Barrett's Esophagus and Endoscopic Therapy

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Objectives

- Relationship of BE, acid reflux and esophageal cancer
- Screening and surveillance guidelines
- Management of dysplasia and early cancers

Esophagogastric Junction

Squamocolumnar junction

View on retroflexion

Esophagogastric Junction

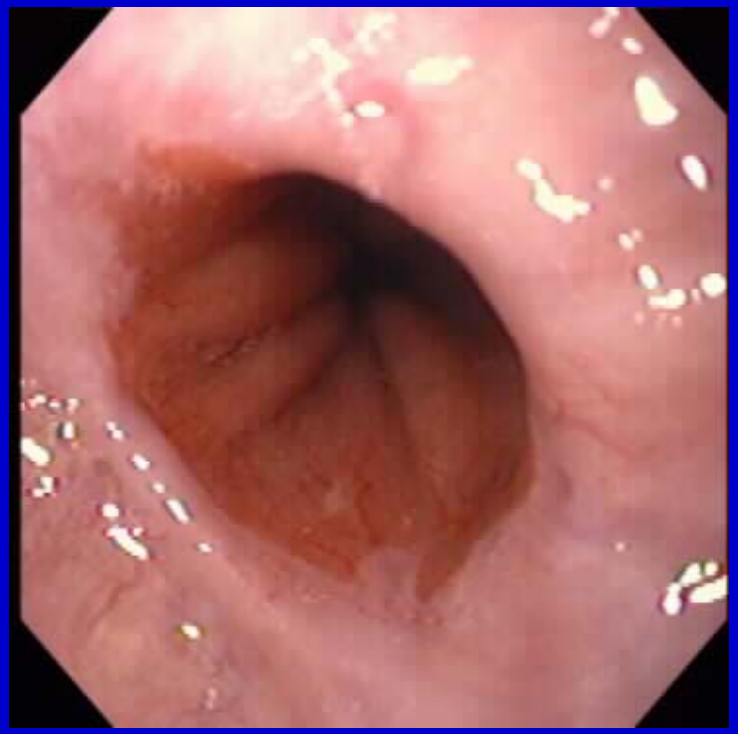
- Definitions
  - Squamocolumnar junction (SCJ) = juxtaposition of the squamous and columnar mucosa
  - Esophagogastric junction (EGJ) = dynamic area including the distal esophagus and proximal stomach
  - Hiatal hernia = foreshortened esophagus with proximal stomach herniated into the chest
  - Columnar lined esophagus = SCJ displaced proximal to EGJ

Acid Reflux and EGJ

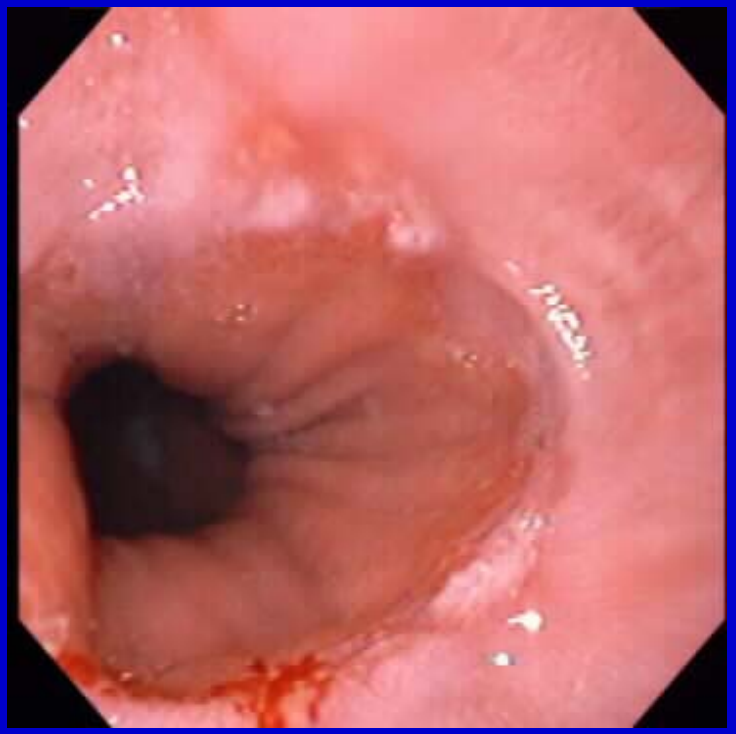
Ring during distention

Same ring during contraction

Hiatal Hernia and Esophagitis



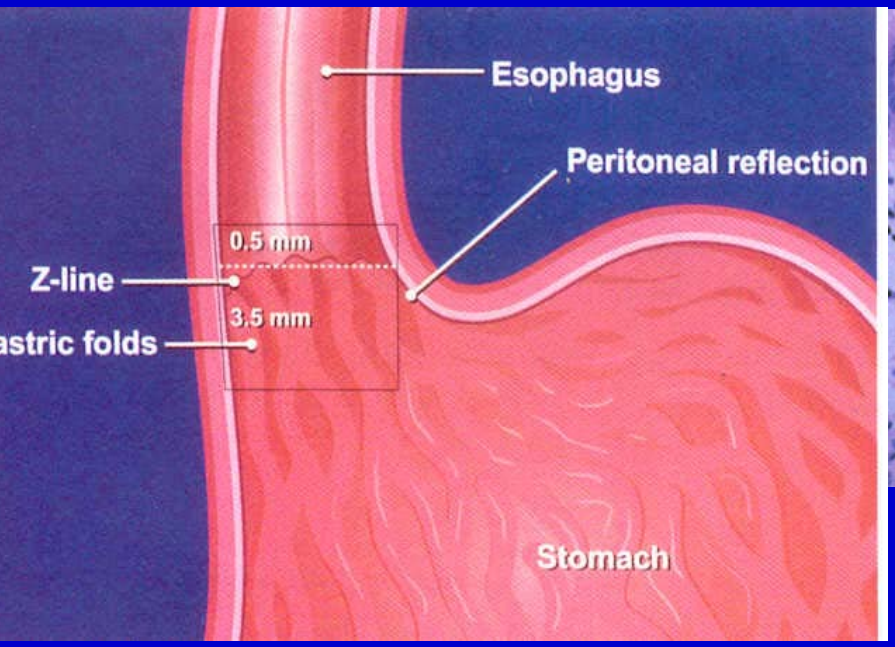
Lax LES

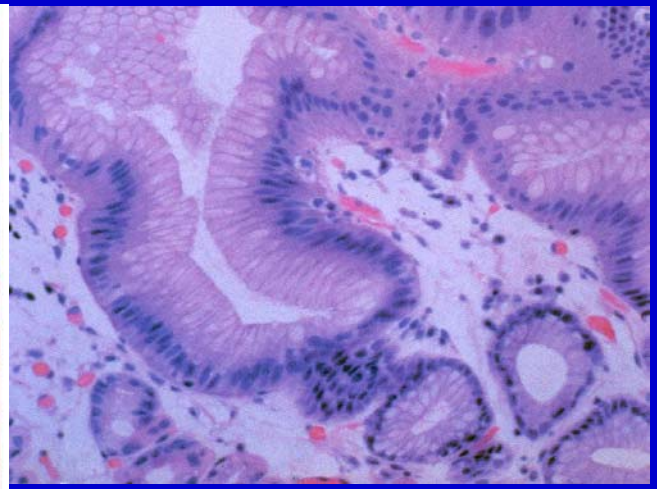


Small erosions

Histology of the EGJ

- Junction-type epithelium
  - Tortuous, tubular mucus secreting glands without parietal cells
    - 1 to 4 mm in children autopsy study

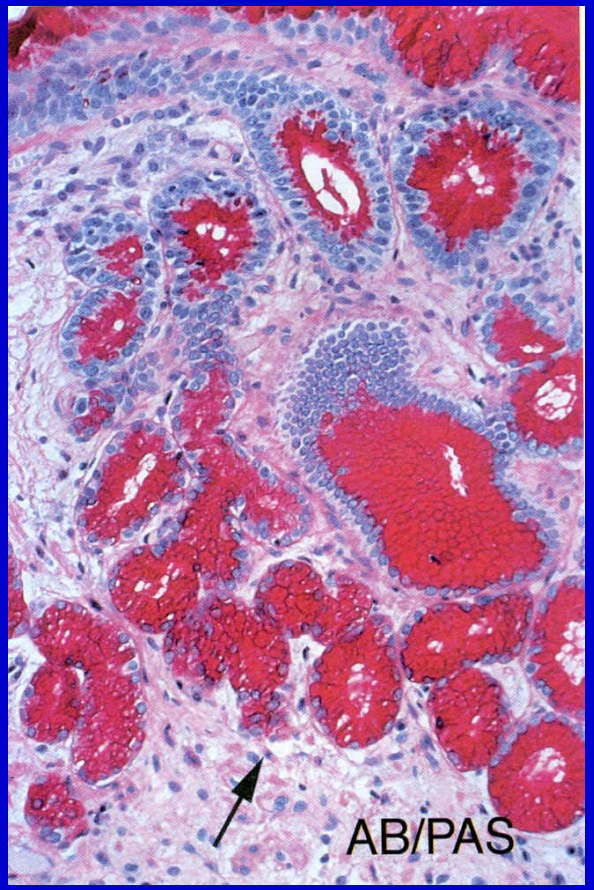




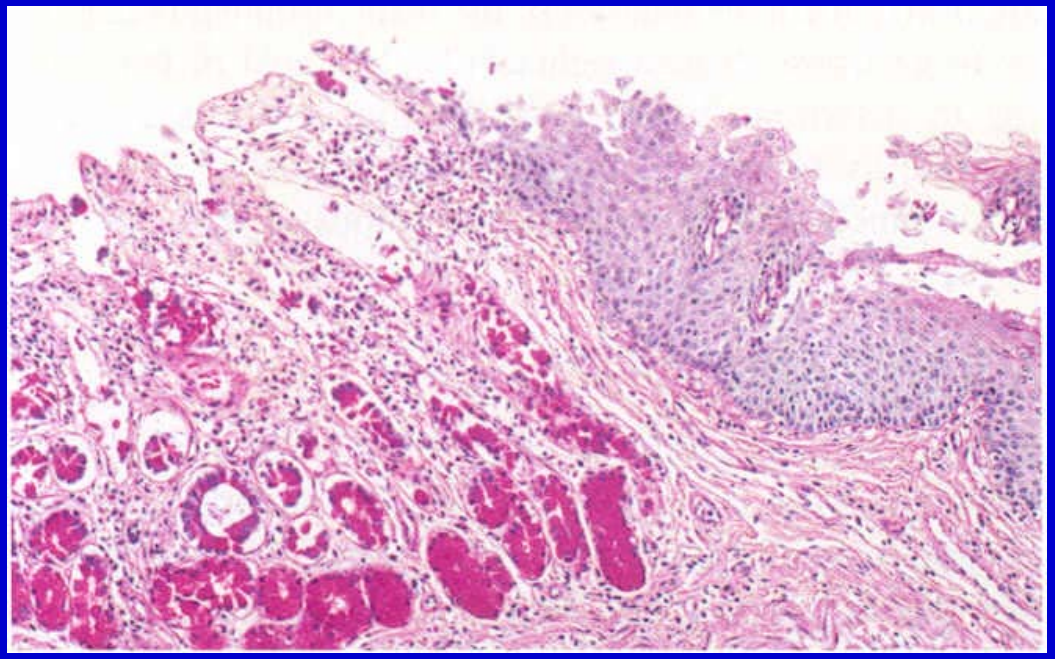
Ormsby, Mod Path 2000
Kilgore, Am J Gastroenterol 1999

Histology of the EGJ

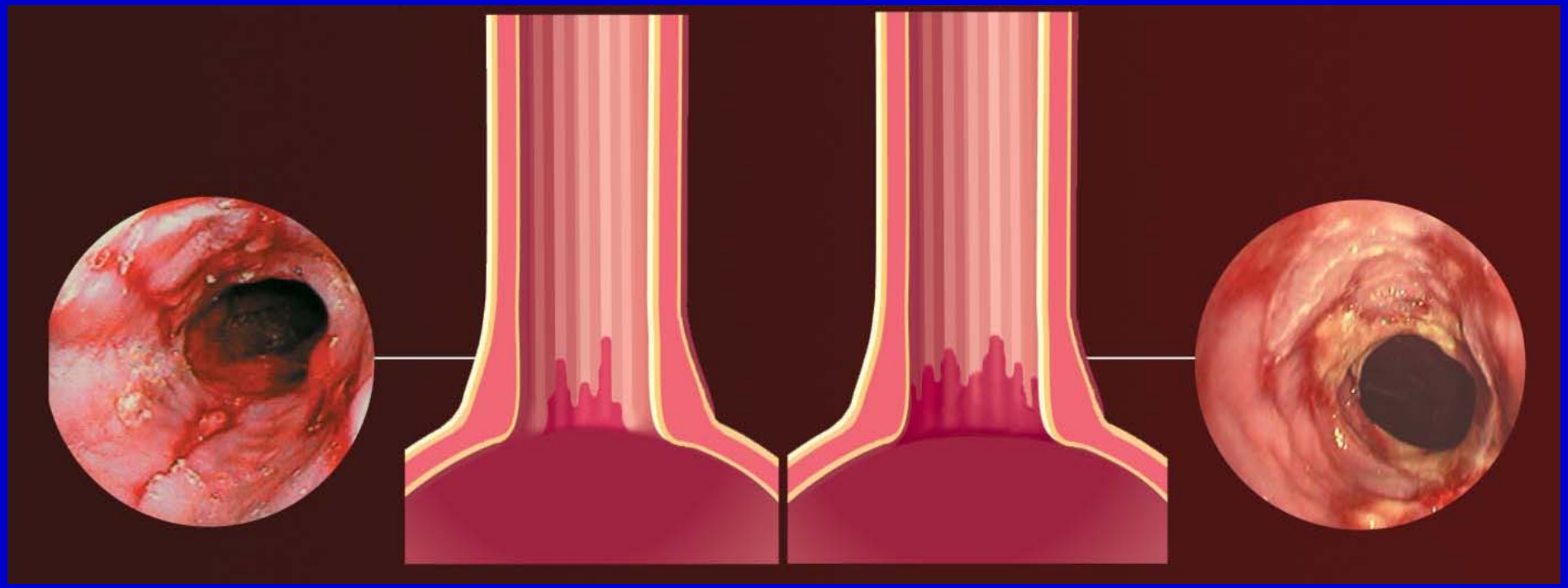
Alcian blue/PAS+



Squamocolumnar Junction



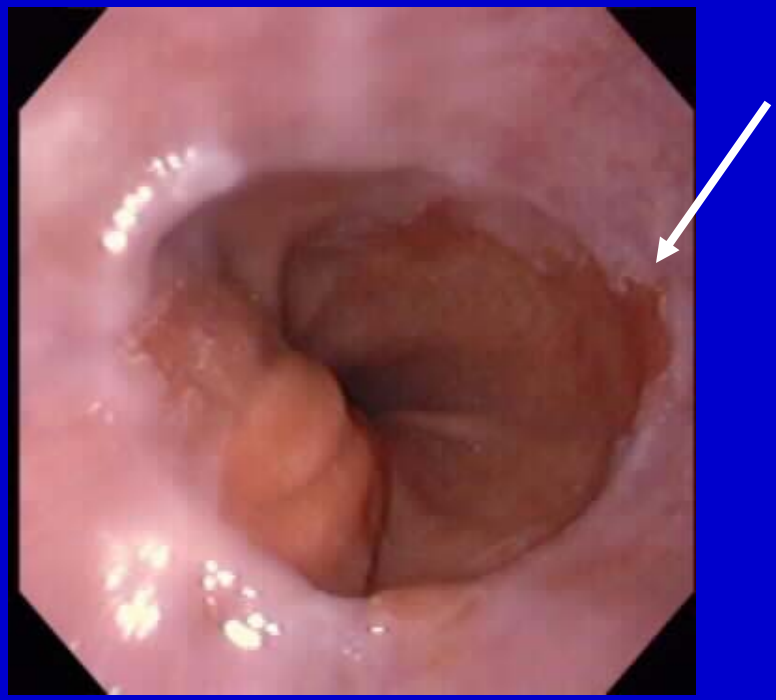
Hiatal Hernia and Erosive Esophagitis



LA Grade C ≥1 mucosal breaks bridging the tops of folds but involving <75% of the circumference

LA Grade D ≥1 mucosal breaks bridging the tops of folds and involving >75% of the circumference

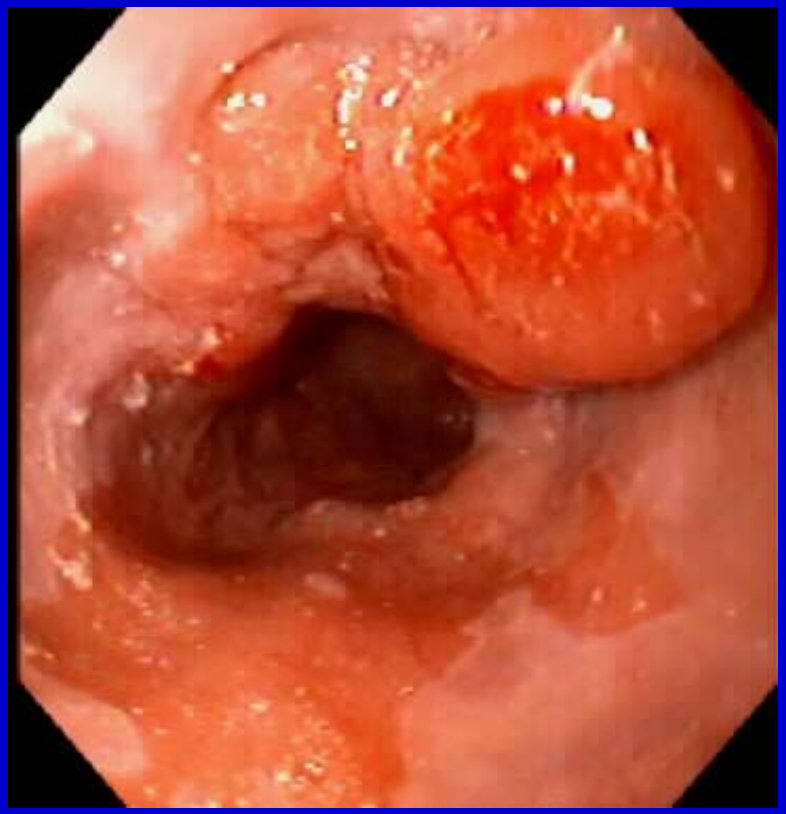
Healing after Erosive Esophagitis



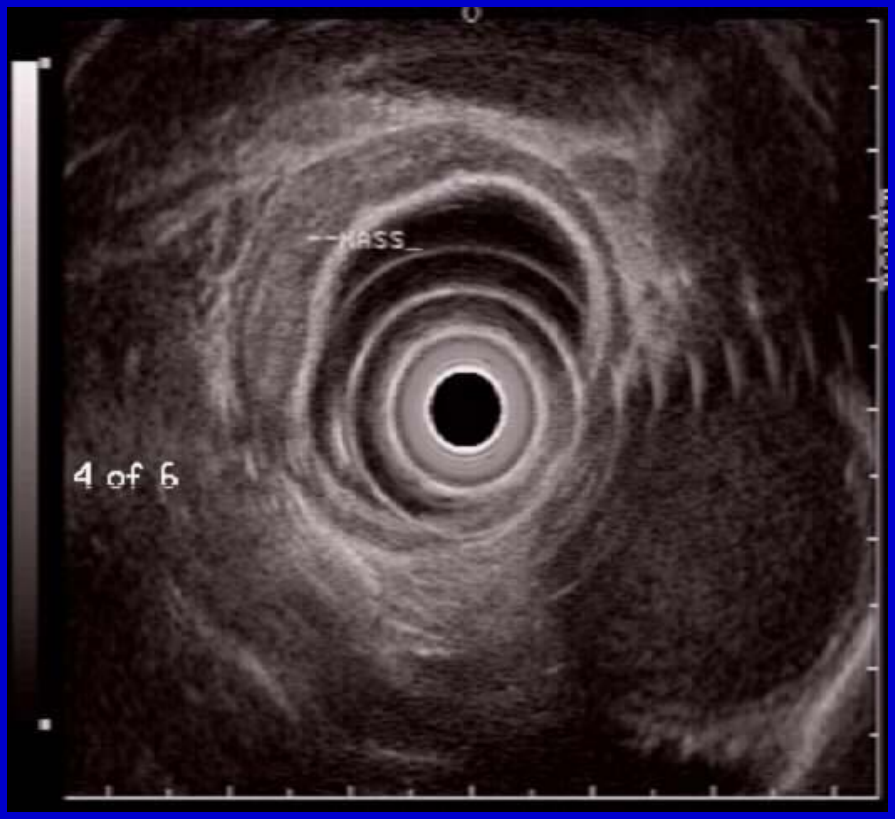
Hiatal hernia with short segment Barrett's

Severe peptic stricture

Barrett's and Esophageal Cancer



Long segment BE
with mass lesion

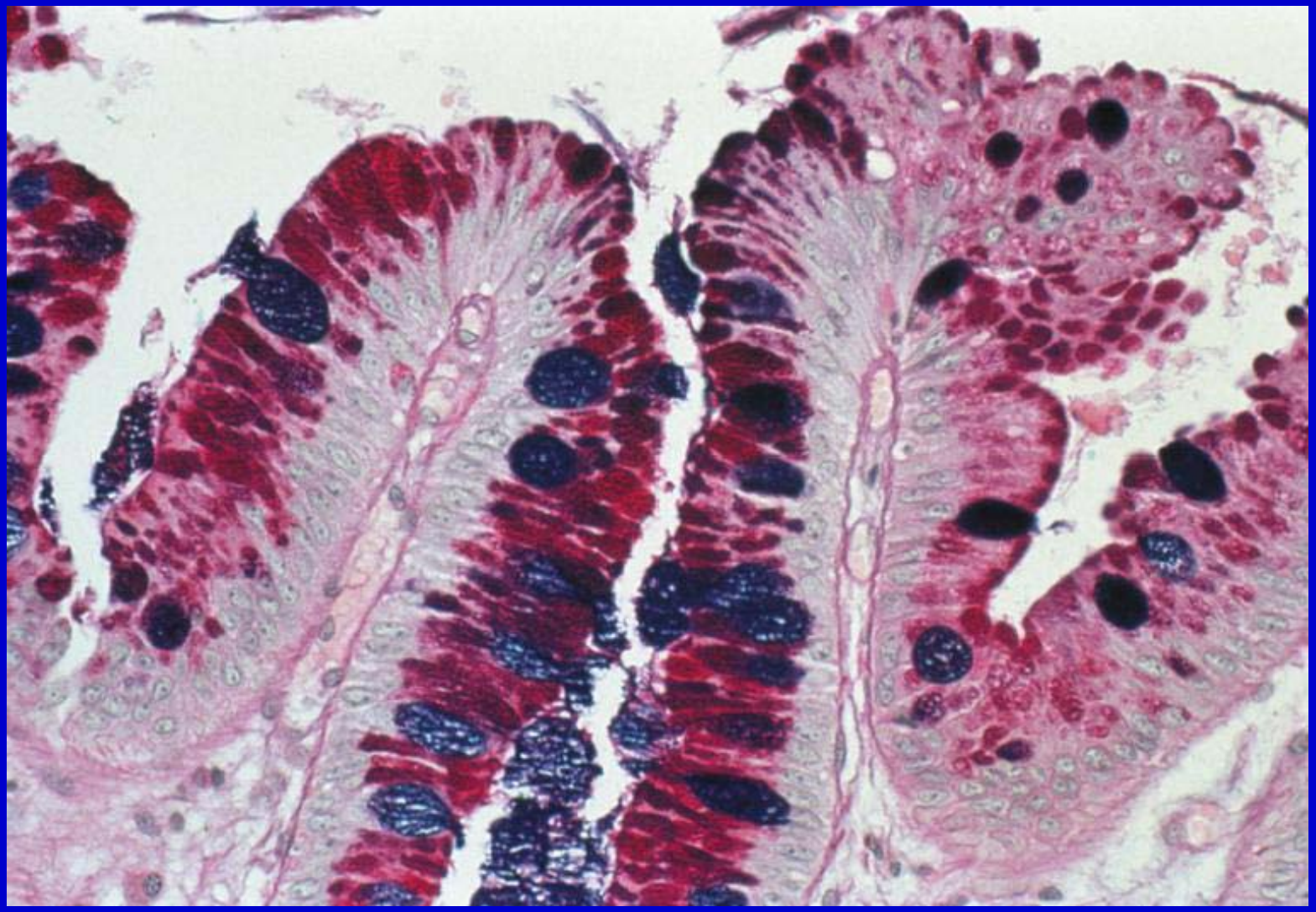


Mass lesion is
EUS stage T2N1

Barrett's Esophagus

- Pathogenesis of Barrett's
  - Repair of injured distal esophageal mucosa
  - Animal model of surgical hiatal hernia with increased acid secretion induces columnar epithelium
  - Cell of origin candidates:
    - esophageal glandular cells
    - gastric cardia mucosa
    - primordial stem cell

Intestinal Metaplasia



Endoscopic Screening for BE

Criteria for Effective Screening Tool	*BE Screening?*
High incidence disease	BE-yes Ca-no
High death/disability rate	BE-no Ca-yes
Early treatment decreases mortality	BE-no Ca-yes
Tool easy to apply and acceptable	No
Inexpensive	No
Accurate test	Yes
Subsequent f/u acceptable	?

Barrett's Screening Rationale

1. Rising incidence of esophageal adenocarcinoma

Esophageal Cancer

- Distal esophageal and GEJ cancer mortality rate increased 4-fold over the last 20 years

- 5- to 6-fold increase from 1940 to 1989
  - Esophagus 3.6 / 100,000 (+3.6 APC)
  - Stomach 4.3 / 100,000 (-2.8 APC)

Estimated New Cancer Cases US 2008

	Both	Men	Women
Digestive system	271,290	148,560	122,730
Colon & rectum	148,810	77,250	71,560
Pancreas	37,680	18,770	18,910
Stomach	21,500	13,190	8,310
Liver	21,370	15,190	6,180
Esophagus	16,470	12,970	3,500
Small intestine	6,110	3,200	2,910

ACS www.cancer.org

Estimated Cancer Deaths US 2008

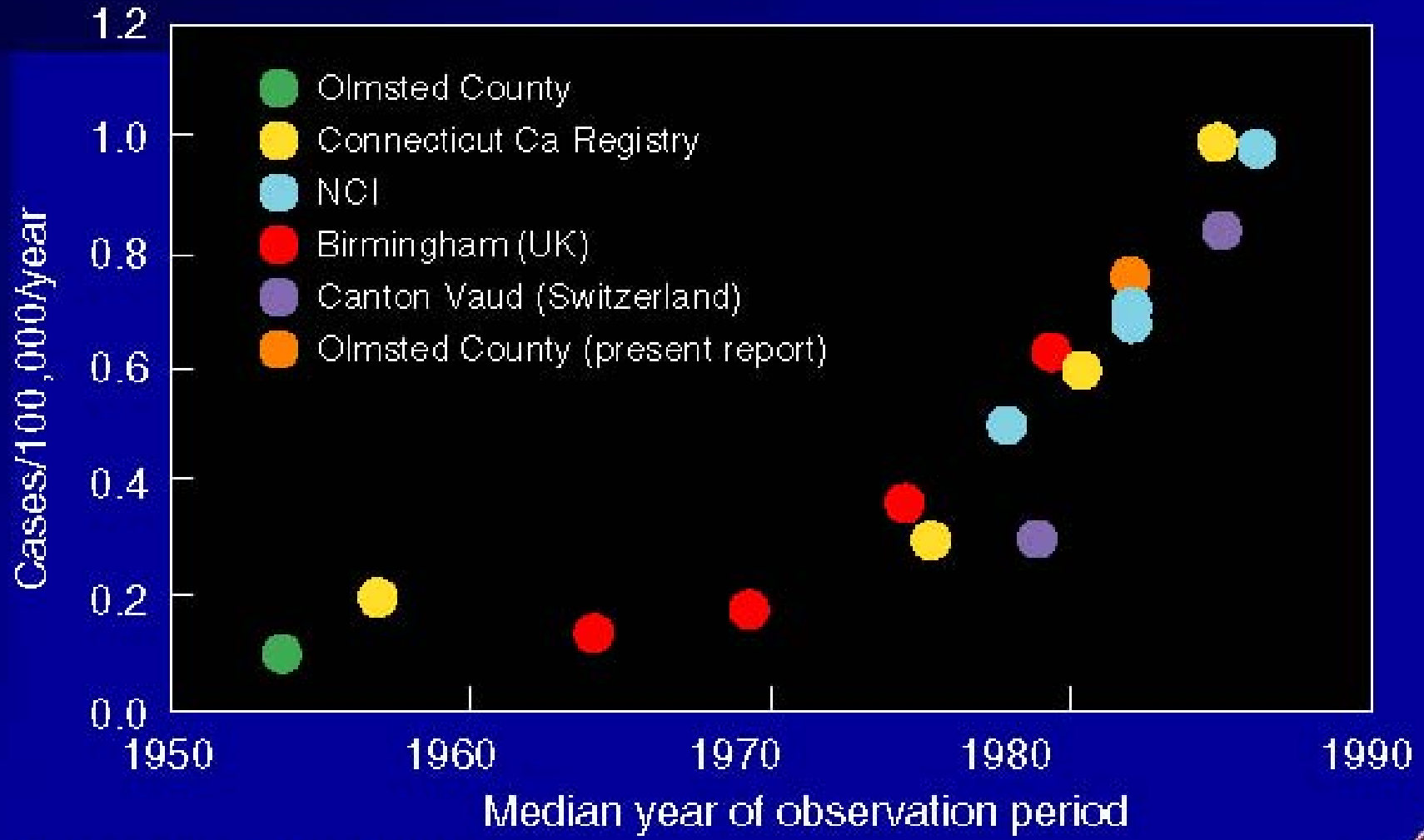
	Both	Men	Women
Digestive system	135,130	74,850	60,280
Colon & rectum	49,960	24,260	25,700
Pancreas	34,290	17,500	16,790
Liver	18,410	12,570	5,840
Esophagus	14,280	11,250	3,030
Stomach	10,880	6,450	4,430
Small intestine	1,110	580	530

ACS www.cancer.org

Male Cancer Deaths 2008

1.	Lung & bronchus	90,810 (31%)
2.	Prostate	28,660 (10%)
3.	Colon & rectum	24,260 (8%)
4.	Pancreas	17,500 (6%)
5.	Liver & intrahep bile duct	12,570 (4%)
6.	Leukemia	12,460 (4%)
7.	Esophagus	11,250 (4%)
8.	Urinary bladder	9,950 (3%)
9.	Non-Hodgkin lymphoma	9,790 (3%)
10.	Kidney & renal pelvis	8,100 (3%)

INCIDENCE OF ESOPHAGEAL ADENOCARCINOMA IN POPULATION BASED STUDIES



om: Pera M et al. *Gatroenterology* 1993.

Esophageal Adenocarcinoma and Colon Cancer Screening

- Esophageal adenocarcinoma incidence
  - 3 per 100,000
- Colon cancer incidence
  - 58 per 100,000

Barrett's Screening Rationale

1. Rising incidence of esophageal adenocarcinoma
2. Reflux symptoms are a risk factor for BE and esophageal cancer

Barrett's Esophagus

How common is BE?

- ≤ 1% of unselected autopsies
- ≤ 1% of patients without GERD symptoms
- 6% - 12% of symptomatic GERD patients

GERD Symptoms and BE

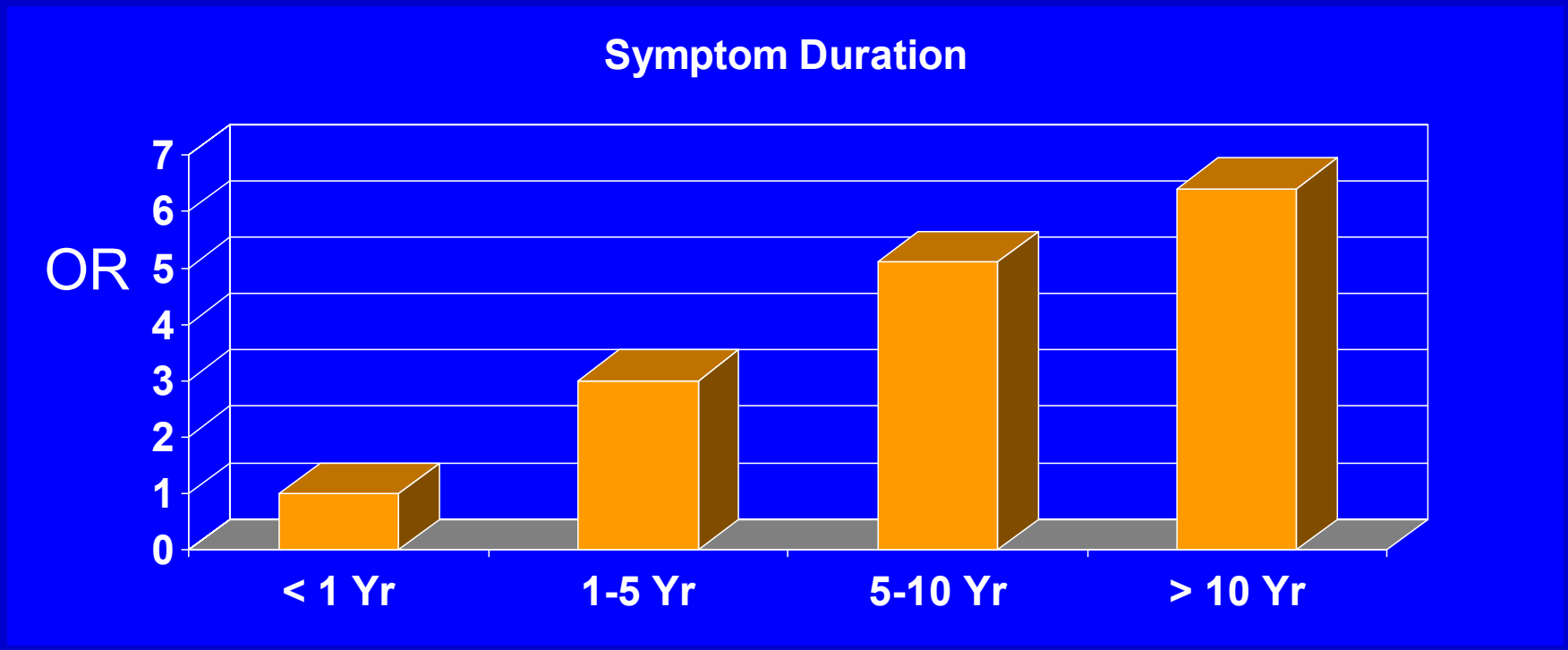
	Barrett's (N=79)	GERD (N=94)	P-value
Severe symptoms	85%	59%	<0.02
Duration (yr)	16.36	11.81	<0.05
Age of onset (yr)	35.3 ± 16	43.7 ± 13	<0.05

Eisen Am J Gastroenterol 1997;92

Barrett's Esophagus

- Who develops Barrett's?
  - Clearly associated with severe GERD
  - Male:female ratio 9:1
  - Hiatal hernia
  - Low LES pressures

BE & Duration of GERD Symptoms



Lieberman Am J Gastroenterol 1997;92:

GERD and Esophageal Cancer

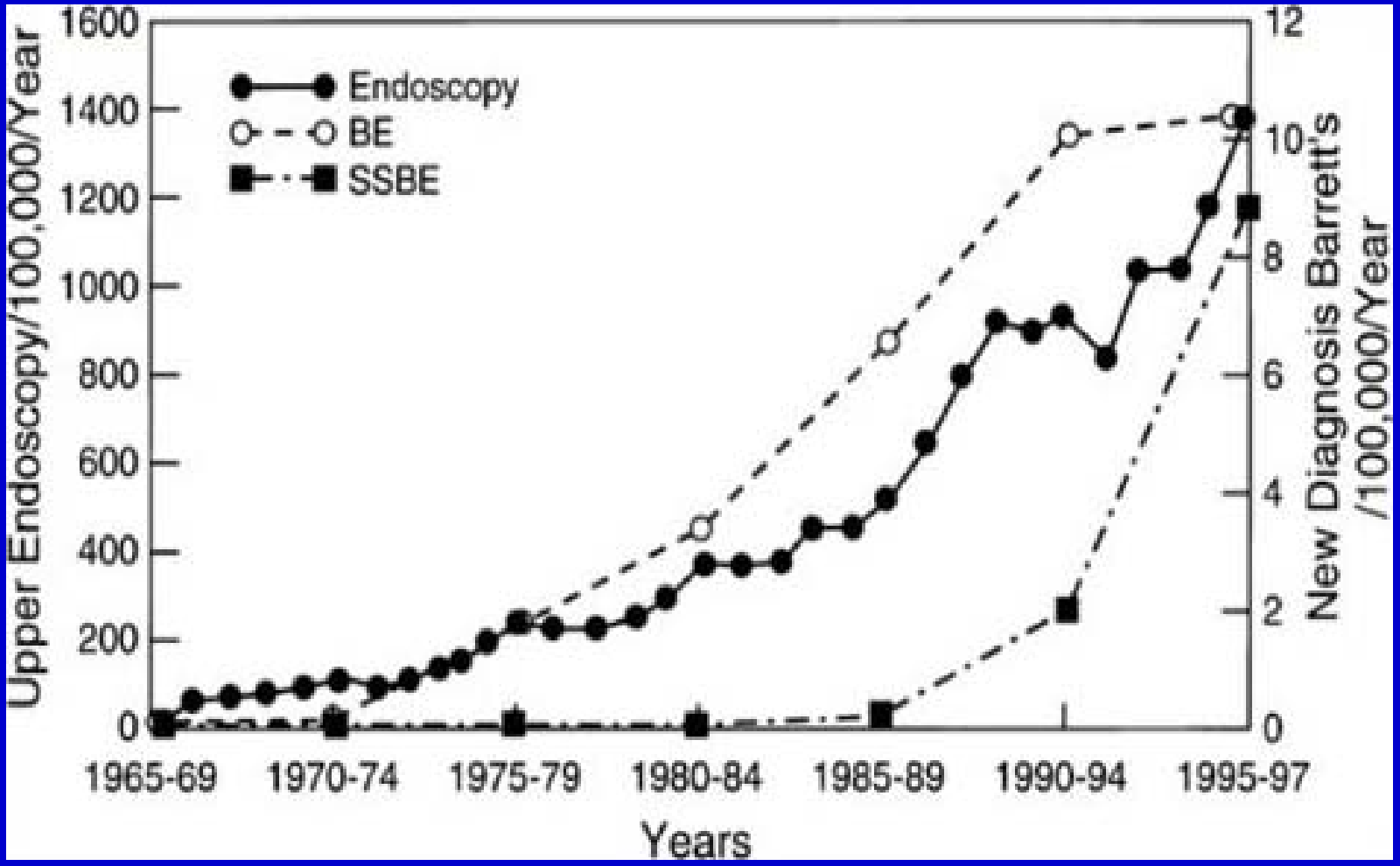
		Odds Ratio
Recurrent reflux	(1 / wk)	7
Frequent reflux	(>3 / wk)	16
Severity & duration	(>20 yr.)	43

Lagergeren NEJM 199

Barrett's Screening Rationale

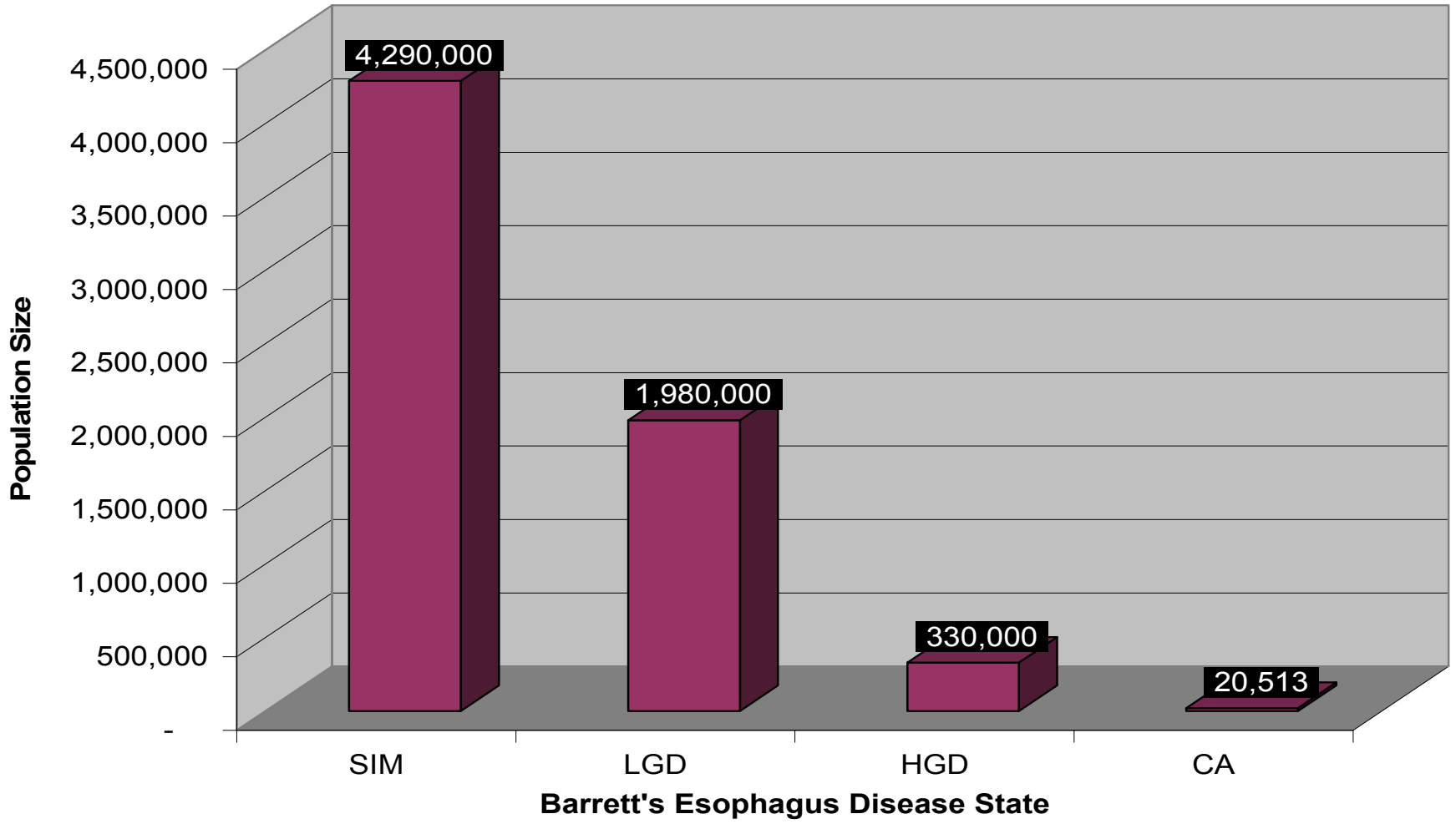
1. Rising incidence of esophageal adenocarcinoma
2. Reflux symptoms are a risk factor for BE and esophageal cancer
3. Barrett's esophagus is the only known intermediate stage

Rising Incidence of BE in Olmstead County



Conio Gut 2001

North America Estimates of Barrett's and Esophageal Cancer



Barrett's and Esophageal Cancer

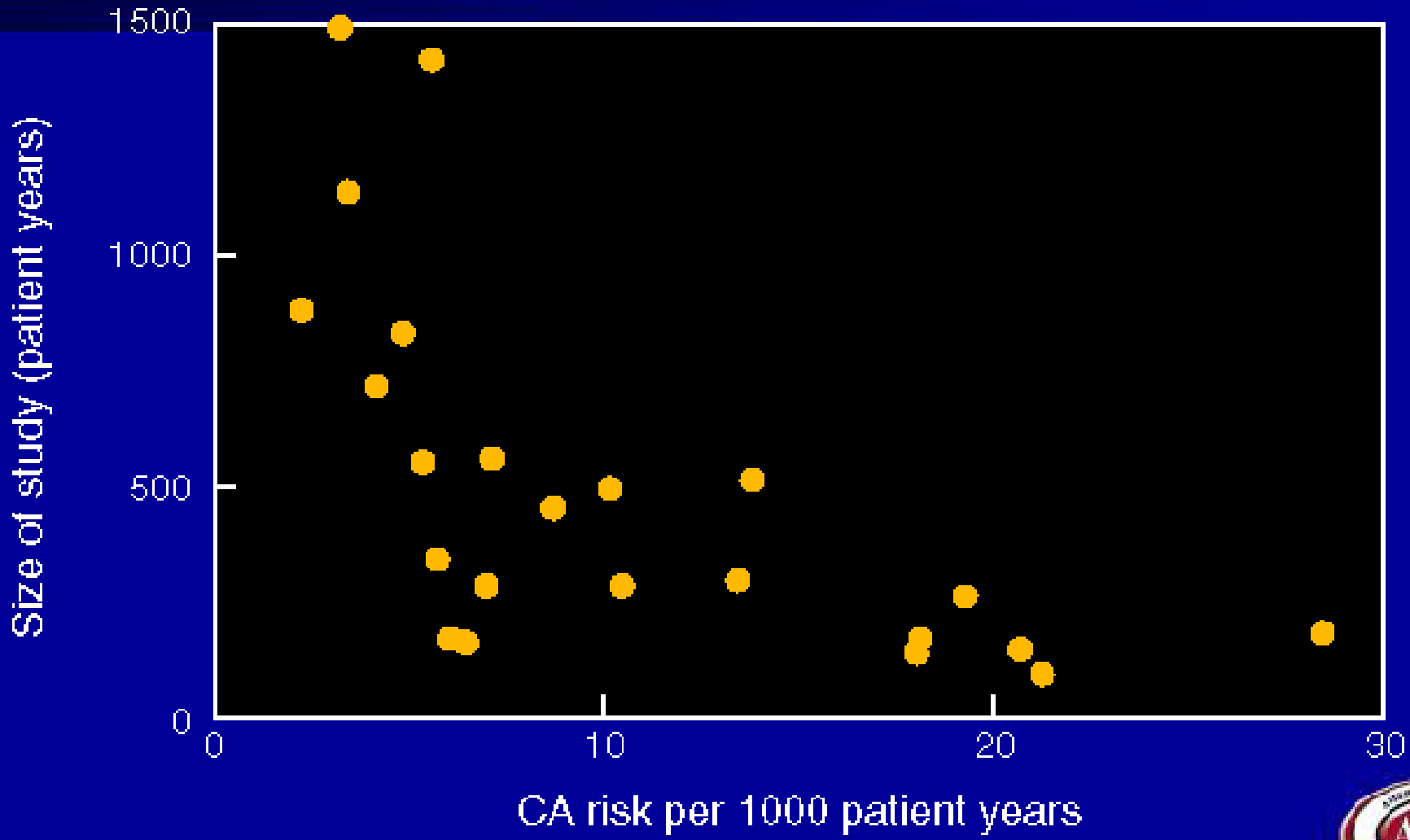
- Mean annual incidence of cancer in long- and short- segment BE is ~0.5%
  - 30-fold increase over the general population

Short segment BE Elevated lesion < 20mm diameter

Short-Segment Barrett's

- Dilemmas of the expanded definition of BE
  - Differentiation from gastric metaplasia
  - Differentiation from cardia intestinal metaplasia
  - Natural history of ultra-short segment BE

REPORTED CANCER RISK IN BARRETT'S ESOPHAGUS VERSUS SIZE OF STUDY



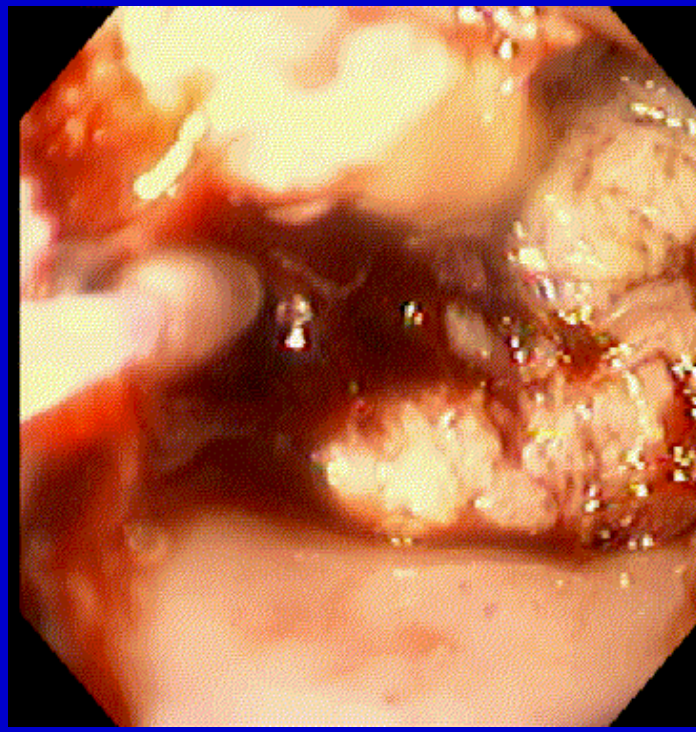
From Shaheen NJ et al. Gastroenterology 2000;119:333-8.

Barrett's Screening Rationale

1. Rising incidence of esophageal adenocarcinoma
2. Reflux symptoms are a risk factor for BE and esophageal cancer
3. Barrett's esophagus is the only known intermediate stage
4. Early detection provides better survival

Barrett's Screening Rationale

- Only 5% of esophageal adenocarcinoma cases occur in patients with *known* Barrett's esophagus

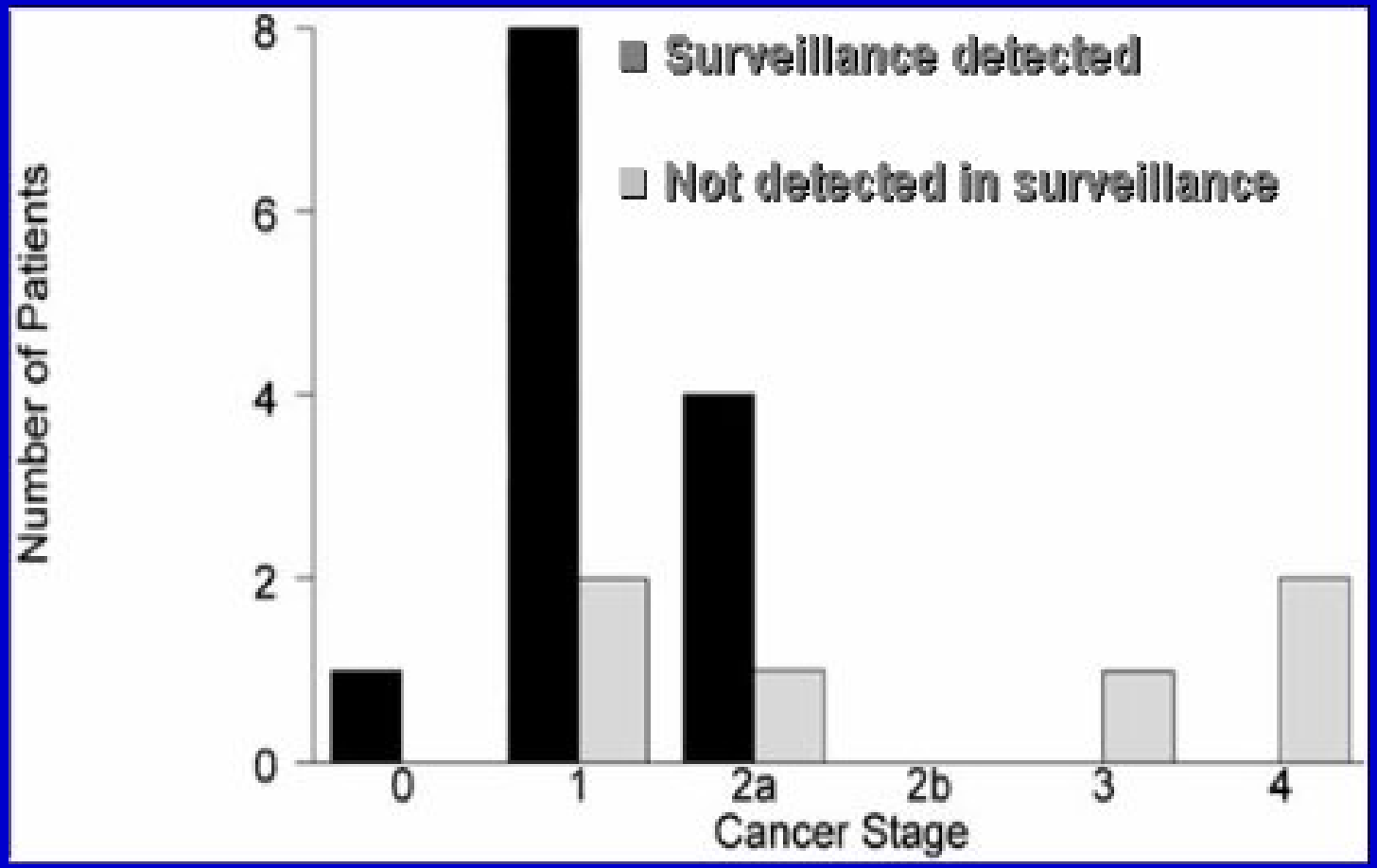


Five-Year Relative Survival Rates by Stage at Diagnosis 1996-2003

	Local	Regional	Distant
Esophagus	33.7	16.9	2.9
Colon & rectum	89.8	67.7	10.3
Breast (female)	98.0	83.5	26.7
Pancreas	20.3	8.0	1.7
Stomach	61.1	23.7	3.4

Ries SEER Cancer Statistics Review, 1975-
www.seer.cancer.gov/csr/1975_2004/, 2007

Impact of Surveillance in Barrett's Associated Cancers



Corley Gastroenterol 20

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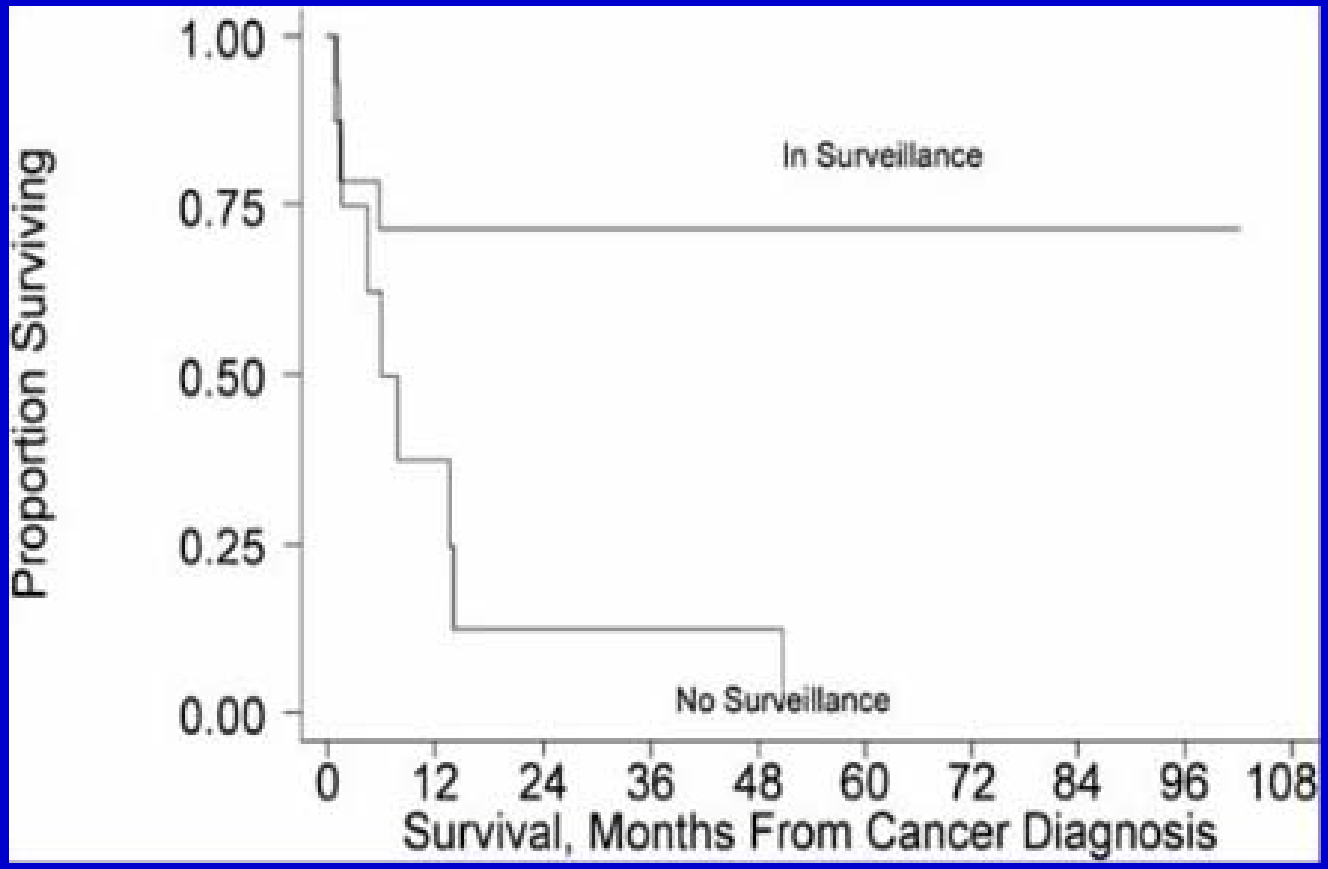
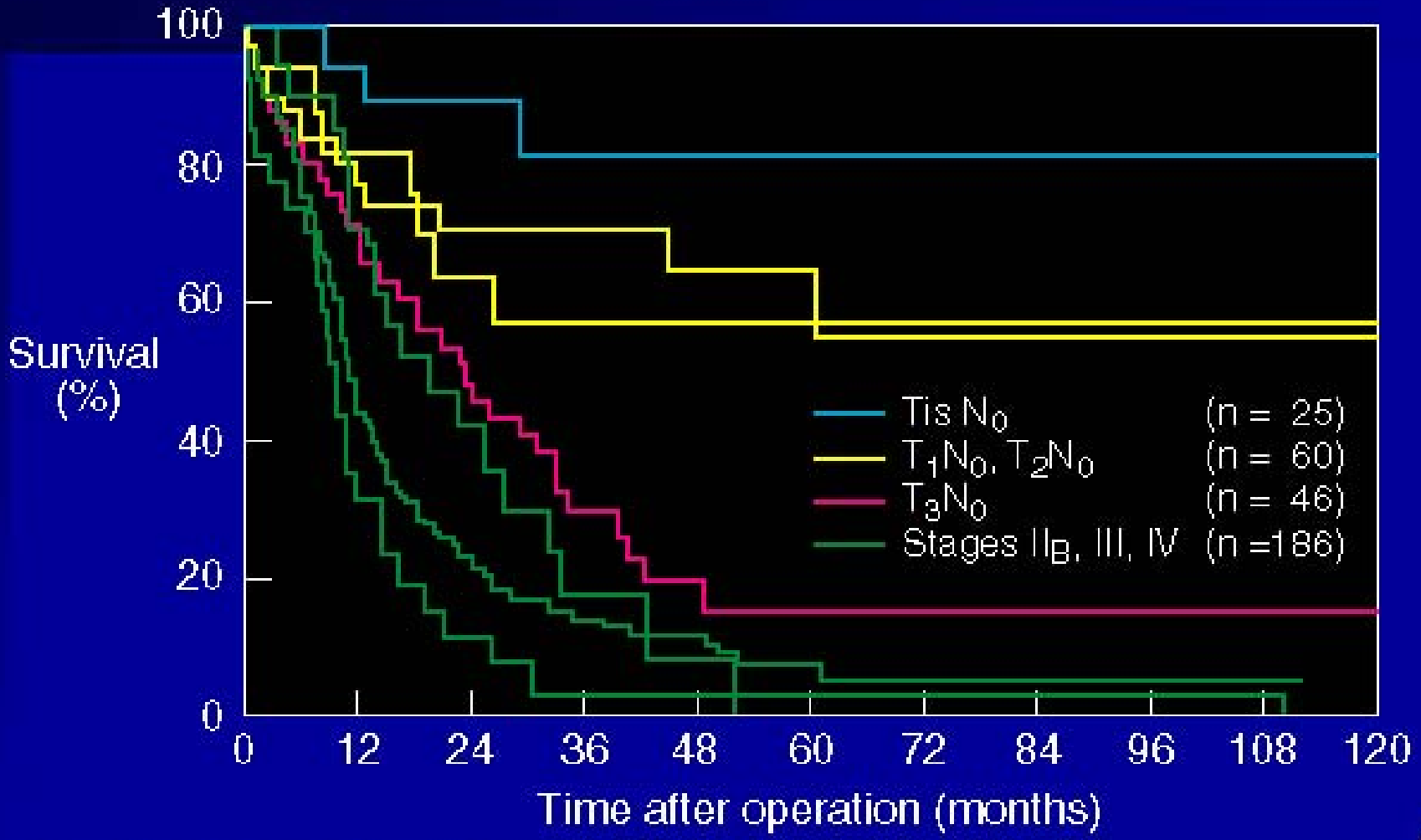


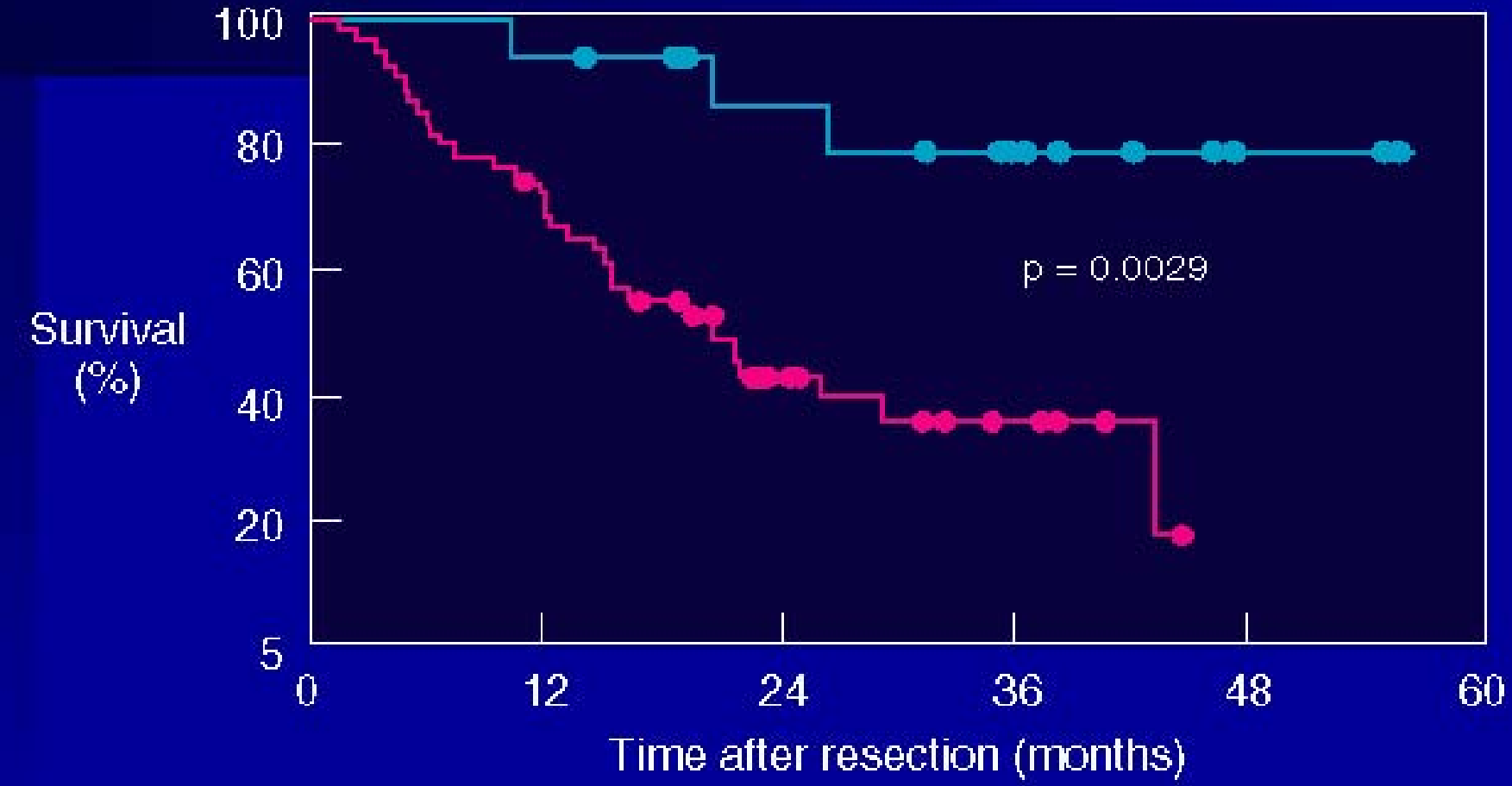
Corley Gastroenterol 20

SURVIVAL AFTER ESOPHAGECTOMY FOR CARCINOMA AT THE CLEVELAND CLINIC: NO NEOADJUVANT THERAPY



om: Rice TW et al. The Gastroentrologist 1997;338:278-94.

IMPACT OF ENDOSCOPIC BIOPSY SURVEILLANCE OF BARRETT'S ESOPHAGUS ON CANCER SURVIVAL



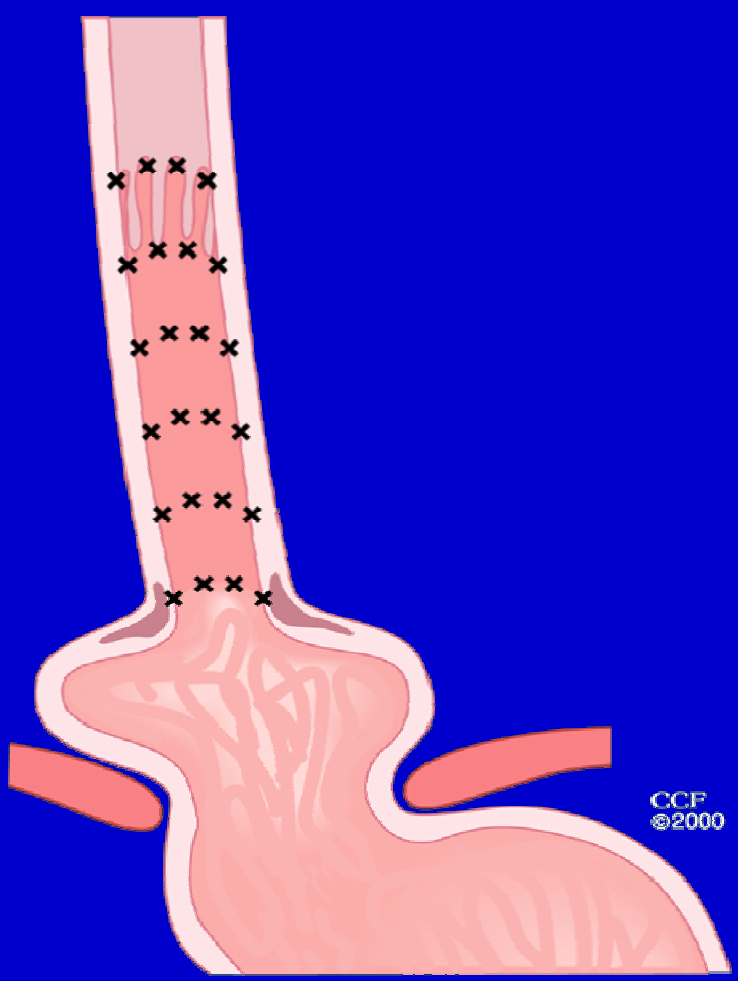
Surveillance (●;n=16)	15	11	6	2	0
Non-Surveillance (●;n=54)	36	15	5	0	0

om: Van Sandick JW et al. Gut 1998;43:216-22.

Screening for BE

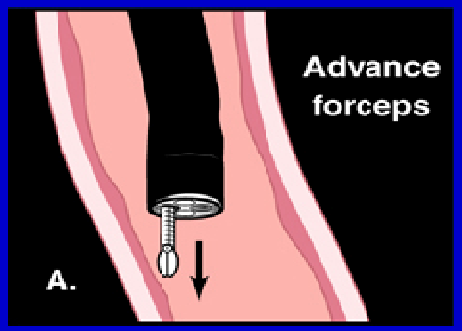
- GERD symptoms for > 10 years
- Endoscopic biopsy:
  - Columnar epithelium
  - Intestinal metaplasia
  - Any length

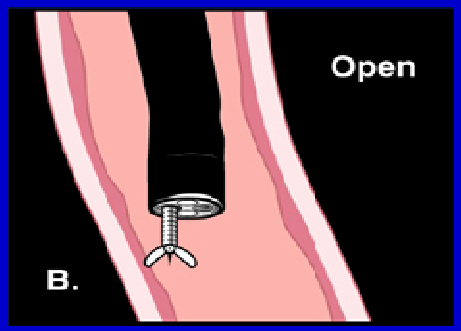
Endoscopic Surveillance of Barrett's

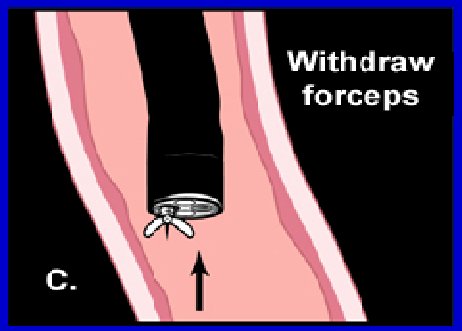


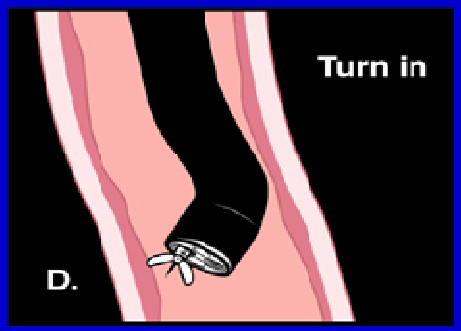
Falk Techniques in GI Endoscopy 2000;2:

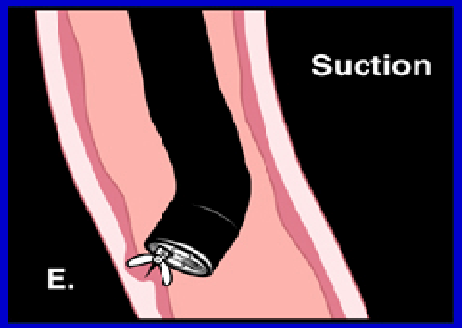
Endoscopic Surveillance of Barrett's

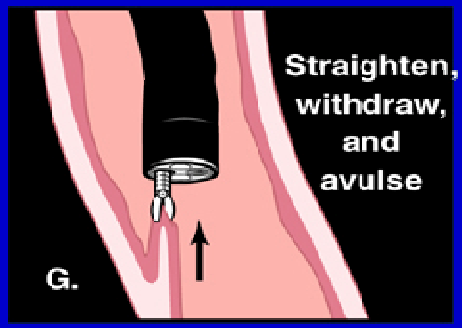






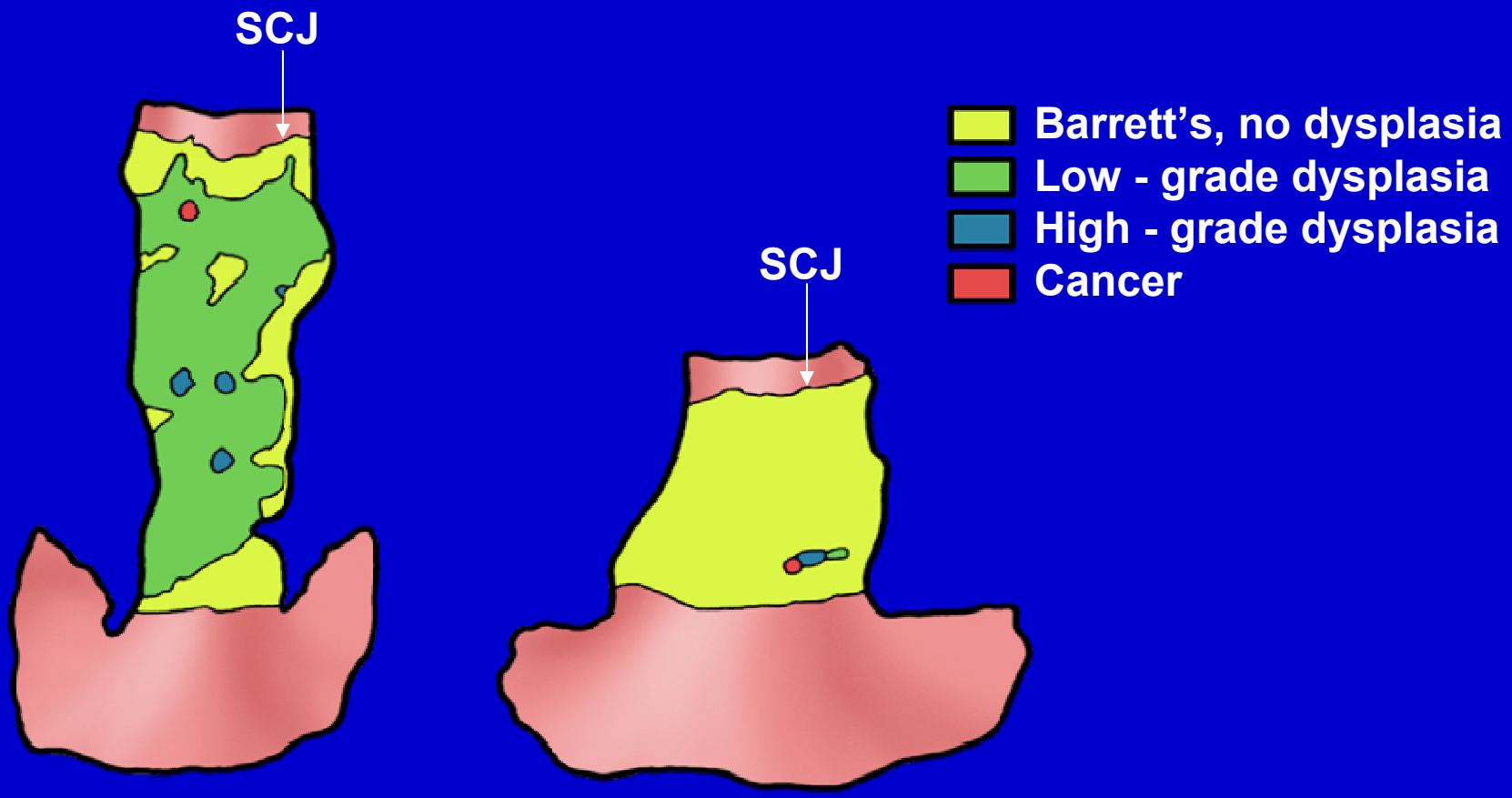




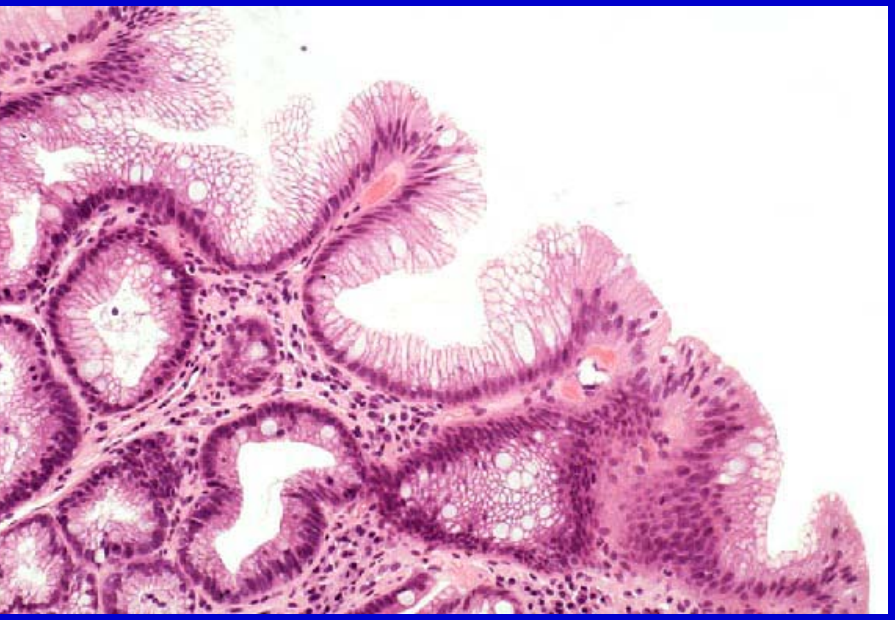


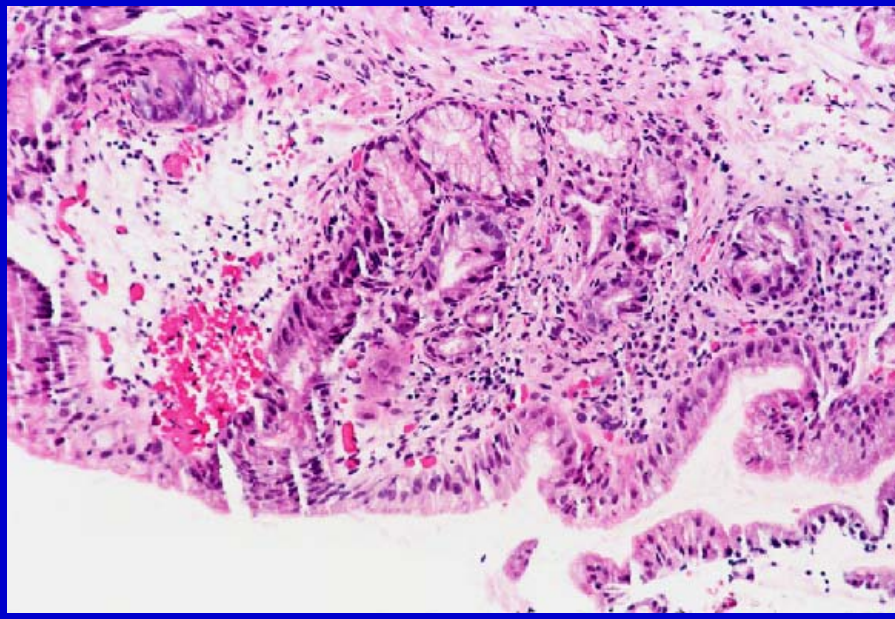
Levine Gastrointest Endosc 1991;37:3

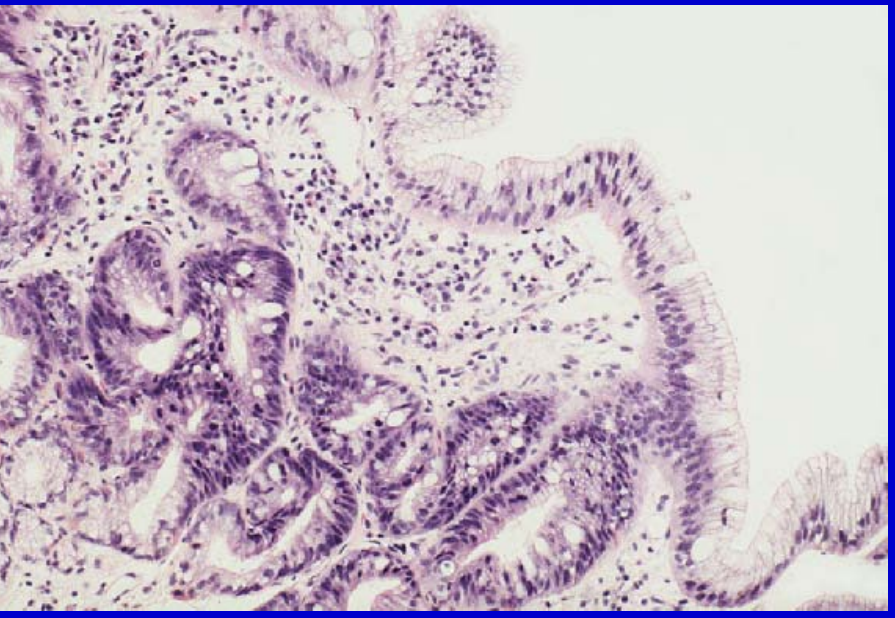
Distribution of Dysplasia and Cancer in Resection Specimens

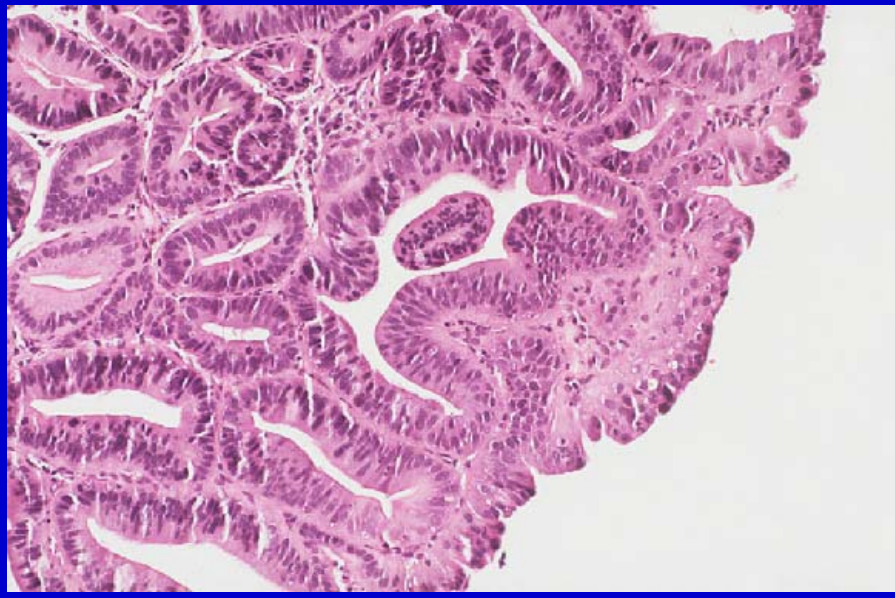


Cameron Am J Gastroenterol 1997;92:58









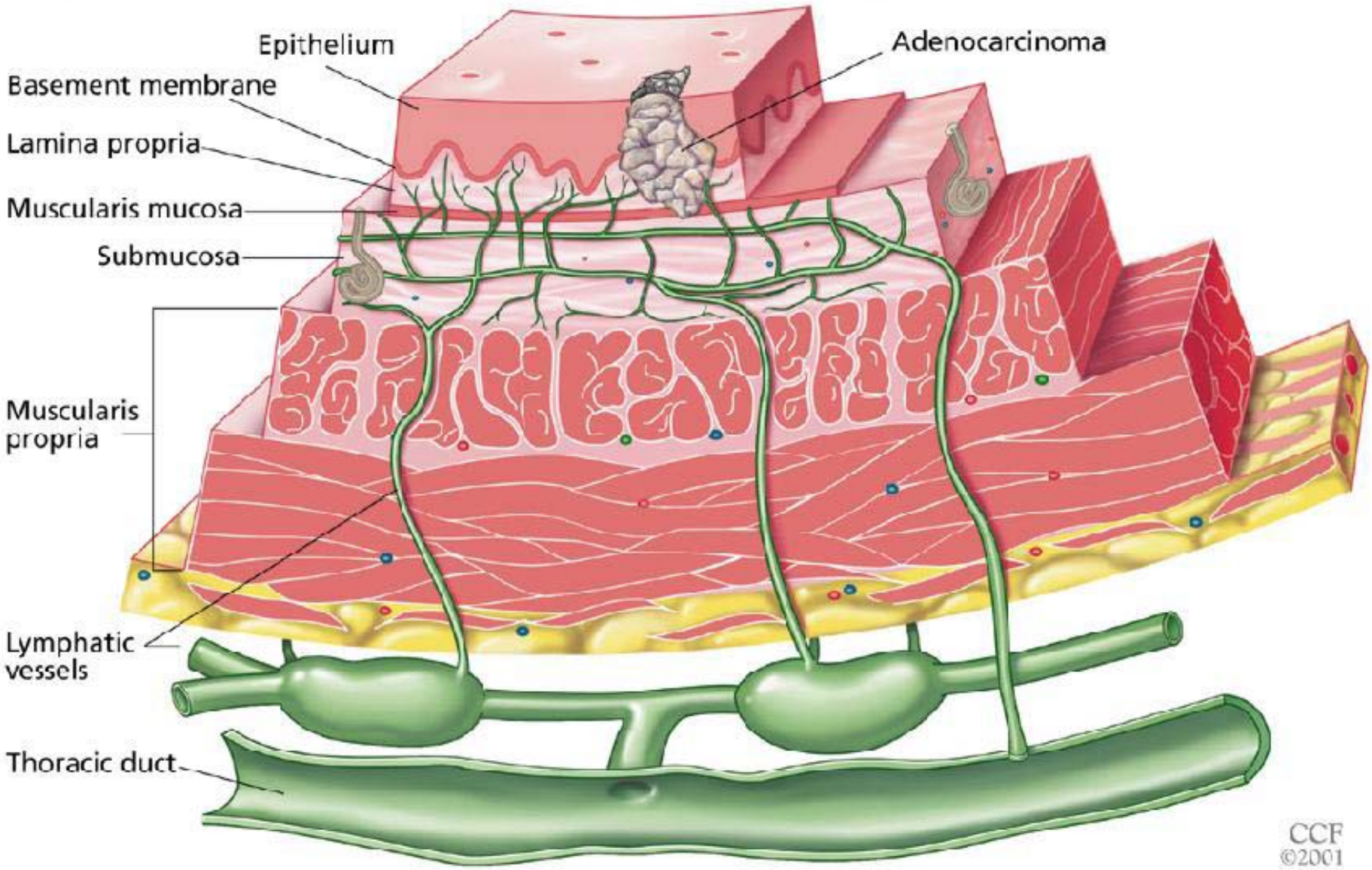
Endoscopic Surveillance of Barrett's

Dysplasia	Interval
None	3 years*
Indefinite	3 to 6 months after PPI
Low-grade	12 months
High-grade	
Focal	3 months
Multi-focal	Intervention or observation?

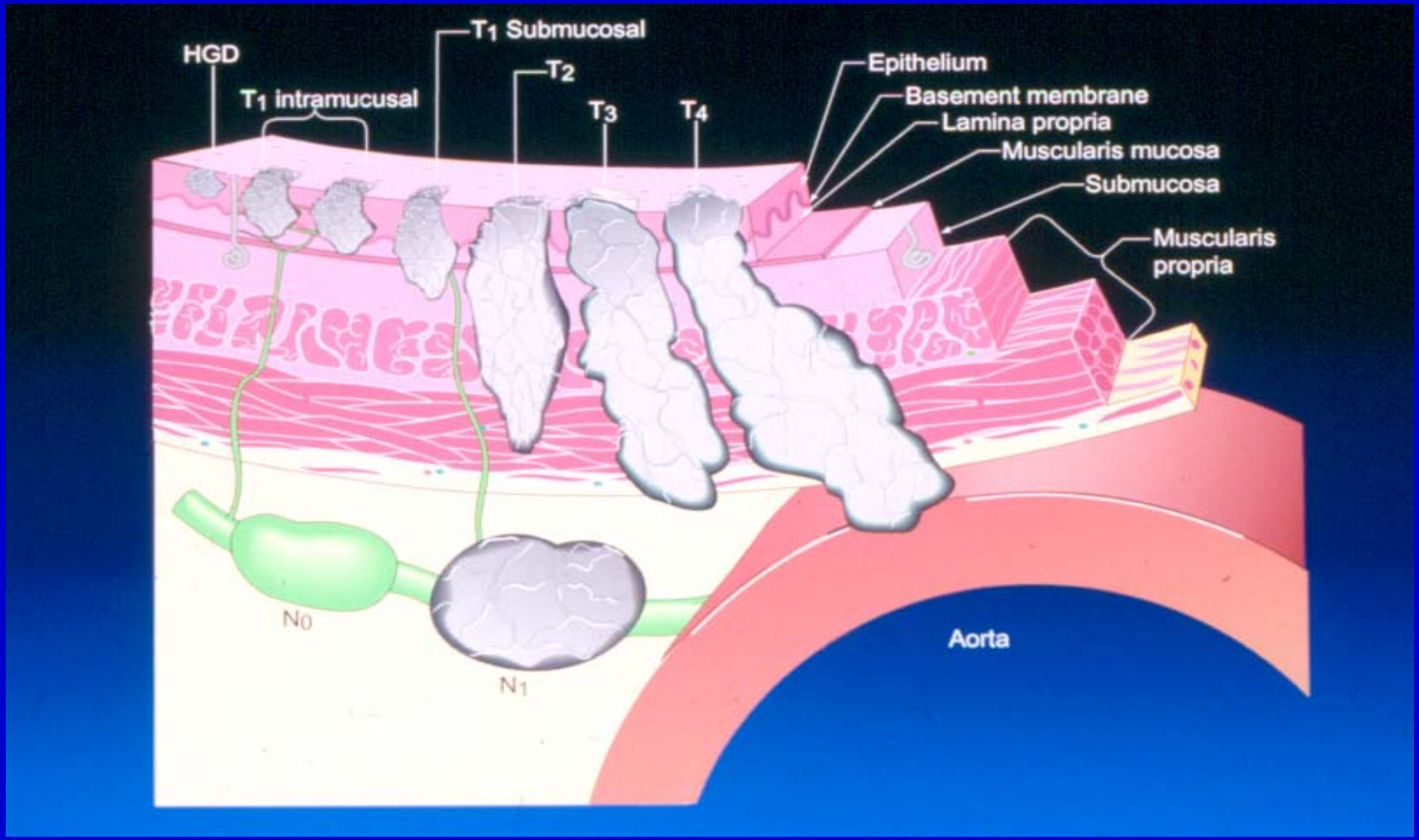
*After 2 exams are negative for dysplasia 1 yr apart

*Requires 4-quadrant biopsies every 1 to 2 cm

Why adenocarcinoma of the esophagus is so malignant



Staging Esophageal Cancer



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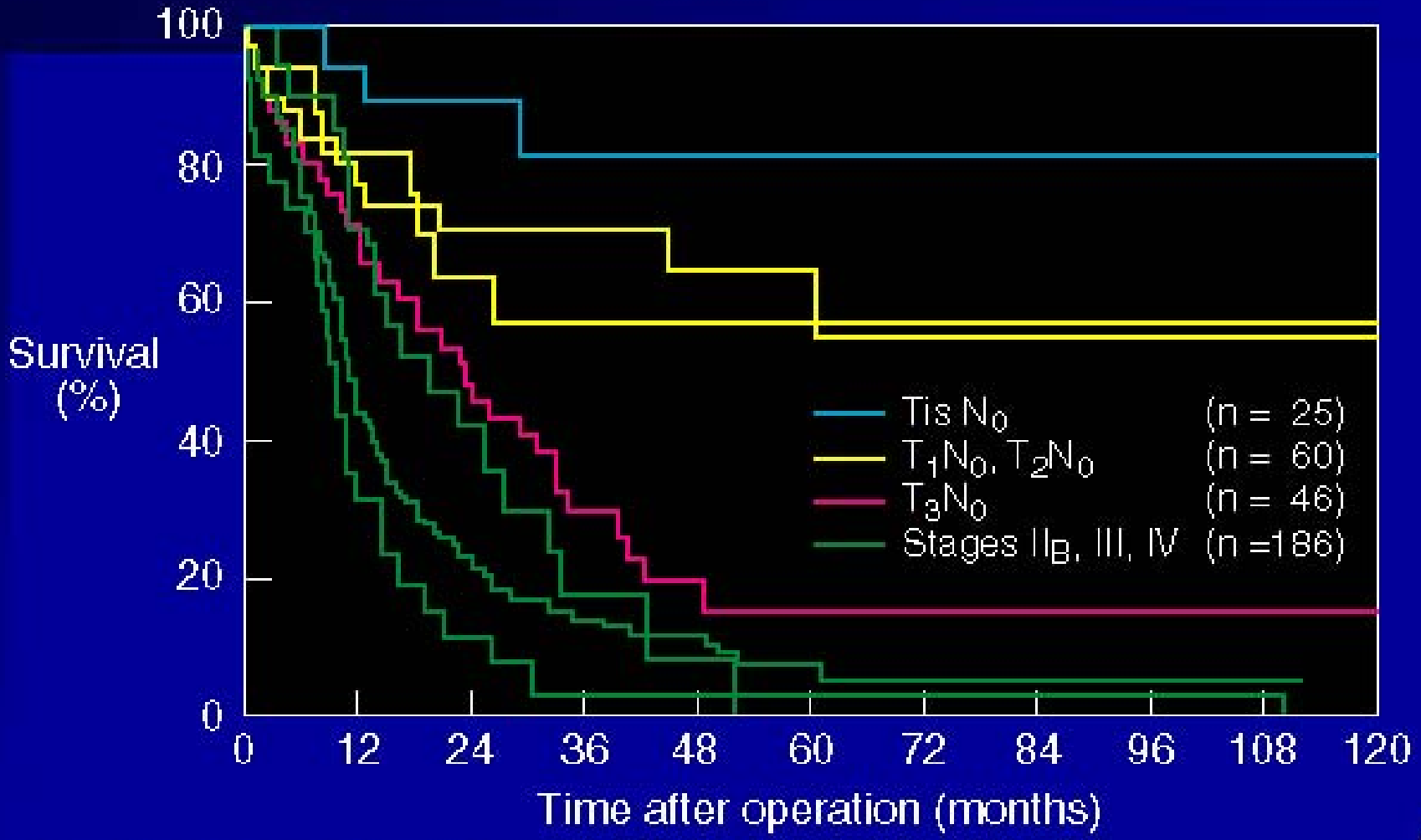
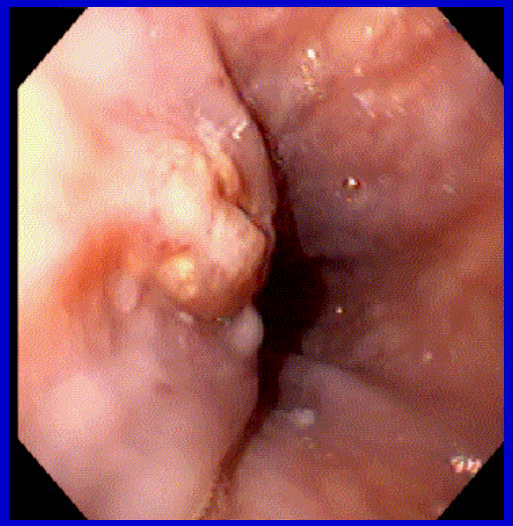
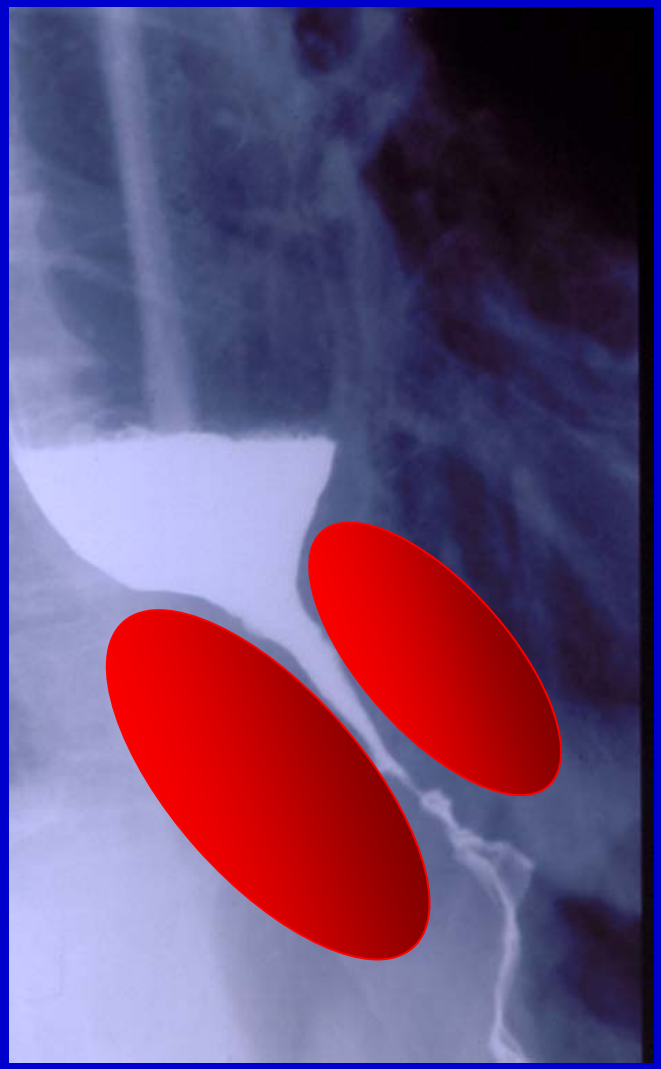


om: Rice TW et al. The Gastroentrologist 1997;338:278-94.

EGJ Cancer

- Extrinsic compression from infiltrative gastric cardia mass
- Prosthetic stent required to maintain lumen





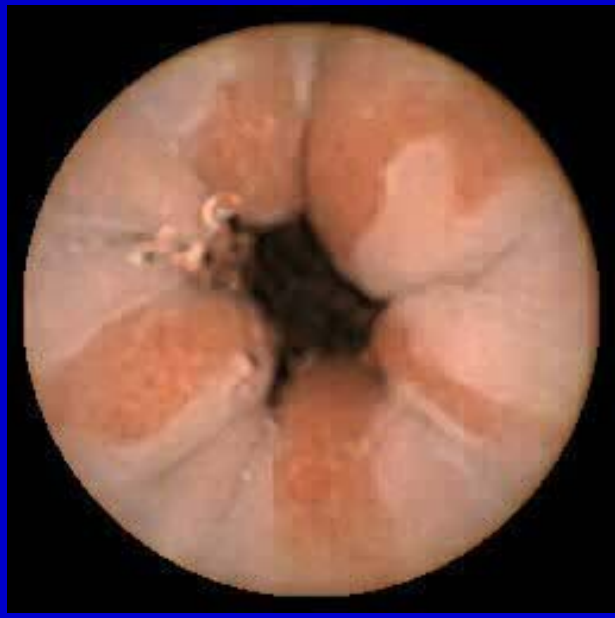
Screening for Barrett's

- Barriers to screening
  - Cost
  - Screening tool not universally accepted
  - Compliance with follow-up
- Future plans for screening
  - Small bore endoscopes
  - Capsule endoscopy
  - Genetic testing

Capsule Endoscopy Screening for BE

Capsule

Recorder



Lower Sphincter with Short Segment BE

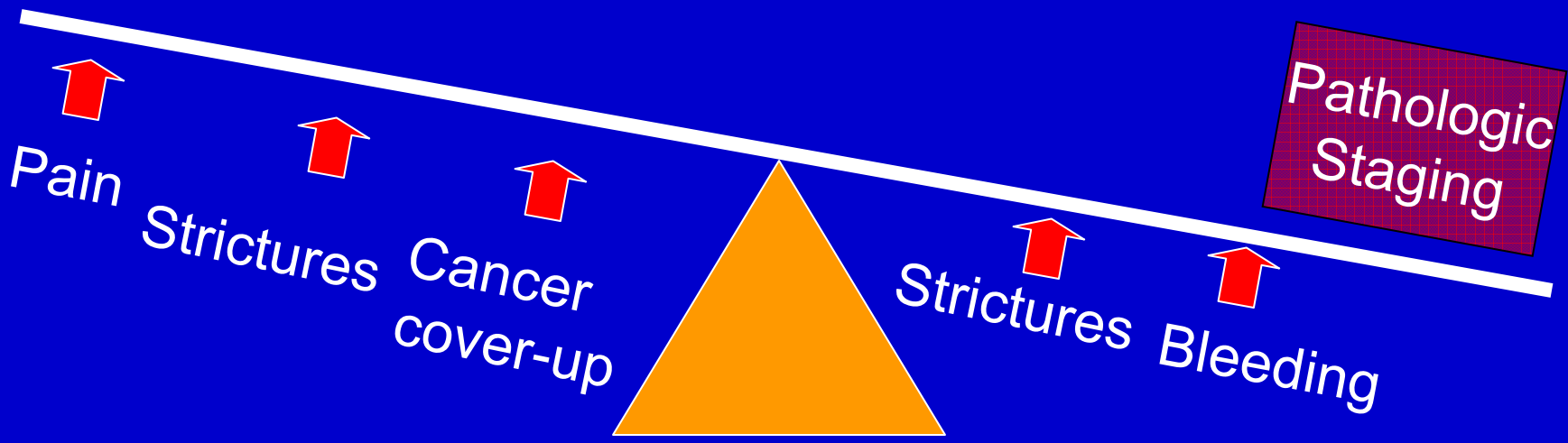
Endoscopic Therapy for BE with Dysplasia?

ASSUMPTIONS

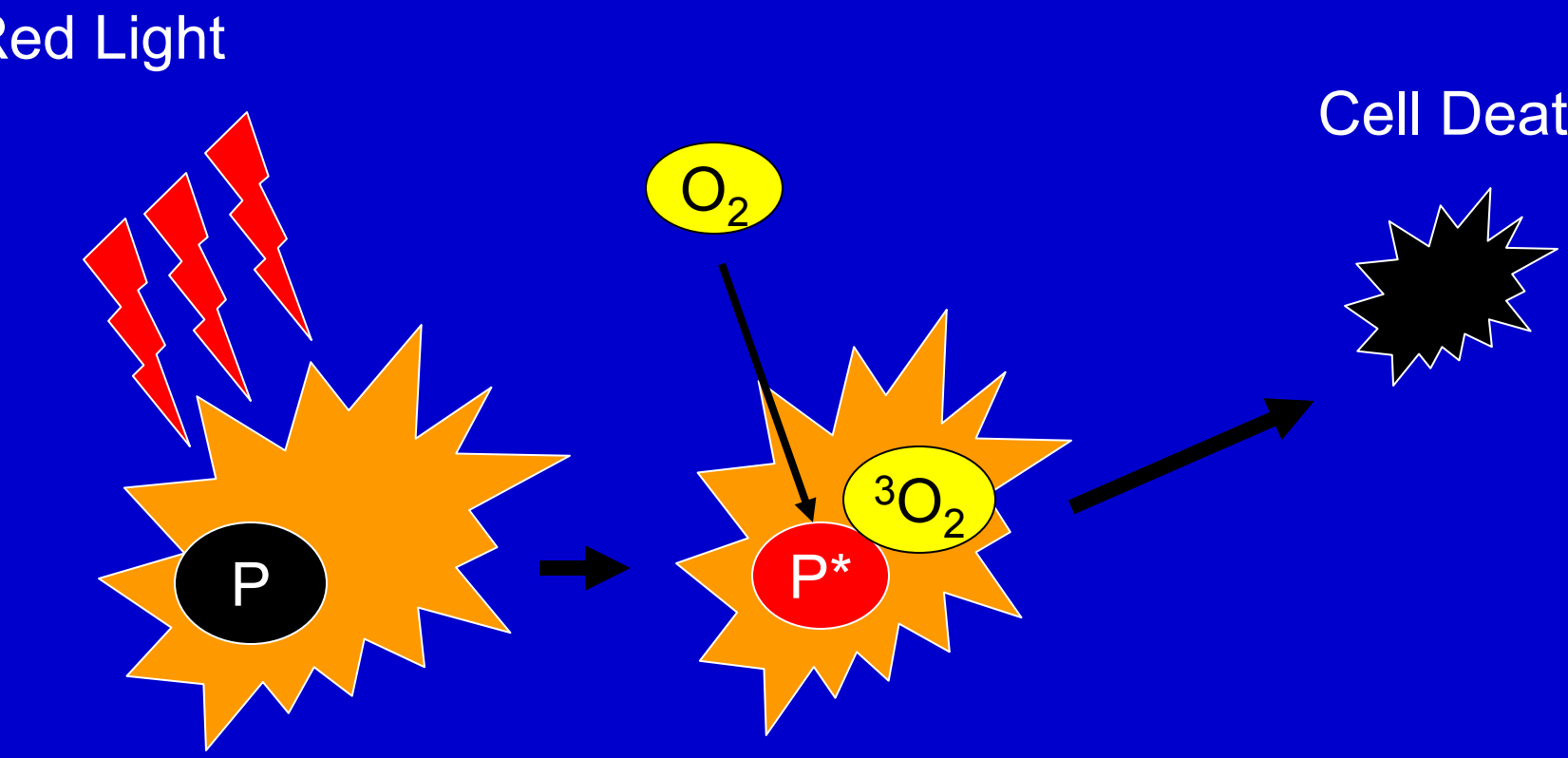
- Esophagectomy may not be in the best interest of all patients
- Observation without intervention may not be the best option in some patients
- Successful eradication of dysplasia and early cancers is possible in some patients

Endoscopic Therapy
Ablation vs. Mucosectomy

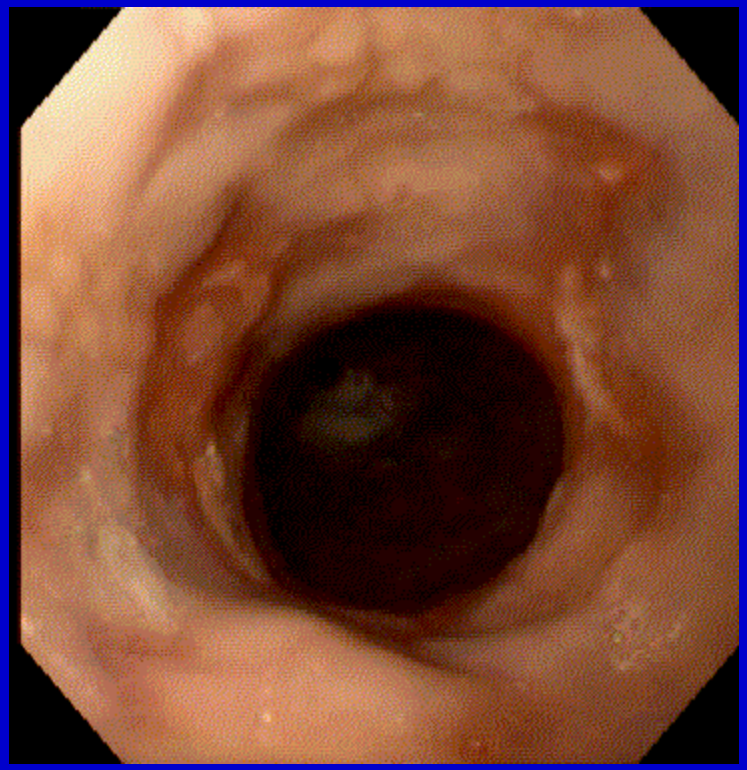
Ablation **EMR**



Photodynamic Therapy (PDT)



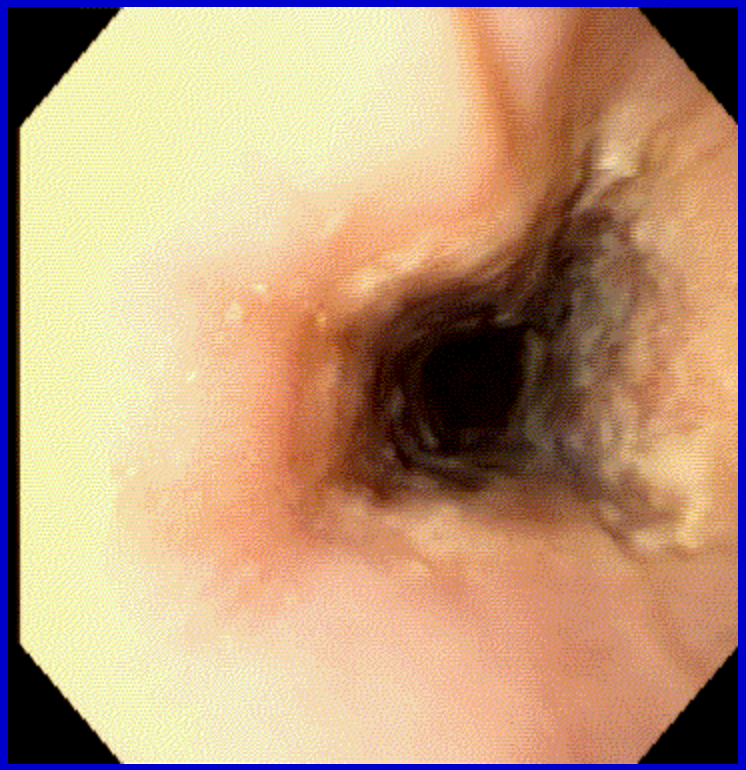
PDT for Barrett's and Early Cancer



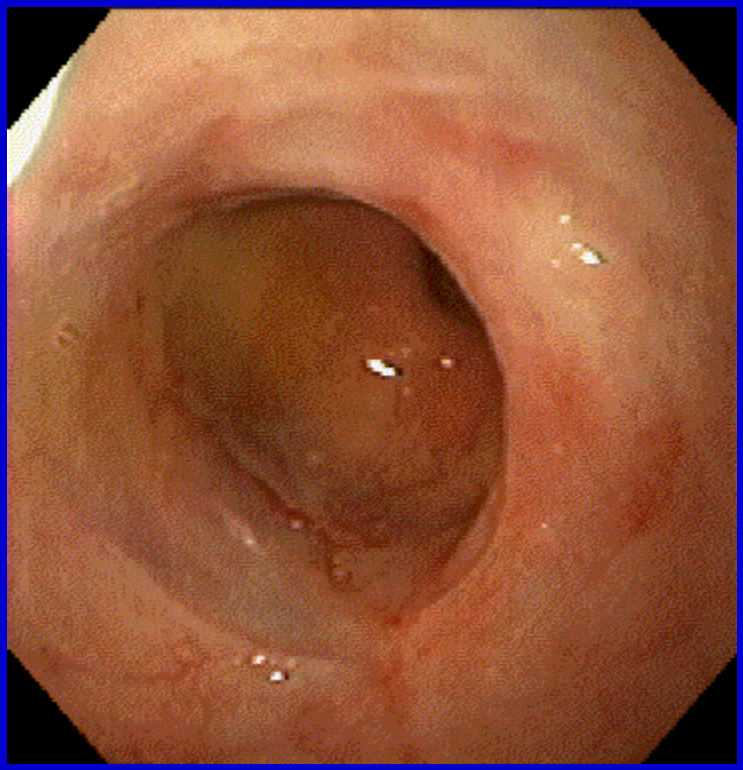
Barrett's segment with IMCa

Cylindrical laser fiber and light

PDT for Barrett's and Early Cancer

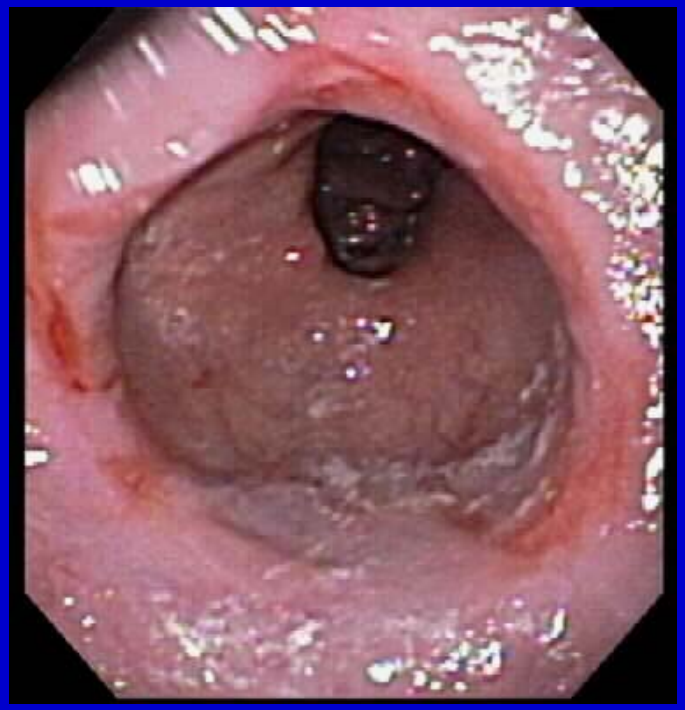


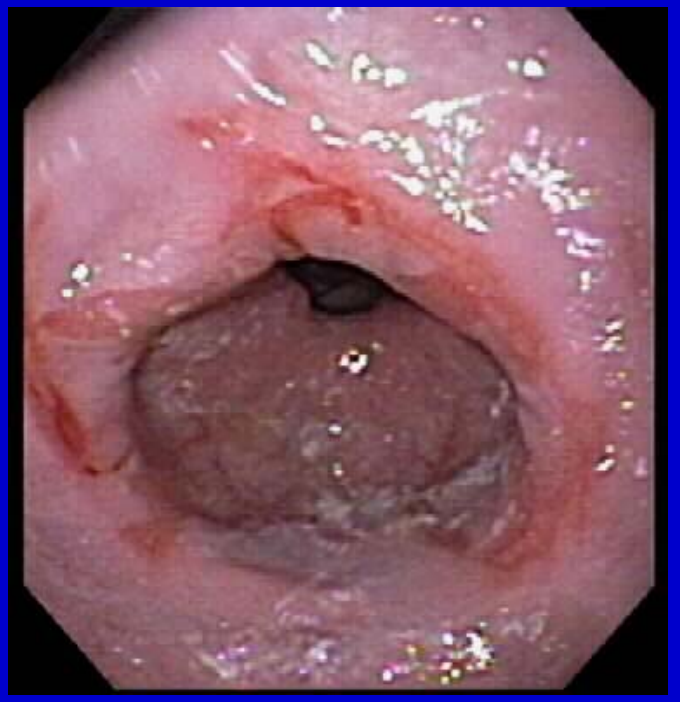
Severe esophagitis – 48 hrs



Follow up surveillance – 1 yr

PDT Long Term Follow-up





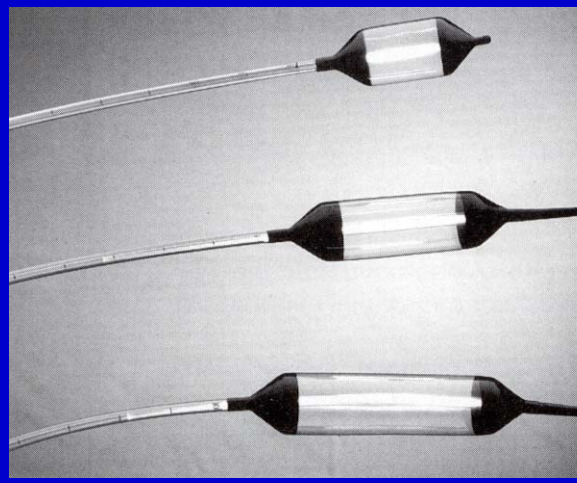
Two year follow-up reveals ongoing esophagitis due to unremitting reflux.

PDT for Barrett's and Early Cancer

- Photofrin® only FDA approved therapy
  - 70% - 80% effective
  - Up to 3 treatment sessions required
- Complications
  - Photosensitivity for 30 – 40 days per session
  - Universal chest pain
  - 30% patients stricture

PDT for Barrett's and Early Cancer

- 100 patients (13 with T1 lesions)
- Light dose 100 to 250 J/cm
- Treatment failures
  - 3 of 13 cancers progressed
- Complications
  - strictures in 34%
  - pain
- Follow up 19 months (4 to 84)



Centering balloons

Overholt Gastrointest Endosc 1

PDT for Barrett's HGD

- Multicenter trial
  - 208 patients (2:1) PDT vs. omeprazole
  - Complete ablation HGD 77% (106/138) PDT compared to 39% (27/70) omeprazole group
  - Multiple treatments
    - 68% PDT patients required 2 treatments
    - 47% PDT patients required 3 treatments

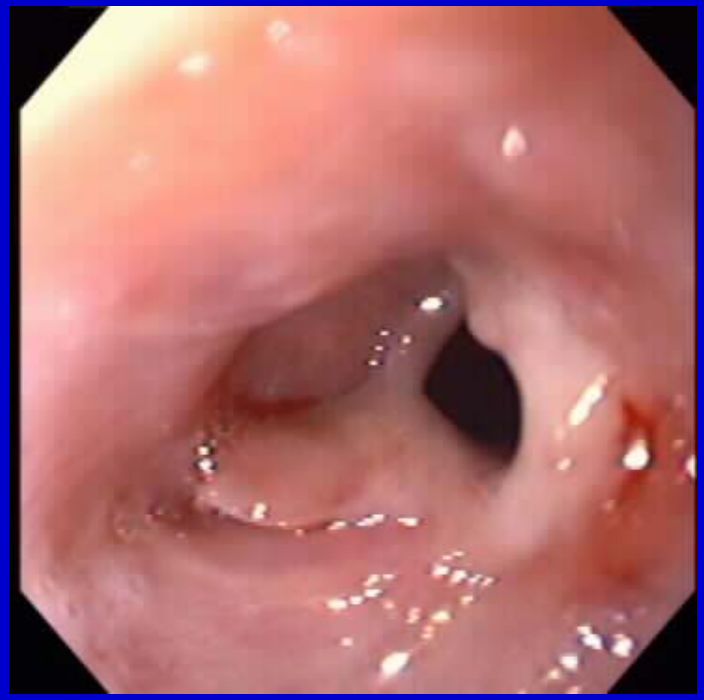
Overholt Gastrointest Endosc 2005;62

PDT for Barrett's HGD

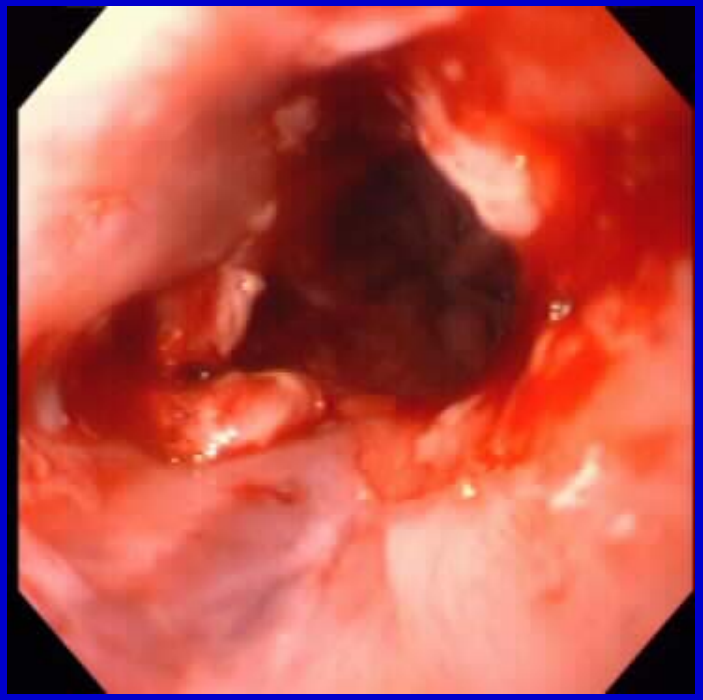
- Multicenter trial – 5 year follow up
  - 208 patients (2:1) PDT vs. omeprazole
  - Progression to cancer 15% PDT compared to 29% omeprazole group

Overholt Gastrointest Endosc 2007;66

PDT Stricture

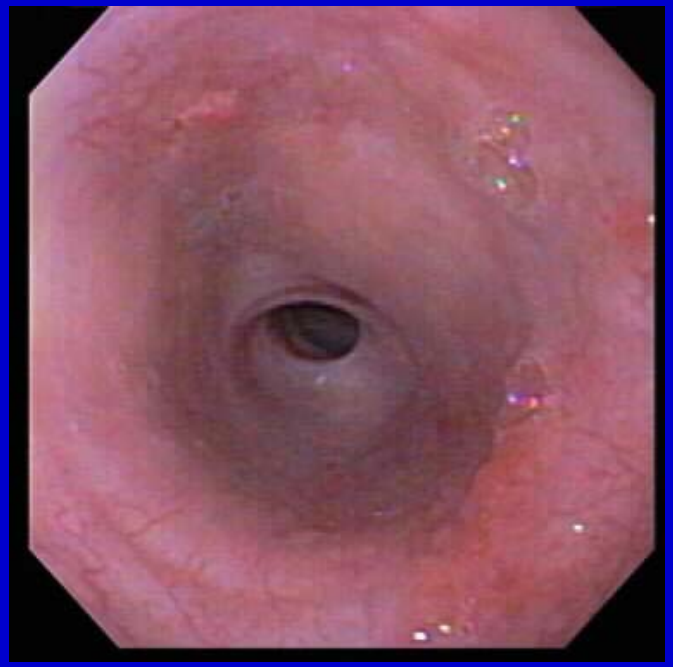


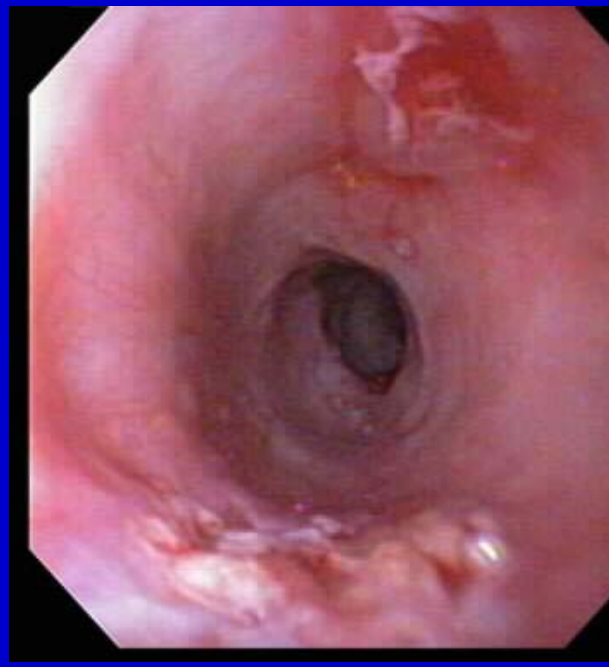
Short inflammatory
5 mm stricture



Balloon dilation to
16 mm

Barrett's Esophagus after PDT



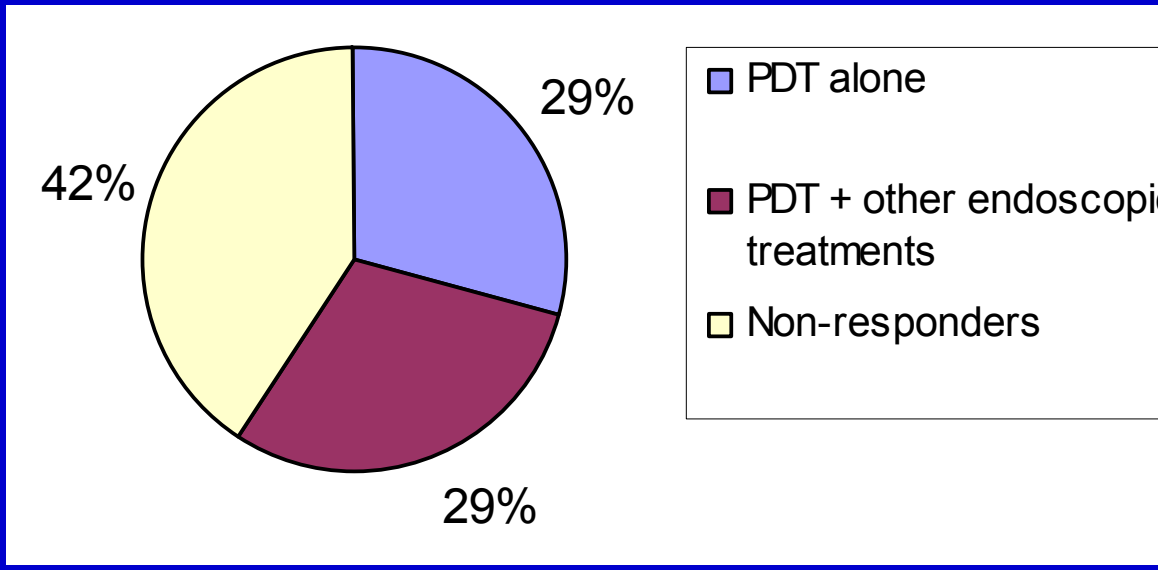


Residual islands of dysplasia

BICAP ablation

Cleveland Clinic Experience with PDT

- 17 patients (12 IMCA / 5 HGD)
  - Follow up 2.3 (±1.7) years
  - Age 78.9 (±5.1)
  - BE length 5.8 (±2.2) cm

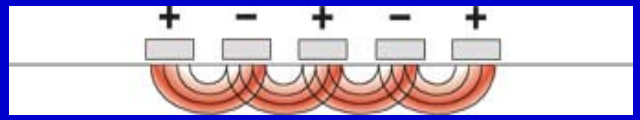


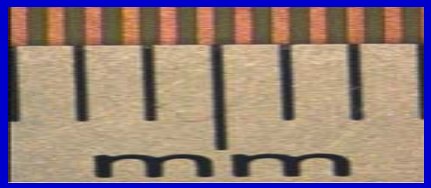
RFA - HALO^{360} System

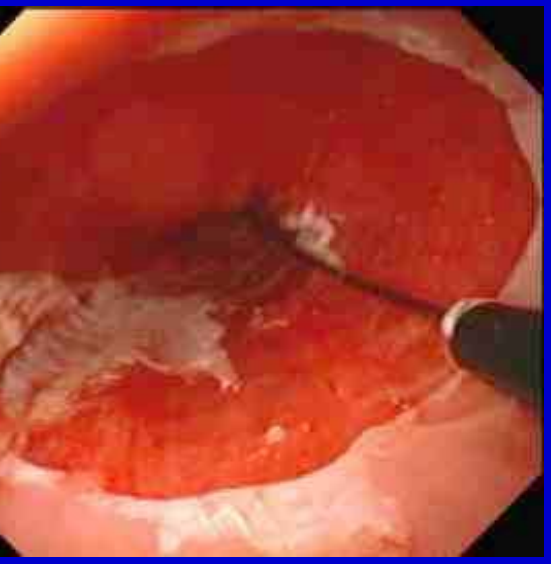
Circumferential balloon-ablation

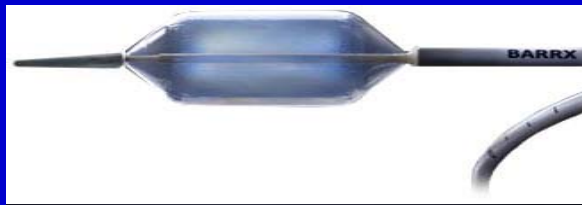
Controlled depth

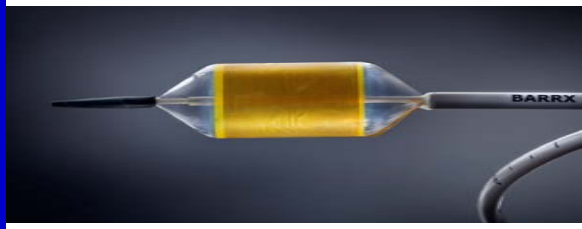
– energy density, electrode geometry





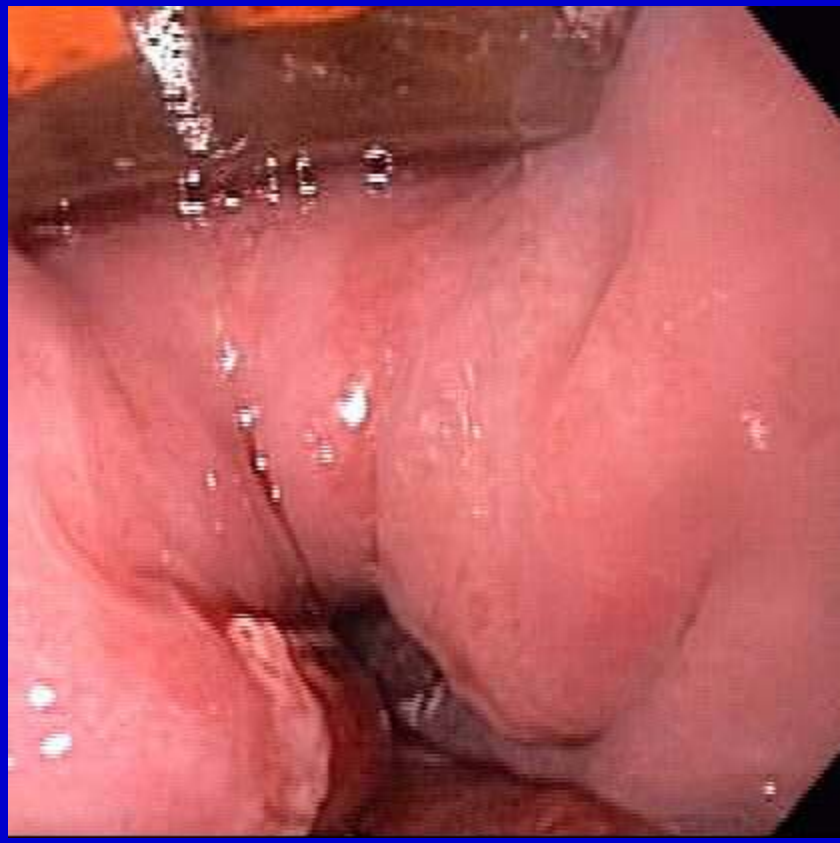




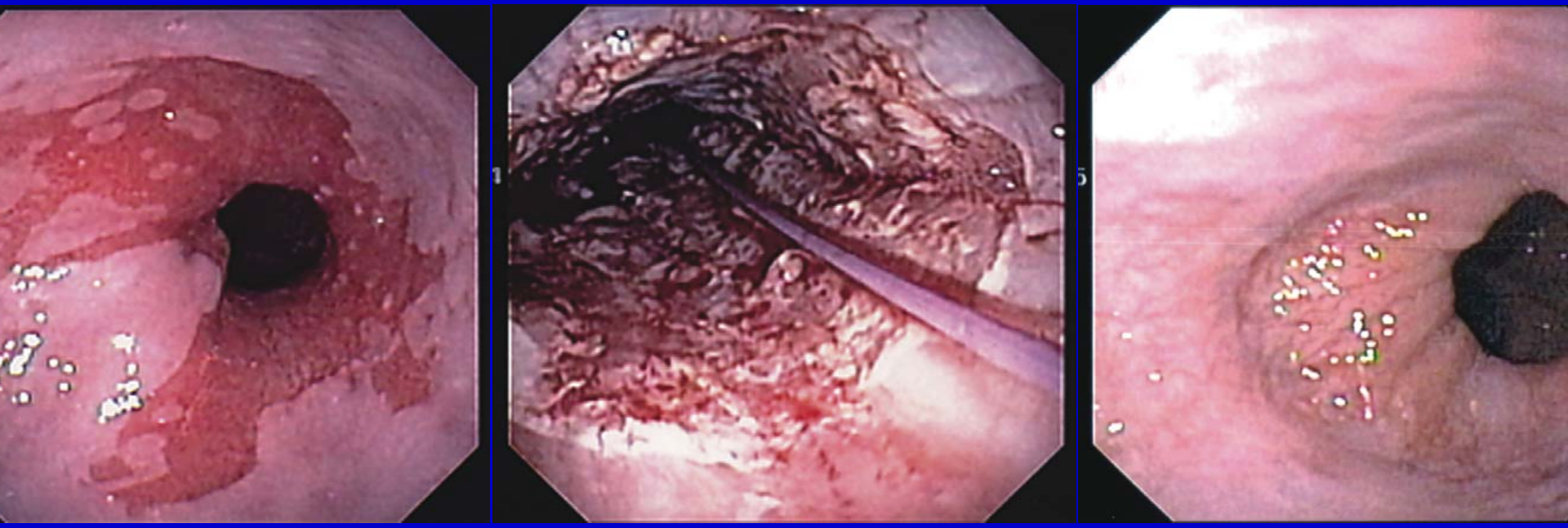


RFA - HALO^{90} System

- Scope-mounted ablation
- Primary therapy
  - short segment Barrett's
  - touch-up residual disease



AIM II Complete Response



Complete response to SIM in 98% patients (n = 70)
2.5-year follow-up after stepwise circumferential and focal ablation

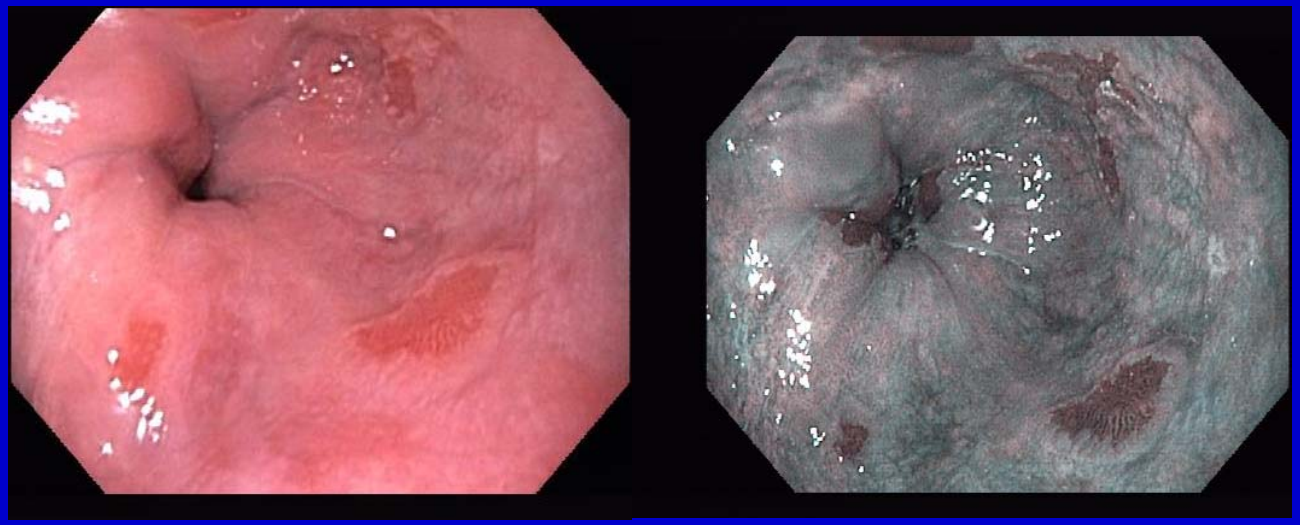
Fleischer Gastrointest Endosc 2008

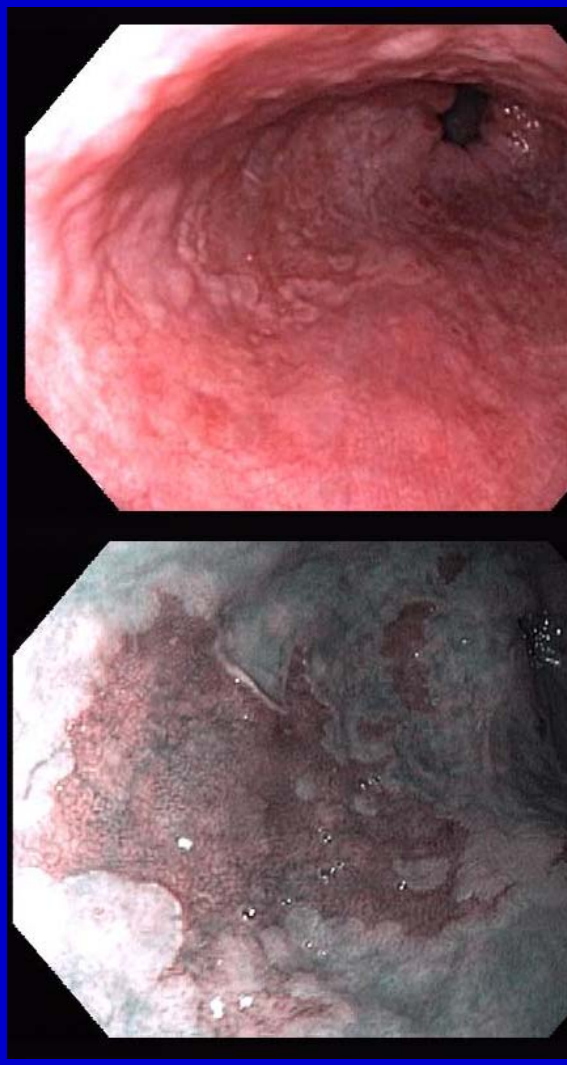
RFA Advantages

- Limited depth of injury
  - Limits strictures
- Immediate effect
- No restrictions on surgical anatomy or complex hiatal hernias

RFA Limitations

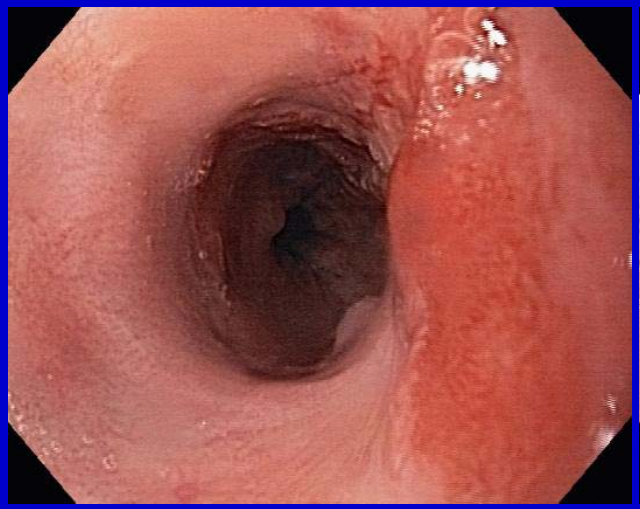
- Limited depth of injury
  - Inadequate for nodular areas
- Requires contact with mucosa
- Skip areas and residual disease

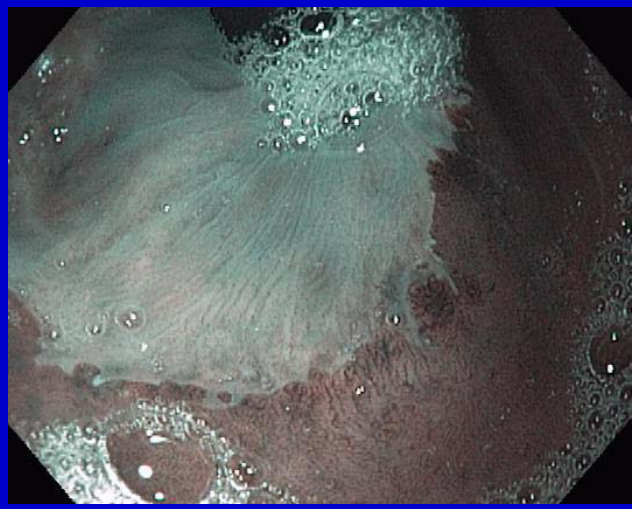




RFA Limitations

- EGJ most like area for failure

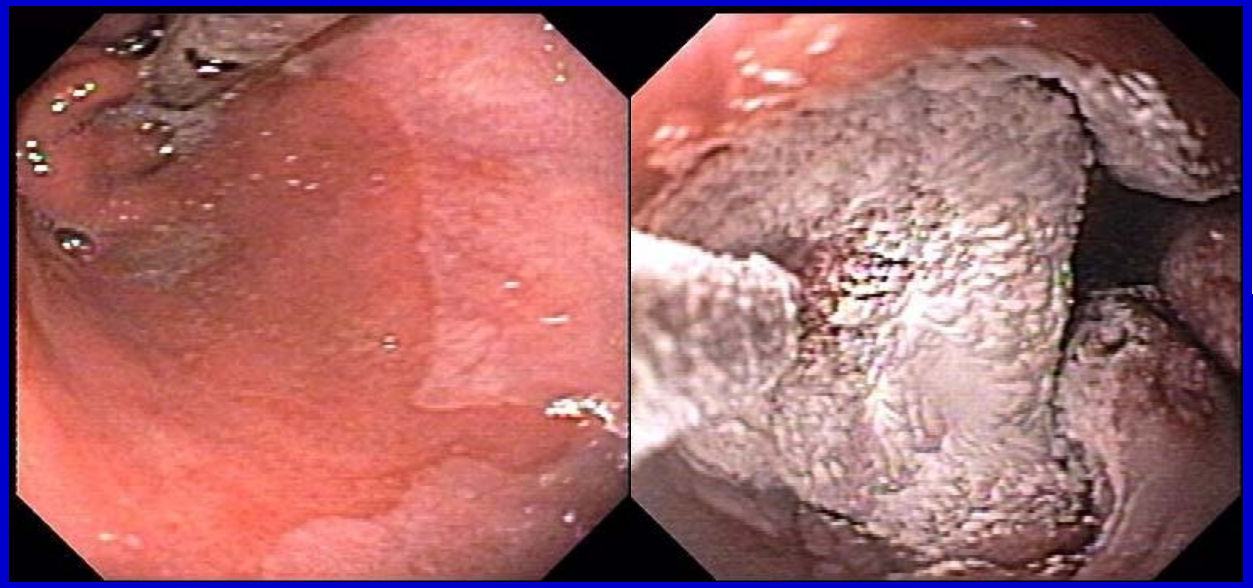




RFA Summary

- 85-98% Complete response IM and dysplasia
  - Elimination of abnormal genetic markers
  - Preservation of esophageal function
  - Safety profile high with low incidence strictures
  - Pain significant and requires management
- Requires contact with the mucosa
  - Difficult to treat in strictures or angulated lumen
  - Inadequate response with nodular mucosa

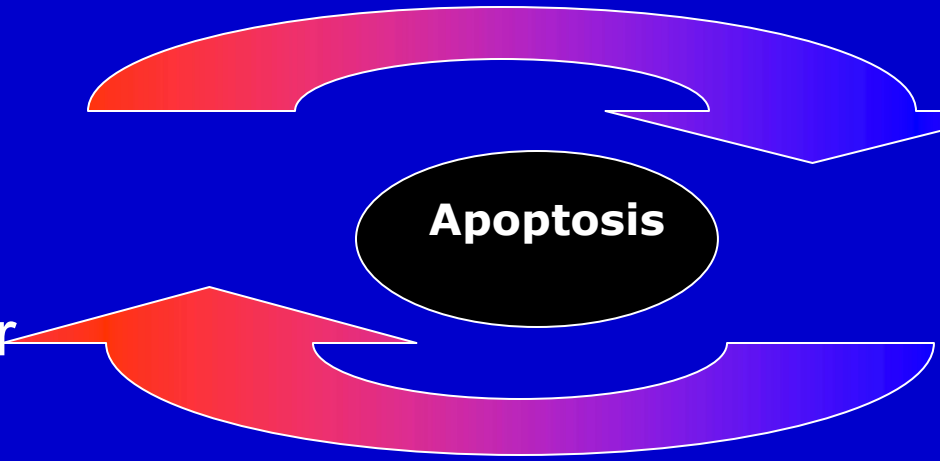
LN CryoSpray Ablation (CSA)



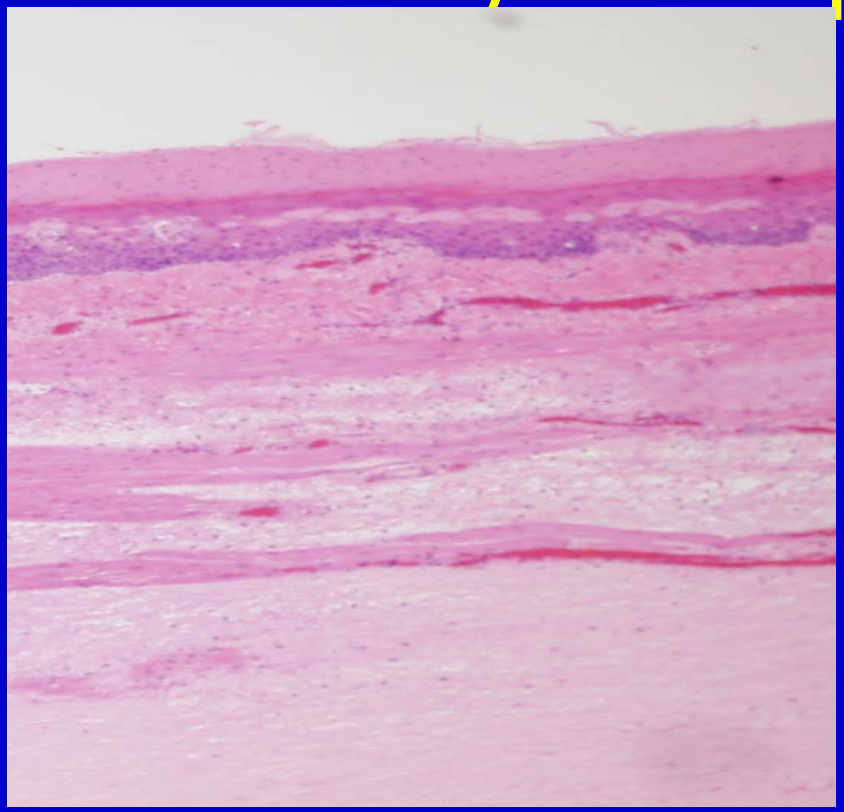
LN Cryotherapy Mechanism of Injury

The freeze-thaw cycle

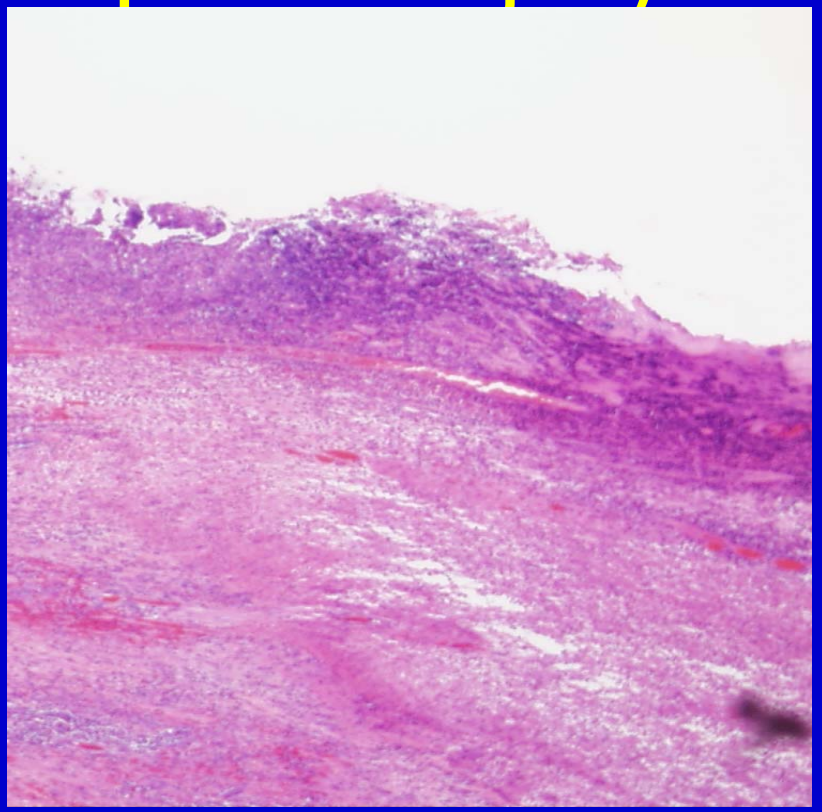
- Ice crystals disrupt lipids and cytoskeleton
- Ischemia and vascular stasis
- Reperfusion injury with cellular leakage and submucosal hemorrhage
- Inflammatory response
- Immune stimulation



LN Cryotherapy Depth of Injury



1 hour: minimal inflammation

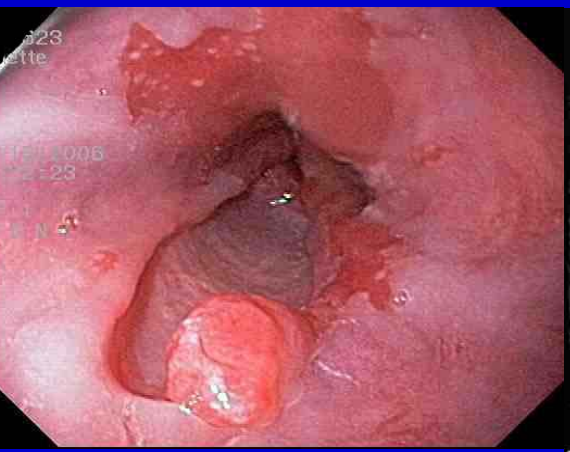


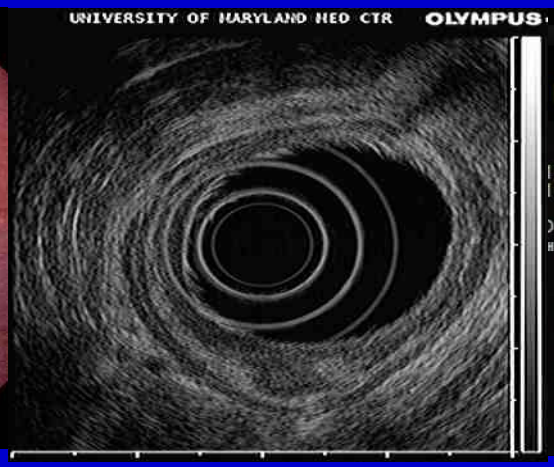
48 hours: marked inflammation

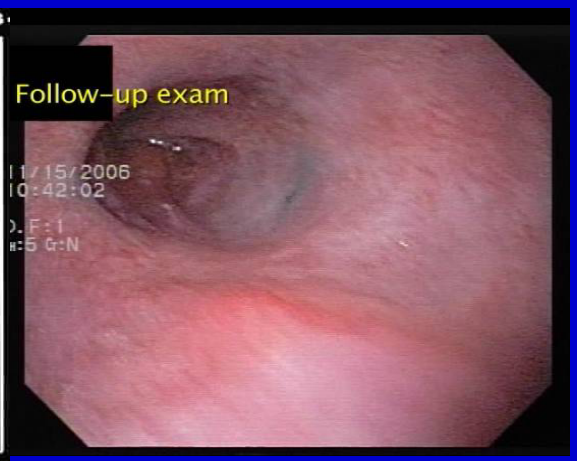
Johnston Gastrointest Endosc 2001 A3448

LN Cryotherapy Advantages

- High patient tolerance
  - Minimal chest pain
  - Familiarity with concept
- Able to treat uneven surfaces
- Possible to treat submucosal lesions



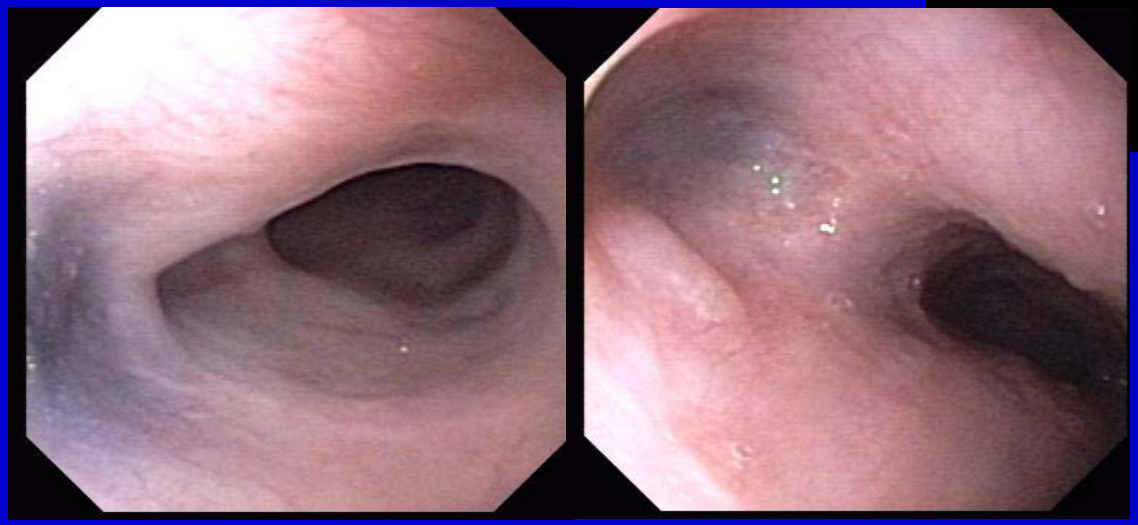




Greenwald DDW 2007

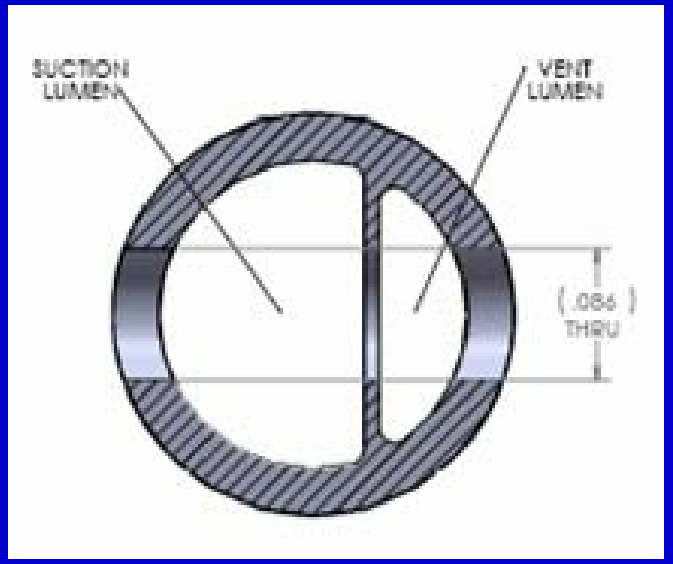
LN Cryotherapy

- Dosimetry
  - Spray duration (10 – 20 seconds)
  - Spray cycles (2 – 4)



LN Cryotherapy Risks

- Liquid nitrogen conversion to gas
  - 20 second spray releases 7 – 8 liters
  - Perforation 3 of 116 patients; 365 cases
    - 2 Gastric rents from over distention
    - 1 Pneumoperitoneum



LN Cryotherapy Risks

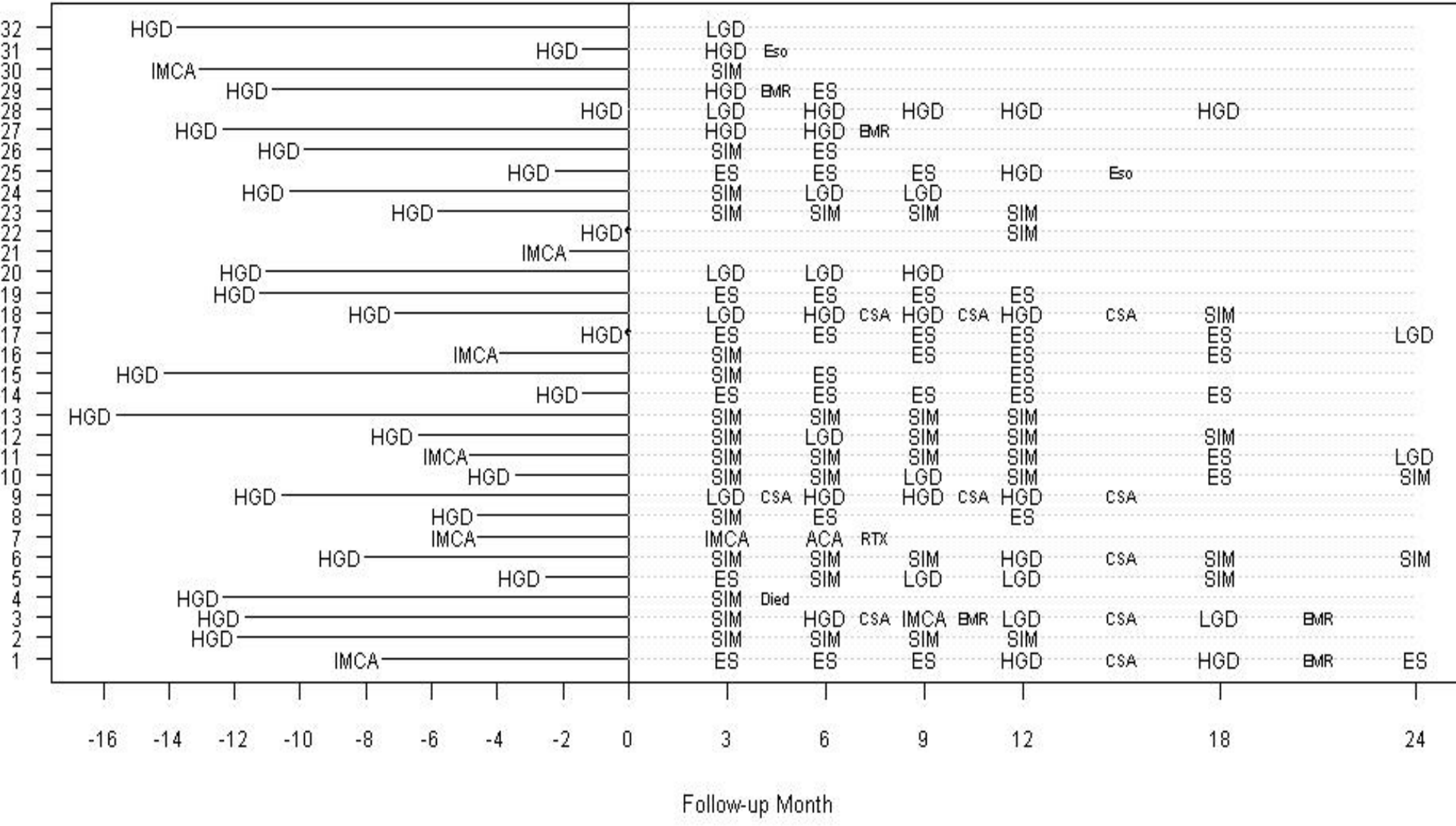
- Strictures 4%
  - Appears limited to those with prior narrowing or therapy
- Lip ulcer
- Pain usually mild – 0 to 5 days

TABLE 1. Cryoablation results

Patient no.	Age (y)	Precryo BE length (cm)	Postcryo BE length (cm)	BE length 6 mo after cryo	No. cryo sessions	Reversal	Histologic reversal at 6 mo	Dysplasia before cryo	Dysplasia after cryo	Subsquamous SIM (no. Bxs) at 1 mo after cryo	Subsquamous SIM (no. Bxs) at 6 mo after cryo
1	56	4	1	1	5	Yes	No	None	None	None (12)	None (12)
2	51	1	0	0	6	Yes	Yes	LGD	None	None (4)	None (4)
3	72	8	2	2	8	Yes	No	LGD	None	None (20)	None (20)
4	74	5	0	0	5	Yes	Yes	LGD	None	None (12)	None (12)
5	57	8	0	0	5	Yes	Yes	IFD	None	None (24)	None (16)
6	60	4	0	0	1	Yes	Yes	IFD	None	None (16)	None (16)
7	57	4	0	0	4	Yes	Yes	LGD	None	None (12)	None (12)
8	53	3	0	0	4	Yes	No	None	None	None (12)	None (8)
9	53	4	0	0	5	Yes	No	LGD	None	None (12)	None (16)
10	50	4	0	0	3	Yes	Yes		None	1 Bx "+" of 12	None (12)
11	64	6	0	0	1	Yes	Yes	HGD	None	1 Bx "+" of 24	None (20)
Mean	59	4.6	0.27		46		64%			2/160 (1.25%)	0/148 (0%)

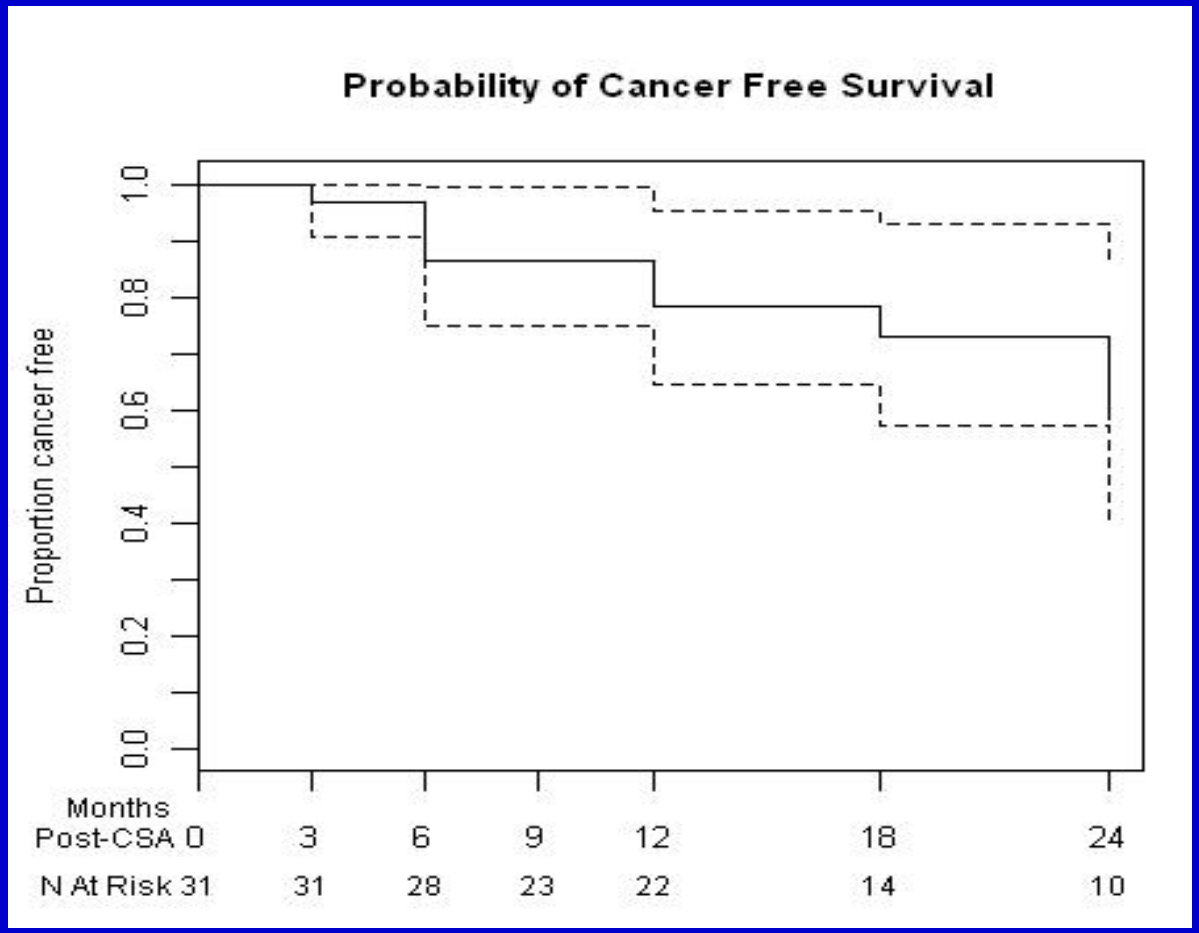
BE, Barrett's esophagus; *SIM*, specialized intestinal metaplasia; *Bx*, biopsy; *LGD*, low-grade dysplasia; *IFD*, indefinite for dysplasia; "+", positive for subsquamous SIM; *HGD*, high-grade dysplasia.

Johnston Gastrointest Endosc 2005



Dumot Gastrointest Endosc 2009

LN Cryotherapy with EMR



Dumot Gastrointest Endosc 2009

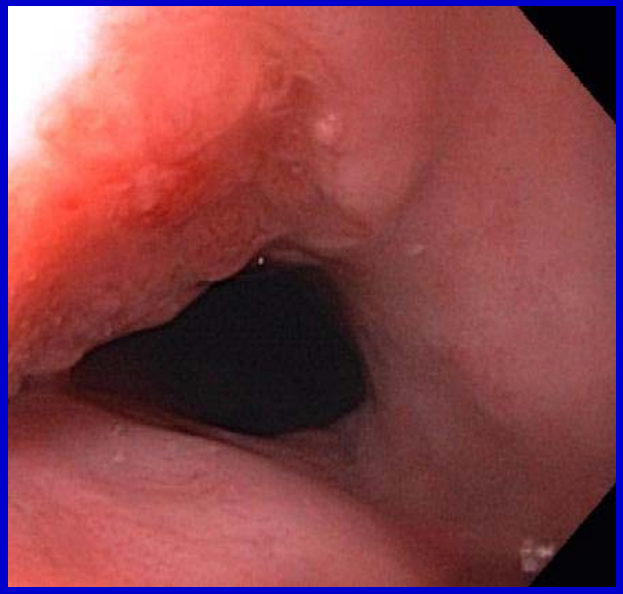
LN Cryotherapy and Squamous Cell Cancer

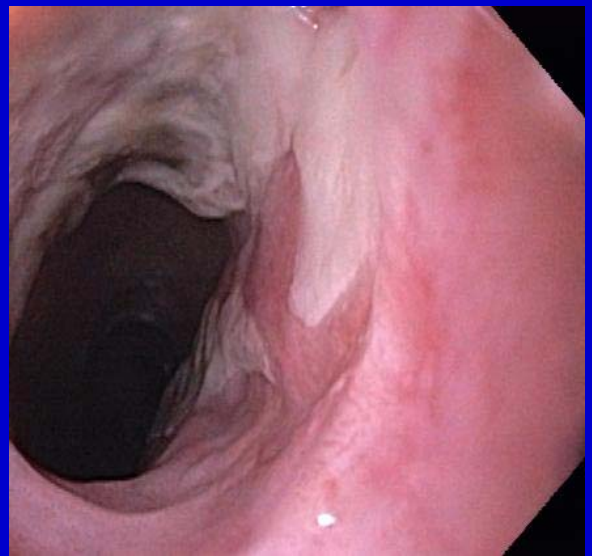
- SSC case series (n = 6)
  - 74 years median age (IQR 65 – 82)
    - 2 Tsm1 and 4 Tm
    - 20 mm median size (IQR 14-26)
    - Cricopharyngeus (3), diverticulum (1), stricture (3), varices (1) and prior radiation therapy (3)
  - Uniform response
    - 5 of 6 local complete response

Dumot DDW 2009

LN Cryotherapy and Squamous Cell Cancer

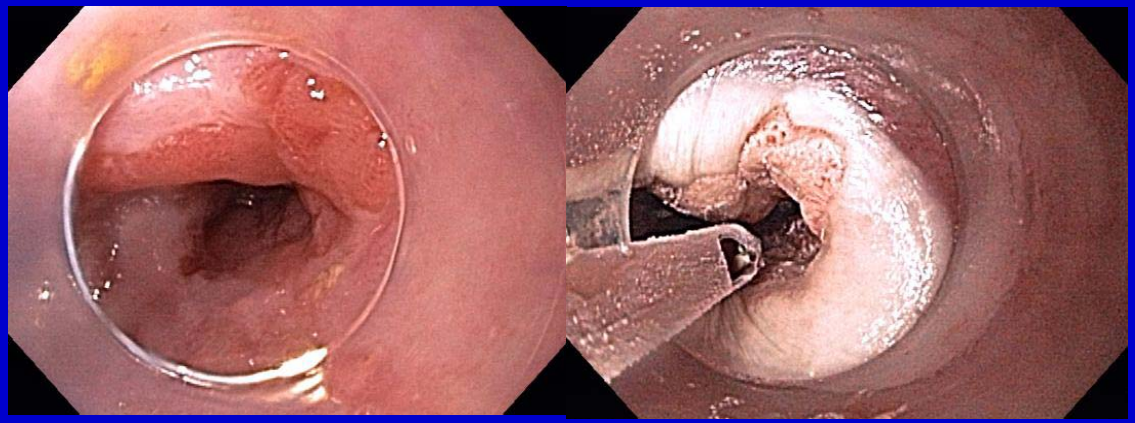
Invasive SCC
PET positive
3rd head / neck ca





Future Goals

- Improve decompression
  - Safety
  - Increase dosimetry (depth of injury)
  - Reduce treatment times
- Improve visibility

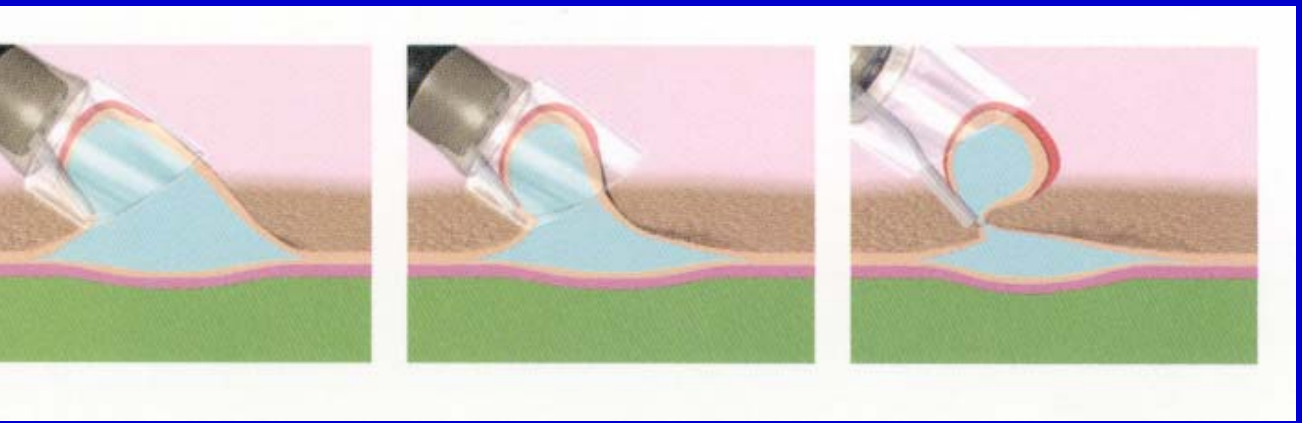


LN Cryotherapy Summary

- Unique mechanism
  - Noncontact technique effective for lesions in difficult topography
  - Depth of injury capable of treating early cancers
- High patient acceptance
  - Low incidence of pain and strictures
  - Patient familiarity

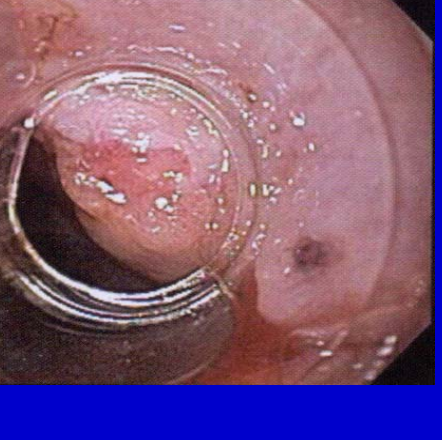
Cap-fitted Technique

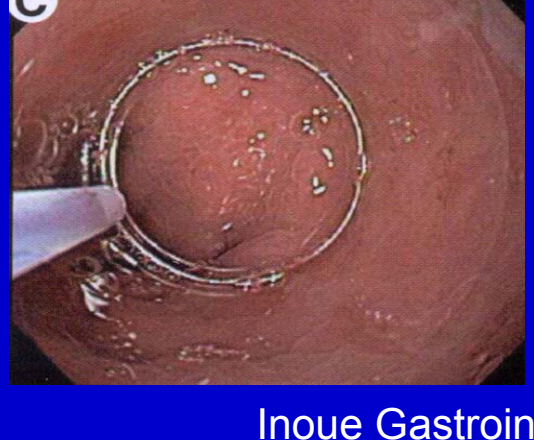
- Crescent-type snare
- Friction fit caps
- Disposable injection needle



Cap-fitted EMR Technique

- Submucosal injection is made in standard fashion
- Crescent-shaped snare is “pre-looped” into the cap rim
- Cap sucks lesion into cap and strangulates lesion
- Snare is closed and suction is released then cut tissue
- Cap is used to aspirate the resected lesion

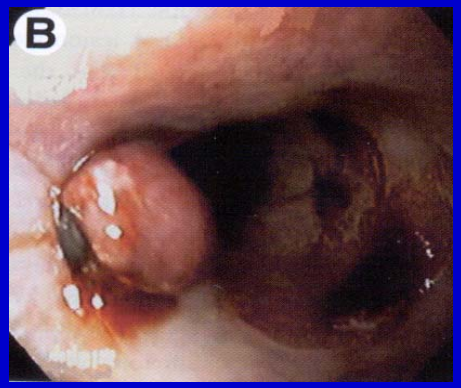


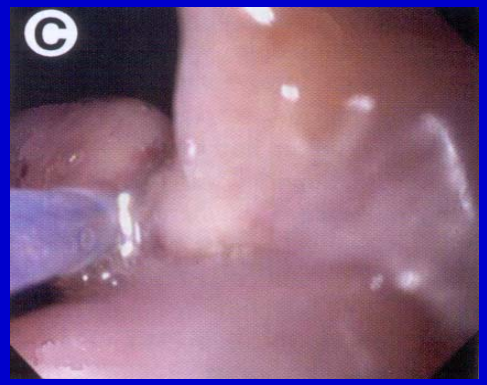


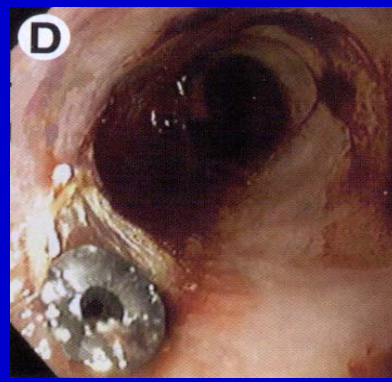
Inoue Gastrointest Endosc 1993;39:
Tada Gastrointest Endosc 1996;44:6

Band-Ligation Technique

- Standard E.V.L. device or Duette®
- Deploy rubber band around lesion
- Hexagon-type snare







Suzuki et al. GE 1999;49:192-
Ell et al. Gastro 2000;119:670

EMR-Ligation vs. EMR-Cap: Early Esophageal CA

- 100 endoscopic resections (72 patients)
  - 50 EMR-L (w/o SM lift)
  - 50 EMR-C (w/ SM lift: diluted epinephrine and saline)
- Specimen (max. dia. / mm) (max. area / mm^2)
  - EMR-L 16.4 x 11 185
  - EMR-C 15.5 x 10.7 168
- Site at 24 hr
  - EMR-L 20.6 x 14.3 314
  - EMR-C 18.9 x 12.9 260

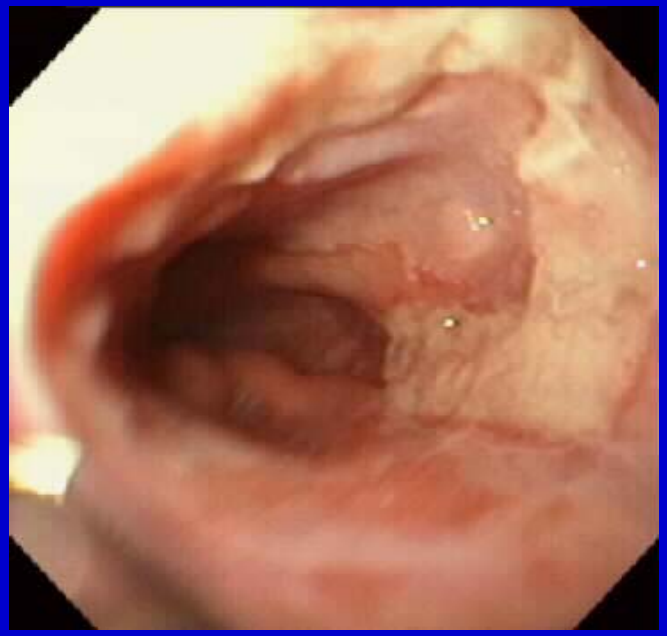
Failure rate:

- 1/50 (2%) EMR-L (due to scarring from prior procedures)
- 6/50 (12%) EMR-C (technical difficulties)

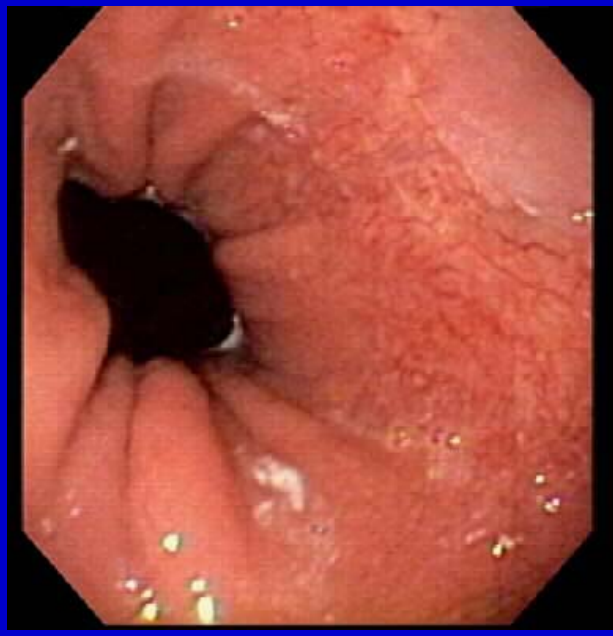
May Gastrointest Endosc 2003;57

Short Segment Barrett's and Esophageal Cancer

Short segment BE with TisN0 mass



1 month after EMR



Surveillance at 6 years

Endoscopic Therapy for Early Cancers in BE: Mayo Clinic Experience

	Surgery (n=64)	EMR/PDT (n=24)
Sex (M/F)	58 / 6	21 / 3
Age (mean±SE)	67 ± 1	68 ± 2
BE length (cm±SE)	6.5 ± .5	5.6 ± .8
Follow up (mo.±SE)	19 ± 3	12 ± 2

Pacifico Clin Gastroenterol 200

Endoscopic Therapy for Early Cancers in BE: Mayo Clinic Experience

	Surgery (n=64) (%)	EMR/PDT (n=24) (%)
Photosensitivity	0	2 (8)
Strictures	10 (16)	2 (8)
Anastomotic leak	5 (8)	0
Wound infections	5 (8)	0
Dumping syndrome	3 (5)	0
Other*	8 (13)	0

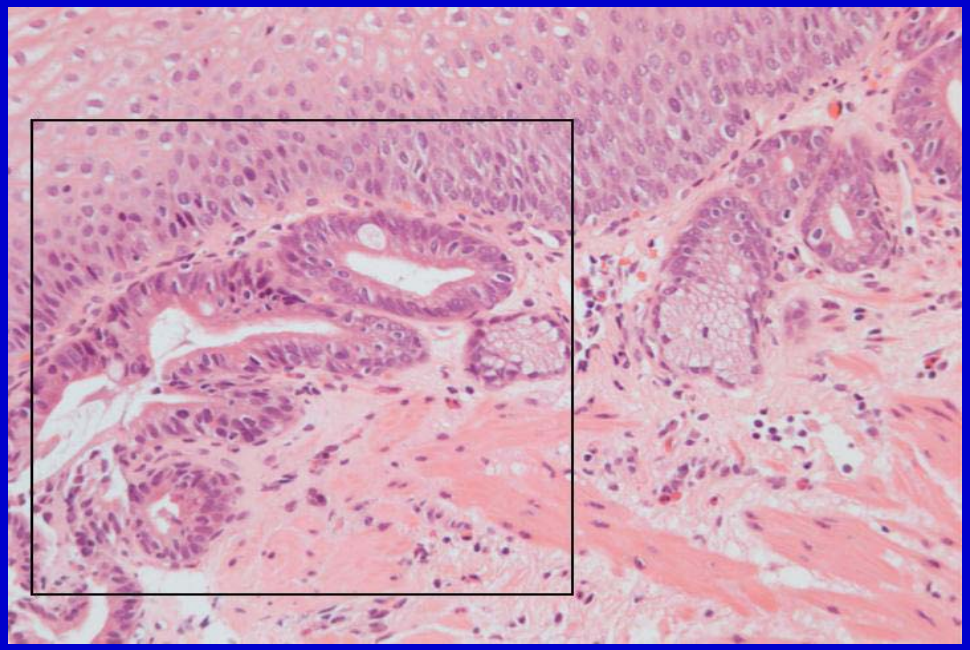
*Empyema, blood transfusions, atrial fib., aspiration, chylothorax)

Endoscopic Therapy for Early Cancers in BE: Mayo Clinic Experience

	Surgery (n=64) (%)	EMR/PDT (n=24) (%)
Death due to therapy	1	0
Unrelated death	1	2
Failed therapy	0	4*
- Ca on 1st F/U Bx		1 - surgery 1 - CRT 2 - died

Ablation Risks – All methods

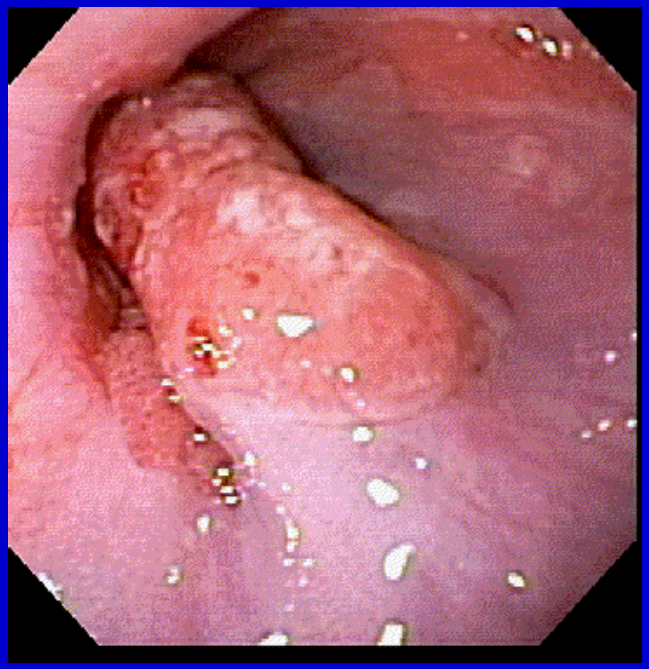
- Failure to continue surveillance
  - Remember squamous overgrowth occurs in treatment naïve patients



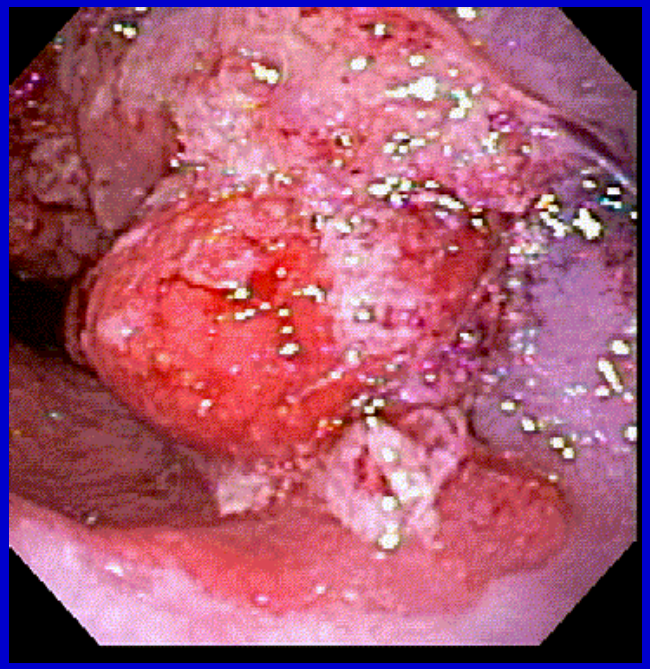
Endoscopic Mucosal Resection

- Provides pathological specimen
  - Margins
    - Peripheral and deep
  - Tumor grade
  - Lymphatic and vascular involvement
- Immediate effect
- Most complications readily apparent
- Well tolerated

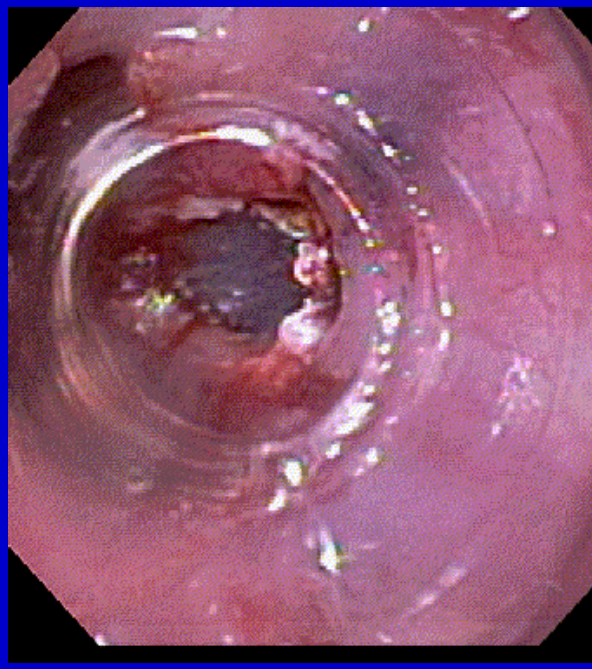
EGJ Cancer Staging with EMR



Thick proximal gastric fold

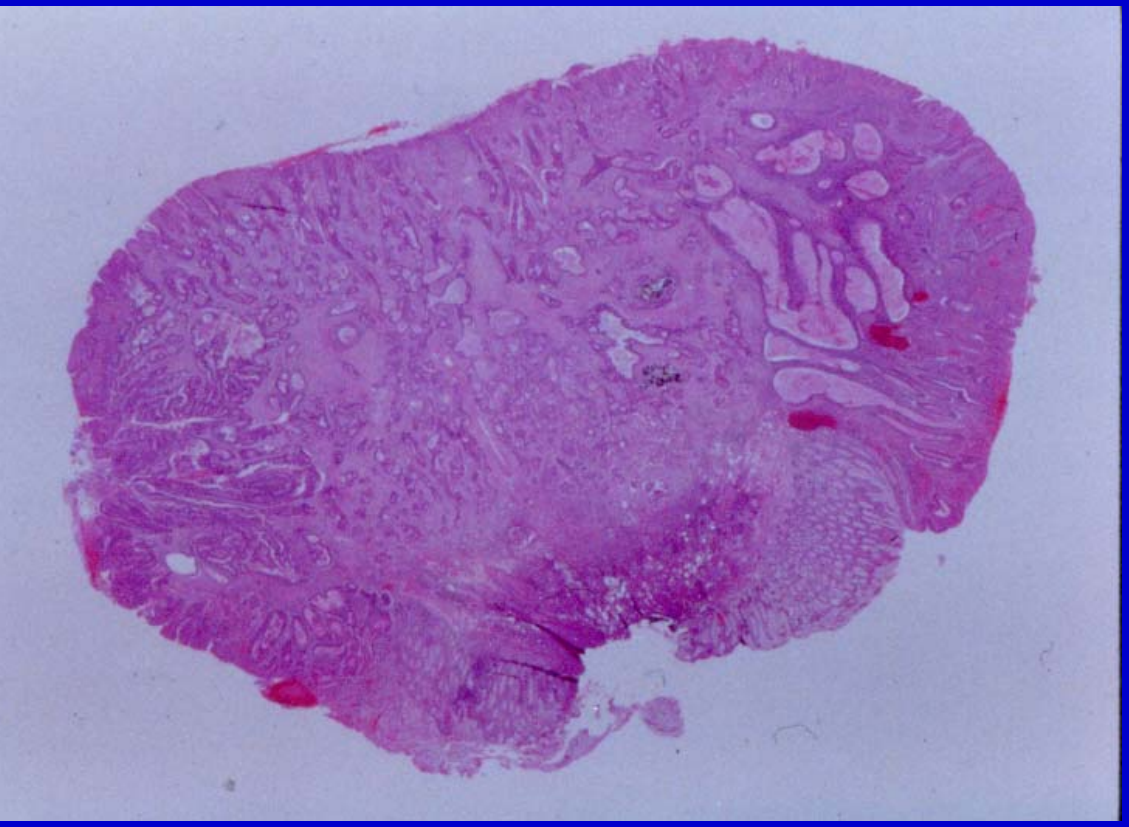


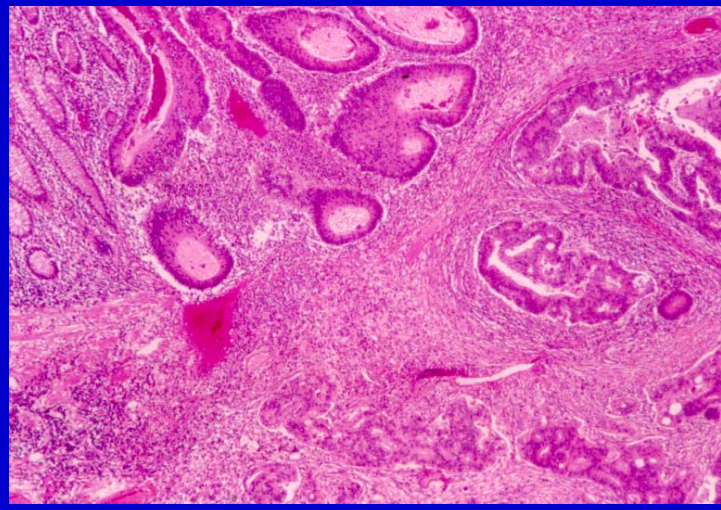
Submucosal saline injection

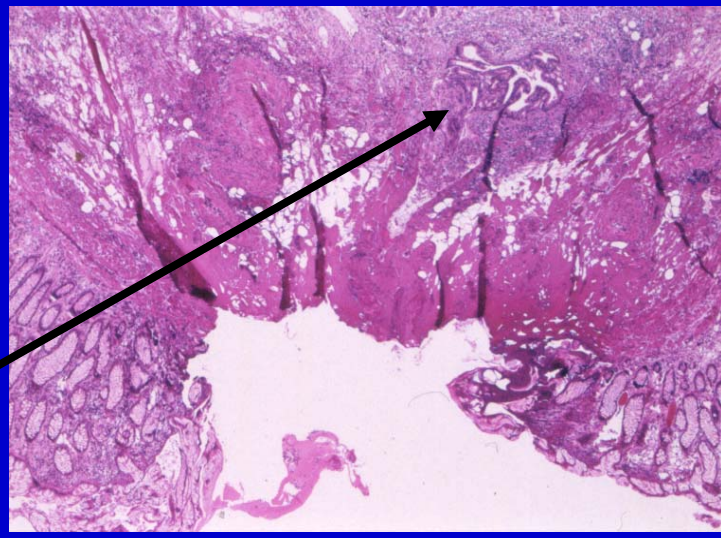


Cap-fitted EMR site

EMR Specimen of EGJ Adenocarcinoma







Polypoid specimen with invasive cancer into the deep submucosal layer

Barrett's and Esophageal Cancer

- 100 patients
- 36.7 month mean follow up

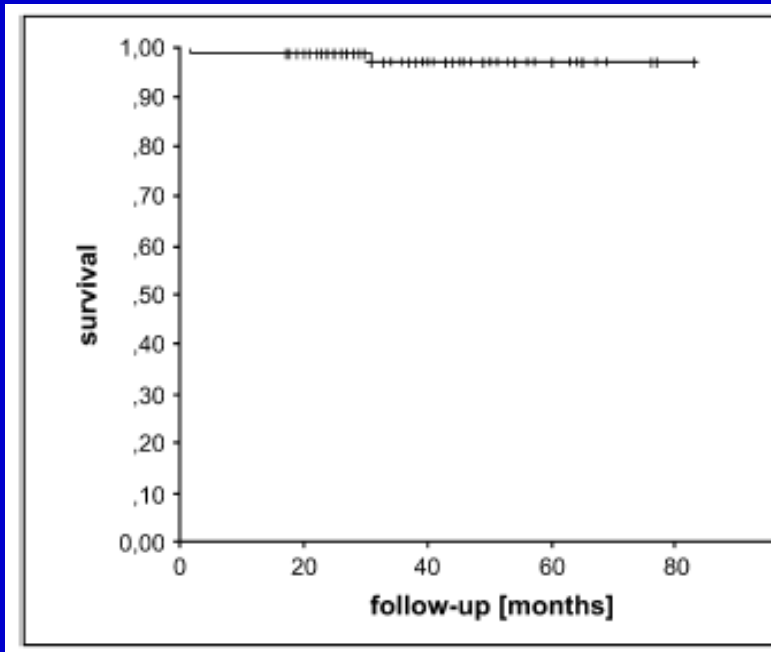
TABLE 1. Low-risk criteria*

Lesion diameter <20 mm; and macroscopically type I, IIa, IIb, or IIc lesions <10 mm; and

Well-differentiated or moderately differentiated adenocarcinoma (grading G1/G2); and

Lesions limited to the mucosa (m type) on the basis of staging procedures and proved by histology of the resected specimen

No invasion of lymph vessels or veins proved by histology of the resected specimen

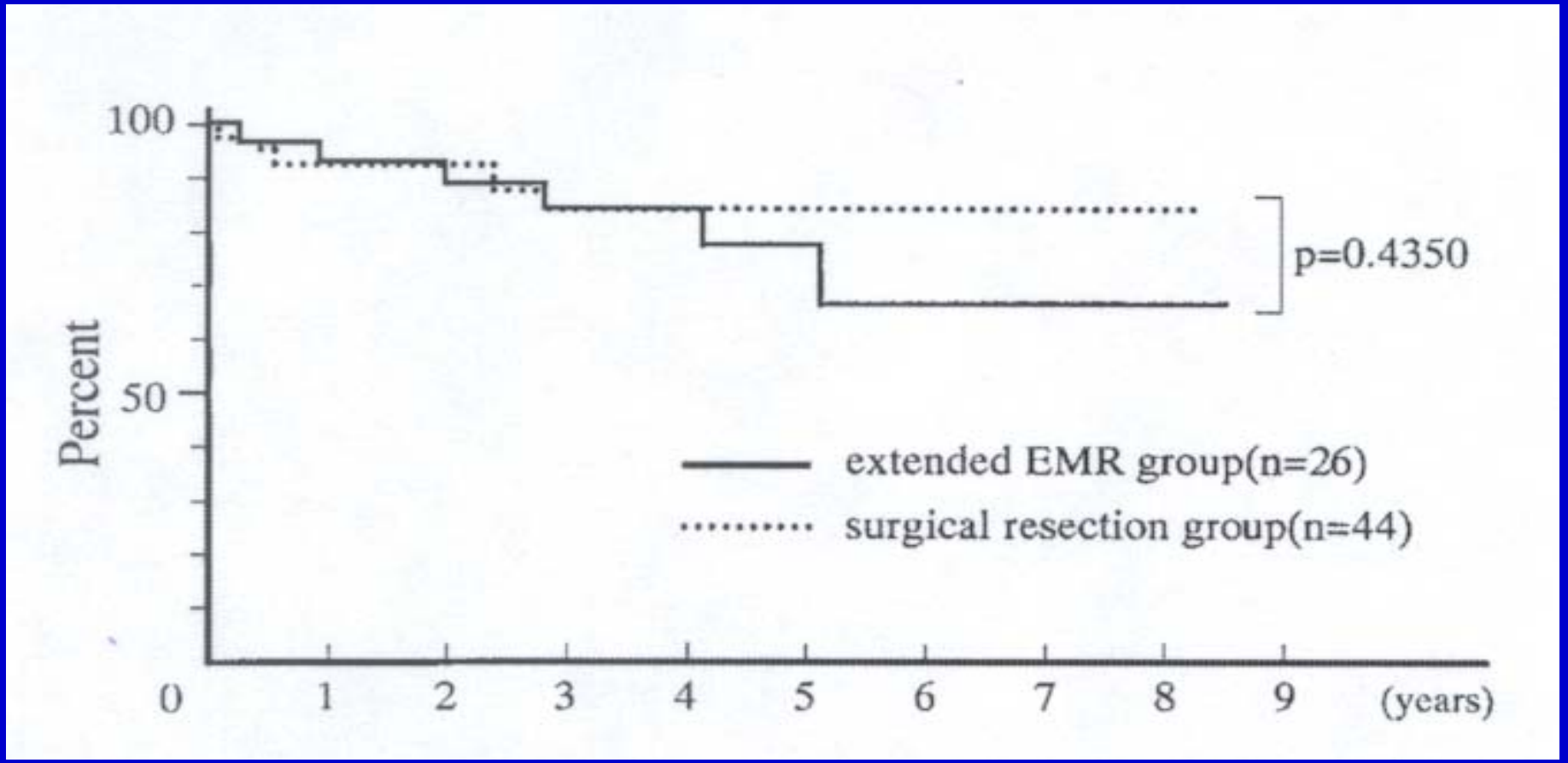


FU [months]	12	24	36	48	60	72
Number of pts at risk	99	80	43	21	11	3

Ell Gastrointest Endosc 2

Squamous Cell Cancer Esophagus

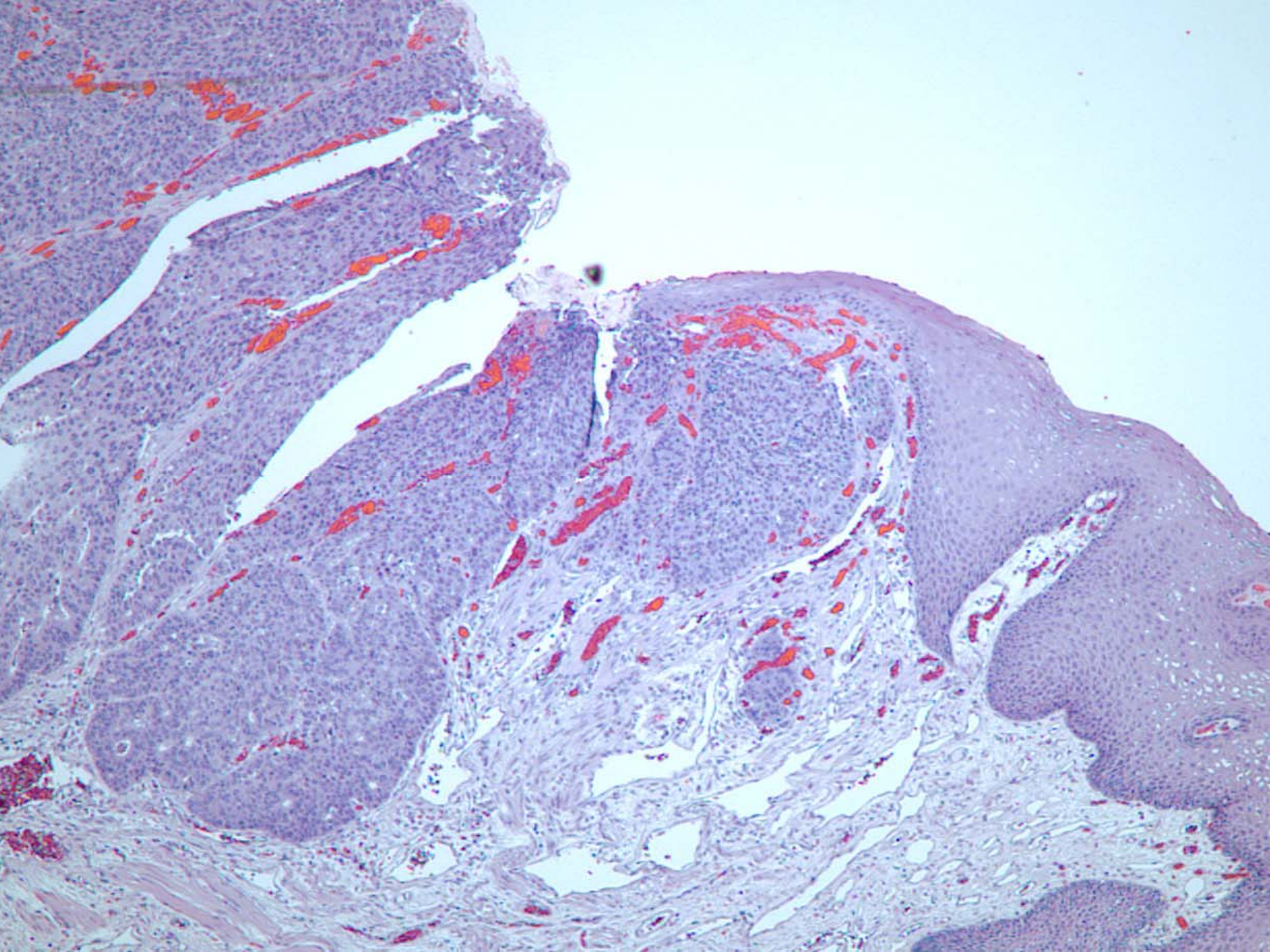
- EMR 5-year survival data for early lesions
  - 84 vs. 77%

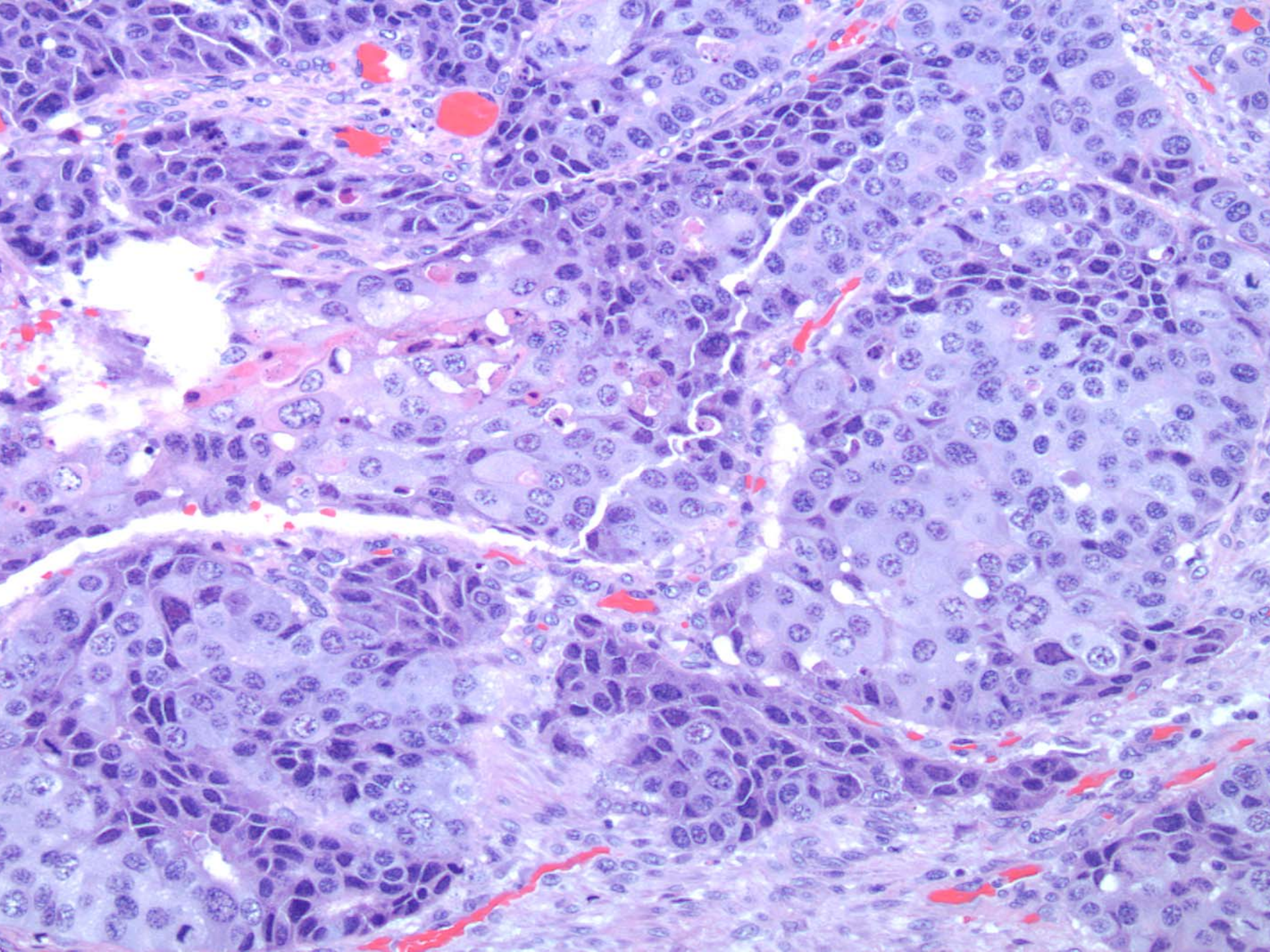


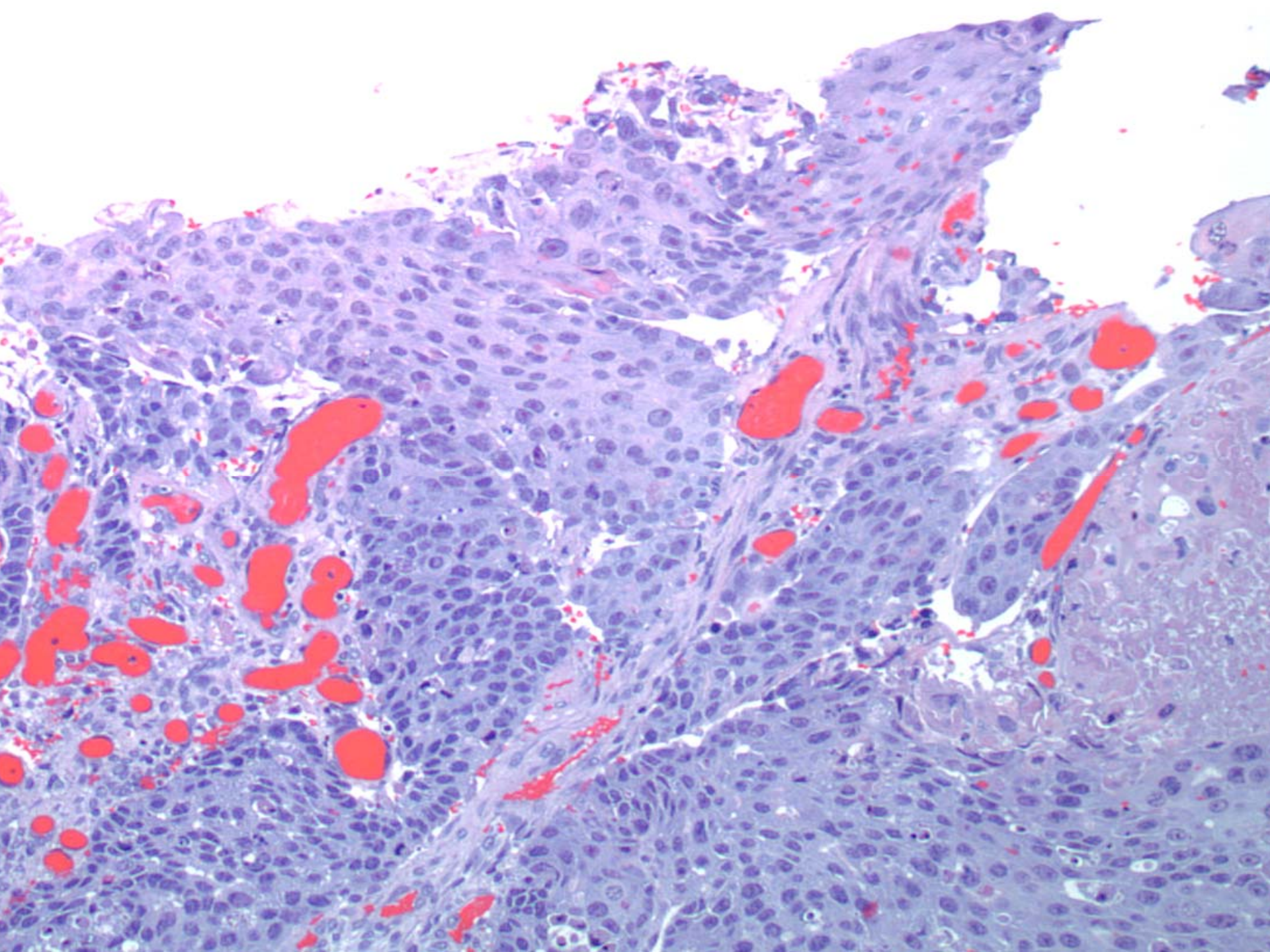
Shimizu Gastrointest Endosc 2002;56

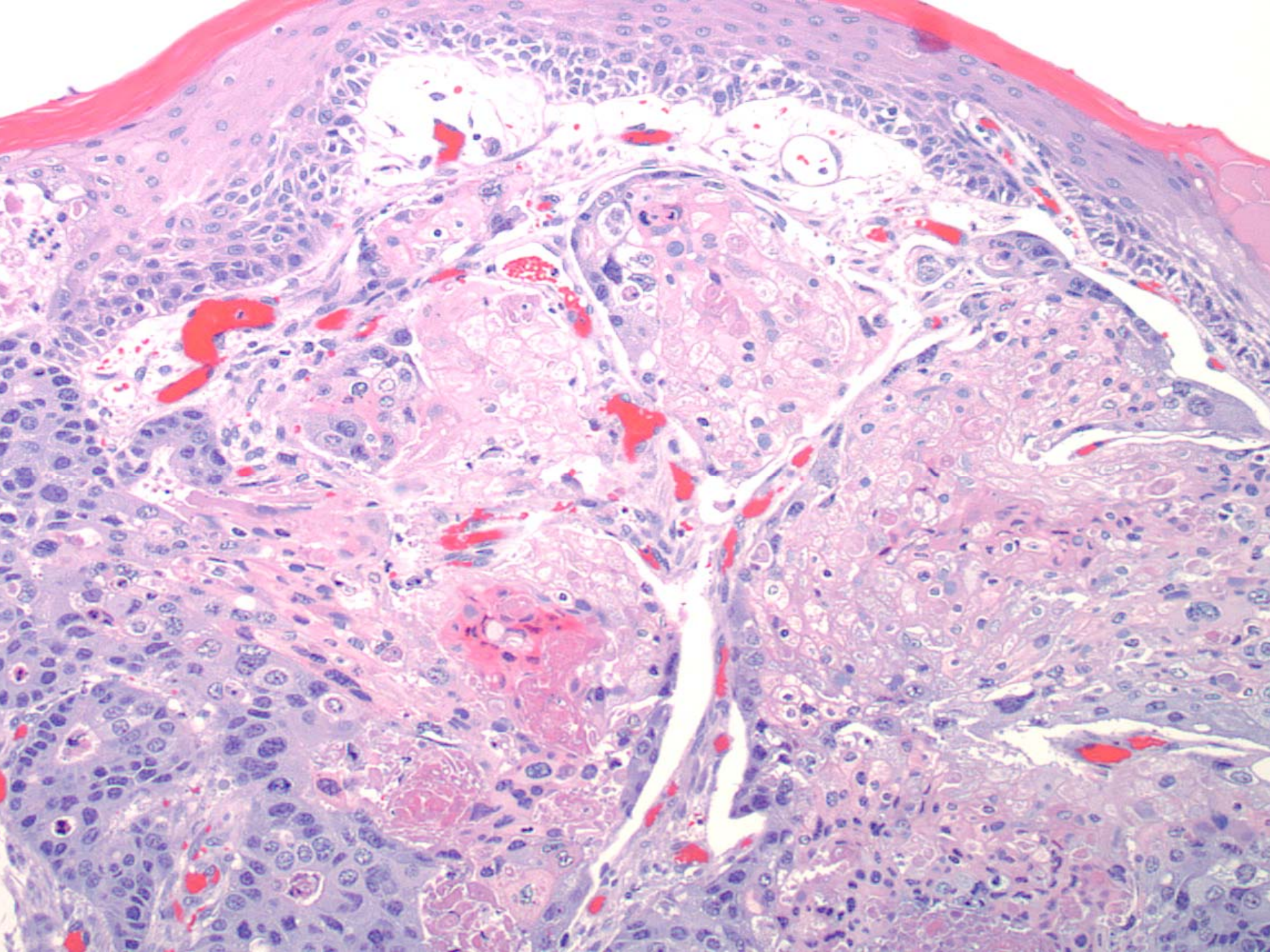
Late Failures

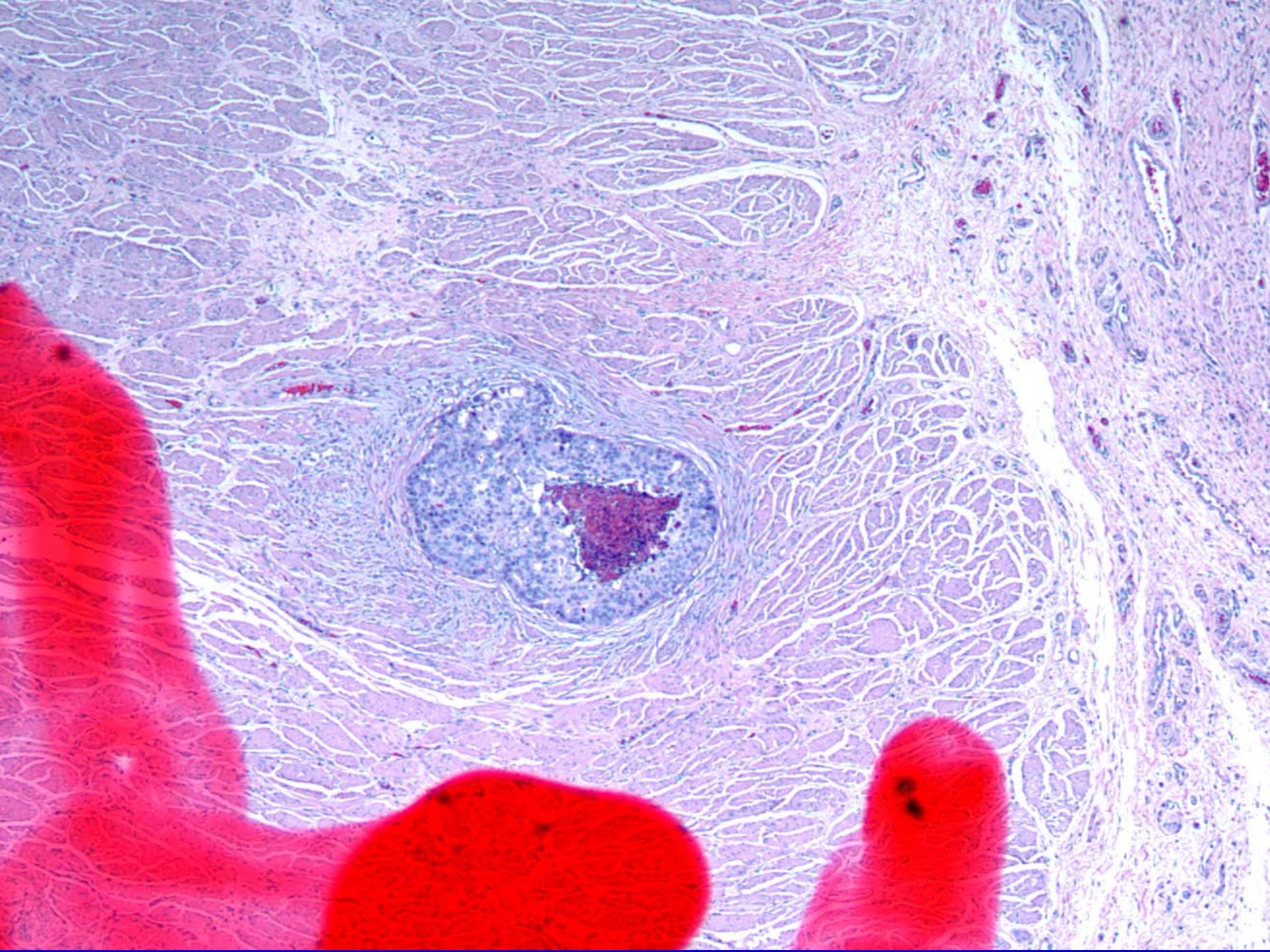
- Long term follow up imperative
- Direct surveillance yourself
- Treat recurrences aggressively











Conclusions

- Endoscopic therapy is effective for dysplasia and some early cancers
  - Well and moderately differentiated cancer
  - Limited to the mucosal layer
- Mucosectomy provides accurate pathologic staging and therapy in some cases
  - Ablation is appropriate for treating large areas of high-grade dysplasia
- Surgical resection provides the only durable cure
  - Endoscopic therapy requires intense life-long surveillance