Barrett’s Esophagus: What to Do for No Dysplasia, LGD, and HGD?

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Outline

• What are the risks of progression in BE?
• What are the management options for ND, LGD & HGD?
  – What data support efficacy of ablative therapy in non-dysplastic & dysplastic BE?
• What is an appropriate algorithm to follow for endoscopic intervention in BE?
Barrett’s Classification and Management

- Non-dysplastic IM
  - Surveillance every 3 years
  - Detect progression to dysplasia or cancer
- LGD (low-grade dysplasia)
  - Surveillance every 6-12 months
  - Detect progression to HGD or cancer
- HGD (high-grade dysplasia)
  - Surveillance every 3 months
  - Esophagectomy
  - EMR and ablation: options at select institutions

Progression to Cancer in HGD

- Buttar et al. N=100: 32% Surveillance Period 8 Years
- Schnell et al. N=77: 16% 7.3 Years
- Reid et al. N=76: 59% 5 Years

Medical Therapy

- All subjects should get PPI
  - Super-therapeutic doses have not been shown more effective
  - Routine pH monitoring not necessary
- Routine ASA not recommended
  - Often indicated on basis of cardiac risk factors
How Benign is Low-Grade Dysplasia?

- 147 subjects with a diagnosis of LGD made in a community practice in the Netherlands
- Path reviewed by 2 expert pathologists
  - Disagreements resolved by consensus
- 85% of cases were down-graded
- In the 15% who were not, the incidence rate of HGD or EAC was 13.4%/pt-yr (mean f/u: 51 months)

Curvers WL et al. Am J Gastroenterol 2010, pub pend

Is It Really Dysplastic?

LGD (n= 83) HGD (n= 129)

Home Institution Diagnosis

Cancer HGD LGD IND/ND-IM
Isn’t the Risk of Cancer too Low in LGD and ND to Justify Intervention?

The risk of cancer in any single year is low for those with ND. The NNT to prevent one cancer in a given year may be >200.

Consider a 40 yo male w/ ND-BE...

- Such an individual may have 40-50 yrs of life expectancy in 2010
- If risks are linear, compounding 0.5% over this time yields an overall cancer risk of 20-25%
- Single year NNT’s are irrelevant
  - Ablation is illogical for someone with a short life expectancy
- The real questions are what the lifetime cancer risk for the individual is, and how much it could be lowered with ablation?
We Don’t Have Good Data on the Longterm Protective Effect of Ablation

- But we can make some estimate of the effect of endoscopic ablation and compare it to natural history studies
- Risk from natural history studies: 6/1000
- Risk from meta-analysis of ablation: 1.6/1000

Using these data, let’s play some hypotheticals...

5 yr survival 10 yr survival 20 yr survival 40 yr survival

Risk from natural history: 6/1000
Risk from meta-analysis of ablation: 1.6/1000

But It Depends on Baseline Risk!

- Natural History
- S/P Ablation
- 1/2 as Effective

Ablation of Lesser Forms of Dysplasia Might be Effective and Cost-Effective

What is the Risk of Death with Esophagectomy?

![Graph showing 30 Day Mortality vs. Number of Esophagectomies/Year]

If an Endoscopic Intervention is to be Pursued...

Birkmeyer et al, NEJM, 2002
Choose Your Weapon!

Fiber Optic Guide
Endoscope
Spacing Balloon
Laser Light
High-Grade Dysplasia

AIM Dysplasia Trial

U.S. multi-center, randomized, single-blind, sham-controlled clinical trial
AIM-Dysplasia Trial

Study Design
• Randomized, sham-controlled design
  – 2:1 RFA vs sham
  – Stratified by:
    • degree of dysplasia (LGD vs. HGD)
    • length of segment (1-4 cm vs 4-8 cm)
  – Maximum of 4 RFA sessions
  – Identical biopsy protocols, equal sampling
  – 12 month cross-over

Methods (cont.)
Primary Outcomes (12 months)
  – Complete eradication of dysplasia
    • all biopsy specimens free of dysplasia
    • RFA vs. control, HGD and LGD analyzed separately
  – Complete eradication of intestinal metaplasia
    • all biopsy specimens free of IM
    • RFA vs. control, all patients

Results (cont.)

*Stricture Occurrence*

- 5 Strictures in 84 patients
  - 5 of 84 patients (6.0%)
  - 5 of 298 cases (1.7%)
- All resolved, mean 2.6 dilations
- All achieved complete eradication of intestinal and dysplasia

What About the Risk of “Buried Barrett’s?”
Results – Buried Barrett’s (SSIM)

Histology: Sub-squamous Intestinal Metaplasia

- Baseline incidence of SSIM (25%)
  - HGD cohort: 21% of patients
  - LGD cohort: 30% of patients
- 12 month incidence of SSIM
  - RFA cohort: 6.8% of patients
  - Sham cohort: 60% of patients*

*p<0.05 Fisher’s exact test, RFA vs. Sham

In this multi-center, randomized, sham-controlled study of radiofrequency ablation in patients with dysplastic Barrett’s esophagus, there was a high rate of complete eradication of dysplasia and intestinal metaplasia and decreased disease progression in the ablation group, as compared with the control group.
What are the True Risks with Ablation?

- Chest Pain
  - Pretty much everyone gets some
  - 23/100 on a VAS in recent RCT
    - Resolves on average by a week or so
- Bleeding
- Perforation
- Stricture
- Buried BE

Given the relatively short-term nature of data after ablation, it is unwise currently to cease surveillance endoscopy after ablative therapy.
Evolving Technology in BE

Cryotherapy in HGD: An Initial Report

- 98 subjects w/ HGD treated at 10 institutions
  - 61 completed Rx, 27 ongoing
- 281 total procedures
  - 4.0 / pt
- No perfs, no buried glands, no bleeds or chest pain requiring hospitalization
- One progression to CA

Algorithm for Endoscopic Intervention in BE

Nodular Disease Should Be EMR’ed!

A
B
C
D
Algorithm, cont.

- For subjects with nodular disease, EMR histology decides further management
  - No cancer, mucosal cancer, or maybe sm₁ cancer -> ablative therapy
  - Worse than sm₁ -> consideration of multimodality Rx and esophagectomy
- Flat HGD -> ablation
  - Given current data, RFA seems most appropriate

Algorithm, cont.

- LGD
  - Unifocal, elderly, and/or wishing conservative Rx -> surveillance endo’s
  - Multifocal, previously nodular, young, family hx of cancer, pathologically worried -> consider ablation
    - Caveats about lack of data on decreasing cancer
- Non-dysplastic
  - Ablation may be preferable, but we await further data
Can It Work in Primary GI Practices?

• Radiofrequency ablation of Barrett’s esophagus: outcomes of 429 patients from a multicenter community practice registry.
  – RFA performed in 4 community practices
    • 76% non-dysplastic subjects
  – Had follow-up in 338 (mean duration, 9 months)
    • 72% had complete eradication of intestinal metaplasia
    • 79% had complete eradication of dysplasia
  – No perforations
  – 2.1% stricture rate

Endoscopy 2010; 42:272-78.