESR’s increased & LES pressures decreased
  - No difference in TLESRs or LESP’s (R or L)
  - Reflux = 2X in right-lateral decubitis position
  - Unknown reasons …

Kapur, Neurogastroenterol Motil 12/1998
Tumor Palliation
GERD-Rx

• New device, “spiral Z-stent”
  – Polyester mesh stent with valve
• 13 patients with unresectable GEJ tumor
  – Good palliation
  – No migration of stent
  – No gas-bloat
• Useful for palliation

Kocher, J Vasc Interv Radiol 11/98
Red or White Wine ???

GERD-Rx

- 20 healthy volunteers
  - 300 ml with standardized meal
    - Red wine, White wine or Water
  - Manometry and pH measured
- LESP’s lowest with white wine (15 mmHg)
  - Water = Red wine LESP’s (20 mmHg)
  - Time pH < 4 lower for wines vs water
  - White wine ➔ more free and stress-induced reflux
- Conclusion: I recommend a red Burgundy

Pehl, Scand J Gastroenterol 2/98
What’s New?
GERD-Rx

“Laparoscopic hiatal hernia repair and repeat sleeve gastrectomy for gastroesophageal reflux disease after duodenal switch”

Parikh & Gagner, Surg Obes Relat Dis 1/2008
Conclusions

1. Fundoplication works
   • Select patients well
   • Beware atypical symptoms
2. Endoluminal suturing may work
3. Obesity presents special options/risks
4. Beware of new devices without testing
Surgical vs Medical
GERD Rx

- 10-year followup, 373 pts, matched pairs
  - 80% response rate
  - 102 laparoscopic, 77 open cases
- GISRS & Psych Gen Well-Being Index
- Fewer reflux symptoms in surgical group
  - 1.34 vs 2.51, p < 0.001
  - More indigestion in surgical group
- No difference in QoL

Surgery more effective

Olberg … Scand J Gastroenterol 40:254, 2005
Medical vs Surgical
GERD Therapy

- Followup RCT, > 9-year followup
  n = 239 found, 160 alive, (VA = 3 women)
  n = 129 with data: 91 medical vs 38 surgical
- GRACI scores, med usage, esophagitis, etc.
  Meds needed regularly: 92% medical vs 62% surgical
  Surgical results better off meds
- No difference strictures, (re)operations, ...
- Lower overall survival in surgical group (cardiac)
  - No difference in esophageal CA

No difference in satisfaction scores
Spechler, JAMA 285:2331, 2001
Endo-Rx Options
GERD Rx

- Plication methods
  - EndoCinch (Bard)
  - Endoscopic Suturing Device, ESD (Cook)
  - Full-thickness Plicator (NDO Surgical)
- Thermal remodeling/neurolysis
  - Stretta (Curon)
- Bulking at LES
  - Enteryx (Boston Scientific)
  - Gatekeeper (Medtronic)

No financial interests
Endoscopic Gastroplasty
Endo-GERD Rx

- N = 64 patients, multicenter
- EndoCinch device … 6-month followup
- Exclusions: dysphagia, 3-4 esophagitis, obesity or >2cm hiatal hernia
- Symptom scores, pH monitoring improved
- Continued PPI usage allowed

Safe & effective (??)

Filipi … Gastrointest Endosc 53:416, 2001
Mucosal Plications?
GERD Endo-Rx

- n = 18 rabbits, laparotomy
  - 3 levels of intraluminal suturing:
    • submucosa, muscularis propria, serosa
  - 3, 10, 60 day sacrifice
  - Fusion & scarring measured
- Fusion of folds absent, all groups
  - Scarring relates to depth of sutures

Plications = Scarring

Feitoza… Gastrointest Endosc 58:868, 2003
RadioFrequency Ablation
GERD Endo-Rx

- n = 20 pigs
- Botulinum toxin-weakened LES
- 4-electrode wires at two LES positions
- Escharification “restores” LES pressures
- Pathology
  - Normal mucosa
  - “Mild fibrosis”

Utley, 7/2000
Stretta Procedure
GERD Endo-Rx

- Conscious sedation
- LES distance measured
- RFA at LES in matrix
- Change in compliance
  - TLESR’s?
  - Neurolysis?

Source: Internet
Does Stretta RFA tighten the LES???

Source: Internet
1-Year Followup
Stretta Procedure

- n = 41 pts
- No change in LES pressures
  - No strictures
- 20/31 pts off PPIs (65%)
  - Mean f/u = 6 months

Controlled trials needed

Houston … Surg Endosc 3/03
Resource Utilization
GERD Endo-Rx

• 1st cases Stretta, n = 13
  – Compare with colonoscopy and EUS
  – Similar patient characteristics
• More sedation with Stretta
• More procedure time with Stretta
• More recovery time with Stretta (colon’y only)

Stretta is resource intense

LES Bulking

- Enteryx™
- Gatekeeper™
Enteryx™
GERD Options

- Inert polymer
- Free-hand injections
- Bulking at LES
- Deep injections …
- Not currently available
GateKeeper™ Assembly
LES Augmentation

- Suction chamber securely holds mucosa in place
- Exact angles and measurements maintained
- Designed to eliminate stray positioning
Hydrogel Expansion
LES Augmentation

- 90% expanded in 6 hours
- Shape maintained indefinitely
- Pliable, sponge-like consistency
Prosthesis Retention
LES Augmentation

Prosthesis Retention
Central Trocar
Beveled Needle

Total of 179 prostheses

(n = number of animals)
6 Month Endoscopy
LES Augmentation
Histopathology
EndoRx GERD

Circular muscle
Submucosa
Prosthesis Cavity
Comparison Trials
GERD Endo-Rx

- Most effective?
- Most durable?
- Most economical?
Fundoplication vs PPIs
Endo-GERD Rx

- 5-year followup RCT, 310 pts
  - Continuous Omeprazole = 155 pts → 133 @ 5-yrs
  - Surgical Fundoplication = 155 → 144 pts → 122 @5
- Followup: QoL scores, symptoms, endoscopy
- Failures:
  - moderate or severe heartburn scores
  - Grade 2 esophagitis or more
  - Crossover: > 8-wks PPIs … antireflux preferred
- More treatment failures with PPI strategy (p < 0.001)
- PPI dose escalation modulates treatment failures

Surgery favored

Enteryx™ vs Sham
GERD Endo-Rx

- n = 64, prospective, randomized, multicenter, 1-blinded
  - 32 Enteryx™ vs 32 Sham endoscopy … 3 mo crossover
  - 3 & 6 month followup evaluations
- PPI reduction ≥50%?
  - 67% treated vs 22% sham
  - 68% vs 41% off PPIs completely
- Improved GERD scores ≥50%?
  - 67% treated vs 22% sham
- Retreatment needed?
  - 19% treated vs 81% sham

Deviere… Gastroenterology 128:532, 2005
**Gastroplasty vs Lap-Fundo**

**GERD Options**

- **Endoscopic Gastroplasty (EndoCinch)** offered to all pts.... LF offered to remainder
  - More hiatal hernia pts in LF group
- **Satisfaction:**
  - EG = 66%
  - LF = 93%
- **Pills needed (PPIs or motility)**
  - EG = 32%
  - LF = 13%
- **3 pts with initial EG → LF**

Cadalavada ... Surg Endosc 12/03
Cost Analysis

PPIs vs. Stretta

• Cost of therapy estimates
  – Based on available data
• Stretta favored after 17 months, but…
• If procedure failures >20% →
• PPIs favored after 29 months

PPIs retain long-term cost advantage

Harewood … Gastrointest Endosc 10/03
Laparoscopic Fundoplication vs Stretta-RFA Procedure

- Stretta used in all suitable pts (n=65)
- Lap Fundo for all others (n=75)
  - LF pts had higher pre-op acid exposure, lower LESP’s and more hiatal hernias (41%)

Results:
1. QOLRAD & SF-12 improved in both groups
2. PPI usage: Stretta = 58% off PPIs, 31% improved
   LF = 97% off PPIs
3. Both groups satisfied

Patient selection critical

Richards … Ann Surg 5/03
Cost-Value
Endo-GERD Rx

- Heartburn treatments are long term
- Many patients need meds after Endo-Rx
- Fewer patients need meds after fundoplication
- Most complete & durable option wins long term
RFA vs G-plication vs PPIs
Endo-GERD Rx

- Decision analysis: costs
  - Stretta vs. EndoCinch vs. PPIs
  - EndoRx ≥ $3,400 … PPIs ≤ $140/month = 2x/day
- Published data for performance-costs
  - 20% annual failure rate
  - 10% partial failure rate
  - 1% complication rate
- Endo-Rx superior after 17 months
  PPIs superior after 29 months
Harewood, Gastrointest Endosc 58:493, 2003
Endo-Rx vs Lap-Fundo
GERD Endo-Rx

- Costs projected… Germany payors
  - Published reports
  - Direct costs only
- Sequential use strategy vs LF only
  - EndoRx → LF for failures vs LF
- Long term success ≤65% for EndoRx

*Endo-Rx “overpriced” by ~30%*

Schiefke … Endoscopy 37:217, 2005
New Therapies
Natural History

Example: Lap Appendectomy

2006

Time

New
Effective?
RCT’s

#
Conclusions
Lap-Rx GERD

1. Fundoplication is a good option for GERD
2. Laparoscopy can duplicate open results
3. Options exist for specific situations
4. Select patients carefully
5. Do not compromise established principles
6. Endoscopic alternatives are being developed
   - Controlled clinical trials are essential
Video Prosthesis Insertion
LES Augmentation
Heartburn Work-up
Lap-Rx GERD

- Endoscopy +/- biopsy
  - Barrett’s metaplasia → dysplasia
- 24-hour pH recordings
  - Rare indication for Bernstein test
- Manometry
- UGI contrast radiographs (optional)
Endoluminal Techniques

EndoRx GERD

- **Bulking**
  - Collagen
  - Polymers… (Enteryx)
  - Hydrogel prosthesis … (Gatekeeper)

- **Suturing/stapling** … (EndoCinch)

- **Escharification**
  - chemical (EtOH)
  - Radio Frequency Ablation … (Stretta)
Video Swallow
LES Augmentation
Principles of Surgical Repair
GERD

- Re-create intra-abdominal esophagus
- Lengthen LES
- Dynamic high pressure zone (HPZ)
- Strengthen LES
- Bulk LES
  - Eliminate TRLES’s
- Close hiatal hernia
Endonetics’ Hypotheses
LES Augmentation

1. Preformed prostheses can be reliably placed at the LES
2. Novel delivery system is
   – Safe
   – Easy to use
3. Bulking can be titrated
   • Bulking may augment LES function
4. Prostheses can be easily removed

Mechanisms
LES Augmentation

- Luminal bulking
- LES occlusion facilitated
- LES lengthening possible
EndoCinch™
GERD Options
EndoCinch™
GERD Endo-Rx

- Two patterns:
  - Linear
  - Circumferential
- Tighten LES?
- Lengthen LES?