Update in Acid Reflux Disease – 2017

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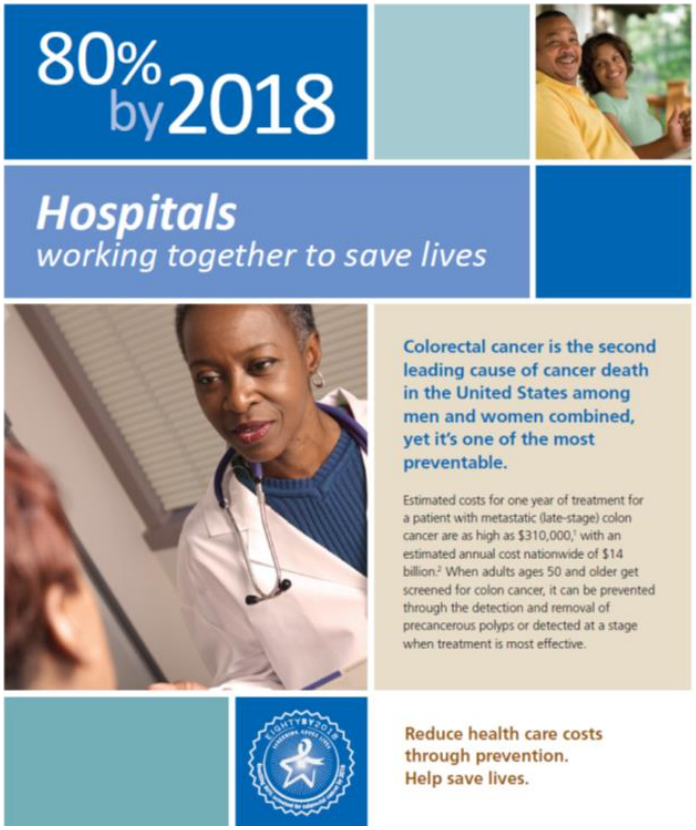
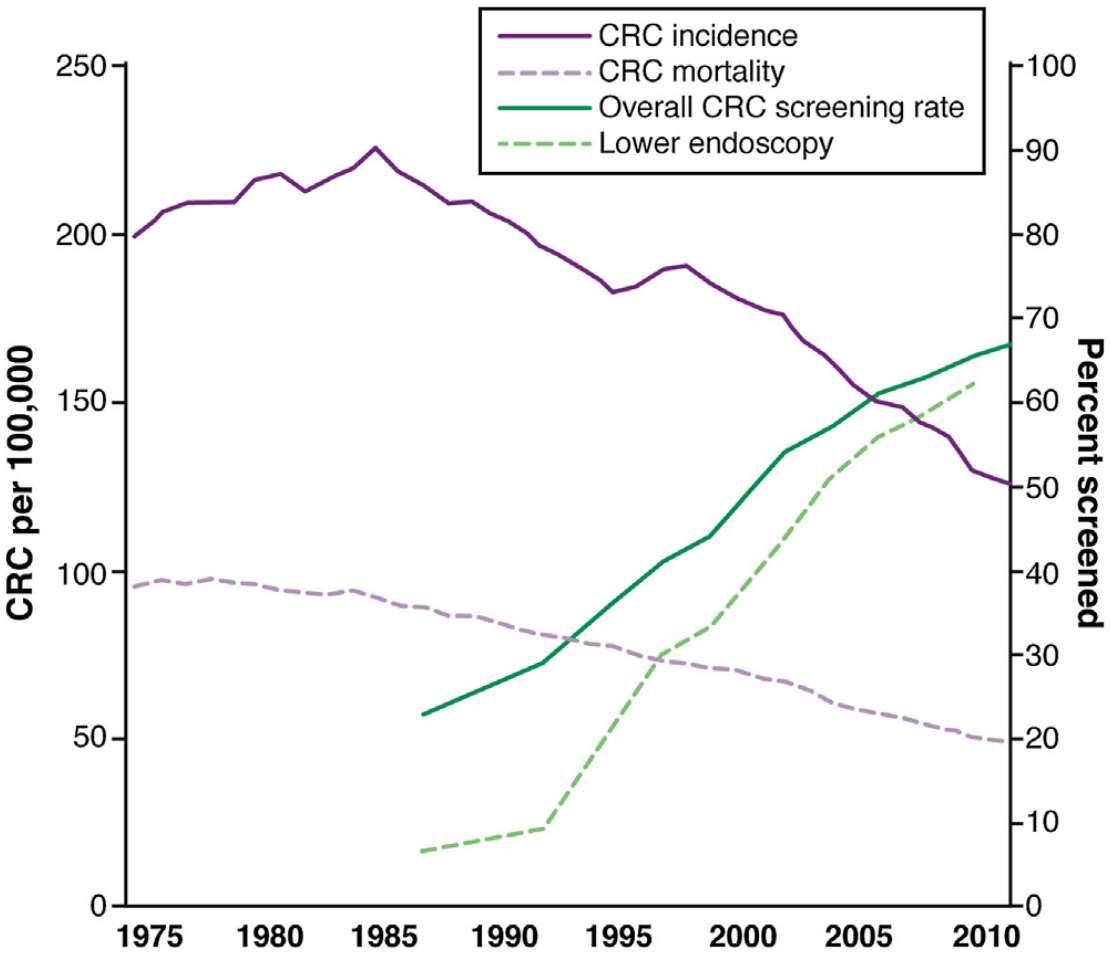
Colorectal Cancer Screening
80 x 2018 Campaign

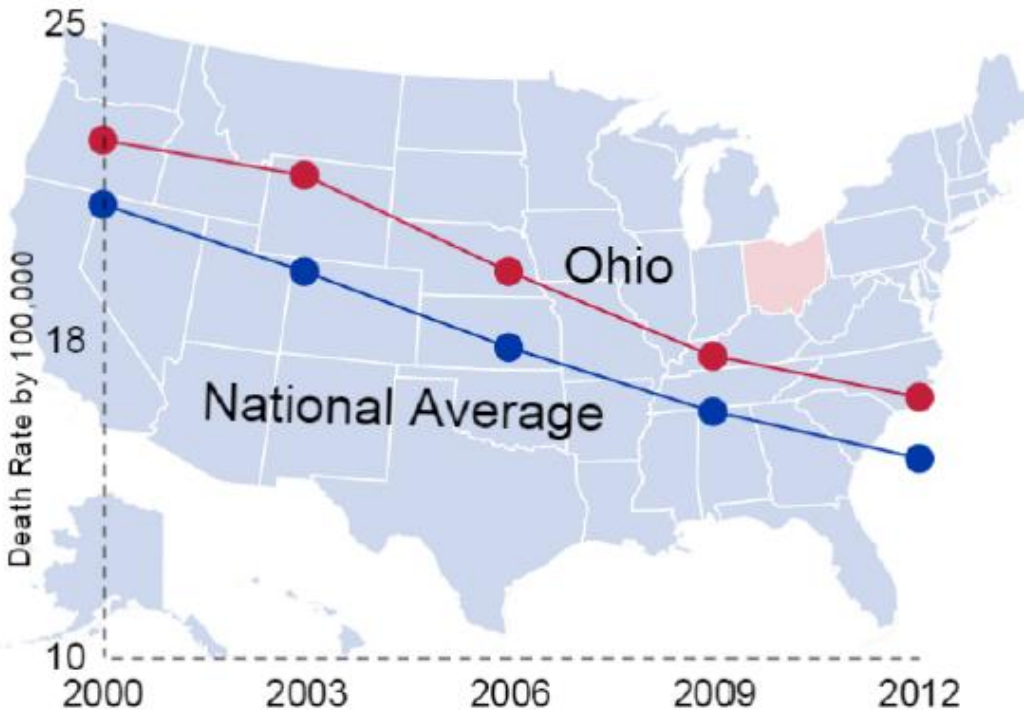
- Colorectal cancer (CRC) screening
  - Second leading cause of cancer death in US
  - Screening rates vary ≈ 60% – 76%
- Do something for every patient
  - High-quality colonoscopy
  - FIT or Cologuard for those adverse to colonoscopy
- Colonoscopy is the only method of colorectal cancer prevention but don't be lulled; it's far from perfect





Patel Clin Gastroenterol Hepatol 2014;12:7-15

Ohio Colorectal Cancer Death Rate vs National Average[6,7]



Objectives

- Define acid reflux disease also known as GERD
- Review the intrinsic causes of GERD
- Determine which patients have severe GERD
- Review testing options for GERD
- Discuss alternative diagnoses to GERD
- Address the concerns of long term medical therapy
- Suggest an approach to choosing patients for anti-reflux surgery
- Introduce available endoscopic anti-reflux procedures
- Summarize Barrett's disease surveillance and treatment options

Acid Reflux or Gastro-Esophageal Reflux Disease (GERD)

- Defined as the retrograde passage of gastric contents into the esophagus
- Typical or classic symptoms
  - Heartburn and regurgitation
- What its not
  - Achalasia
- GERD phenotypes and pathologic sequel
  - Non-erosive (NERD)
  - Esophagitis
  - Barrett's esophagus
  - Esophageal ring or stricture

Mechanism of GERD

- Structural – hiatal hernia
- Functional – transient or persistent lax lower esophageal sphincter

Define which Patients have Severe GERD

- Pathologic sequel
  - Esophagitis
  - Barrett's esophagus
  - Esophageal stricture

Atypical GERD

- Defined as the retrograde passage of gastric contents into the esophagus causing a variety of symptoms NOT including Heartburn and Regurgitation
- What it may be associated with
  - Noncardiac chest pain
    - Hypersensitive esophagus
    - Esophageal spasm
  - LaryngoPharyngeal Reflux (LPR) theory
    - Laryngitis – hoarseness, excessive throat clearing, globus
    - Chronic cough and asthma
    - Dysphagia, post-nasal drip, ear infections
    - Pepsin implicated as a marker or causative agent
    - Otolaryngologists' Irritable Bowel Syndrome
      - Reflux Symptom Index (RSI)
      - Reflux Finding Score (RFS)

Refluxgate.com Sept 2017

"The combination of symptoms helps a lot to make the diagnosis. But it is also something that can lead to confusion even among physicians, if they are not specialized in LPR"

What are the Alternative Diagnoses for GERD symptoms?

- Separate out alternative diagnosis vs associated atypical symptoms
  - Noncardiac chest pain
  - Cough
  - Laryngitis and ear symptoms

- Major diagnoses may coexist
  - Eosinophilic esophagitis
    - Responds to PPI, Six food elimination diet and topical steroids
  - Pill induced esophagitis
    - Common in patients with esophageal strictures, rings and poor motility
  - Connective tissue disease
    - Scleroderma
  - Radiation induced esophagitis
  - Nasogastric tube induced esophagitis

Define which Patients have Severe GERD

- Complete assessment requires endoscopy – EsophagoGastroDuodenoscopy (EGD)
  - Durability of EGD findings is high
    - Normal or limited findings will persist
  - Limited clinical alternatives
    - Video esophageal capsule
    - Swallowed tethered capsule for cytology or genetic testing

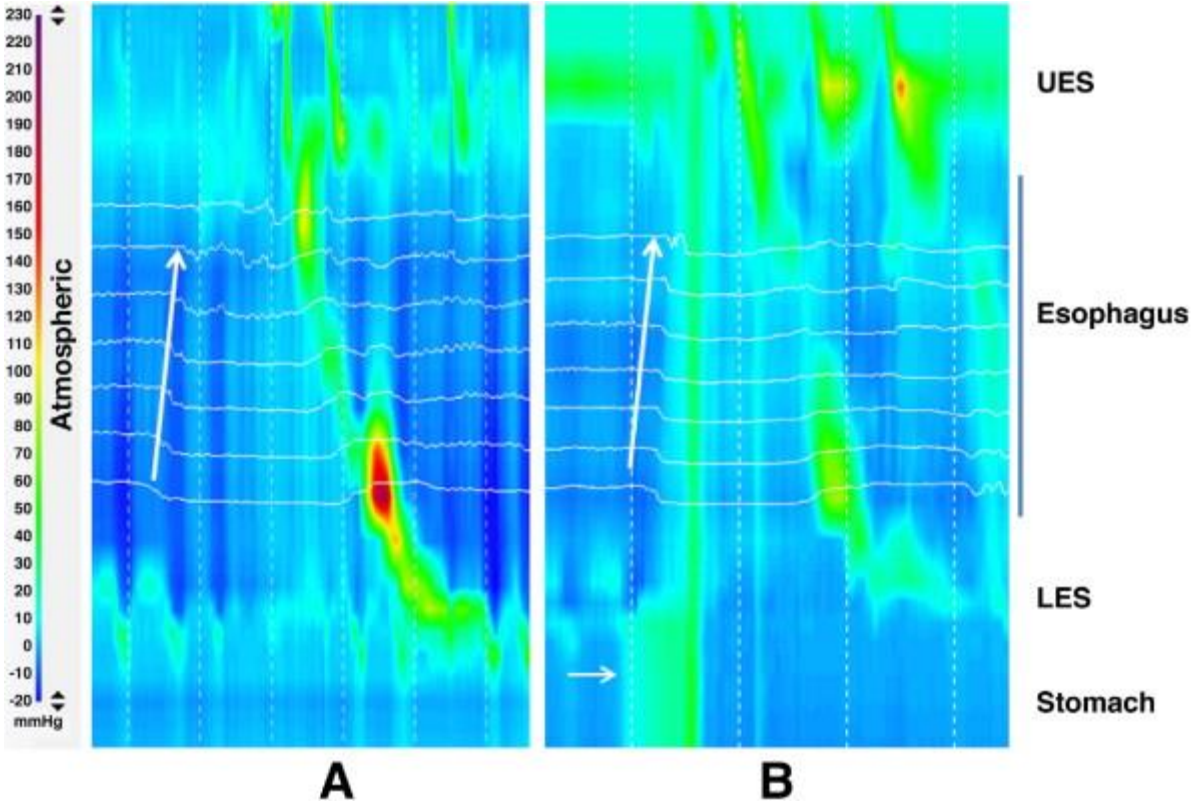
- Barium esophagram
  - Good starting point in some patients
  - Low sensitivity for Barrett's esophagus

- Esophageal function testing
  - Underutilized in difficult cases
  - Provides objective data

Esophageal pH vs Impedance Testing

1. 24 hour pH with impedance naso-esophageal catheter
2. 24 hour dual pH probe with LPR testing
3. 48 hour pH esophageal capsule (Bravo®)

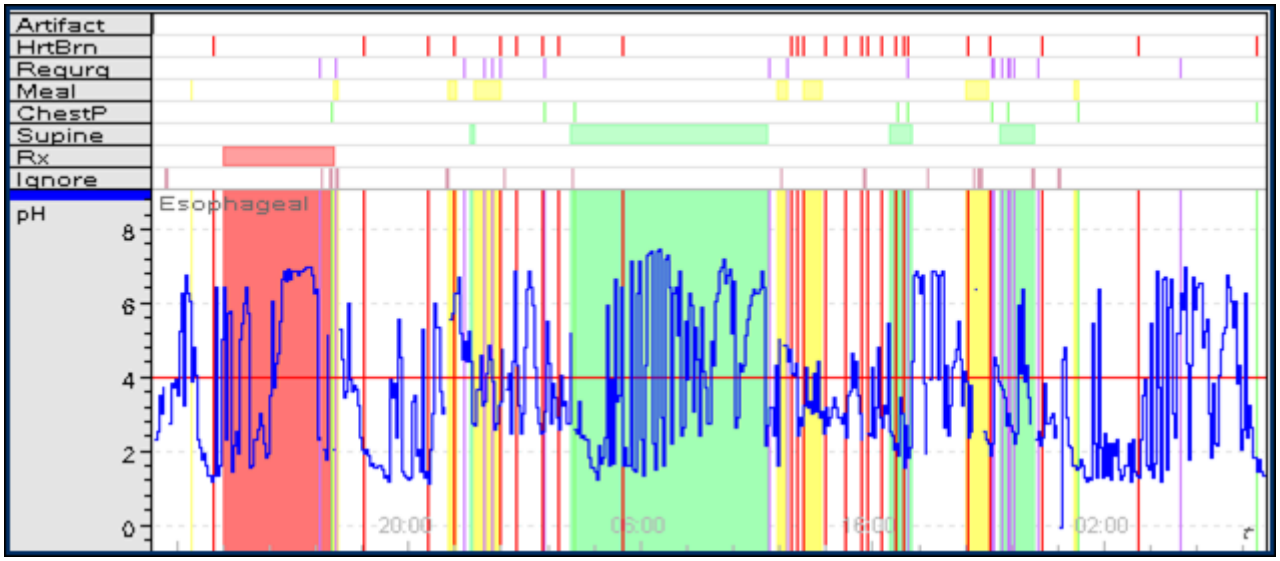
Esophageal Motility Testing (EMOT)



Normal GERD

Testing On or Off Acid Suppression Medications?

- Testing OFF acid suppression medications provides the best assessment



Testing On or Off Acid Suppression Medications?

- Test **OFF** medication
  - Determines the underlying disorder
    - Typical GERD with NERD, EE or BE
    - Functional heartburn and reflux hypersensitivity
  - Needed to document GERD exists in atypical presentations before surgical intervention

- Test **ON** medication
  - Generally a low yield scenario
  - Non-acid reflux detection requires impedance technology
    - Symptom index is crucial for clinical decisions in PPI failure patients
  - Confirms acid control in selected patients
  - Patients with > 50% response to PPI
  - Consider in patients with high pretest probability of GERD when PPI fails

Concerns about Long-term GERD Medical Therapy

- Differentiate PPI vs non-PPI therapies
  - PPI associated hyper-gastrin state
    - Durable acid control for patients suffering from typical GERD
  - Histamine receptor antagonists associated tachyphlaxis
    - Fast acting and better for short courses as needed
- PPI adverse effects
  - Bone disease
  - Risk of C. difficile infection
  - Renal health
  - Brain health
  - Fundic gland polyps
- The risk of side effects is greatest in those that do not really benefit from long term therapy
- Functional heartburn and Endoscopy-Negative Reflux Disease (ENRD)
  - Patients may respond better to tricyclic antidepressants or serotonin uptake inhibitors

Limsrivilai Am J Gastroenterol 2016;111:217-24

Concerns about Long-term GERD Medical Therapy

- Esophageal Cancer Awareness Network (ECAN)
  - 14% of US adults aware of association of heartburn and cancer
  - Petitioning FDA for labeling PPI with warning
  - PPI use improves symptoms without reducing neoplasia risk

  - "Persistent heartburn can indicate increased risk of developing esophageal cancer. This medication will not eliminate that risk. Ask your doctor before use if you have had heartburn for over 3 months. This may be a sign of a more serious condition. Stop use of the product and see your physician if your heartburn continues or worsens; or if you need to take more than 1 course of treatment every 4 months."

Choosing Patients for Anti-reflux Surgery

- Pathologic sequel
  - Esophagitis
  - Barrett's disease
  - Esophageal stricture
- Structural abnormality
  - Hiatal hernia
- Risk of recurrence
  - 17.7% overall recurrence rate over median of 5.6 years in 2655 patient Swedish cohort
    - 83.6% resorted to long term medical therapy
    - 16.4% revision surgery
  - Lowest risk group is young health males
    - Age – less than 45 yrs. < 45-60 yrs. < over 60 yrs.
    - Gender – Women 22% vs Men 13.6% [HR 1.57 95% CI 1.29-1.90]
    - Comorbidity
  - Recurrence was not associated with hospital volume

Maret-Ouda JAMA 2017;318:939-6

Endoscopic Anti-reflux Procedures

- Transoral Incisionless Fudoplication (TIF or EsophyX®)
  - 20,000 patients world wide – 1300 unique patients in clinical trials from 60 centers
  - 75% able to stop PPI – 10 studies (n = 527 weighted average follow up 13 months)
  - 82% healed esophagitis – 4 studies (n = 82 weighted average follow up 18 months)
  - Improvement in QoL, LES pressure, and pH studies
  - Limited to hiatal hernias ≤ 2 cm

Alternative Surgical Anti-reflux Procedure

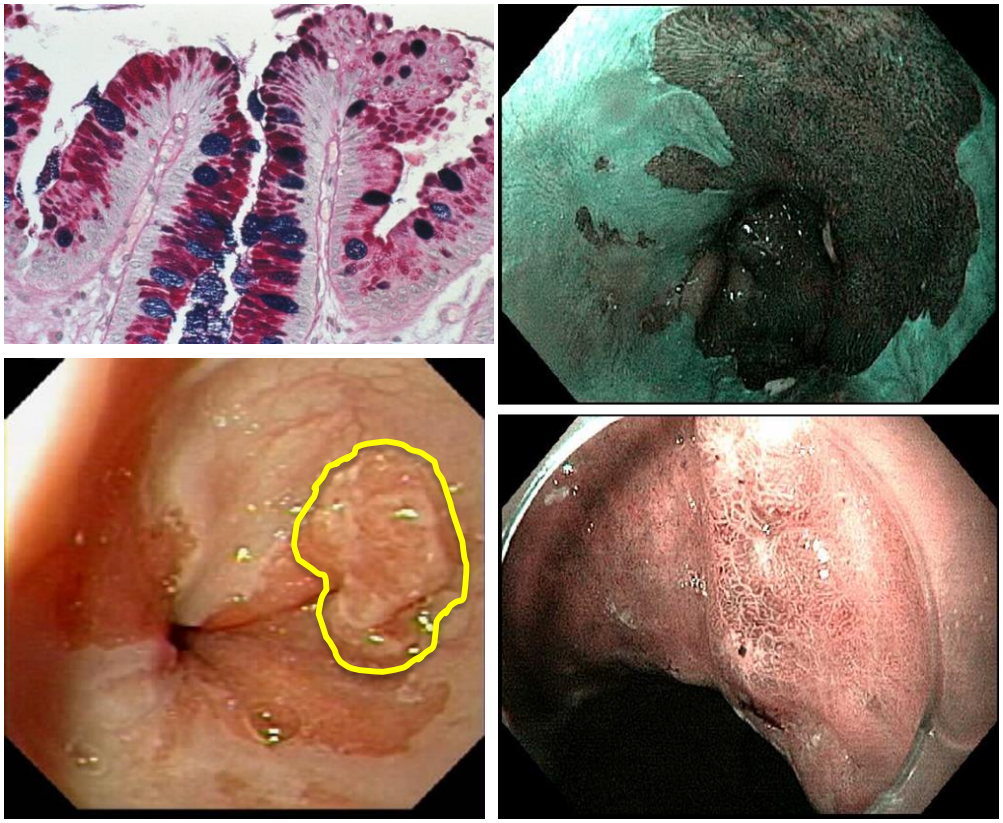
- Magnetic augmentation of the LES (Linx®)
  - Approved by the FDA in 2012 for laparoscopic implantation
  - May be the treatment of choice for GERD after Gastric Sleeve bariatric surgery
  - Limited to hiatal hernias ≤ 2 cm with normal esophageal motility
  - MRI safe if magnet strength ≤ 1.5 tesla

Barrett's Esophagus

- Associated with esophageal adenocarcinoma
- Screening is not cost effective
- Surveillance is even less cost effective
- Endoscopic therapy can save lives
- Ablation durability
  - 3 meta-analyses now range from 6.9-13% (U. Chicago, Mayo, and UNC)
  - Critical need for reflux control after achieving complete remission of intestinal metaplasia

Quality Indicators for Accurate Diagnosis

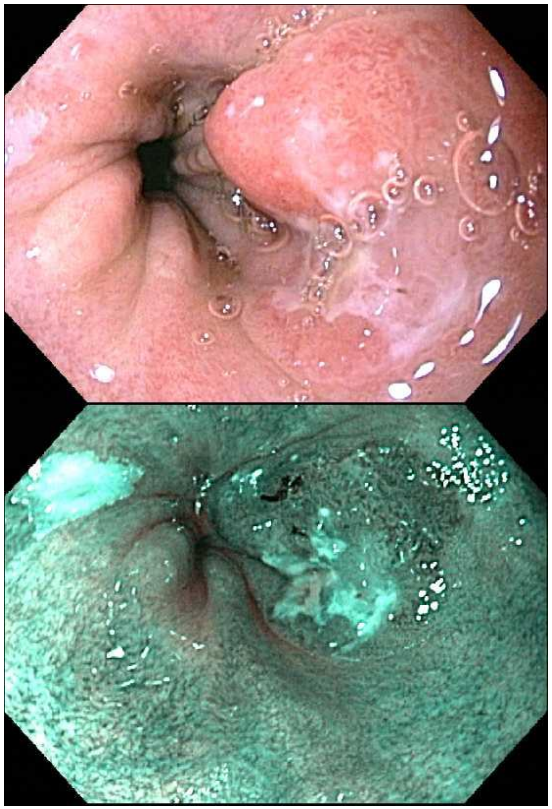
1. BE = Columnar lined epithelium of the esophagus + Intestinal Metaplasia (IM) on biopsy ≥1 cm
2. Prague classification (CxMx)
3. Identify **lesions** within BE segment
4. Understand what is not BE
   - IM of the gastric cardia
   - Irregular Z line <1 cm
   - Columnar epithelium without IM (unless you are British)



Shaheen Am J Gastroenterol 2016;111:30-50

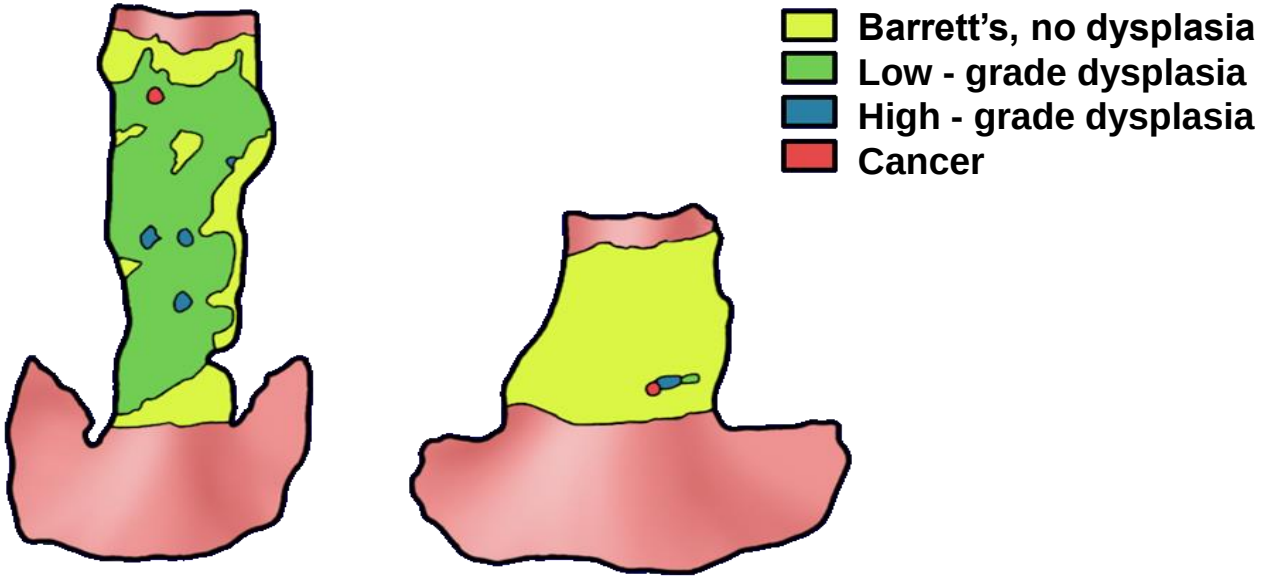
High-Quality Surveillance

- Begins at the initial diagnostic exam
  - Guidelines dropped the 1-year follow-up exam
- High definition white light – look carefully before biopsy
  - Longer inspection times are associated with higher detection of high-grade dysplasia (HGD) and esophageal adenocarcinoma (EAC)
  - Attention to the right wall
- Adequate number of biopsies
  - 4 quadrant every 2 cm for non-dysplastic
  - 4 quadrant every 1 cm for dysplastic



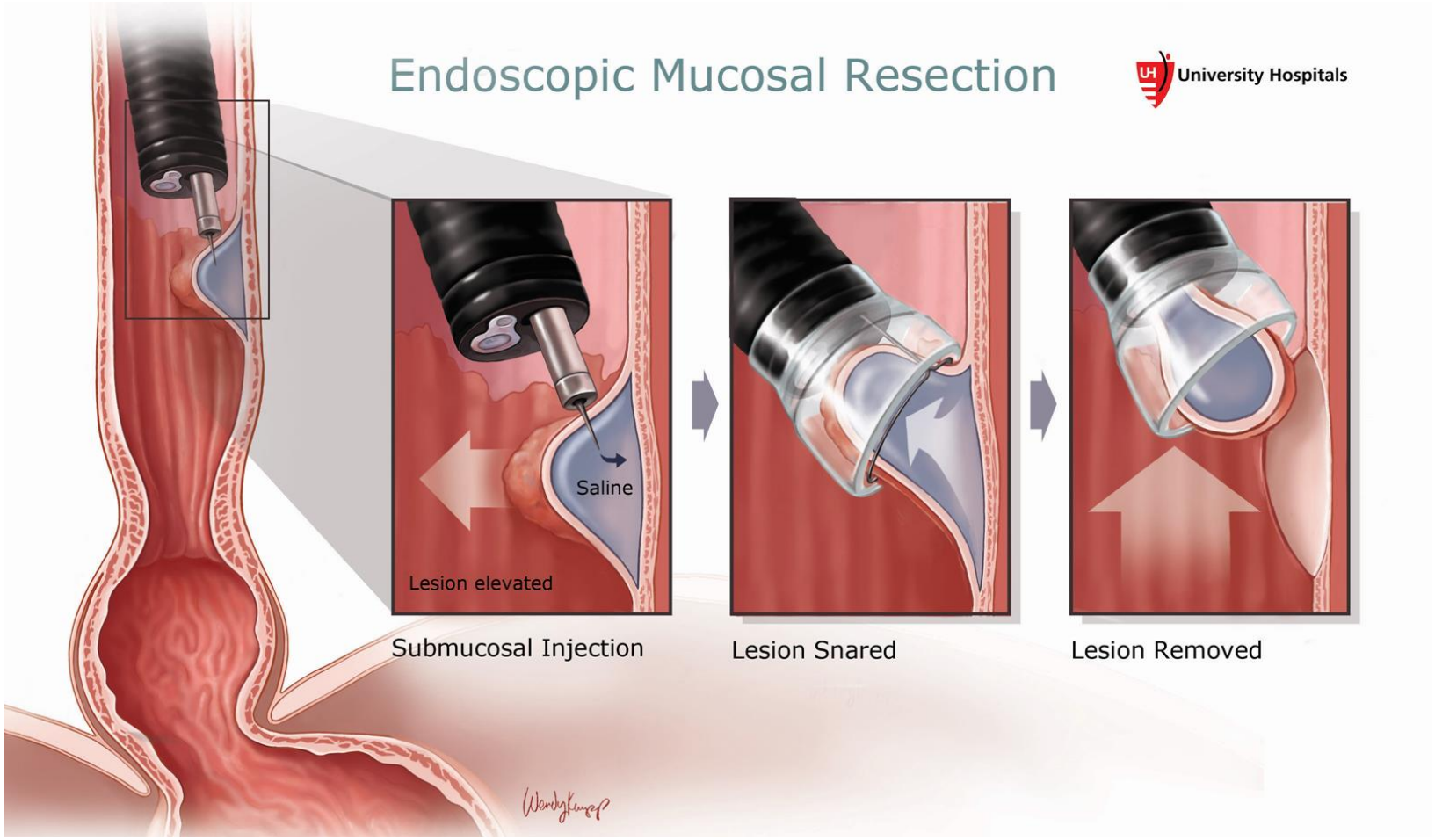
Gupta Gastrointest Endosc 2012;76:531-8
Enestvedt Gastrointest Endosc 2013;78:462-7
Fitzgerald Dig Dis Sci 2001;46:1892-8

Distribution of Dysplasia and Cancer in Resection Specimens



Cameron Am J Gastroenterol 1997;92:586

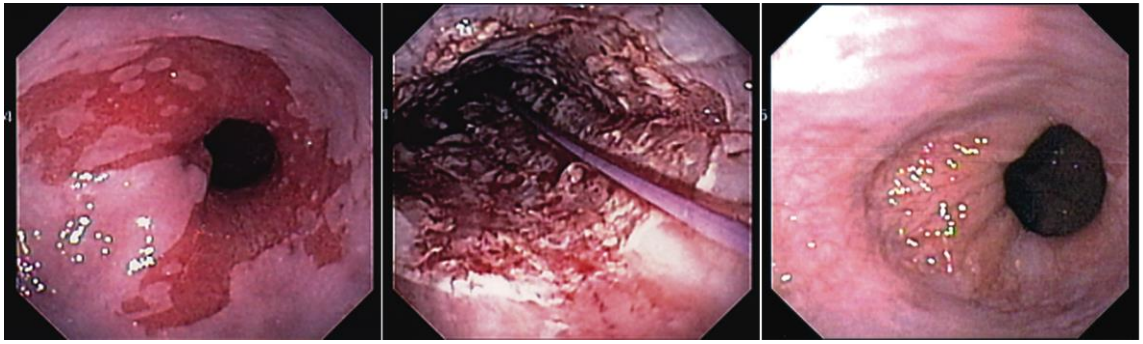
Endoscopic Mucosal Resection (EMR)



Radiofrequency Ablation vs Stepwise EMR

- RFA combined with focal EMR improves safety over stepwise or complete EMR

	CE-N	CE-IM	EAC	Recurrence Dysplasia	IM
F-EMR + RFA (774)	93.4%	73.1%	1.4%	2.6%	16.1%
S-EMR (751)	94.9%	79.6%	0.7%	3.3%	12.1%



Desai Gastrointest Endosc 2017;85:482-495

Case

- 69 year old retired male engineer referred for failed RFA with recurrent HGD
  - No family history of esophageal cancer
  - Original diagnosis on EGD after Roux-en-Y gastric bypass C7M7
  - Occasional heartburn on PPI
  - Barrett's segment with residual disease and ulcerations C0M7 after several sessions of RFA

Case

- Failed RFA with recurrent HGD requires aggressive intervention – T1a carcinoma found

Patient Groups for Endoscopic Therapy - Community

Yes

- Confirmed LGD
  - Alternative: surveillance in 1 year
- HGD
  - Endoscopic therapy is preferred strategy
- Intramucosal cancer – T1a
  - Provided lesion can be completely removed in initial EMR session

No

- BE without dysplasia

Patient Groups for Endoscopic Therapy – BE Center

Yes

- Confirmed LGD
  - Alternative: surveillance in 1 year
- HGD
  - Endoscopic therapy is preferred strategy
- Intramucosal cancer – T1a
- Early submucosal cancer – T1b with prohibitive surgical risk

No

- BE without dysplasia

Maybe

- Strong family history EAC
- Ultra-long segment in young
- BE with dysplasia and life-limiting comorbidities

Conclusions and Take-away Points

- GERD is a diverse problem to manage
- Testing is very effective in determining the best treatment option and outcomes
- Patient satisfaction requires options and inclusion in decision making
- Anti-reflux surgery has a long-term treatment failure in 1:5 patients
- Endoscopic therapy for Barrett's esophagus requires a complete skillset and plan for treatment failures in 1:10 patients