

Journal Club

Endoscopic Ablation of Barrett's Esophagus

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Objective

- Familiarize audience with
 - The methods used with the HALO-360 Ablation System
 - Evidence behind using RFA for BE
 - Selection of patients appropriate for RFA
- i.e. Everyone should be able to do it and know why they are doing it.

My Patient

- 54 y/o wm with long h/o gerd, undergoing surveillance for Barrett's esophagus (5cm segment).
- July 2008: small nodule biopsied: hgd in setting of lgd
- Plan repeat scope to confirm and begin 3 month surveillance
- Sept, Dec 2008: LGD only, no nodule despite NBI and jumbo forceps biopsy (4 quadrant q 1cm)
- Result: Fellow/Patient dissatisfaction

The Perfect Solution

- Reduces or removes risk of cancer (and need for surgery)
- Cost effective
- Minimal side effects
- Reduces or removes need for surveillance
- “inflict an injury deep enough to eradicate all of the metaplastic and dysplastic stem cells but not so deep as to cause complications”

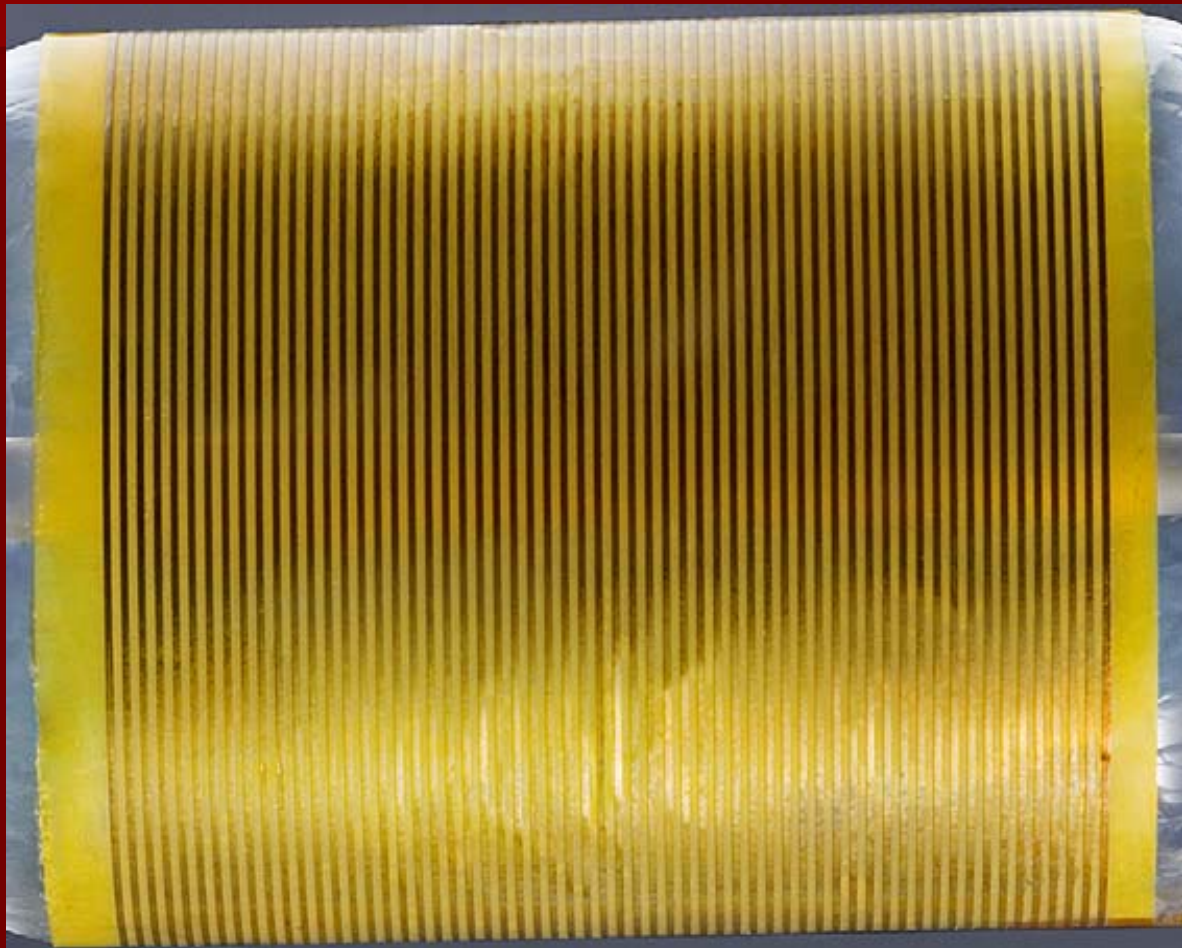
Background: Barrett's Esophagus

- 10–15% chronic GERD patients
- 30- to 50-fold greater risk of developing EAC
- incidence of development of adenocarcinoma ~0.5% annually
- LGD appears to be ~0.6% per year
- HGD patients ~5% risk per year
- Current recs: surveillance +/- emr vs surgery vs other modality

Background: RFA

- HALO-360 Ablation System (BARRX Medical, Sunnyvale, CA)
- 3 cm long ablation catheter
- 60 rings spaced 250 μm apart
- Delivers rf energy at predetermined density (10-12 J/cm²) for < 1 sec.
- Automated sizing balloon
- Contraindications: varices and/or previous radiation and/or ? surgery (other than nissen) and/or cardiac device



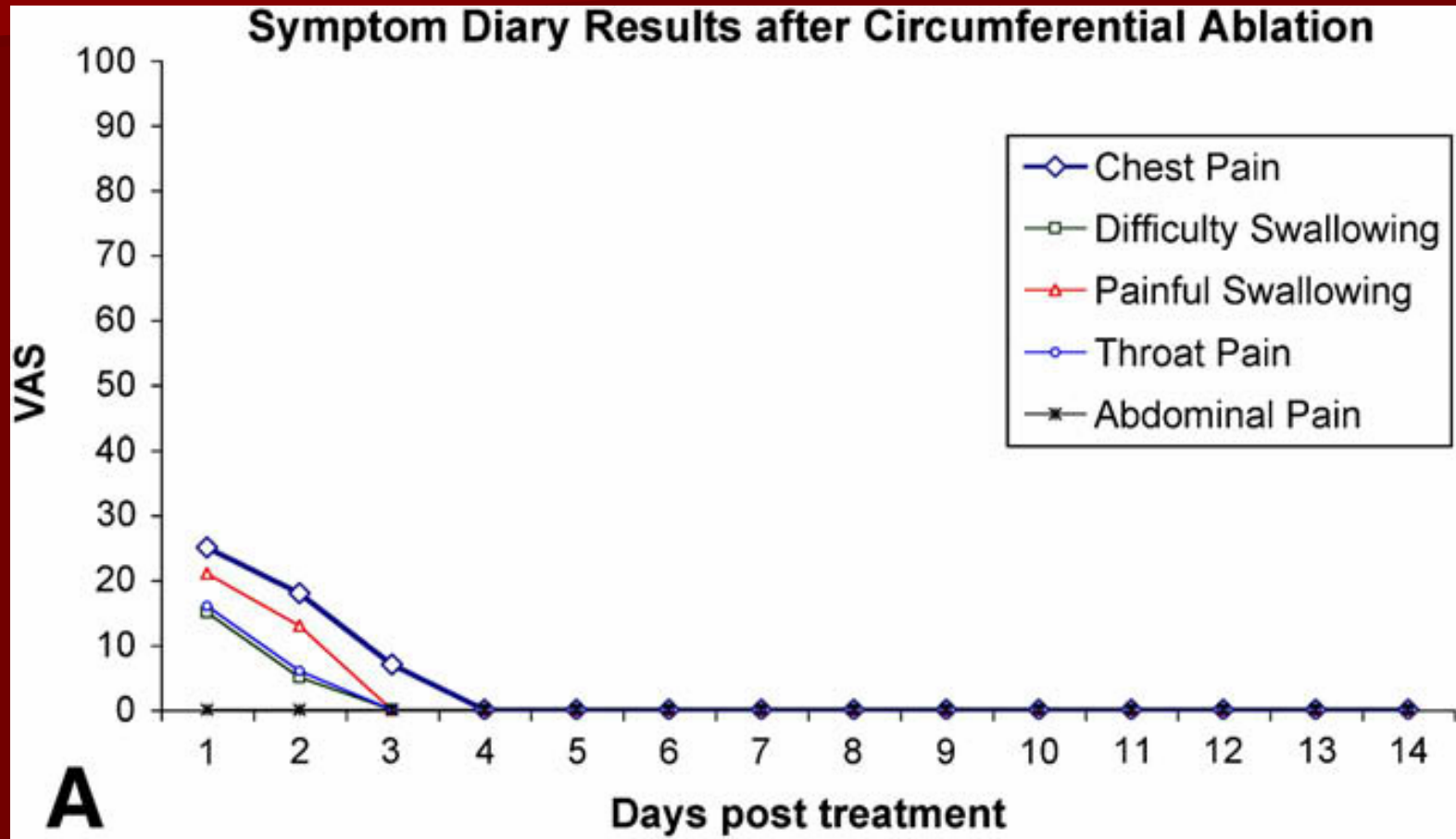


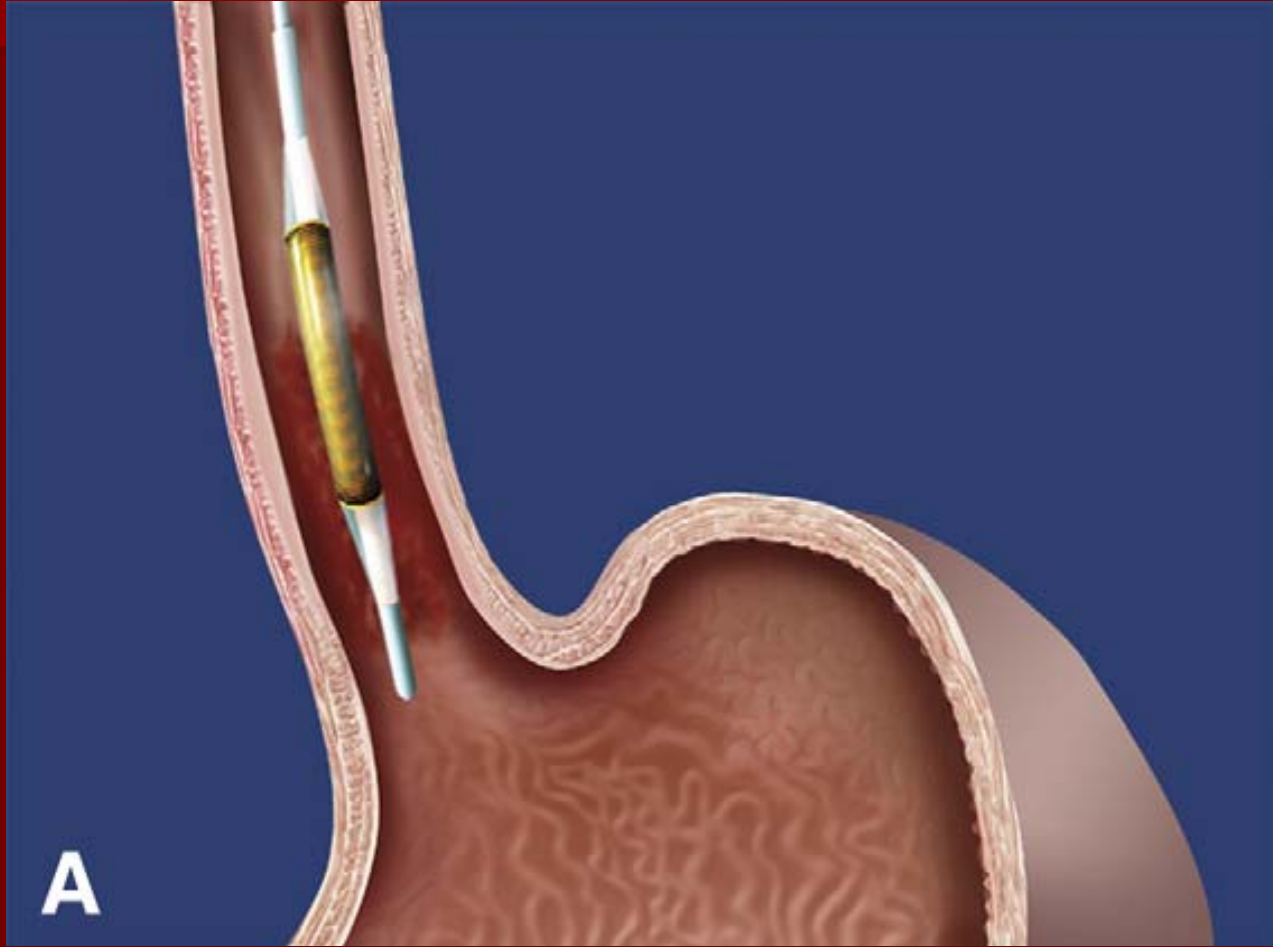
Background: RFA

- Focal ablation catheter
- electrode array mounted on an articulated platform (13 mm wide, 20 mm long).
- Device is mounted on distal end of gastroscope.



RFA: Side Effects

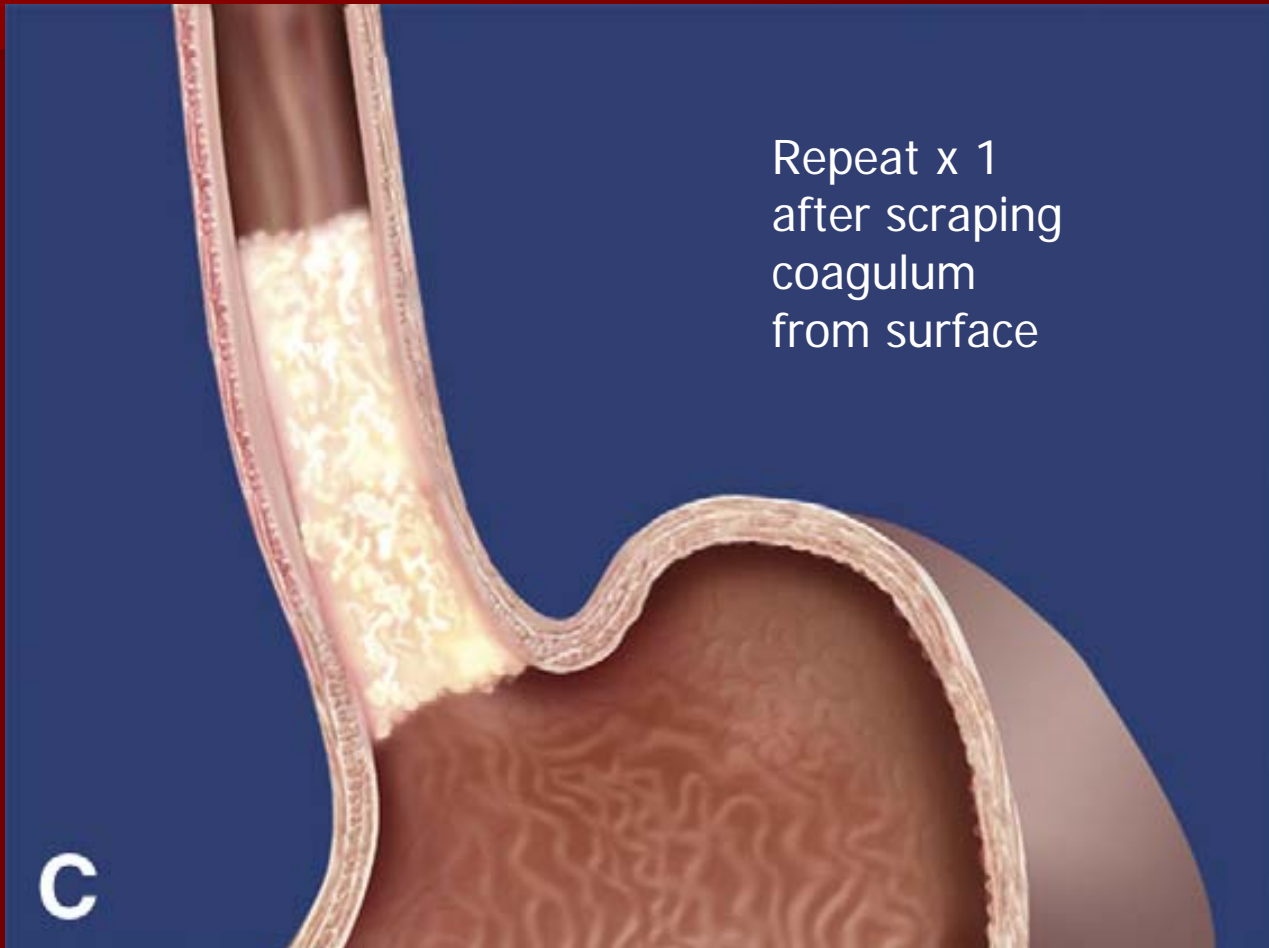


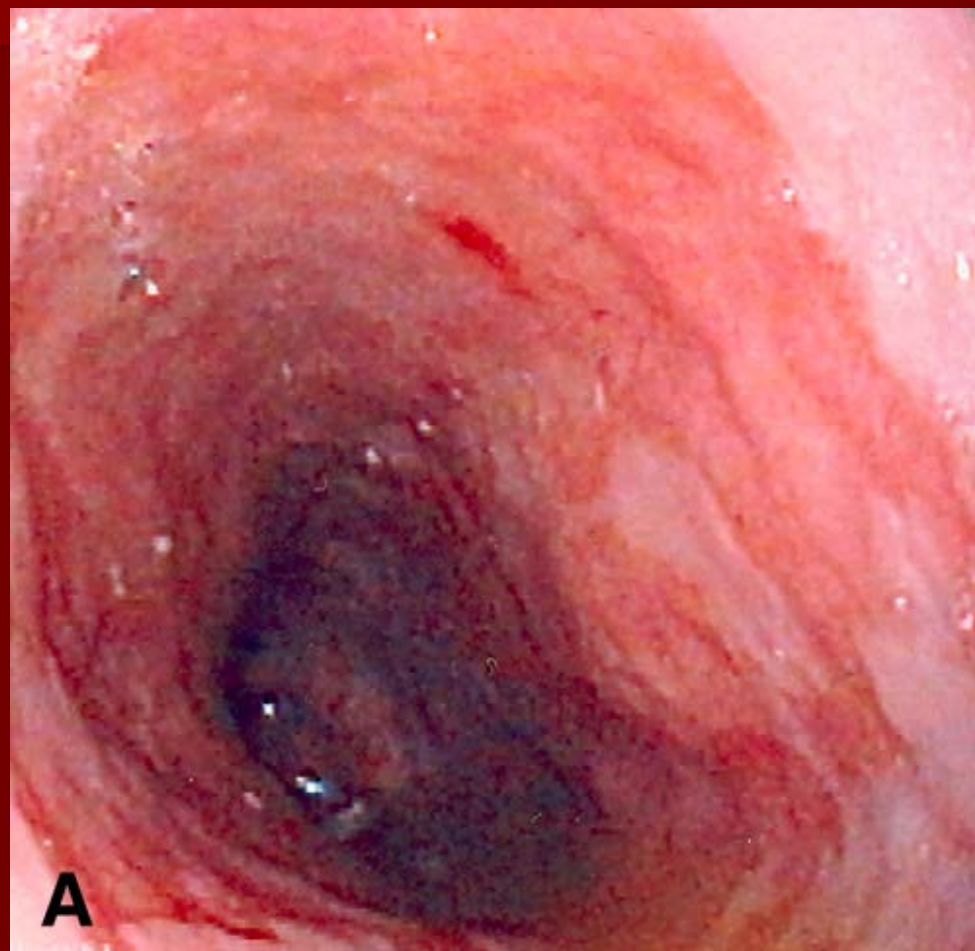


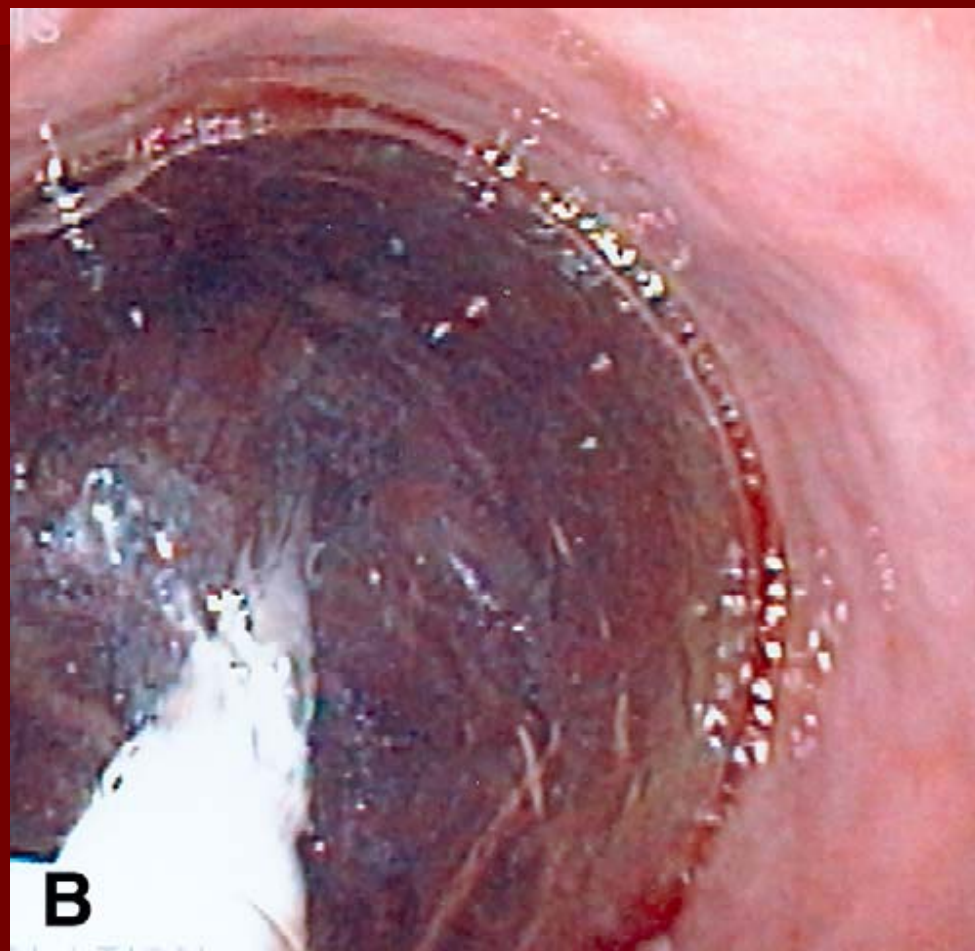


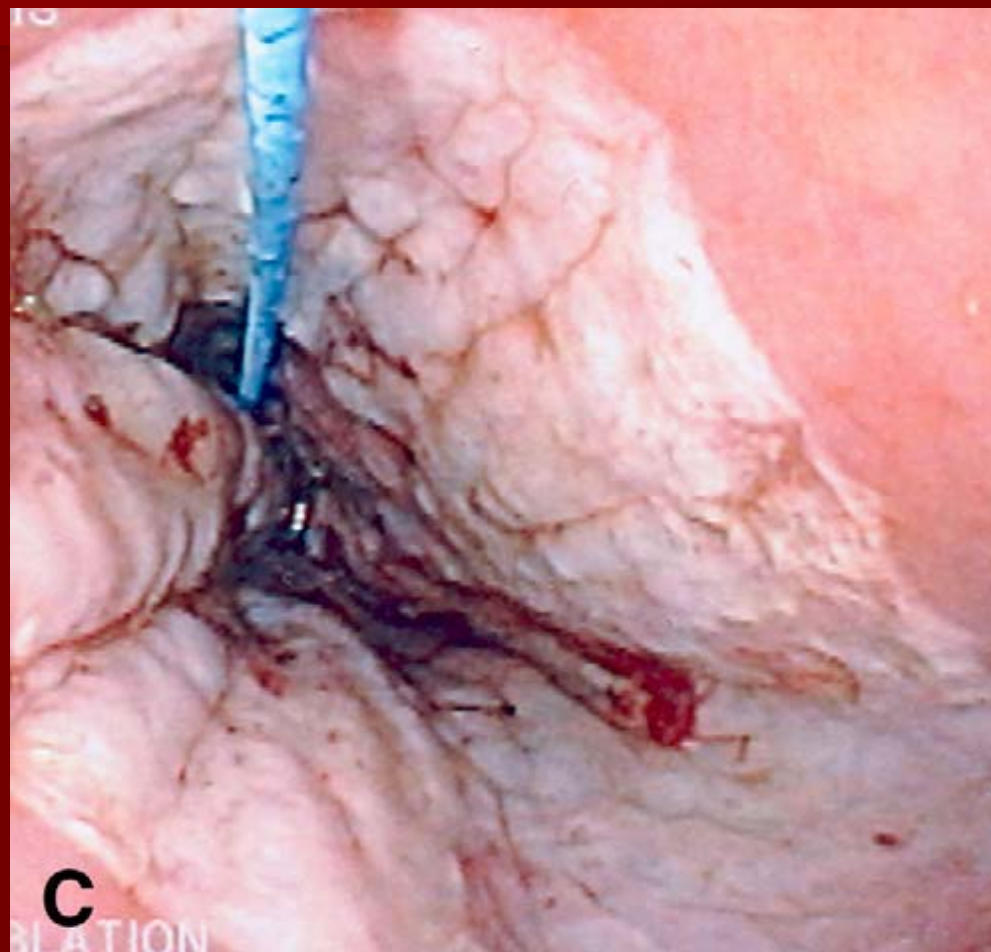
Repeat x 1
after scraping
coagulum
from surface

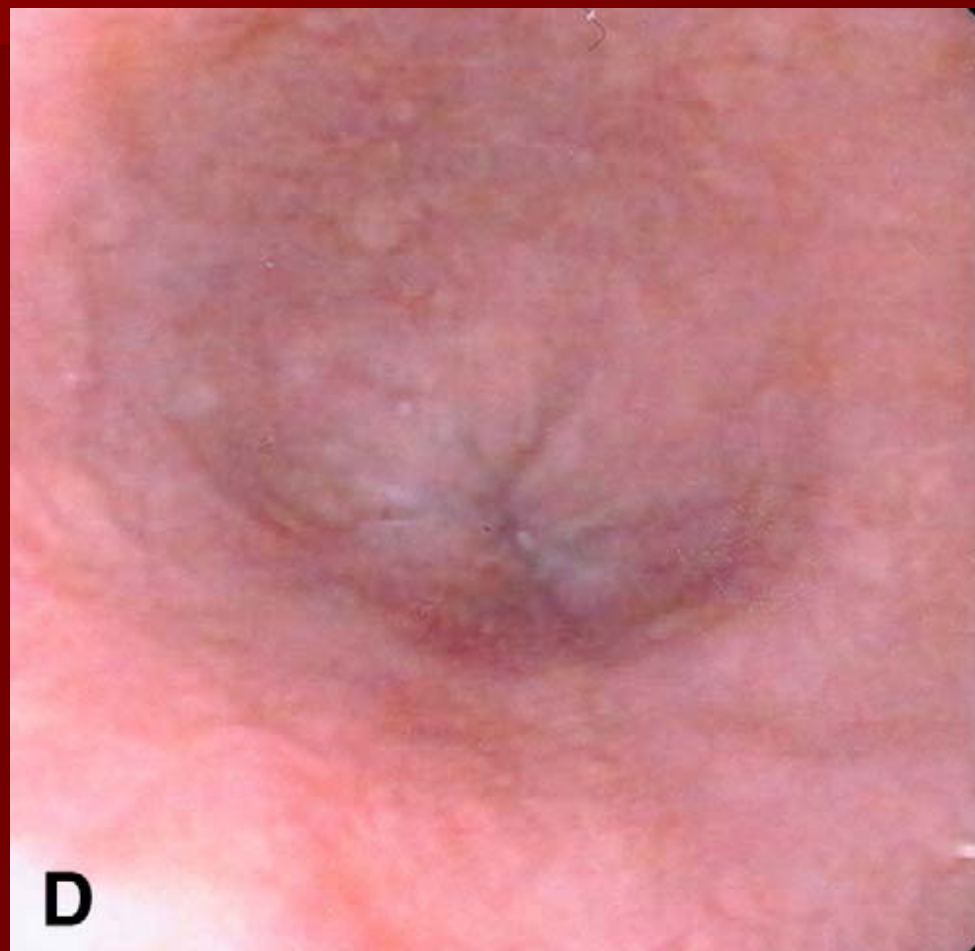
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Circumferential ablation of Barrett's esophagus that contains high-grade dysplasia: a U.S. multicenter registry

Ganz et al.

GIE Volume 68, Issue 1, Pages 35-40 (July
2008)

- Objective: To assess the safety and effectiveness of endoscopic circumferential balloon-based ablation by using radiofrequency energy for treating BE HGD.
- Design: Multicenter U.S. registry.
- Setting: Sixteen academic and community centers; treatment period from September 2004 to March 2007.

- Patients: histologic evidence of intestinal metaplasia (IM) that contained HGD confirmed by at least 2 expert pathologists.
 - A prior EMR was permitted, provided that residual HGD remained in the BE region for ablation.

Outcomes

1. all biopsy specimen fragments obtained at the last biopsy session were negative for HGD (CR-HGD),
2. all biopsy specimens were negative for any dysplasia (CR-D), and
3. all biopsy specimens were negative for IM (CR-IM).

Design

- 142 patients (median age 66 years) who had BE HGD (median length 6 cm, IQR 3-8 cm) underwent circumferential ablation (median 1 session, IQR 1-2).
 - prior EMR in 24 patients (17%), 5 of whom demonstrated intramucosal adenocarcinoma (IMC) with negative deep and lateral margins.
- Repeat endoscopy at 3-month intervals.
 - 92 patients received 1 follow up biopsy session
- persistent BE was evident = repeat ablation
- If no endo evidence of BE: 4-quadrant biopsy specimens q 1 to 2 cm of the original BE-segment length.
- 2 pathologist reviewed pathology (not centralized)

Results

- No serious adverse events were reported.
 - There was 1 asymptomatic stricture
 - no buried glands.
- 92 patients had at least 1 follow-up biopsy session (median follow-up 12 months, IQR 8-15 months).
 - CR-HGD: 90.2%
 - CR-D: 80.4% (9 patients had persistent LGD)
 - CR-IM: 54.3%.
 - Results were the same for prior and no prior emr
- 5 patients with baseline mucosal adenocarcinoma resected with an EMR before ablation, all achieved CR-IM on the last biopsy.

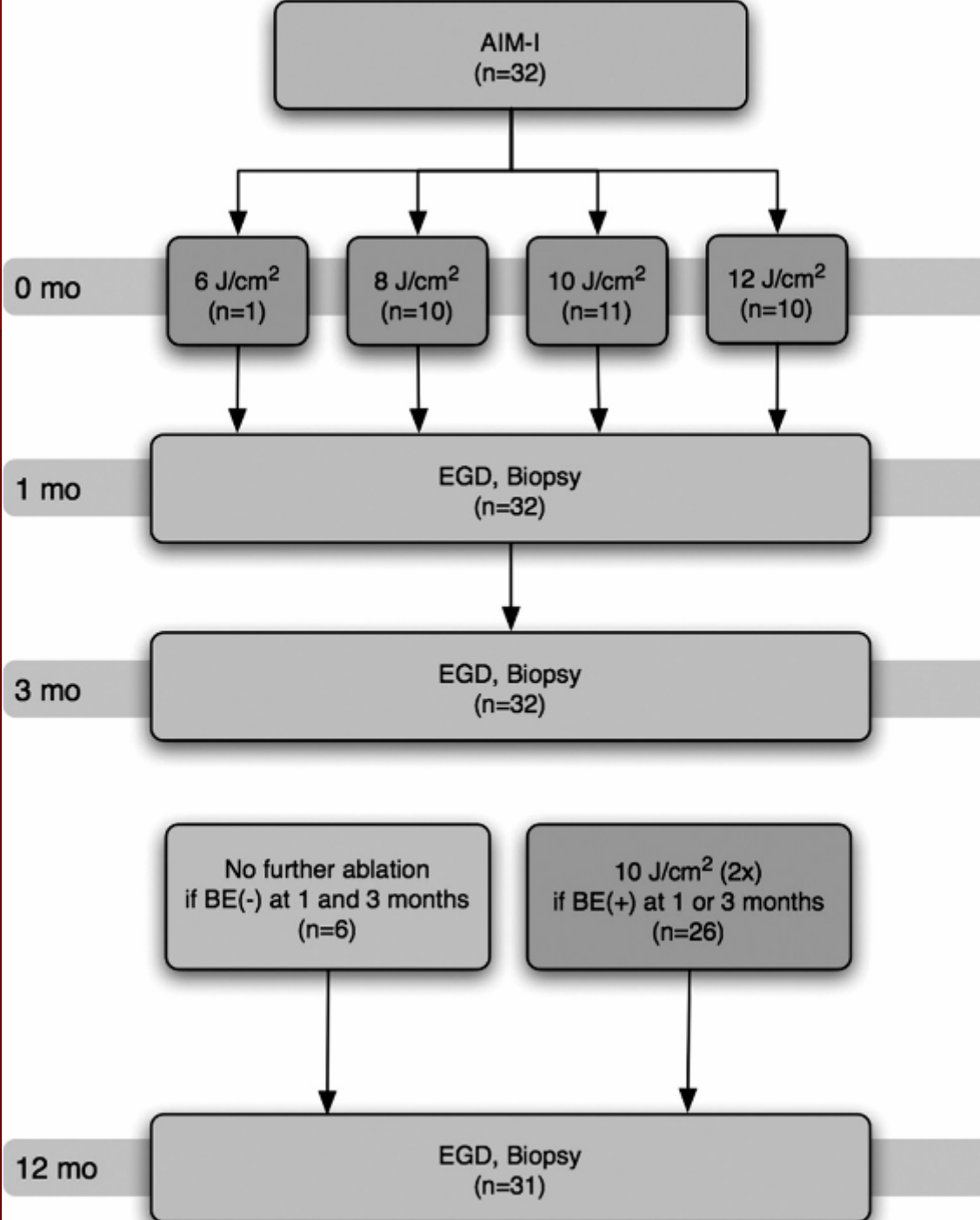
Limitations

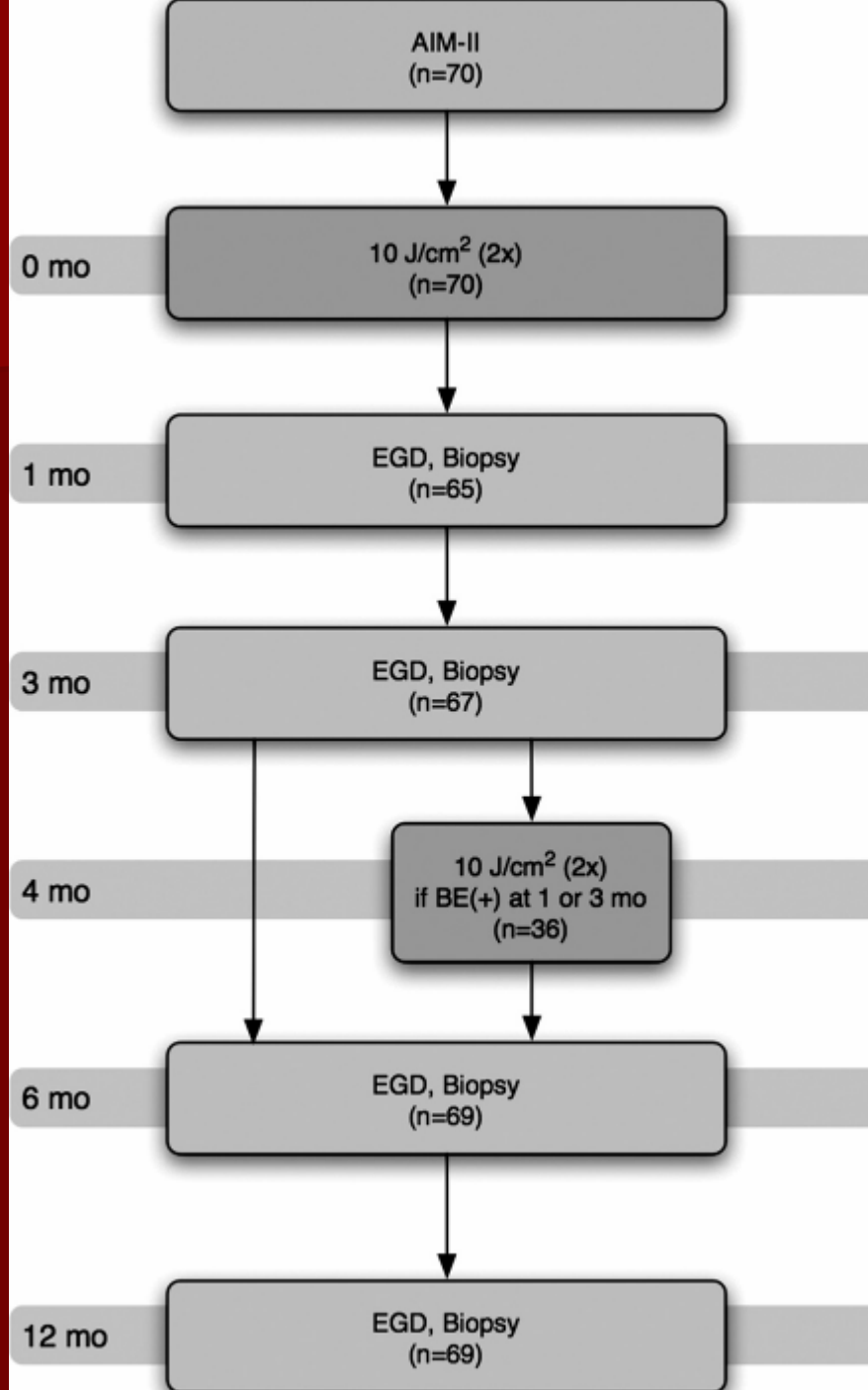
- A nonrandomized study design
- without a control arm
- lack of centralized pathology review
- ablation and biopsy technique not standardized
- relatively short-term follow-up
- They did not remove balloon between ablations (for cleaning)

Endoscopic ablation of Barrett's esophagus: a multicenter study with 2.5-year follow-up

David E. Fleischer, MD, Bergein F. Overholt, MD,
Virender K. Sharma, MD, Alvaro Reymunde, MD,
Michael B. Kimmey, MD, Ram Chuttani, MD, Kenneth J.
Chang, MD, Charles J. Lightdale, MD,
Nilda Santiago, MD, Douglas K. Pleskow, MD, Patrick J.
Dean, MD, Kenneth K. Wang, MD

■ (Gastrointest Endosc 2008;68:867-76.)







- Objective: To provide longer follow-up and to assess the long-term safety and efficacy of step-wise circumferential ablation with the addition of focal ablation for BE.
- Design: Prospective, multicenter clinical trial (NCT00489268).
- Setting: Eight U.S. centers, between May 2004 and February 2007.

Patients

- Ages: 18-75
- + IM w/o dysplasia and reconfirmation within 6 months
- 2-6 cm BE
- Excluded: prior ablation, esophageal stricture or varices, active esophagitis, prior emr, dysplasia or malignancy, implanted electrical device

Patients & Interventions

- 70 subjects with 2-6 cm of BE and histologic evidence of IM.
- Circumferential ablation at baseline and at 4 months if there was residual IM.
- Follow-up biopsy specimens were obtained at 1, 3, 6, 12, and 30 months.
- Specimens were reviewed by a central pathology board.
- Focal ablation was performed after the 12-month follow-up for histological evidence of IM at the 12-month biopsy (absolute indication) or endoscopic appearance suggestive of columnar-lined esophagus (relative indication).
- Subjects received esomeprazole for control of esophageal reflux.

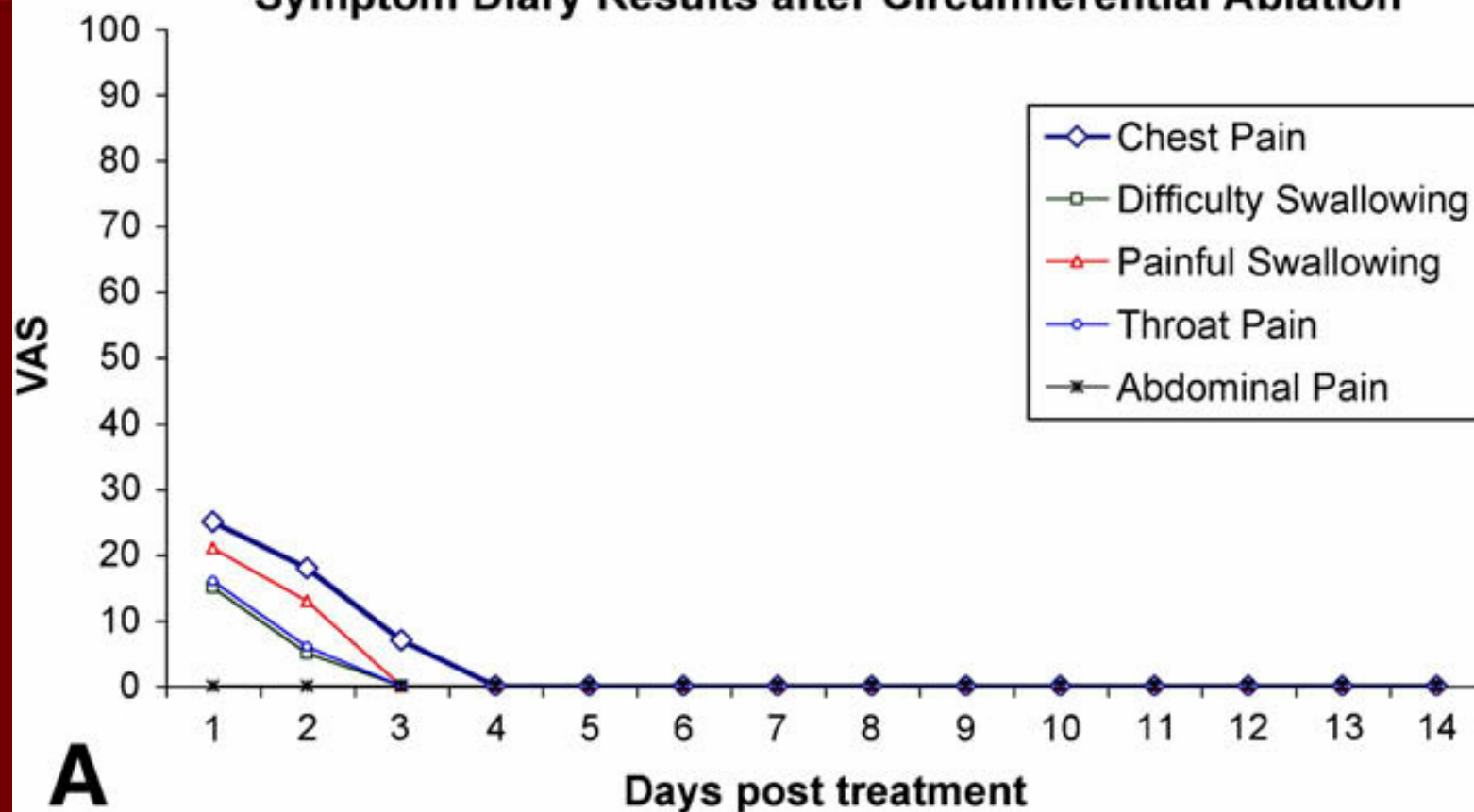
Main outcome measurements

- Complete absence of IM per patient from biopsy specimens obtained at 12 and 30 months, defined as complete remission–IM (CR-IM).

Results

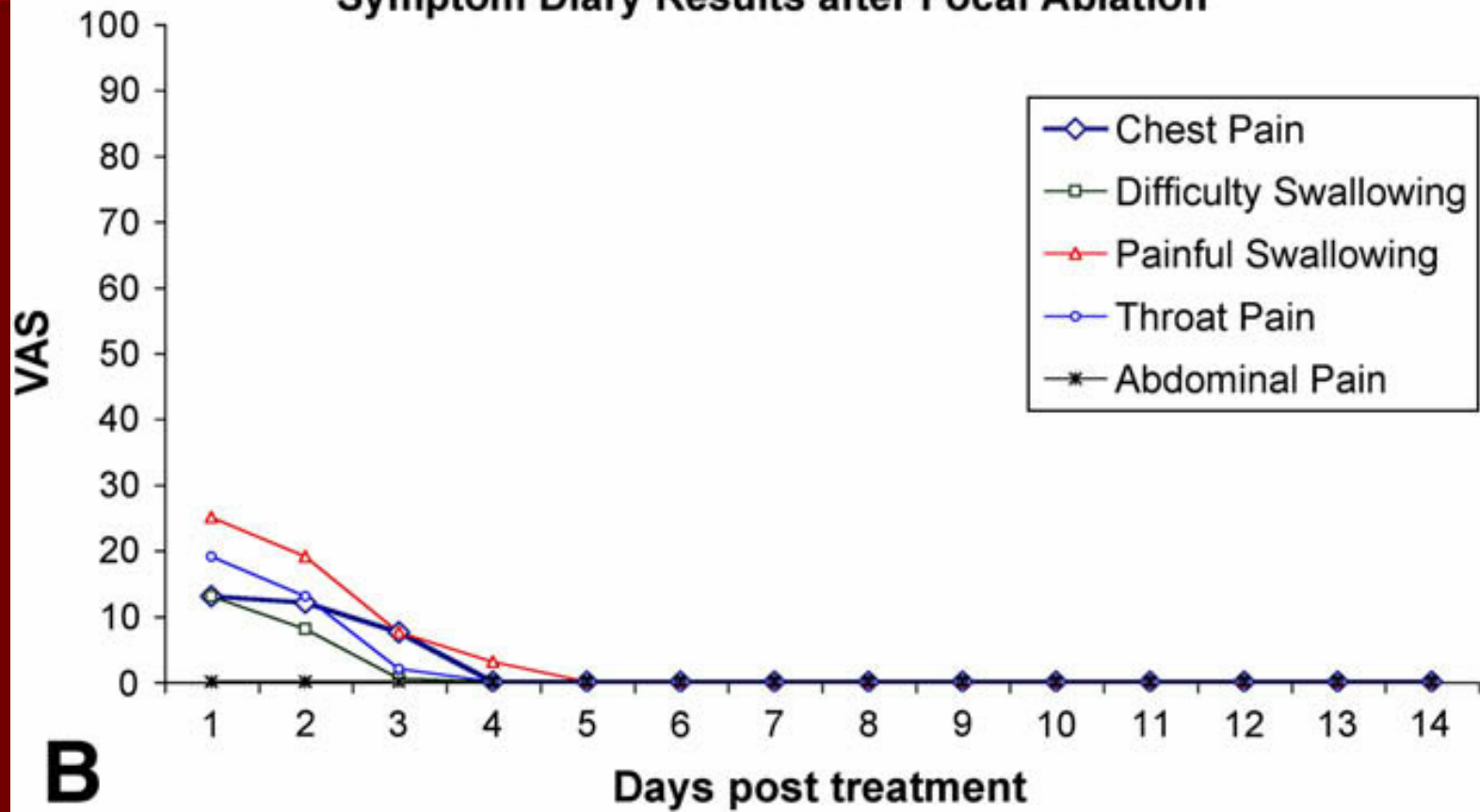
- At 12 months, CR-IM was achieved in 48 of 69 available patients (70% per protocol [PP], 69% intention to treat [ITT]).
- At 30 months after additional focal ablative therapy, CR-IM was achieved in 60 of 61 available patients (98% PP, 97% ITT).
- No strictures
- No buried glands
- No serious adverse events.

Symptom Diary Results after Circumferential Ablation

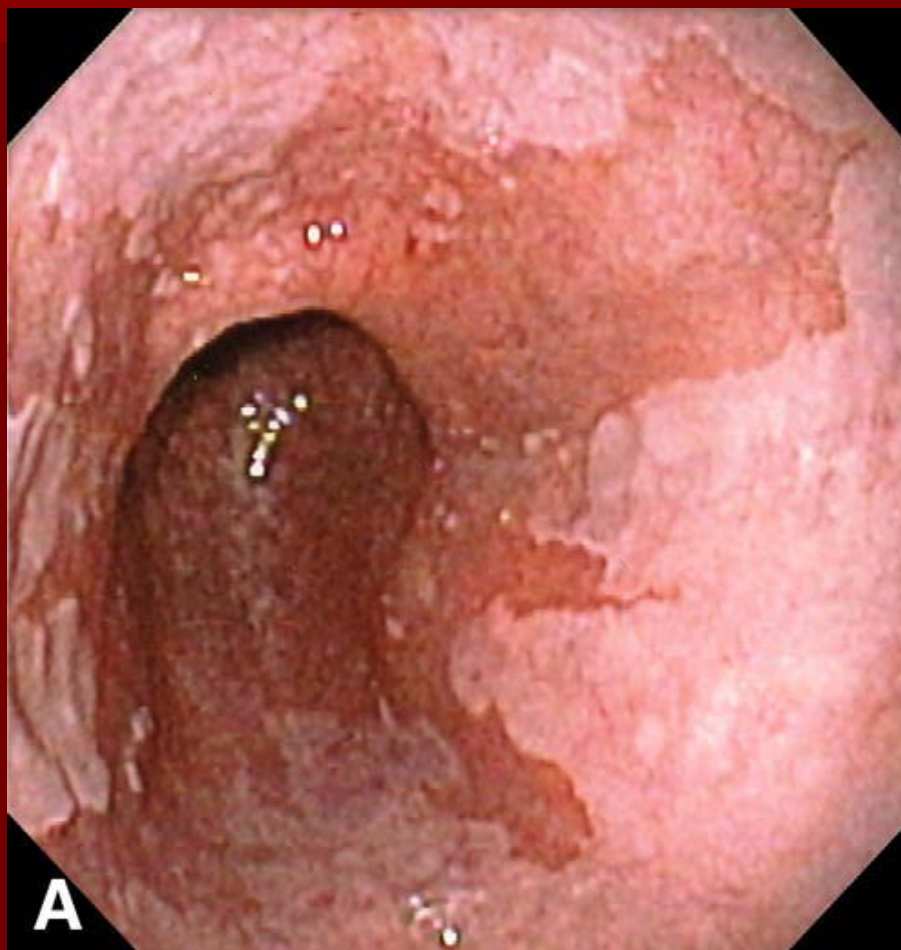


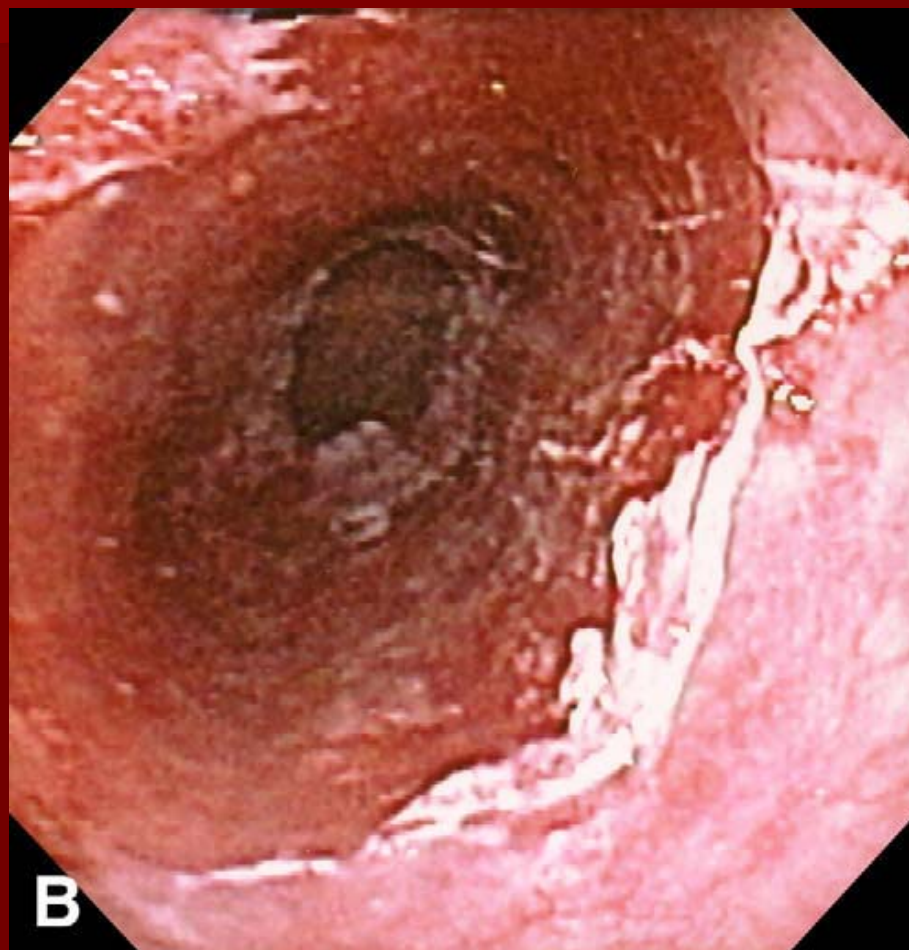
A

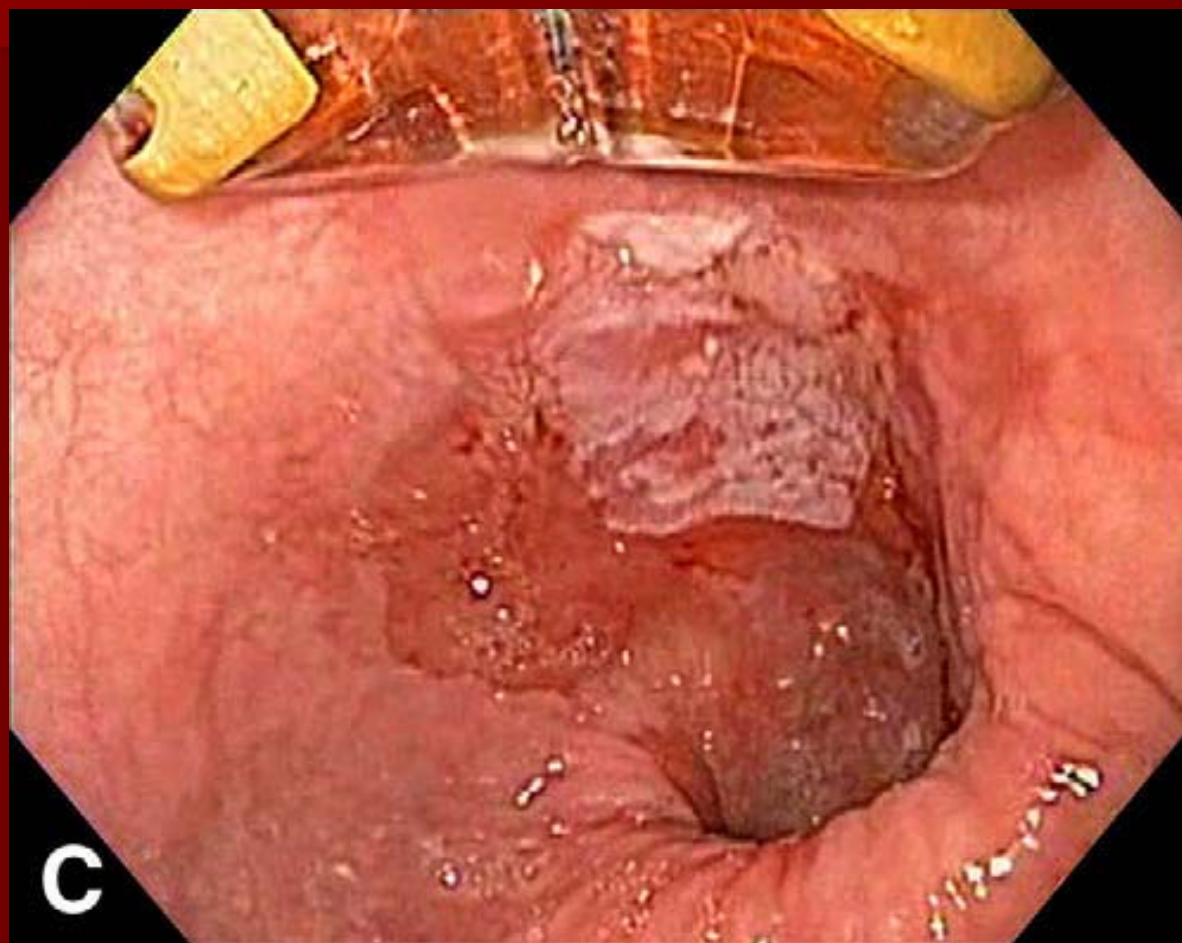
Symptom Diary Results after Focal Ablation

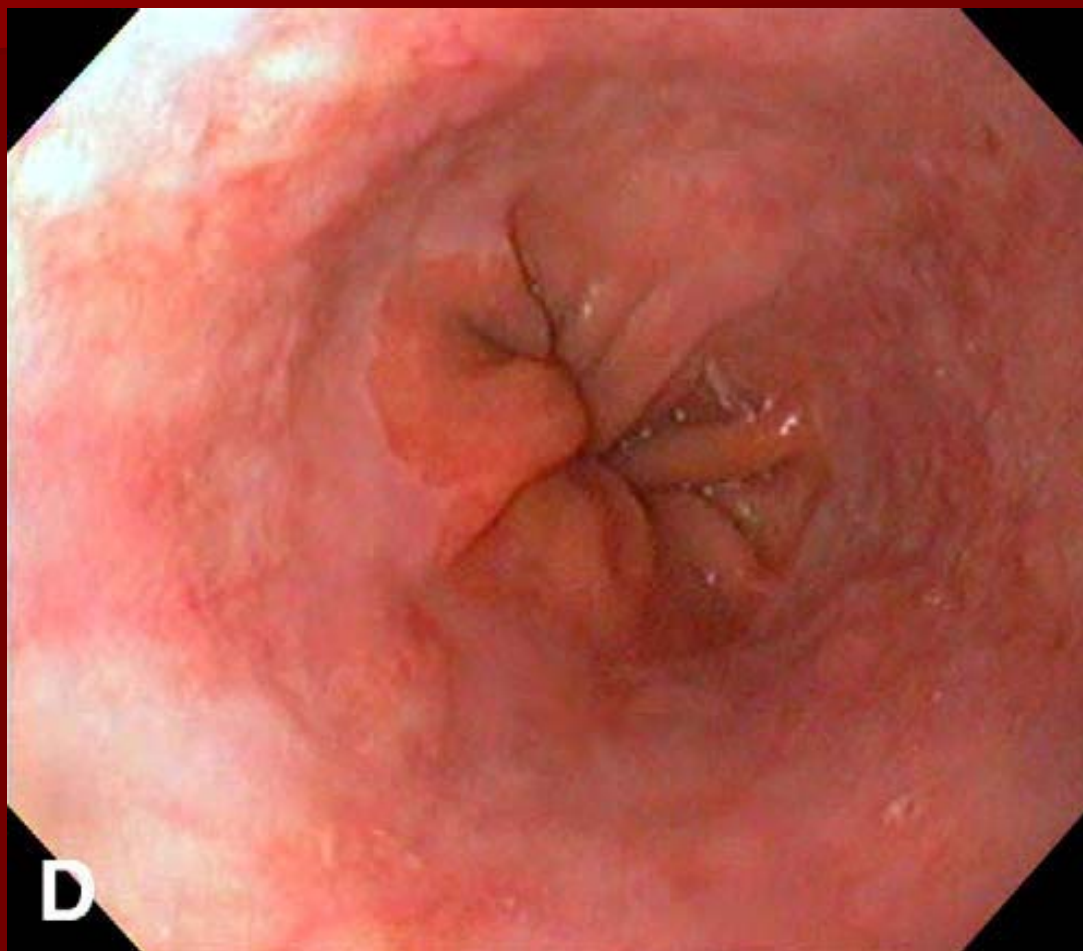


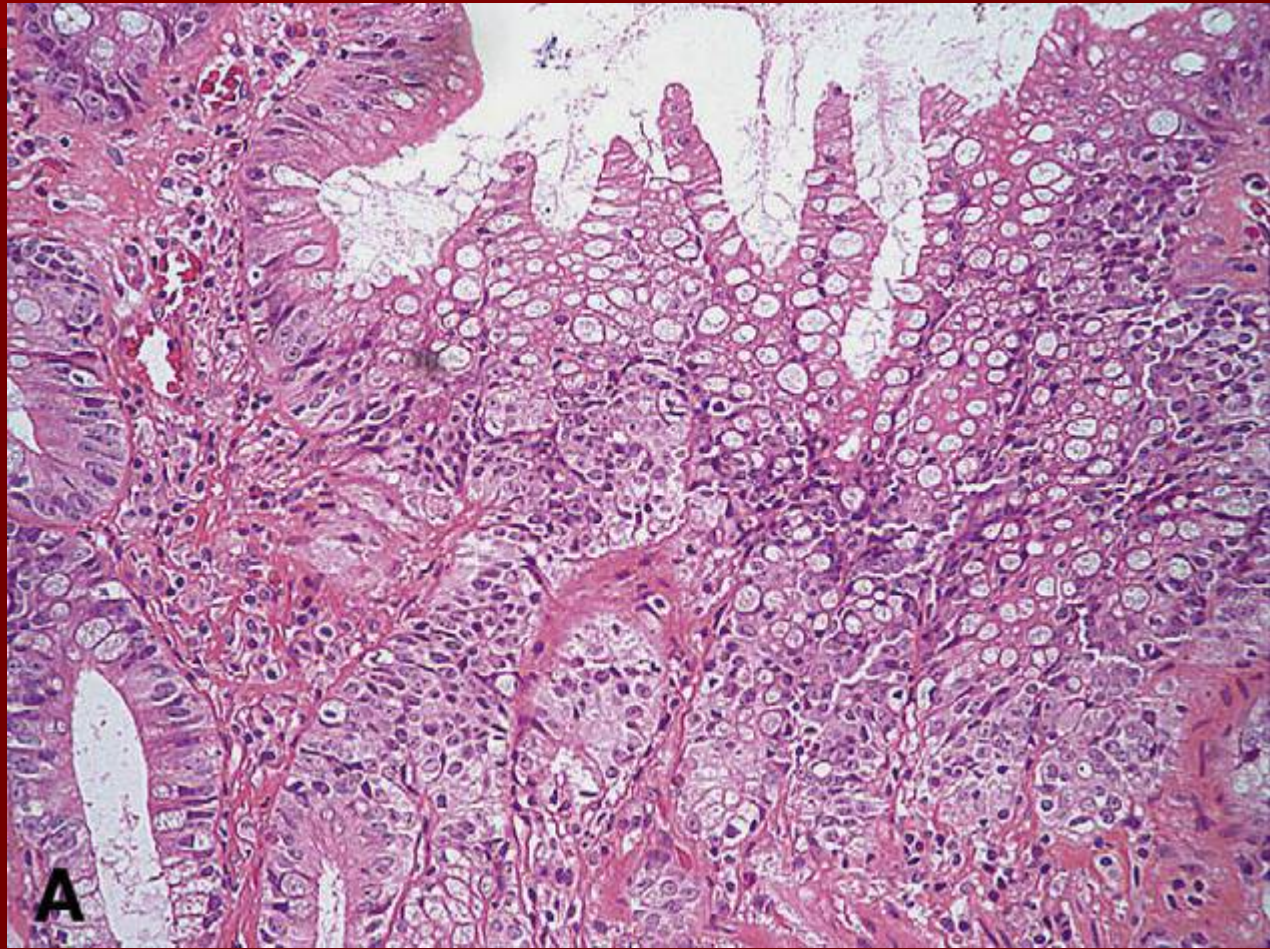
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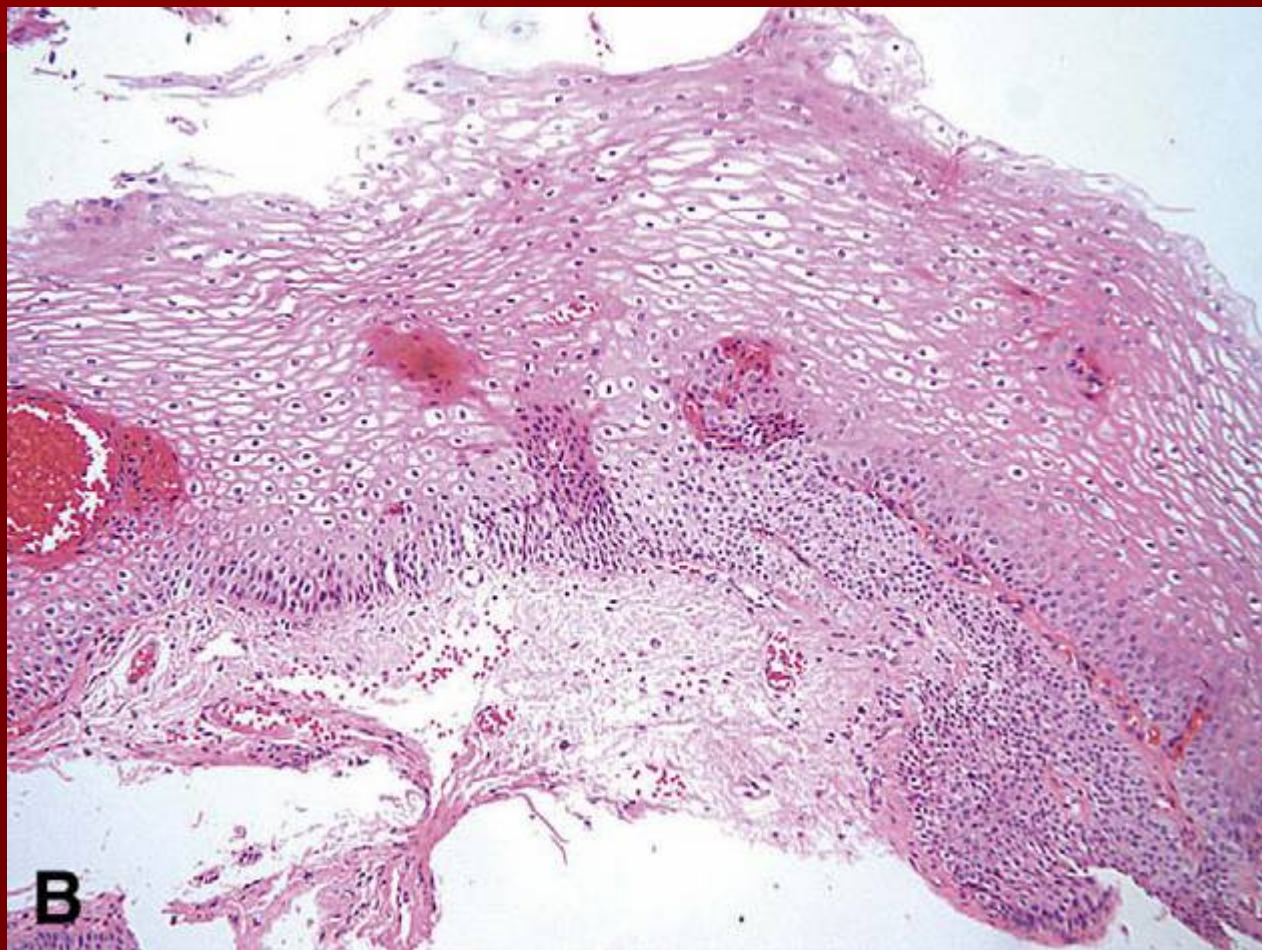






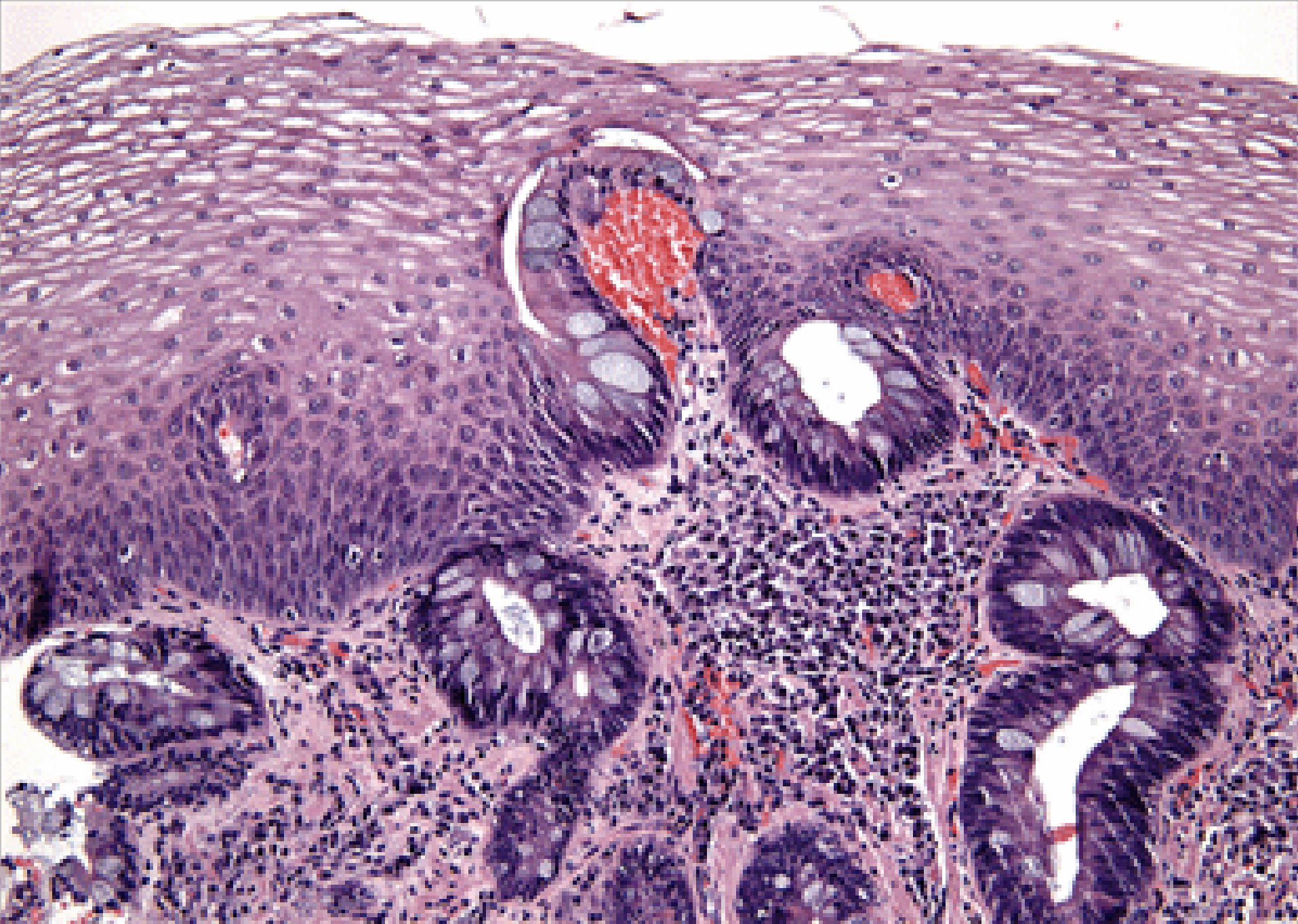






Limitations

- No control arm



“Buried glands”

- Squamous epithelialization over underlying IM = we can't see salmon tongue
- To accurately detect: biopsies should contain some lamina propria
- The mean thickness of nondysplastic Barrett's epithelium in vivo has been estimated at 0.6 mm, with a range of 0.5 to 0.7 mm.
- >4000 biopsy specimens reviewed in these two studies: no buried glands (@ 1 and 2.5 yr follow-up)
- Recent small study with 3/15 patients

Stem cells

- If one dysplastic cell remains
 - We probably won't see it
 - It will be allowed to proliferate unnoticed

Are we curing people?

- Traditional thought with epithelial malignancy: no recurrence at 5 yrs = cure (stem cells wouldve shown themselves)
- HGD in Barrett's esophagus, CA rate of 5% per year
- it may not be appropriate to conclude that the cancer risk has been eliminated for a patient who has survived 5 years after the treatment of dysplasia in Barrett's esophagus.
- Surveillance?

Is RFA Cost Effective?

- RFA of HGD could increase life expectancy by 3 quality adjusted years at an incremental cost of < \$6,000, compared with no intervention.
- Patients with LGD or no dysplasia can also be optimally managed with ablation, but continued surveillance after eradication of metaplasia is expensive.
- If ablation permanently eradicates at least 28% of LGD or 40% of non-dysplastic metaplasias, ablation would be preferred to surveillance.

Future directions

- Cancer risk after ablation (long term follow up)
- RFA for patients with + tissue biomarker assesment to determine those more likely to progress to cancer (e.g. aneuploidy)
- RFA + EMR
- RFA + Nissen
- Issues with surveillance

Question 1

A 55-year-old man with BE and HGD is referred to you for endoscopic ablation. You review the patient's histology and endoscopic video before counseling about the outcome of radiofrequency ablation of BE. Which endoscopic/histologic findings predict an effectively complete ablation without residual disease?

■ **Possible answers (A-D)**

- A. 5 cm BE and multifocal HGD with no visible lesions
- B. 3 cm BE and unifocal HGD with an ulcer
- C. 5 cm BE and unifocal HGD with a nodule
- D. 5 cm BE and multifocal HGD with nodules

CORRECT RESPONSE: A

- **Rationale for correct response:**
- Practical approach to endoscopic ablation of BE with HGD:
- Patients without endoscopically visible lesions could be considered for endoscopic ablation.
- Patients with esophageal nodularity or ulceration should undergo endoscopic mucosal resection of the nodule/ulcer to assess the depth of penetration of the disease.
- Patients with T1b (submucosal invasion) should be considered for surgery.
- Patients with T1a disease (intramucosal) could be offered endoscopic ablation.

Question 2:

- **How good is radiofrequency ablation of Barrett's esophagus with or without dysplasia?**

A 55-year-old man with GERD and histologically confirmed Barrett's esophagus is referred to you for consultation regarding the role of radiofrequency ablation. You review recent studies on this new treatment modality and explain to him the endpoints, such as histological complete response (CR) of intestinal metaplasia (IM).

- Which one of the following ablation approaches leads to over 90% CR of IM?
- **Possible answers (A-D)**
- A. Single-session circumferential radiofrequency ablation
- B. Single-session focal radiofrequency ablation
- C. Circumferential ablation, followed by focal ablation
- D. Focal ablation, followed by circumferential ablation

CORRECT RESPONSE: C

- **Rationale for correct response:**

- **RF ablation of BE with HGD**

- Circumferential ablation results in elimination of HGD in 90.2% of patients, dysplasia in 80.4%, and IM in 54.3% of cases.¹

- **RF ablation of BE with LGD**

- A stepwise regimen of circumferential balloon ablation followed by focal ablation eradicated IM in 90% and dysplasia in 100% of cases at 2-year follow-up, without stricture formation or buried IM.²

- **RF ablation of BE without dysplasia**

- A stepwise circumferential balloon ablation followed by focal ablation resulted in complete eradication of IM in 98% of patients at 2.5-year follow-up, without any esophageal strictures or buried glandular mucosa noted on standard surveillance biopsies.

Questions

