IBD Surveillance Intervals and Techniques

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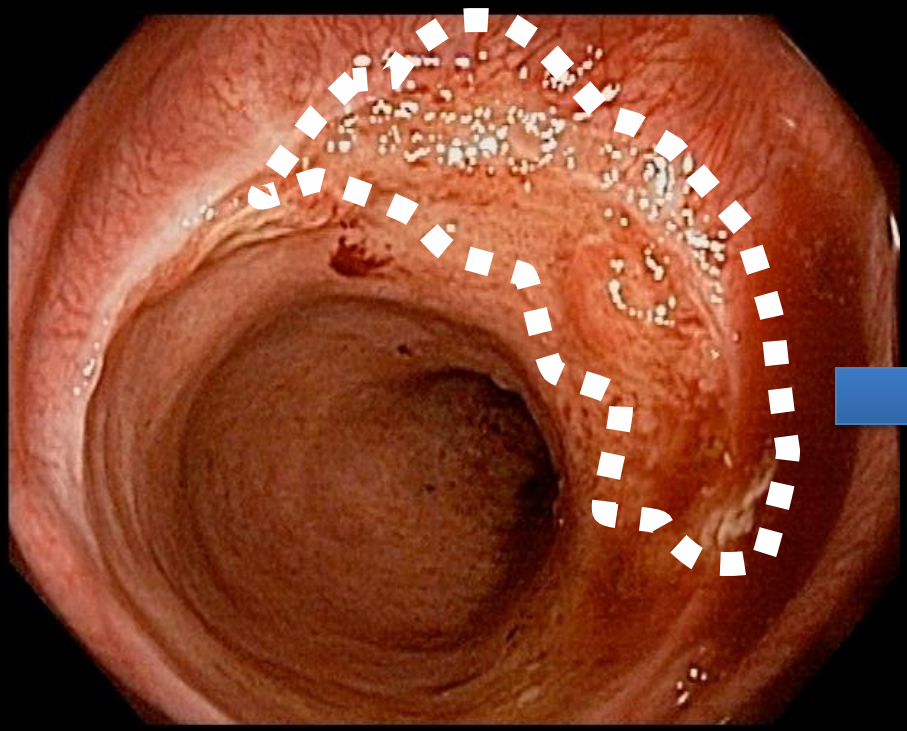
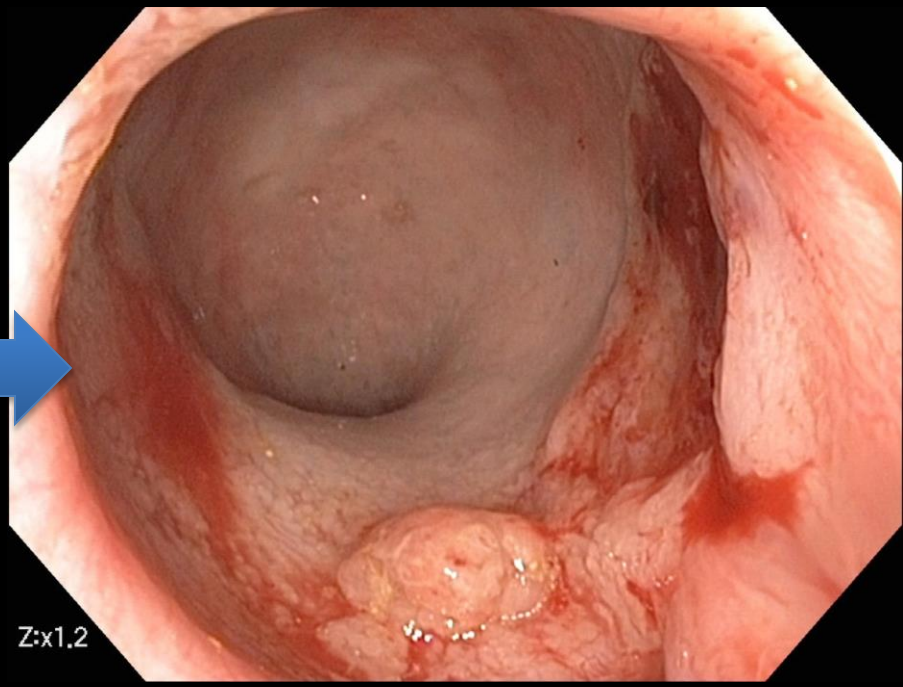
A True Case

- A 48 y/o man with extensive ulcerative colitis X 10 years undergoes routine surveillance.
- No lesions are seen
- 32 random four-quadrant biopsies taken: non-dysplastic





Unrecognized Non-polypoid Neoplasm

12 months later: T2N2 Poorly Differentiated CA

Courtesy: Roy Soetikno

Major Teaching Points

- Was this preventable? Yes
- Why did it occur? Ongoing misconception about dysplasia in IBD.
  - Most dysplasia (>90%) is visible
  - Random biopsies contribute little
  - Most dyplastic lesions are non-polypoid
- We need to change our surveillance approach
  - Revised IBD surveillance guidelines
  - Chromoendoscopy with targeted biopsies is *preferred* surveillance method

Risk of CRC in IBD Increased…but How Much?

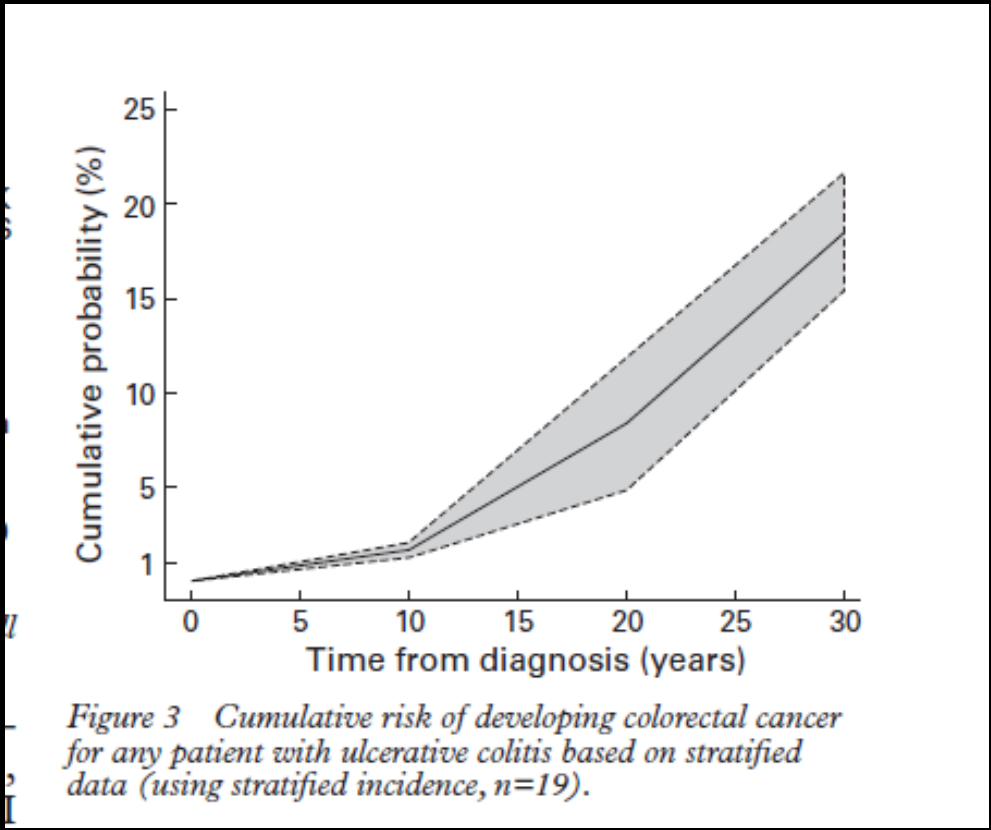


Figure 3 Cumulative risk of developing colorectal cancer for any patient with ulcerative colitis based on stratified data (using stratified incidence, n=19).

- Eaden J. Gut 2001
  - Meta-analysis 116 reports of CRC in UC
  - Estimated risk of CRC:
  - 10 yrs: 2%
  - 20 yrs: 8%
  - 30 yrs: 20%

Recent Meta-Analysis: CRC Risk Lower Than We Thought?

TABLE 2. Reported Colorectal Cancer Risk in Patients with IBD

IBD Type (Study References); Subgroup Analysis	No. of Patients	PYAR[a]	Observed CRC	Pooled SIR	95% CI	I^2 (%)
IBD[2,7,8,16,22,34,35,37,65]; population-based	13,010	259,266	210	1.7	1.2–2.2	64
IBD[20,21,30,31]; referral center	2098	29,799	57	6.9	4.1–9.7	43
UC[2,7,8,16,34,35,37,65]; population-based	8964	161,154	188	1.7	1.03–2.4	73
UC[21,30,31]; referral center	1585	22,375	48	8.3	5.9–10.7	0
CD[7,8,22]; population-based	4046	98,112	22	1.7	1.01–2.5	0
CD[20]; referral center	513	7424	9	4.4	1.5–7.2	NA

I^2 is heterogeneity statistic: higher percentages depict higher heterogeneity between pooled studies.

Lutgens MW, Inflam Bowel Dis 2013; 19:789-99.

- Systematic review: IBD cohort studies (population-based and referral center) on CRC risk
- 9 most recent (1988 to present) assessed
- SIR for <u>all</u> UC pts: 1.7 (1.2-2.2)

And, Cumulative Risk in All IBD-colitis Not As High As Thought

TABLE 6. Colorectal Cancer Risk Stratified for Disease Duration Grouped by Population

Disease Duration (Study References)	Population-based Studies	PYAR	Pooled CRC/1000 PYAR	95% CI	Cumulative Risk (%)
<10 yr[8,13,14,37]	4	45,744	0.8	0.4–1.4	0.8
10–20 yr[8,13,14,37]	4	19,184	1.4	0.8–2.4	2.2
>20 yr[8,13,14,37]	4	7695	2.4	0.8–7.2	4.5

- Based on 2 population studies and 1 referral-site study
  - Includes all colitis: proctitis, left-sided, extensive, and Crohn's

Lutgens MW, Inflam Bowel Dis 2013; 19:789

But , Risk IS High With Extensive Disease

TABLE 4. Colorectal Cancer Risk Stratified for Extent of Disease

IBD Type (study References); Subgroup Analysis	No. of Patients	PYAR[a]	Observed CRC	Pooled SIR	95% CI	I^2 (%)
Extensive colitis UC[1,7,8,34]; population-based	1887	41,640	88	6.9	1.9–11.9	84
Extensive colitis UC[21,31]; referral center	681	11,164	38	21.6	15.0–31.0	0
Left-sided UC[illegible]; population-based	1093	13,148	19	1.7	0.6–4.5	47
Left-sided UC[21,31]; referral center	628	8872	7	2.0	1.01–4.1	0
Proctitis CD[8,13,37,39]; population-based	172	12,427	16	1.0	0.5–1.6	21
Proctitis CD[31]; referral center	132	1005	0	NA	NA	NA

Lutgens MW, Inflam Bowel Dis 2013; 19:789

High Risk With Extensive Colitis and Young-age Onset Disease

Risk in Extensive Colitis			
Disease Duration	Incidence/1000 Pt-years	95 % CI	Cumulative Incidence
< 10 years	1.7	0.9 – 3.3	2 %
10 – 20 years	10.9	7.1 – 16.7	12%
> 20 years	11.2	6.8 – 18.6	21%
Risk According to Age of Onset			
Age of Onset	Pooled SIR	95 % CI	
< 30 yrs old	8.2	1.8 – 14.6	
> 30 yrs old	1.8	0.9 – 2.7	

Lutgens MW, Inflam Bowel Dis 2013; 19:789

Summary: Risk Factors for CRC in IBD-Colitis

- Long duration
- Extensive colonic involvement
- Family history of CRC
- Primary sclerosing cholangitis
- Young age IBD onset
- Severity of inflammation
- Strictures

Current Surveillance Recs

- Who:
  - All UC patients with extensive or left-sided disease
  - Crohn's colitis > 1/3 of colon
- Initial screen:
  - 8 years after symptom onset
- Subsequent surveillance
  - W/in 1-2 years
  - If 2 negative exams, surveillance interval lengthened

2010 AGA Guideline: Farraye F, et. Gastroenterology 2010; 138:738.
2015 ASGE Guideline: Shergill A, et al. Gastrointest Endosc; 2015:81:1101.

Individualized Intervals

High risk: 1 year

- Extensive disease with active inflammation
- Family hx CRC
- PSC
- Anatomic abnormality: stricture, foreshortening
- Extensive pseudopolyps
- Prior dysplasia

Medium risk: 2-3 years

- Left-sided colitis
- Extensive disease – inactive
- Crohn's colitis >1/3 of colon

Low risk: 3 years

- Two prior colonoscopies: histologically/macroscopically normal
- Crohn's colitis < 1/3 of colon

British Society of Gastroenterology 2010
Cancer Council of Australia 2011
ECCO 2012
ASGE 2015

‘Standard’ Approach to Surveillance Colonoscopy

- Visible lesions (“DALMS”) biopsied or endoscopically resected
- At least 33 random biopsies (4 quadrant, q 10 cm) to detect “non-visible” dysplasia
  - ? 90% confidence to detect dysplasia, if present in at least 5% of colon
- Endoscopic resection: “adenoma-like DALMs”
- Surgery: endoscopically unresectable lesions, invisible HGD, multifocal LGD

2010 AGA Guideline

Evidence That Current Surveillance Practice Effective in Reducing CRC?

- No RCTs
- Case-control studies, population-based cohort studies suggest earlier CRC stage at diagnosis and improved survival
- Cochrane analysis: no clear evidence that surveillance improves survival (Collins PD; 2006: CD 000279)

Recent Cause for Celebration?

- Retrospective cohort study: 6823 IBD-colitis pts followed ≥ 3 yrs (2 tertiary hospitals)
  - 154 CRC
- Incidence:
  - Colonoscopy w/in 6-36 mos: 1.6%
  - No colonoscopy w/in 36 mos: 2.6%
- Colonoscopy w/in 6-36 mos:
  - Reduced CRC incidence: OR 0.56 (CI, 0.39-0.80)
  - Reduce CRC mortality: OR 0.34 (CI, 0.12-0.95)

Ananthakrishan A, Clin Gastroenterol Hepatol 2015; 13:322.

Current Practice: Not Based on Strong Evidence

- "The most appropriate technique of surveillance has never been subjected to a randomized clinical trial"
- "The optimal surveillance interval has not been clearly defined"
- "There are no prospective studies that have determined the optimal number of biopsy specimens that should be obtained"
- "Randomized controlled trials have not been performed to prove that surveillance colonoscopy is effective"

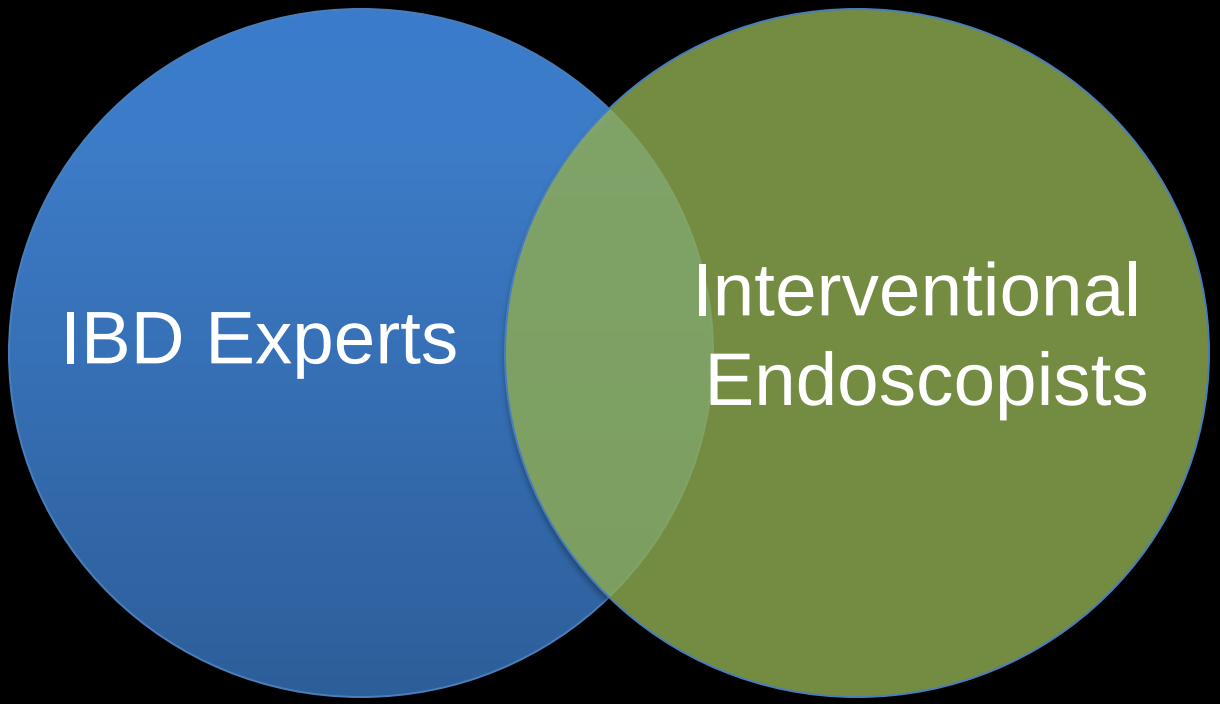
Farraye F, et al. AGA Technical Review on the Diagnosis and Management of Colorectal Neoplasia in IBD. Gastroenterology 2010; 138:746

Why There Was Need for a Change in Guidelines

- "…cynicism about the value of AGA guidelines as the technique continues to be touted as the standard of good practice" (Marion J, Gastro 2015)
- Increased awareness of non-polypoid adenomas and SSAs in non-IBD patients
- Growing use of EMR techniques in non-IBD patients
- Increasing use of electronic image enhancement in endoscopy (e.g. Barrett's, diminutive polyps)
- Advent of high-definition scopes: we all see more
- Growing number of RCTs (US and international) of chromo in IBD-surveillance

Marion JF, Editorial. Gastroenterology 2015; 143:462

Two Different Worlds



SCENIC International Consensus Conference

- EBM Experts: Laine L, Barkun A, Ioannidis J, Yang YX
- IBD: Farraye F, Feagan B, McQuaid K, Rubin D, Rutter M, Subramanian V, Ullman T, Velayos F
- Endoscopists: East J, Kaltenbach T, Matsumoto T, Monkemuller K, Sanduleanu S
- Pathologists: Odze R, Rubio C
- Academic and private practice: McCabe R, Picco M
- Surgeon: Michelassi F
- RN, Patient representative
- Non-voting content experts: Kiesslich R, Shergill A, Soetikno R

International Consensus on the Diagnosis & Management of Colorectal Neoplasia in Inflammatory Bowel Disease Patients

Systematic review

Formulate the organizer

Formulate the question

Select outcomes in IBD

Rate importance

Outcomes across studies

Synthesize evidence profile

Panel review and rating

Rate quality of evidence for each outcome

Panel re-review and rating

Loren
Alan
Ken
Roy
Tonya

P
I
C
O

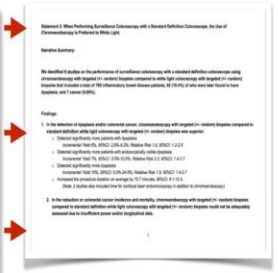
- Detection of dysplasia/CRC — Critical
- Reduction of CRC incidence — Critical
- Reduction of CRC mortality — Critical

Select Panelist

May 2013 — June 2013

Cochrane Group
4946 to 92 articles

July 2013



11 statements

January 2014

The SCENIC Recommendations Platform on the WWW

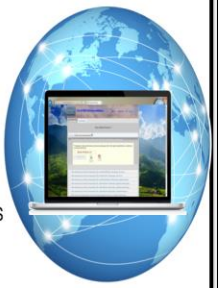
High
Moderate
Low
Very low

RCT start high, obs data start low

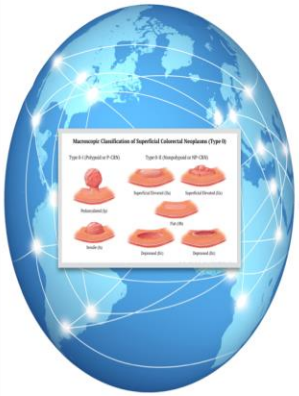
Grade down
1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

Grade up
1. Large effect
2. Dose response
3. Confounders

February 2014



Guideline development



Implementation

Nomenclature

New Guidelines

- "We recommend using .."
- "We suggest …"
- "We recommend against …"
- "We suggest against …"

Formulate recommendations:

- Agreed or disagreed (direction)
- Strong or weak (strength)

By considering:

- Quality of evidence
- Balance benefits/harms
- Values and preferences

Revise if necessary by considering:

- Resource use (cost)

Supported by unrestricted gift from The Maxine and Jack Zarrow Family Foundation and The Warren Foundation

CONSENSUS STATEMENT

SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease

CONSENSUS STATEMENT

SCENIC International Consensus Statement on Surveillance and Management of Dysplasia in Inflammatory Bowel Disease

Loren Laine,[1,2] Tonya Kaltenbach,[3] Alan Barkun,[4] Kenneth R. McQuaid,[5] Venkataraman Subramanian,[6] and Roy Soetikno,[3] for the SCENIC Guideline Development Panel

Endorsed by:

American Gastroenterological Association
American Society for Gastrointestinal Endoscopy
Asian Pacific Association of Gastroenterology
British Society of Gastroenterology
Canadian Association of Gastroenterology
European Society of Gastrointestinal Endoscopy
Japan Gastro-enterological Endoscopy Society

Disclosures

- I was part of SCENIC Consensus conference
- I know some people do not agree with all of its recommendations
- I do NOT have an agenda to push
- I believe in evidence-based medicine
- I believe where evidence is lacking we must make the best recommendations based upon available data

What Are We Looking For and How Do We Describe It?

Dysplasia-associated Lesion or Mass (DALM)

- Coined in 1981 by Dr. M Blackstone (Gastroenterology 1981; 80:366.)
- “In performing colonoscopy…on 112 patients with long-standing ulcerative colitis, a dysplasia-associated lesion or mass (DALM) was found in 12. This appeared as either a single polypoid mass (5 cases), a plaquelike lesion (2 cases), or multiple polyps (5 cases). In 7 of the 12 cases carcinoma was subsequently found.”

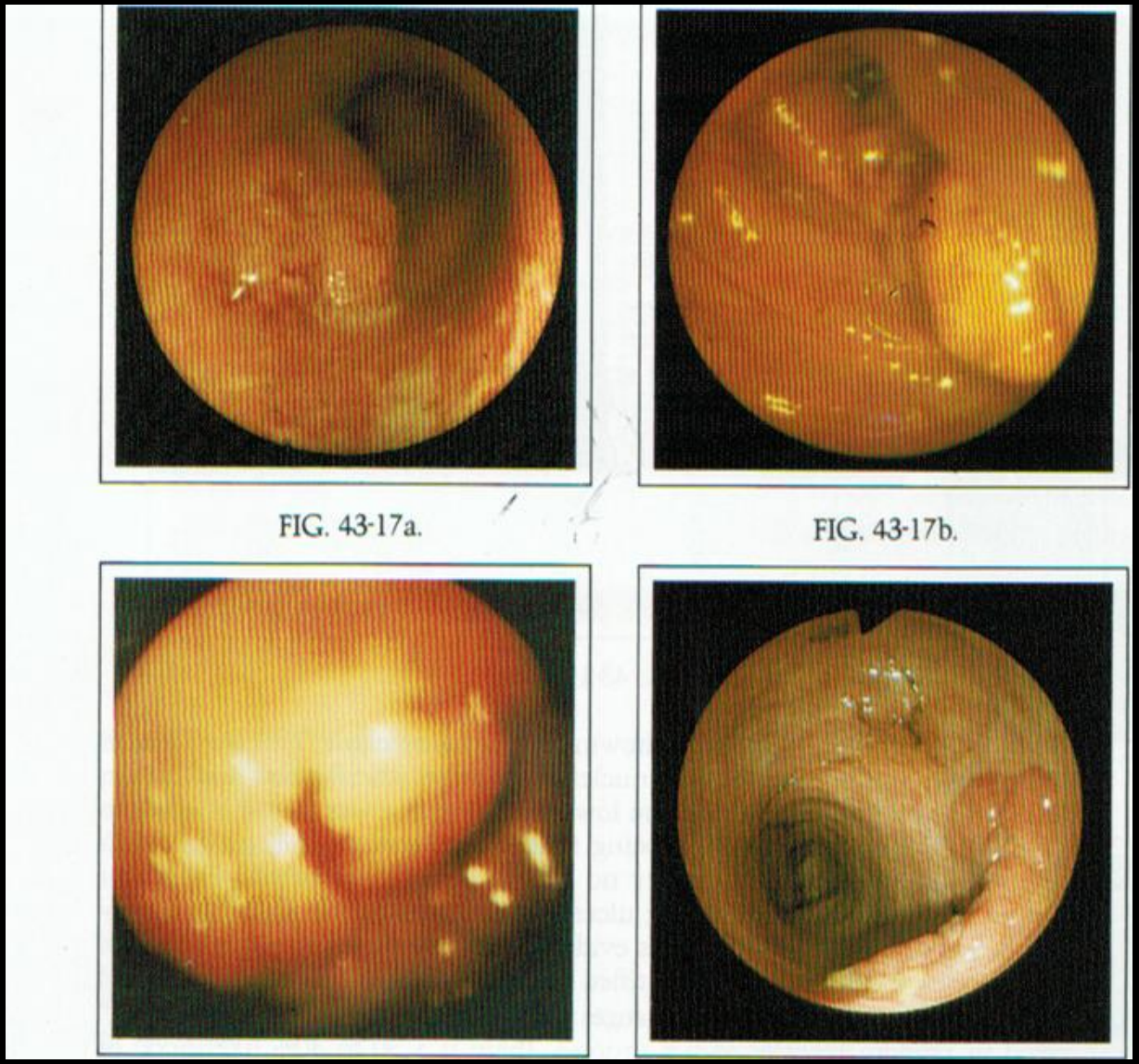


FIG. 43-17a.

FIG. 43-17b.

Blackstone M. Endoscopic interpretation: normal and Pathological appearaance of the gastrointestinal tract. Raven Press, 1984.

DALM

DALM

DALM

DALM

DALM

DALM

DALM

DALM

DALM

DALM

DALM

Confusion Grew

- "Since the Blackstone publication, several other studies have confirmed the high associations of DALMS with cancer."
- "However, these studies are quite diverse with the definitions used, the gross features of DALMs…and the clinical and endoscopic features of the lesions."
- "…it is now apparent that DALMs are a heterogeneous population of tumors that may endoscopically appear as a plaque, mass (irregular, broad-based or stricture lesion), a discrete sessile nodule, or polyp. The cancer risk is not equal among these subtypes."

Odze RD. Adneomas and adnenoma-like DALMS in chronic ulcerative colitis: a clinical, pathological, and molecular review. Am J Gastroenterol 1999; 94:1746

…and Grew

- “There is a lack of consistency in the literature with regard to the criteria and methods used to designate endoscopically visible lesions as DALMS.”
- “There is discordance with regard to the definitions used…and the clinical and endoscopic features of the lesions.”
- “…few studies actually present representative photographs of DALMS. As a result, there is variability in the reported frequencies of cancers associated with DALMS…”

Farraye F et al. AGA Technical Review on the Diagnosis and Mgmtof Colorectal Neoplasia in IBD. Gastroenterology 2010; 138:747.

The Refinement of DALM

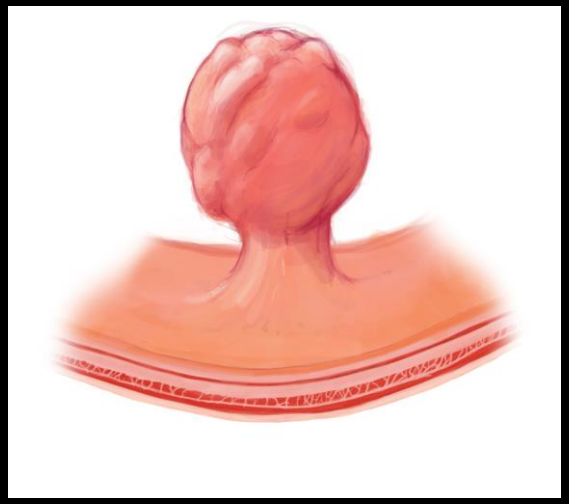
- Sporadic adenomas: occurring outside area of involved colon
- Adenoma-like DALM:
  - ‘appear similar to non-IBD related sporadic adenomas’
- Non-adenoma-like DALM:
  - ‘do not resemble adenomas’

Farraye F. AGA Tehnical Review. Gastroenterology 2010

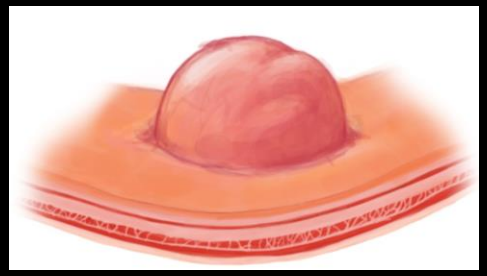
What would Blackstone have done if the Paris Classification was extant in 1981?

Superficial Neoplasms (Type 0)

Type 0-I:Polypoid or Sessile

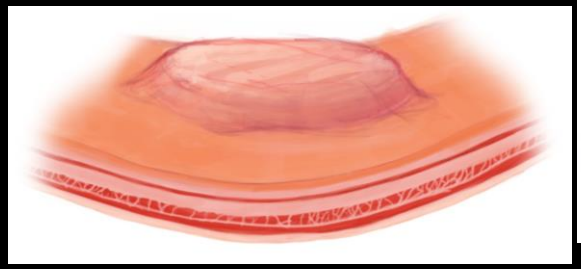


Pedunculated (Ip)

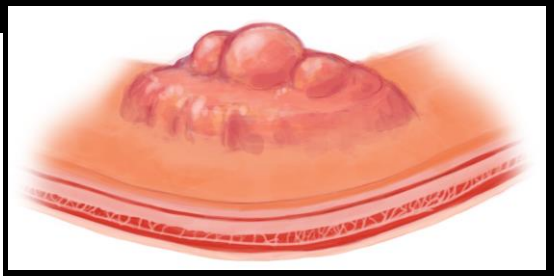


Sessile (Is)

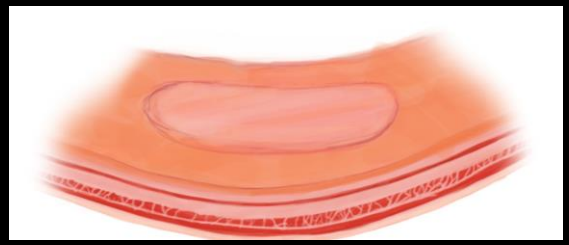
Type 0-II Nonpolypoid



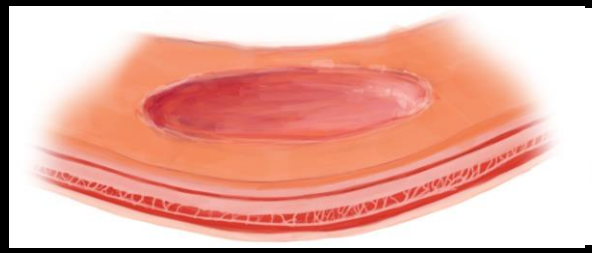
Superficial Elevated (IIa)



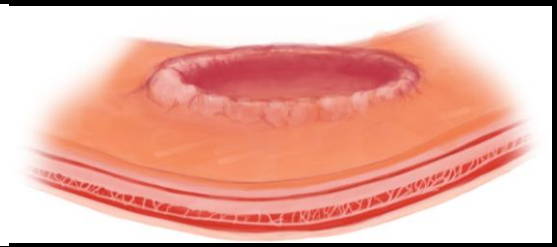
Superficial Elevated (IIa)



Flat (IIb)



Depressed (IIc)



Depressed (IIc)

Soetikno, Kaltenbach,.... Rouse. JAMA 2008; March 5.

SCENIC Classification for IBD-related Colorectal Neoplasia*

VISIBLE Dysplasia (>90%)

- Polypoid neoplasia
  - Sessile
  - Pedunculated
- Non-polypoid neoplasia
  - Slightly elevated
  - Flat
  - Depressed
- Descriptors:
  - Ulcerated
  - Distinct border: discrete and distinguished from surrounding mucosa
  - Indistinct border: lesion is not discrete; cannot be distinguished from surrounding mucosa

INVISIBLE Dysplasia (<10%)

- Identified on random (non-targeted) biopsies of colonic mucosa without a visible lesion

Chromoendoscopy in IBD-Surveillance: Areas of Uncertainty

- Yes, it picks up more dysplasia…
  - Significance and natural history of these subtle lesions uncertain
  - No proof that detection/resection will prevent CRC, save colons, or save lives
  - Inherent biases: healthier cohort, lead-time bias, length-time bias (example: prostate CA)
- Optimal patient populations
  - Risk stratification
  - Appropriate intervals
  - Efficacy in active inflammation
- Will we help or hurt patients?
  - More procedures
  - Increased referral for surgeries?

Practice Costs

- Equipment:
  - High definition scopes
  - Chromo: pumps for forward wash
- Supplies
  - Chromo: Indigo carmine vs. methylene blue
  - Sterile water (?), syringes, tubing
- Staining: clothes, floor (MB)

Practice Expense

- Increased procedure time: 10 min?
  - Greater inspection time
  - Resection or biopsy of lesions found
    - False positives vs. true positives
  - ? savings if random biopsies abandoned
- Increased report generation time
  - Need software should have templated reporting of chromoendoscopy, optimal description of IBD-related findings/lesions, and resection techniques

Educational Materials: All Free

- Atlas of non-polypoid neoplasms in inflammatory bowel disease. Soetikno R, et al. Gastrointest Endosc Clin N Am 2014; 24:483-520. (Available FREE)
- ASGE Video: Chromoendoscopy with targeted biopsy to detect non-polypoid colorectal neoplasia in IBD (Soetikno R, et al; 2014 ASGE AV Award Winner)
- 2014 SCENIC International Consensus Guidelines on Surveillance and Management of Dysplasia in IBD : (Laine L, Kaltenbach T, Barkun A, Soetikno R, McQuaid K) (Gastrointestinal Endoscopy and Gastroenterology, March 2015)

Death to the DALM!

Recommendations: 2015 SCENIC Consensus and ASGE Guideline

1. When performing surveillance with standard definition colonoscopy, *chromoendoscopy is preferred rather than white-light colonoscopy* (strong recommendation; moderate-quality evidence)
2. When performing surveillance with high-definition colonoscopy, *chromoendoscopy is suggested rather than white-light colonoscopy* (conditional recommendation; low-quality evidence)

Meta-analysis: 8 RCT's of Chromoendoscopy vs. Standard Definition White Light

Outcome	No. of Studies	No. of Patients or Lesions	Summary Statistic (95% CI)
No. of patients with visible dysplastic lesions	7	100/811	Incremental yield: 6% (3-9%)
Detection of endoscopically visible dysplastic lesions	8	217	Incremental yield: 162 vs 55; Relative Risk in 4 tandem studies: 21.9 (1.4-2.7)

The Leeds Teaching Hospitals NHS
NHS Trust

Leeds Centre for Digestive Disease

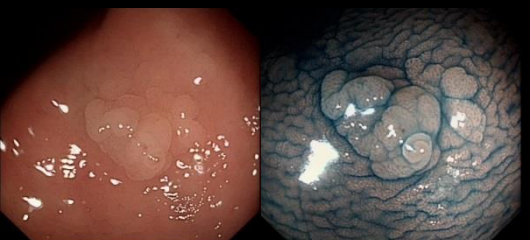
High Definition white light endoscopy versus High Definition with Chromoendoscopy in the detection of dysplasia in long standing ulcerative colitis: A Randomized Controlled Trial.

Venkat Subramanian

Clinical Associate Professor and Consultant in Gastroenterology

St James University Hospital

University of Leeds



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The Leeds Teaching Hospitals NHS
NHS Trust

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High Definition white light endoscopy versus High Definition with Chromoendoscopy in the detection of dysplasia in long standing ulcerative colitis: A Randomized Controlled Trial.

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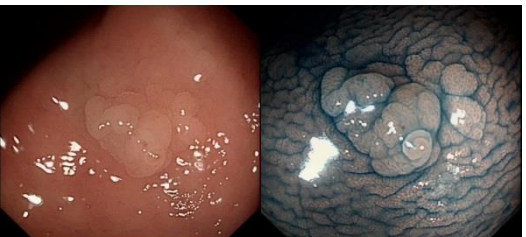

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Results

	HDWLE (n=53)	HDCE (n=50)	P value
No. of Patients with dysplasia	5 (9.4%)	11 (22%)	0.04 (Incremental yield of HDCE)*
Total number of dysplastic lesions**	6 (all low grade)	14 (1 high grade and 13 low grade)	--
Mean number of dysplastic lesions	0.12±0.4	0.26±0.6	0.04 (differences in means)*
Right sided lesions	2/6	5/14	
Mean withdrawal time (minutes)	13.6±3.3	21.2±5.8	<0.001

* Single tailed t test given null hypothesis that HDCE > HDWLE

** All lesions detected on targeted biopsy

Technique for Chromoendoscopy

- Excellent bowel prep: wash residue
- Disease in remission
- Agents:
  - Methylene blue: 0.1%
  - Indigo carmine: 0.03 to 0.2%
    - 10 cc (2 amps of 0.8%) in 250 mL = 0.03%
- Application during withdrawal:
  - Forward wash jet/pump (preferred)
  - Anatomic segments or 10 cm intervals

See 2014 ASGE DVD "Chromoendoscopy for IBD" by Soetikno R, et al. Available FREE in ASGE Learning Library and YouTube

Purpose	Technique	Method	Dilution*	Color	
Lesion detection	Pan chromo-endoscopy	Water jet channel using auxillary foot pump or biopsy channel using spray catheter	Indigo carmine (0.8%, 5ml ampule): 2 ampules + 250ml water (0.03%) Methylene blue (1%,10ml ampule): 1 ampule + 240ml water (0.04%)		
Lesion characterization and delineation of borders	Targeted chromo-endoscopy	Syringe spray through biopsy channel	Indigo carmine (0.8%, 5ml ampule): 1 ampule + 25ml water (0.13%) Methylene blue (1%,10ml ampule): 1 ampule + 40ml water (0.2%)		

*Various dilutions ranging from 0.03-0.2% of indigo carmine and methylene blue have been reported for for panchromoendoscopy.

Free Review Materials

- Atlas of non-polypoid neoplasms in inflammatory bowel disease. Soetikno R, et al. Gastrointest Endosc Clin N Am 2014; 24:483-520. (Available FREE)
- 2014 ASGE Video Award: Chromoendoscopy with targeted biopsy to detect non-polypoid colorectal neoplasia in IBD (Soetikno R, et all; available FREE through YouTube ("ASGEGIEndoscopy")

Short Video of Chromo Technique

Options During Shortage of Indigo Carmine Solution

- Indigo carmine powder
  - PCCA Rx (www.pccarx.com: order # 30-2388)
  - 25 grams = $107
- Mayo Jacksonville:
  - Autoclave powder before mixing
  - 1 g/1L = 0.1%
    - 300 mg/1L = 0.03%
- U of Indiana:
  - Dilute to 0.8 % (5 mL vials)
  - Filter; the culture confirm sterility

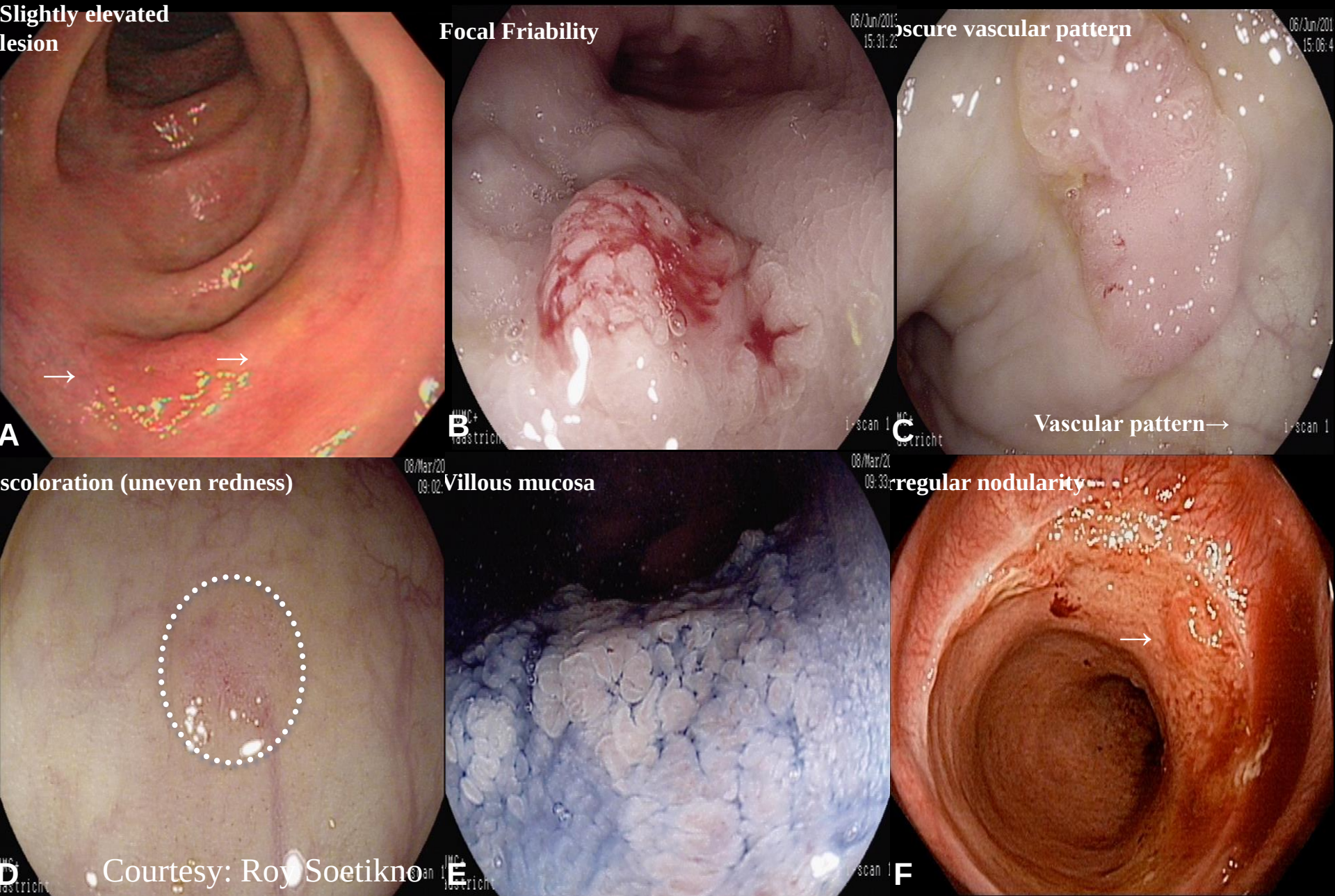
Mike Wallace: YouTube

Doug Rex ASGE Tip of Week: April 15, 2015

What are you looking for?

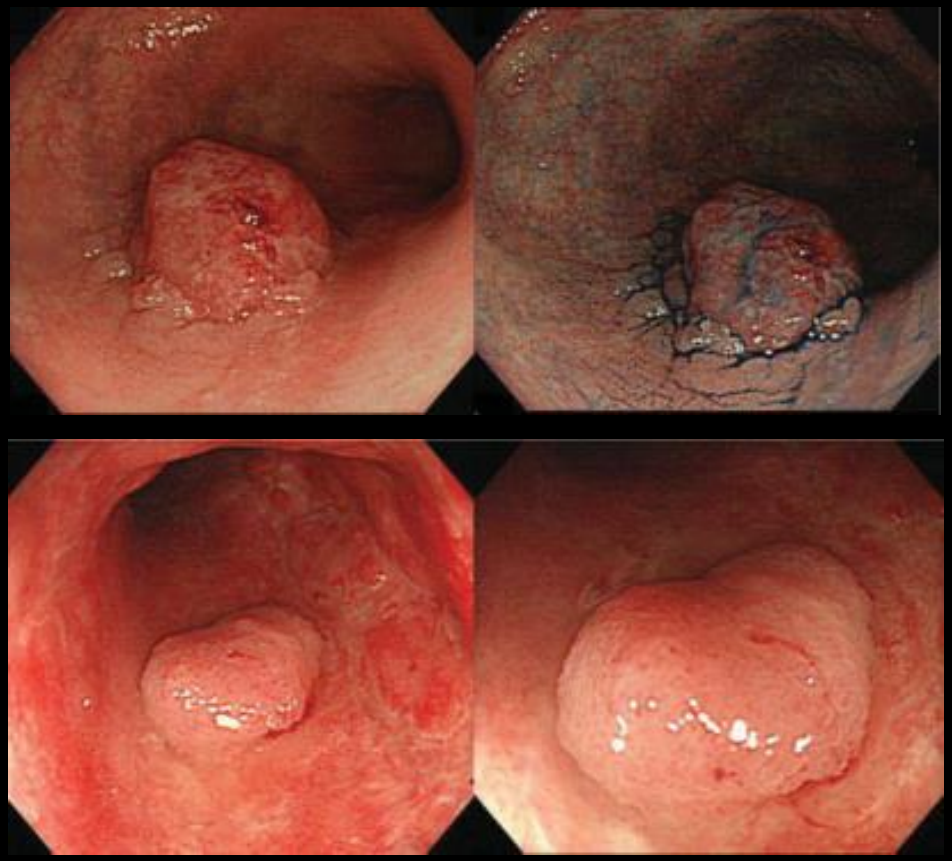
- Areas ‘of concern’: examine closely
  - Irregularity, nodularity
  - Slight elevations
  - Villous-type mucosa
  - Discoloration (uneven redness)
  - When in doubt….spray…examine again…and biopsy!
- Lesions: polypoid or non-polypoid

What You Are Looking For: Areas of Concern



Courtesy: Roy Soetikno

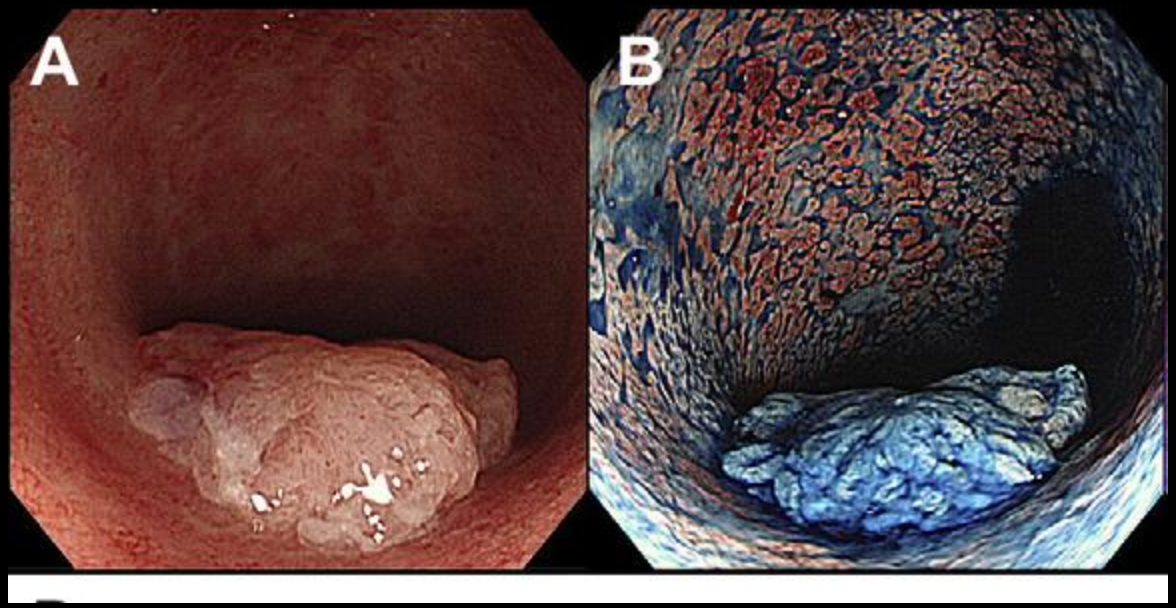
Sessile Lesions: 0-Is



Both lesions: well-differentiated adeno CA extending to submucosa

Matsumoto T, Inflamm Bowel Dis 2008; 14:259
Atlas featuring dysplastic lesions in UC.

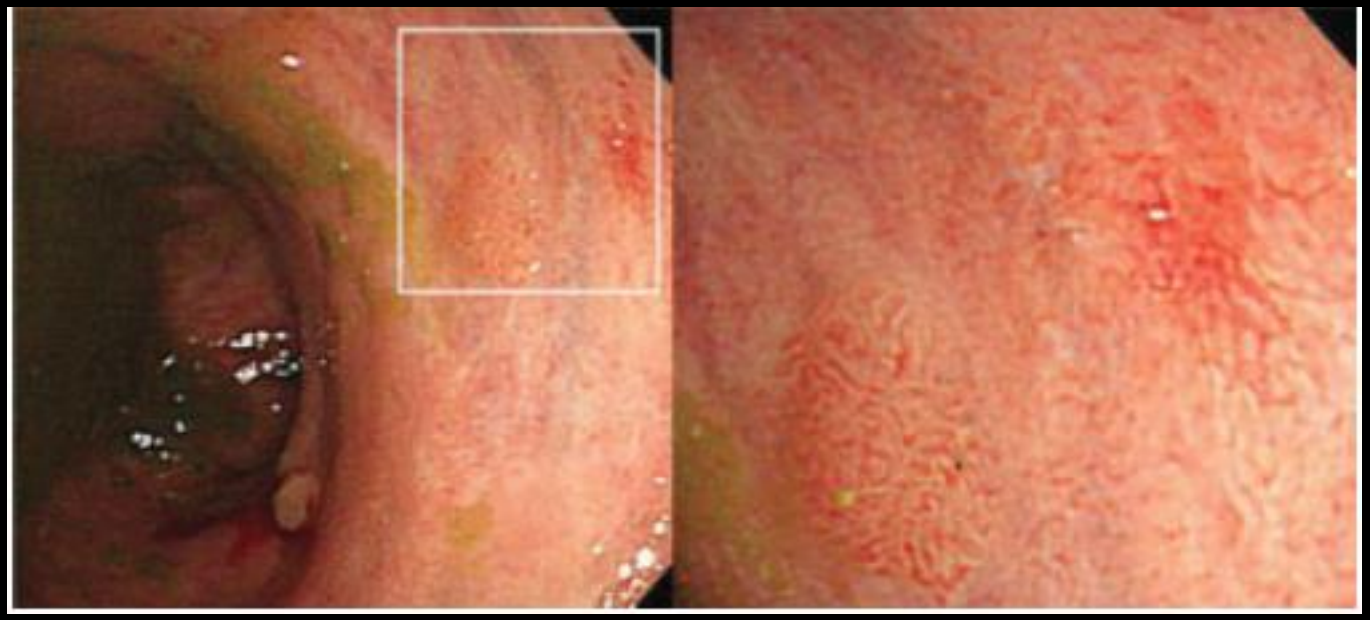
0-Is: sessile polyp



- Malignant polyp: moderately differentiated CA in adenoma

Ueno Y, GI Endosc Clin North Am 2010; 525.

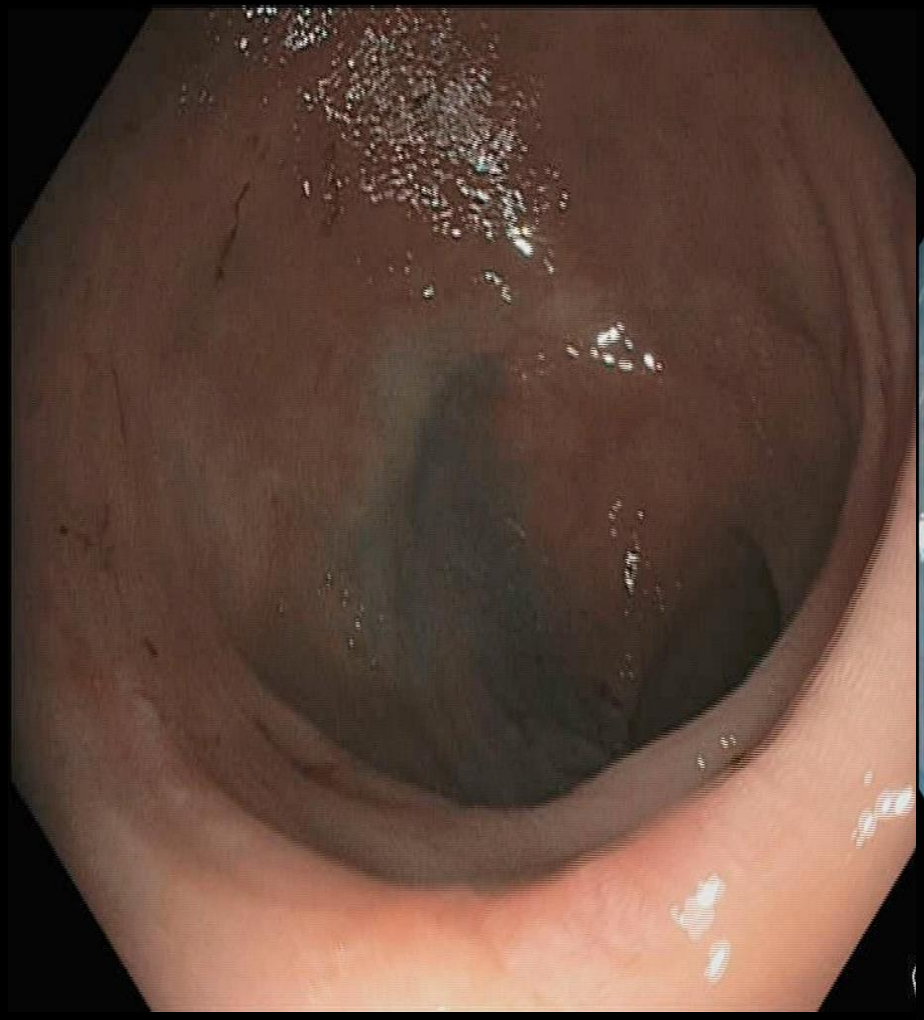
Non-polypoid (0-IIb): flat, border indistinct

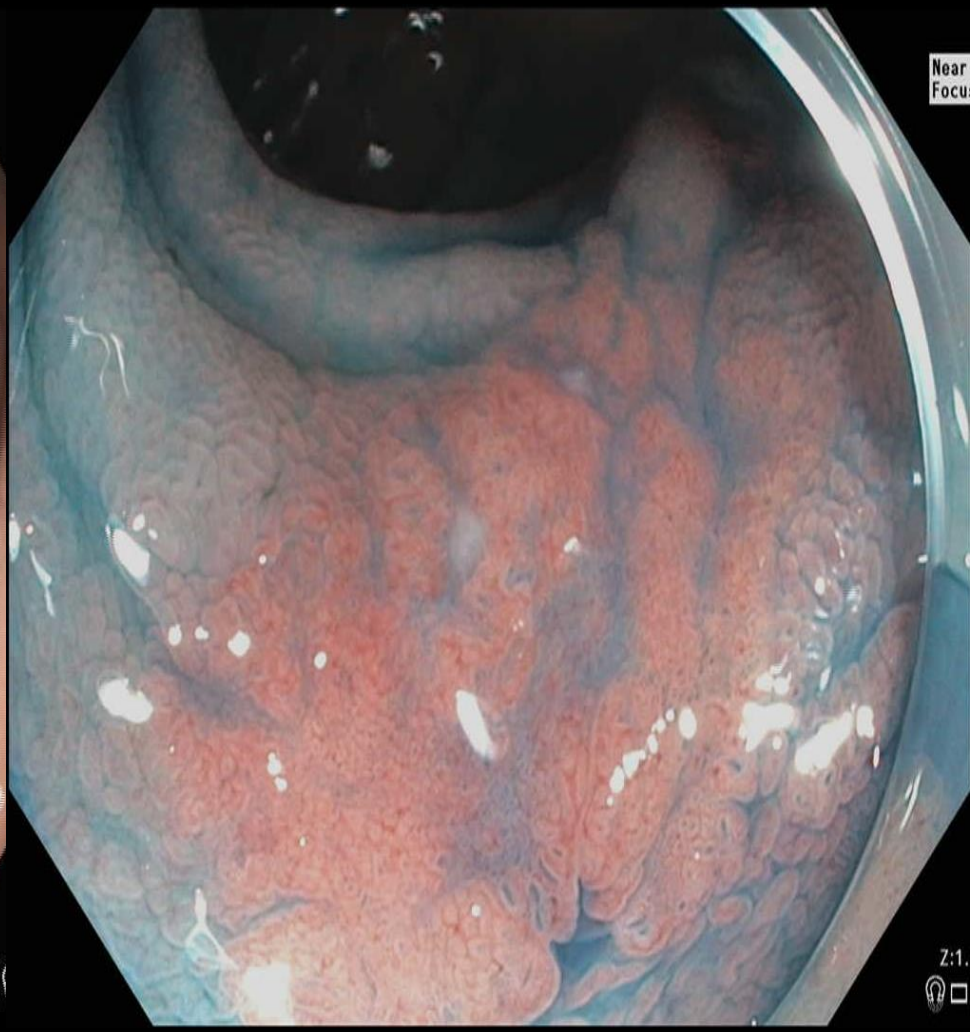


Low-grade dysplasia

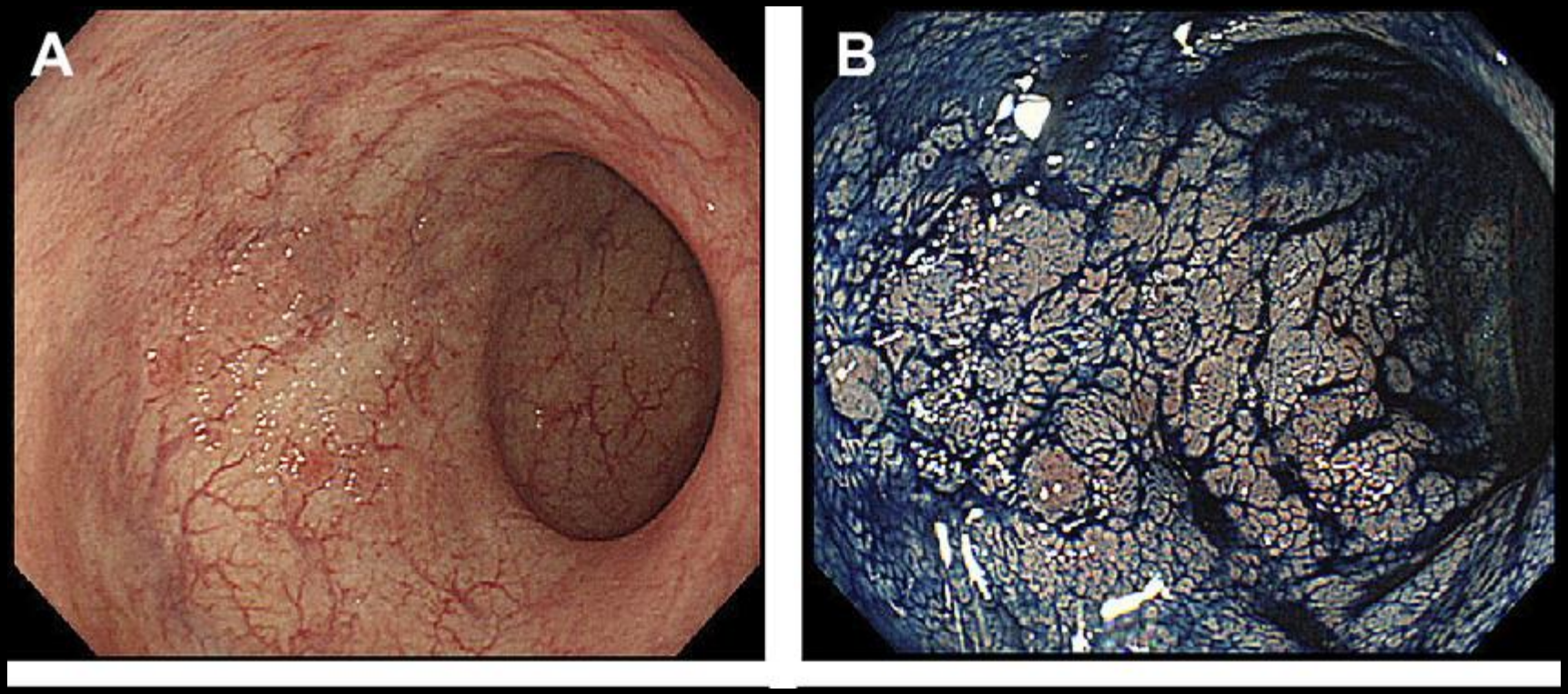
Matsumoto T. Inflamm Bowel Dis 2008; 14:259.

Chromoendoscopy Aids Detection and Characterization of Non-polypoid Lesions





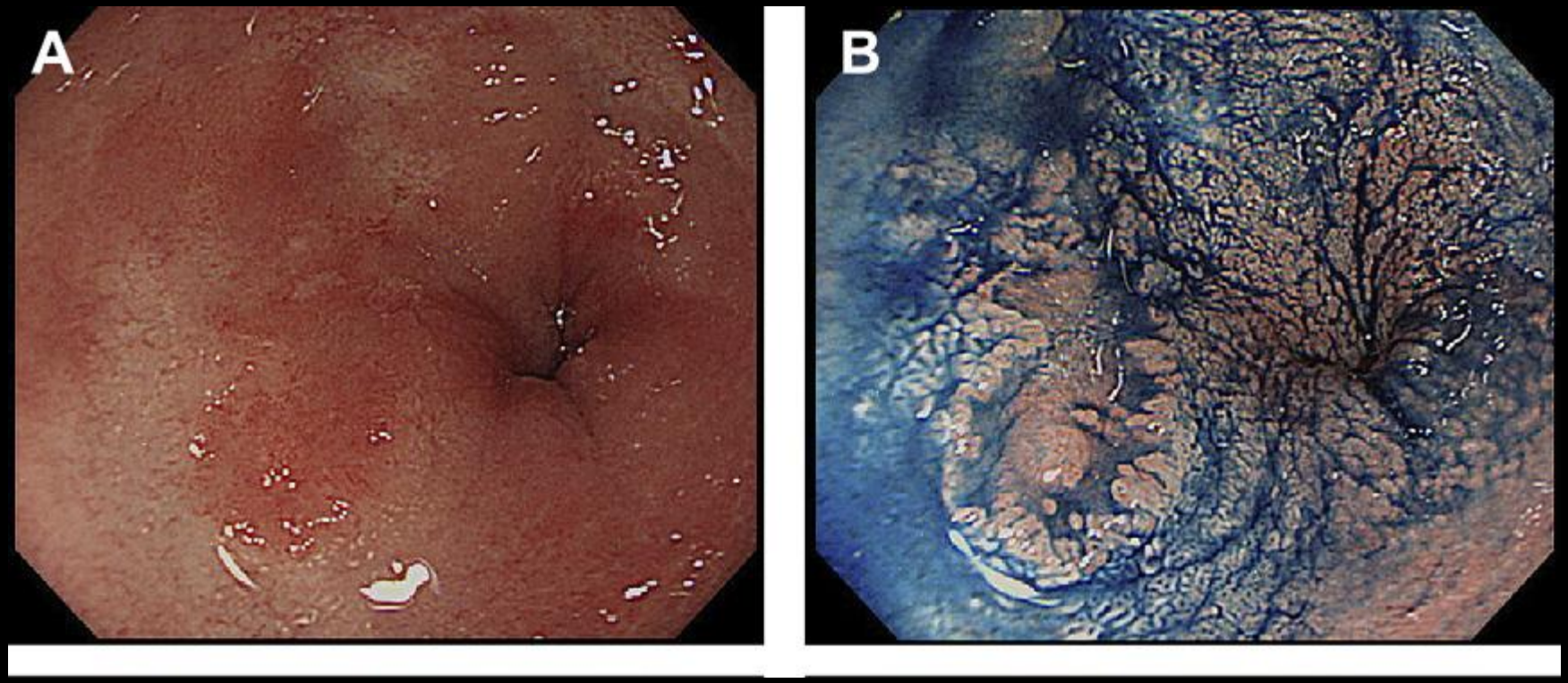
No you don’t see it…now you do



- 0.5 % indigo carmine
- Colectomy: well-differentiated adenoCA

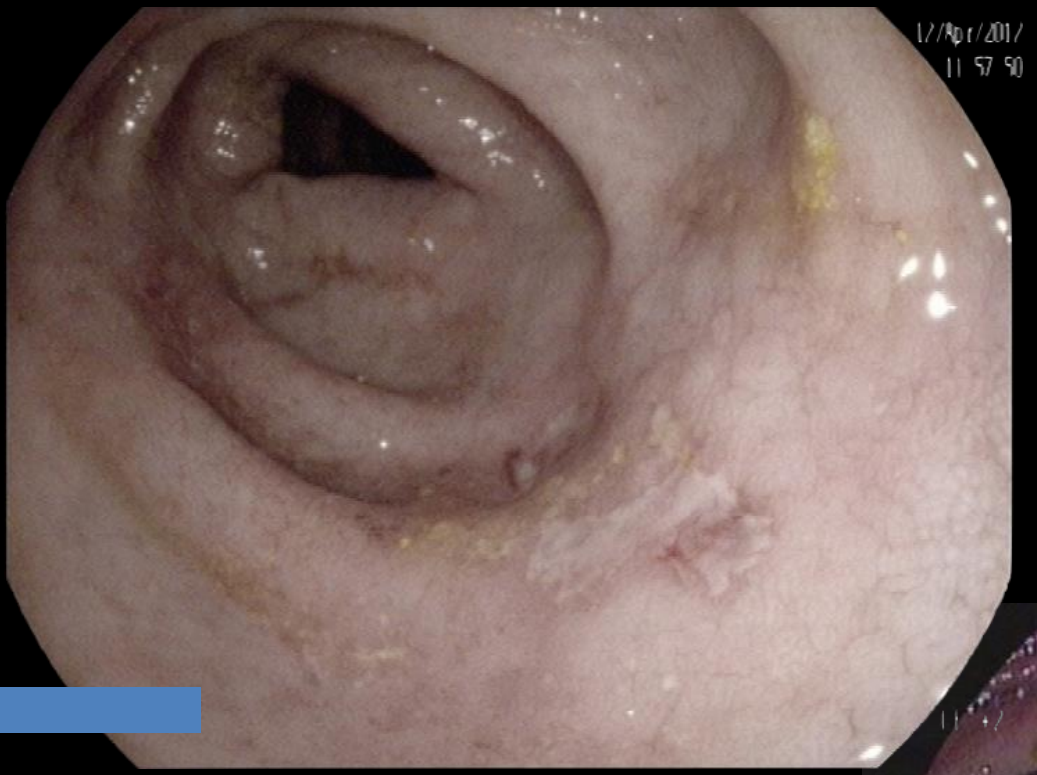
Ueno Y, GI Endosc Clin North Am 2010; 525.

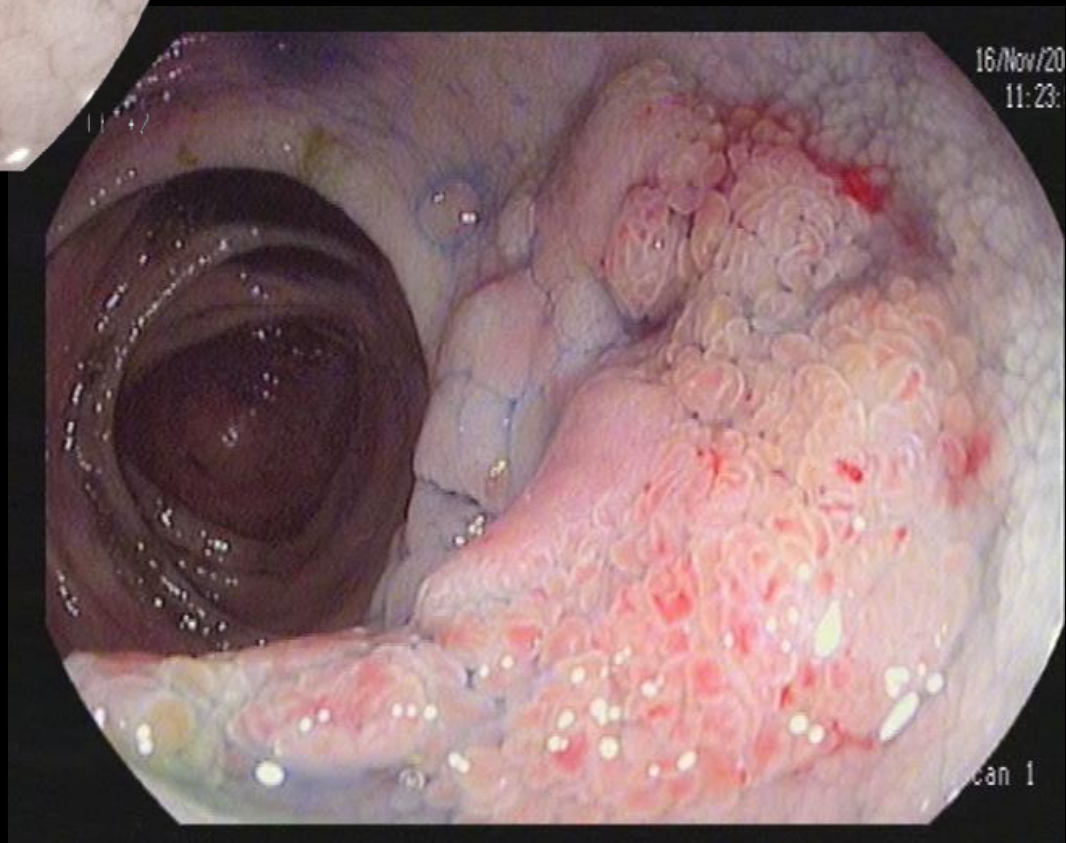
If you’re not convinced….



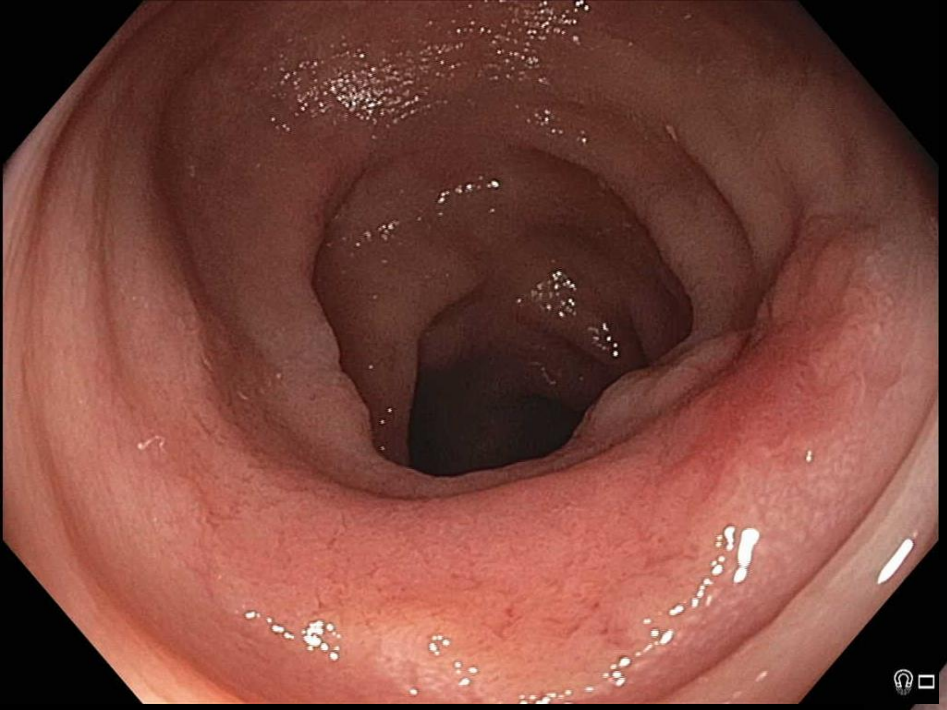
- Indigo carmine 0.5 %
- Colectomy: adenoCA

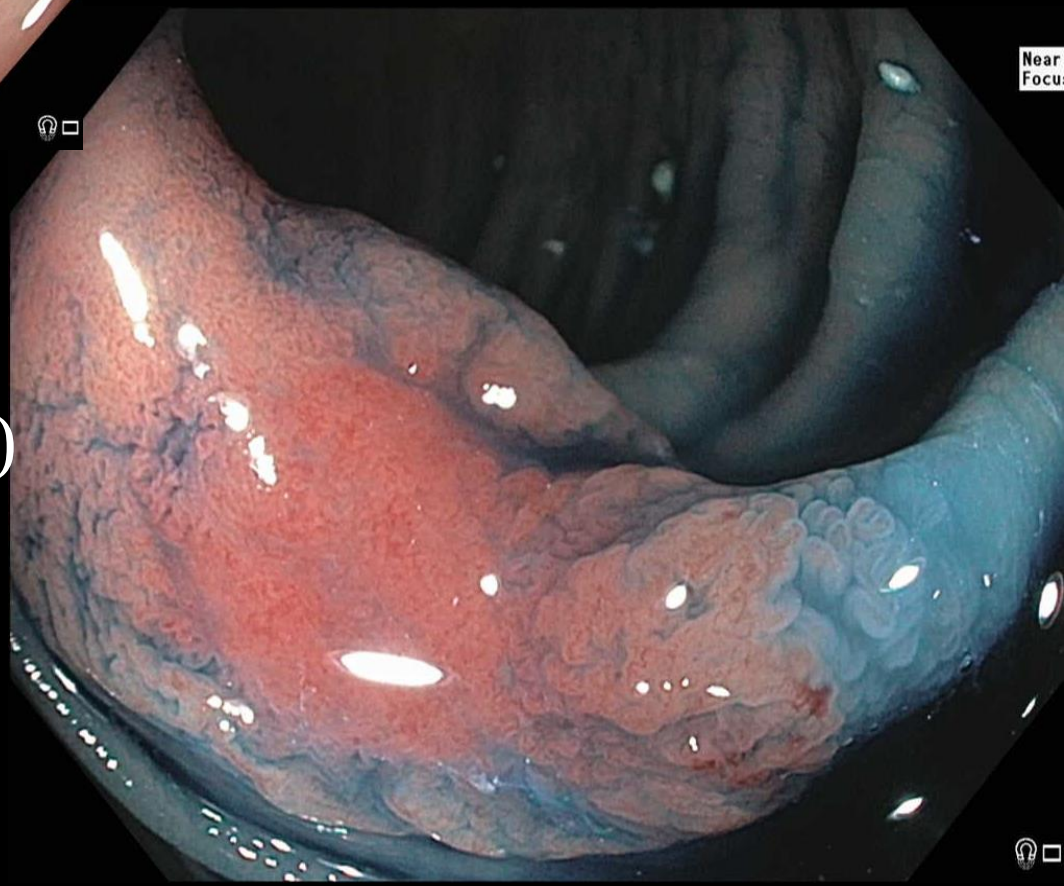
Ueno Y, GI Endosc Clin North Am 2010; 525.



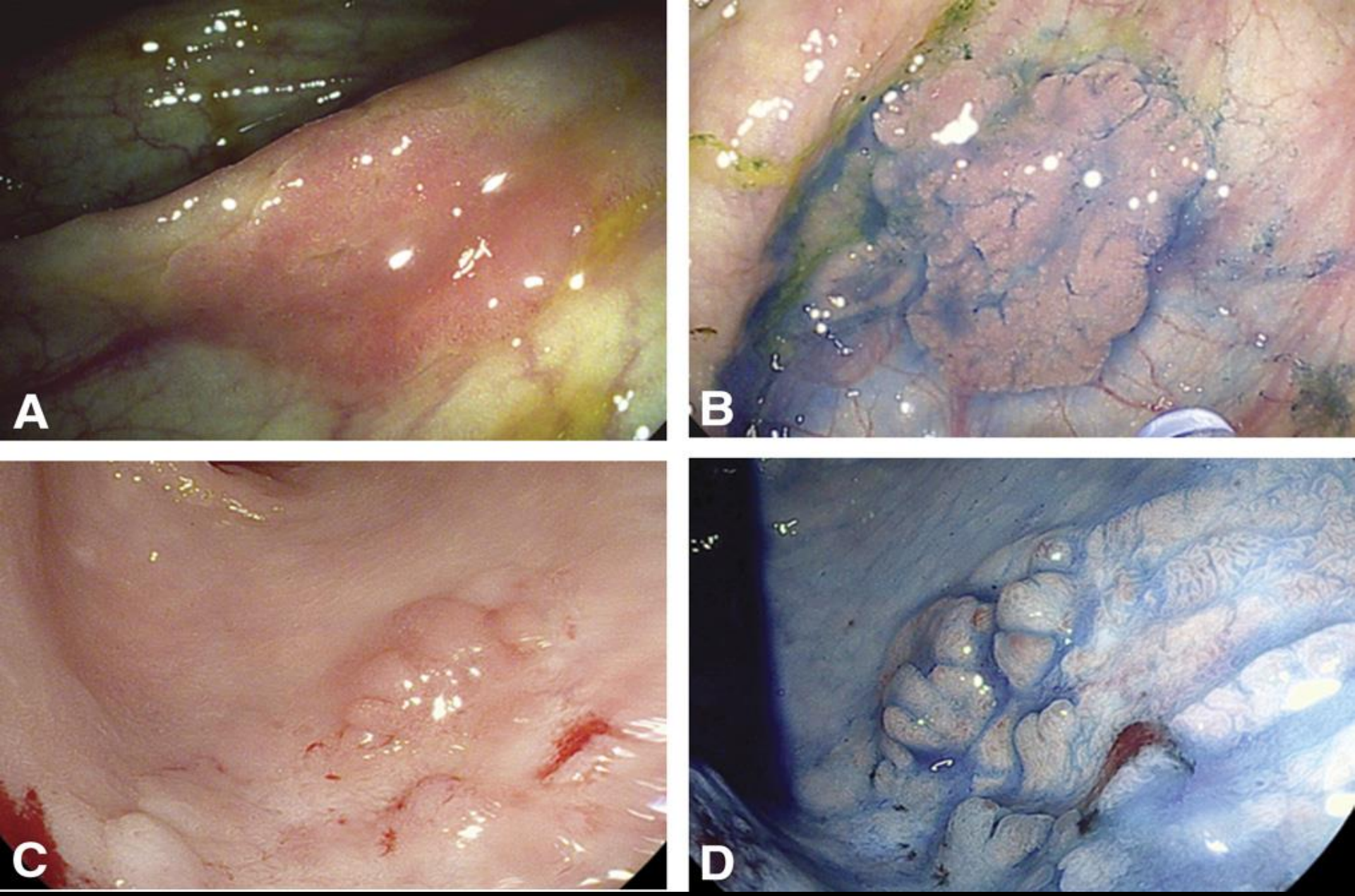


Non-polypoid lesion:
Superficial elevation (IIa);
border (?)





Non-polypoid lesion:
superficial elevation (IIa)
Distinct border (?)



Murthy S, Kiesslich, R. Gastrointest Endosc 2013; 77:352.

Question: Can We Abandon Random Biopsies?

MOST DYSPLASIA IN PRE-VIDEO-ENDOSCOPIC ERA WAS INVISIBLE

Systematic Review from Pre-Video-endoscopic Era

Proportion of patients with dysplasia identified only on random biopsies	**87%** **(10 studies; N=312)**

WHAT WAS THE BASIS FOR THE MINIMUM NUMBER OF RANDOM BIOPSIES?

- **AGA cited Rubin et al (Gastro 1992;103:1611)**
  - **44 colonoscopies with dysplasia, mean 68 biopsies/procedure**
    - **33 biopsies to achieve 90% confidence to detect dysplasia**
    - **56 biopsies to achieve 95% confidence**
- **ASGE cited CCFA guidelines (CCFA: 33, not 32)**
- **CCFA did not provide citation**
- **Mathematical model: confidence that dysplasia involves ≥5% of colon (Awais et al. Gut 2009;58:1498)**
  - **80%: 32 biopsies 90%: 45 biopsies 95%: 58 biopsies**

Farraye et al Gastro 2010;138:738; Leighton et al. GIE 2006;63:558; Itzkowitz et al. IBD 2005;11:314

In VIDEO Era: What Proportion of Dysplasi1 is Picked up on Random Biopsies?

Pooled Analyses from SCENIC Systematic Reviews

	Standard-definition	Chromo-endoscopy	High-definition
Proportion of patients with dysplasia identified only on random biopsies	19.6%(11.5-31.2%)* (12 studies; N=270)	9.8% (6-15%) (7 studies; N=158)	9.4% (4.1-19.9%) (4 studies; N=59)
Proportion of patients surveyed found to have dysplasia only on random biopsies	2.6% (1.1-6.0%)* (11 studies; N=1735)	1.2% (0.8-2.0%) (7 studies; N=1289)	1.6% (0.7-3.6%) (4 studies; N=382)
Proportion of all random biopsies positive for dysplasia	0.1% (0.1-0.3%)* (11 studies; N=25,238)	0.1% (0.0-0.3%)* (11 studies, N=48,522)	0.2% (0.0-1.2%)* (5 studies; N=8739)

*Statistical heterogeneity (Q, I^2 > 95%)

Can You Abandon Random Biopsies?

- 2015 ASGE Guideline: "When chromoendoscopy is used for IBD surveillance, random biopsies are unnecessary."
- 2015 SCENIC Consensus: *60% agreed that random biopsies are unnecessary* (80% agreement needed for recommendation)

Challenges in Clinical Practice

- Training: chromo, lesion recognition, resection techinques
- Should it be performed by experts or everyone?
- Increased procedure time (mean: 11 min)
- Lack of CPT code and reimbursement
- Shortage of indigo carmine and methylene blue

Options During Shortage of Indigo Carmine Solution

- Indigo carmine powder
  - PCCA Rx (www.pccarx.com: order # 30-2388)
  - 25 grams = $107
  - Mix:
    - Autoclave powder before mixing
    - 1 g/1L = 0.1%
    - 300 mg/1L = 0.03%

Courtesy: Mike Wallace, Mayo Jacksonville:
https://www.youtube.com/watch?v=6PJ91qYUPcE

Management Algorithm for Dysplasia

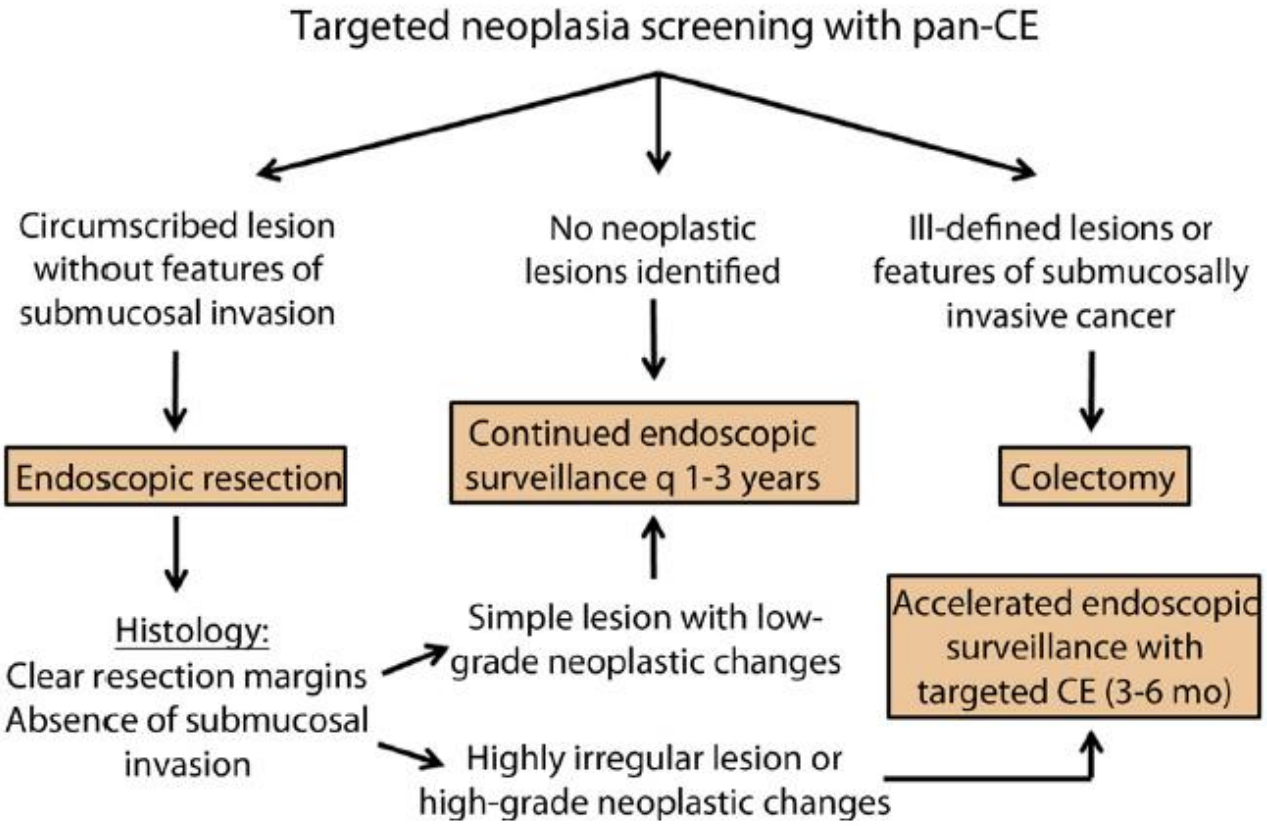


Figure 4. Proposed algorithm for neoplasia surveillance and management in inflammatory bowel disease. *CE*, chromoendoscopy; *pan-CE*, pancolonic chromoendoscopy.

Murthy S, Kiesslich, R. Gastrointest Endosc 2013; 77:352.

SCENIC Statements on Dysplasia Management

#7: After complete removal of endoscopically resectable polypoid dysplastic lesions, surveillance colonoscopy is recommended rather than colectomy (100% agreeement; strong recommendation; low-quality evidence)

#8: After complete removal of endoscopically resectable non-polypoid dysplastic lesions, surveillance colonoscopy is recommended rather than colectomy (80% agreement; conditional recommendation; very low-quality evidence)

#9: For patients with endoscopically invisible dysplasia (confirmed by a GI pathologist), referral is suggested to an endoscopist with expertise in IBD surveillance using chromoendoscopy with high-definition endoscopy (100% agreement; conditional recommendation; very-low quality evidence)

Management of Visible Dysplasia: Endoscopically Resectable or Not?

Endoscopically Resectable

- Border: well defined
- Well circumscribed
- Smooth surface
- Nonulcerated
- No stricture

Resect en bloc (EMR or ESD) whenever possible (biopsy margins to be sure complete!)
OR, tattoo and refer to expert

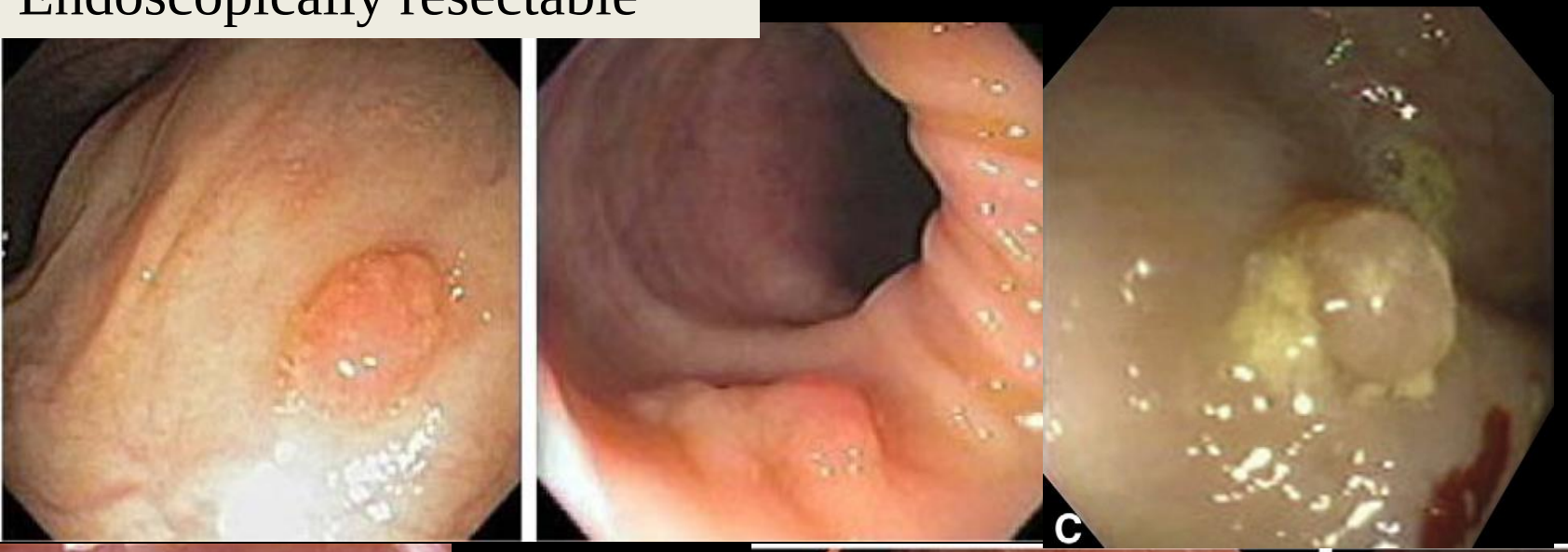
Not endoscopically resectable

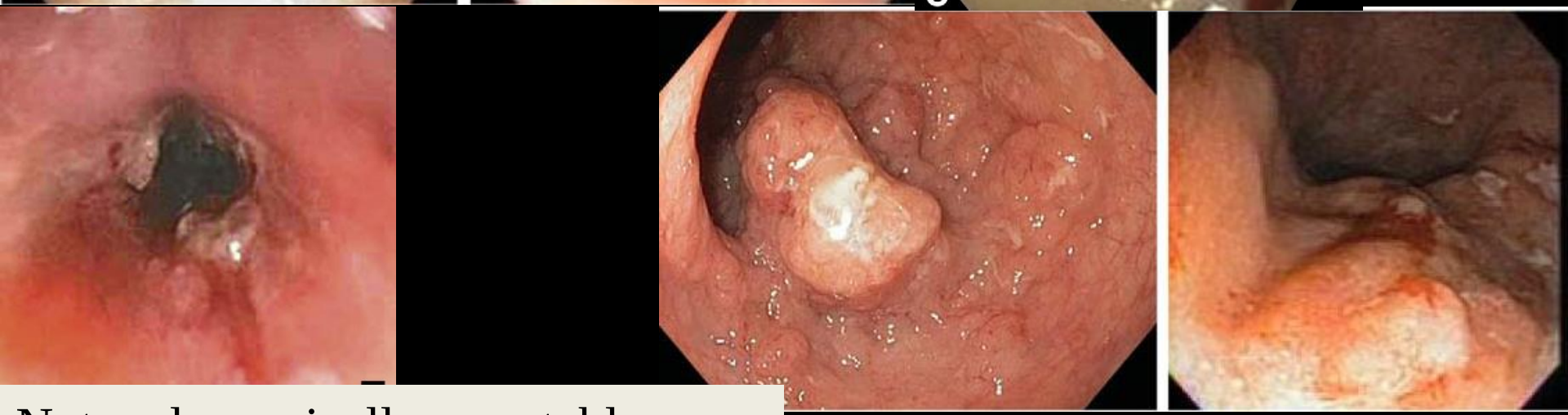
- Velvety patches, plaques, wart-like bumps
- Poorly circumscribed
- Irregular surface
- Indistinct border
- Ulceration / necrosis
- Stricture
- Tethering

Biopsy and tattoo
Refer for surgical resection

Prototypical Examples:
The Easy Ones

Endoscopically resectable

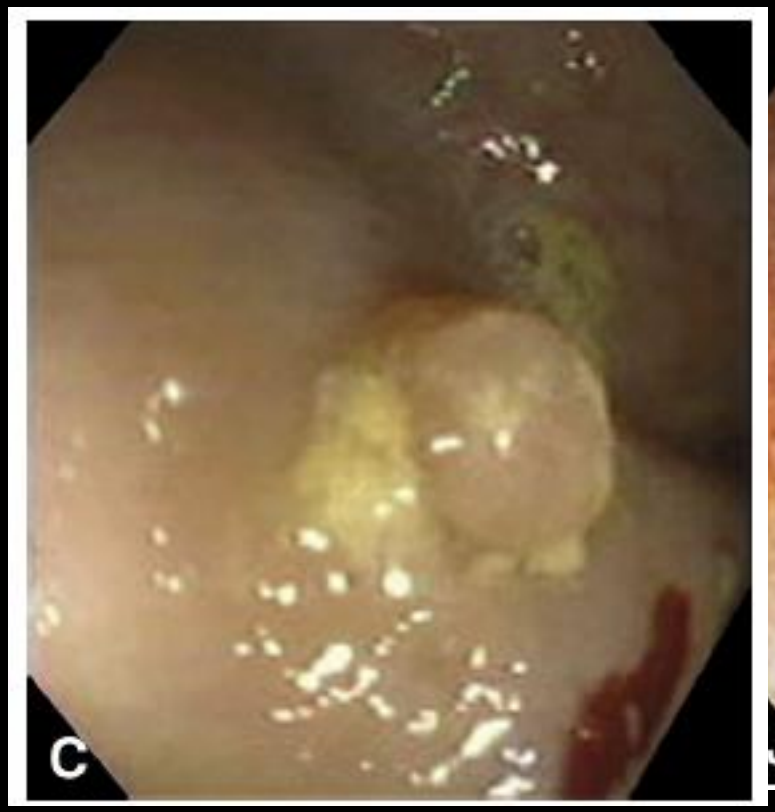




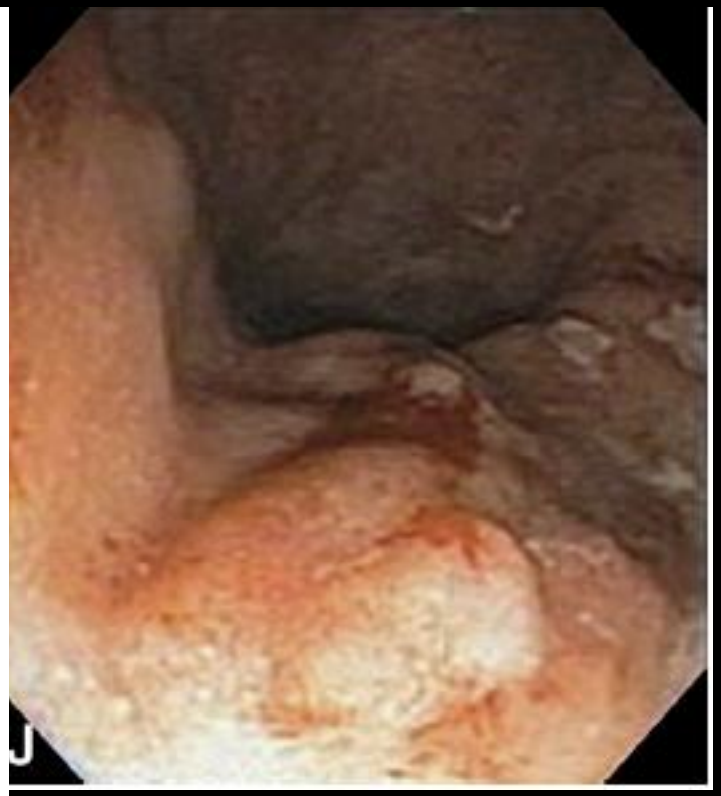
Not endoscopically resectable

Farraye, GIE, 2007; 66:519.

Not So Easy



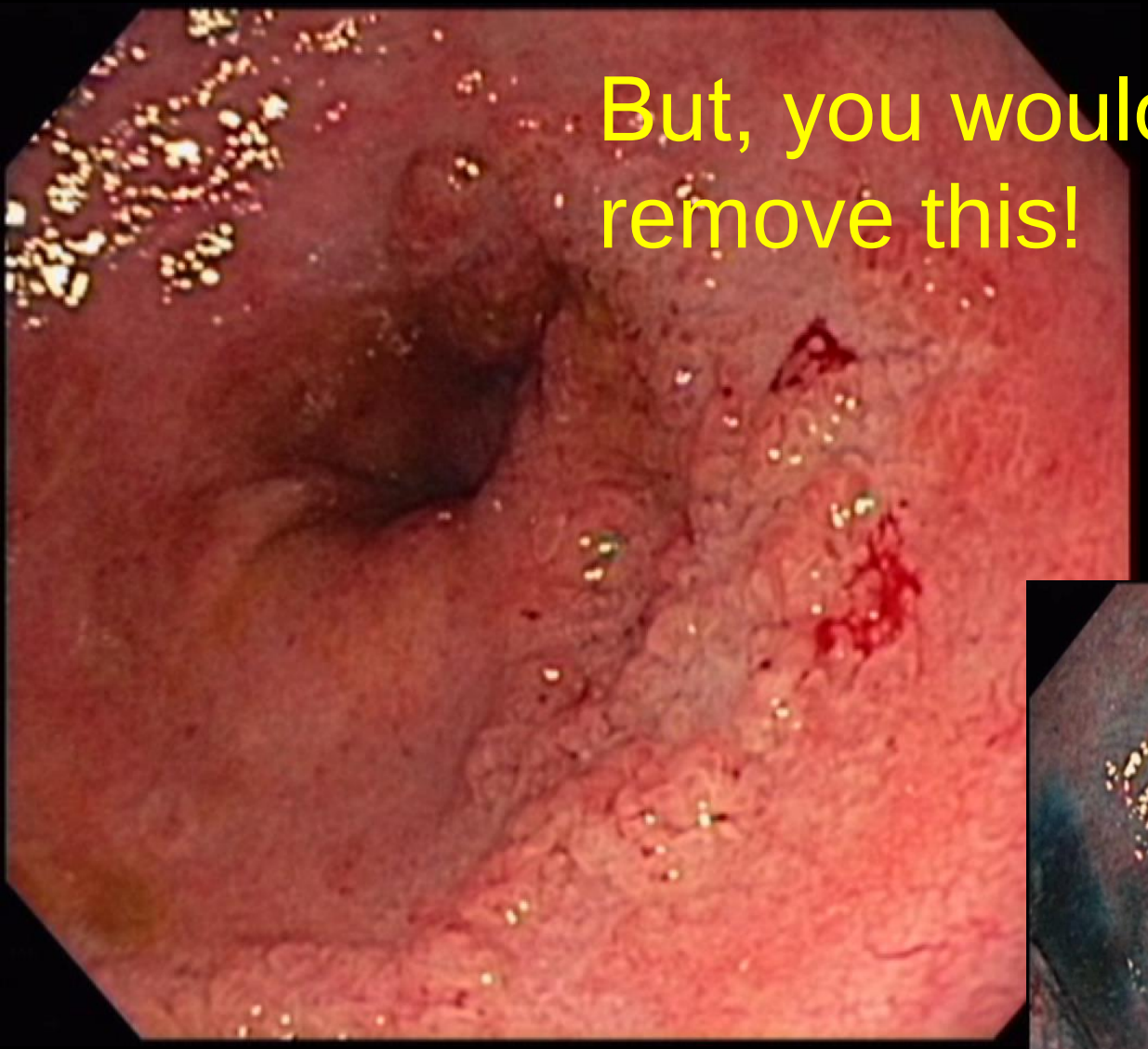
Adenoma-like
DALM

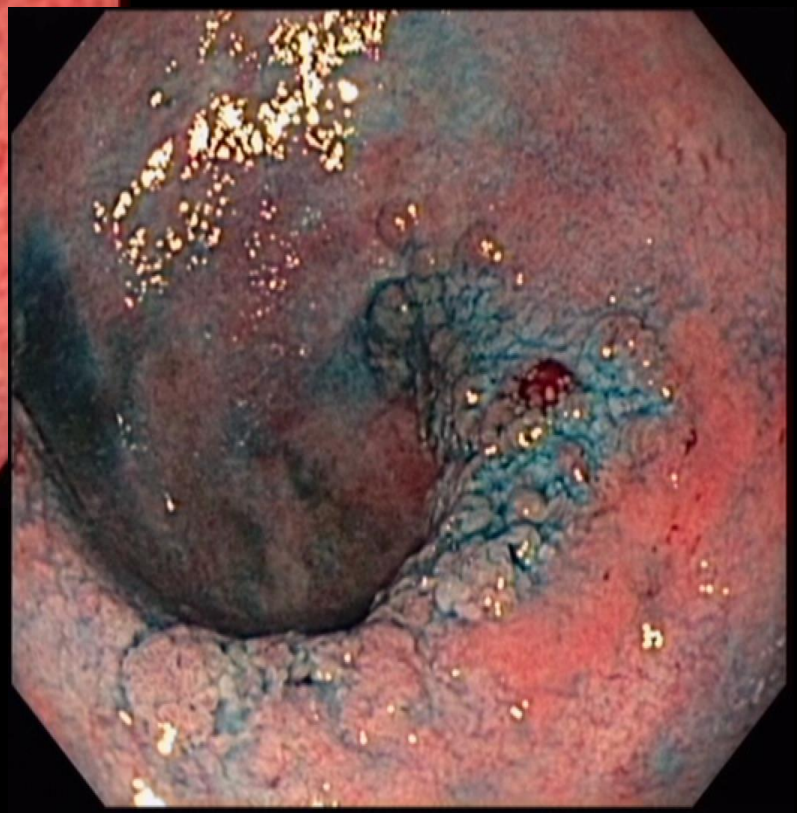


Non-Adenoma-like
DALM

Farraye F, GIE 2007

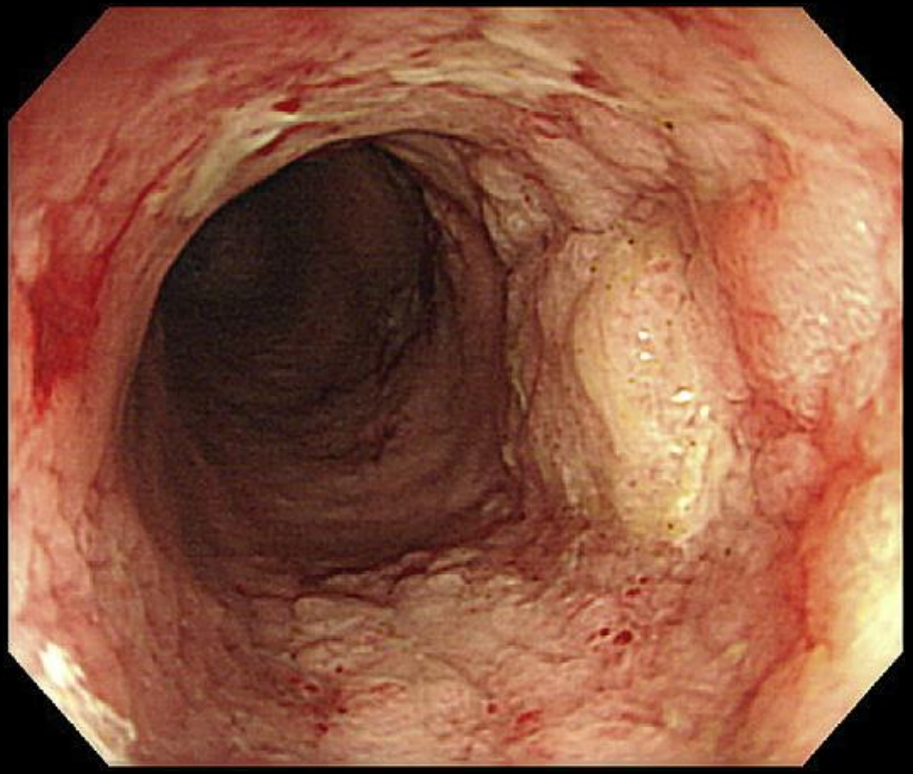
But, you wouldn’t attempt to remove this!





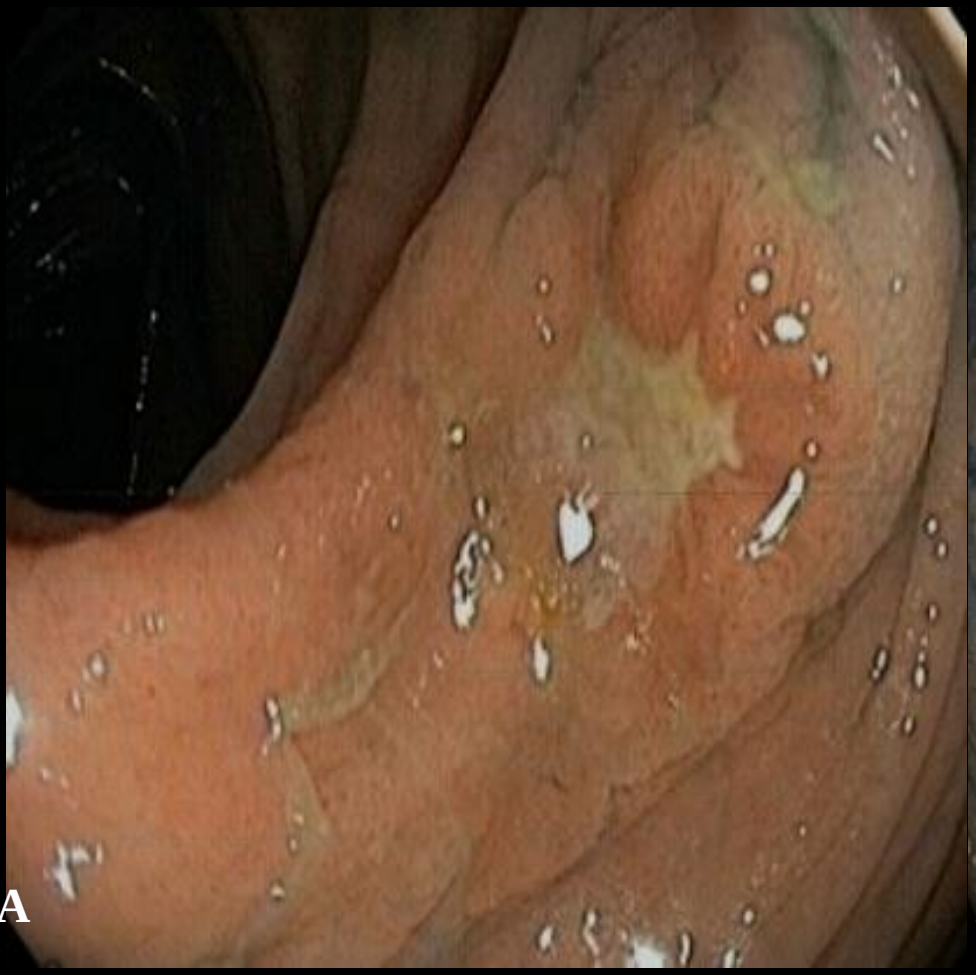
Courtesy: Roy Soetikno

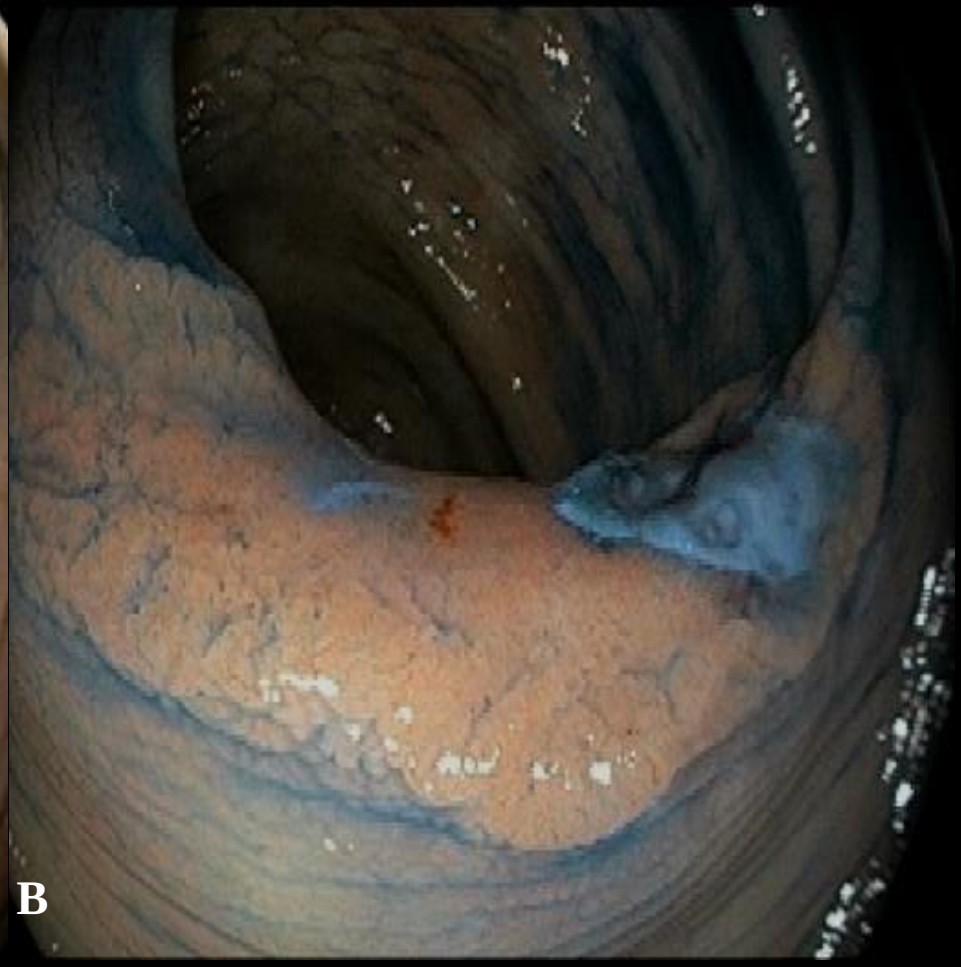
And not this…



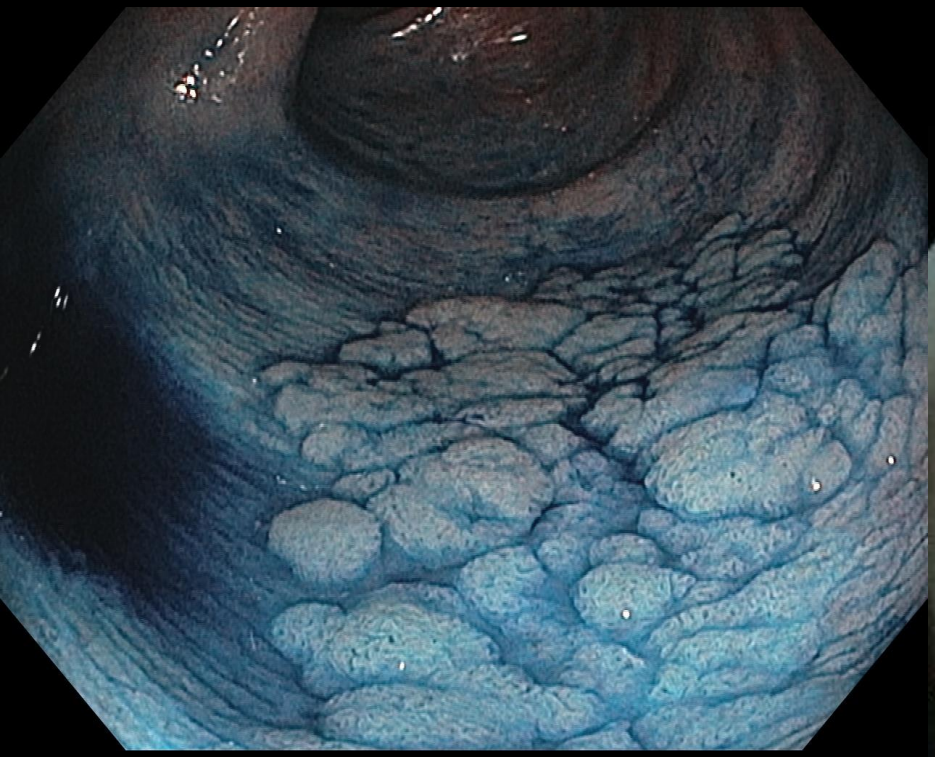
Ueno Y, GI Endosc Clin North Am 2010; 525.

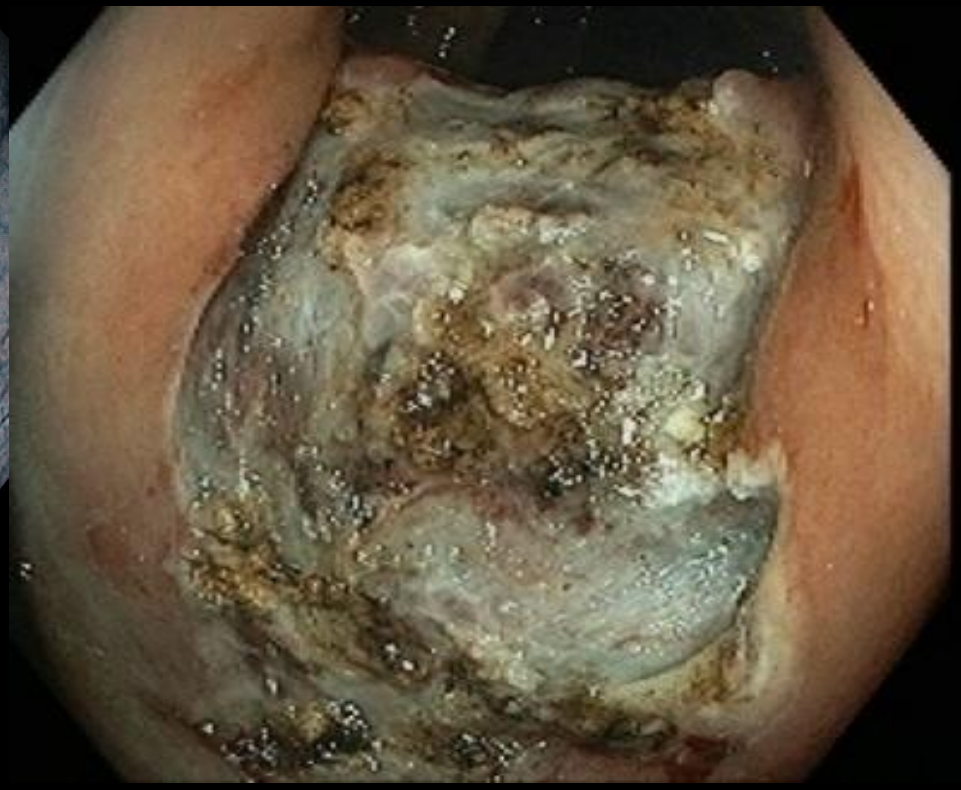
Or, this: Ulcerated superficially elevated lesion: cancer





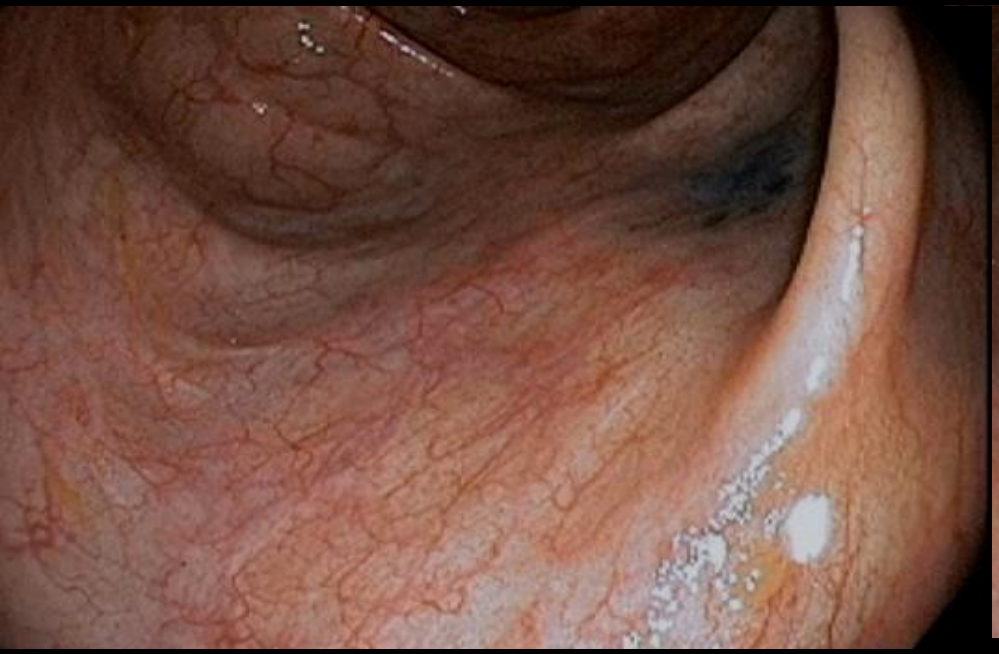
But, what about this? Should you?

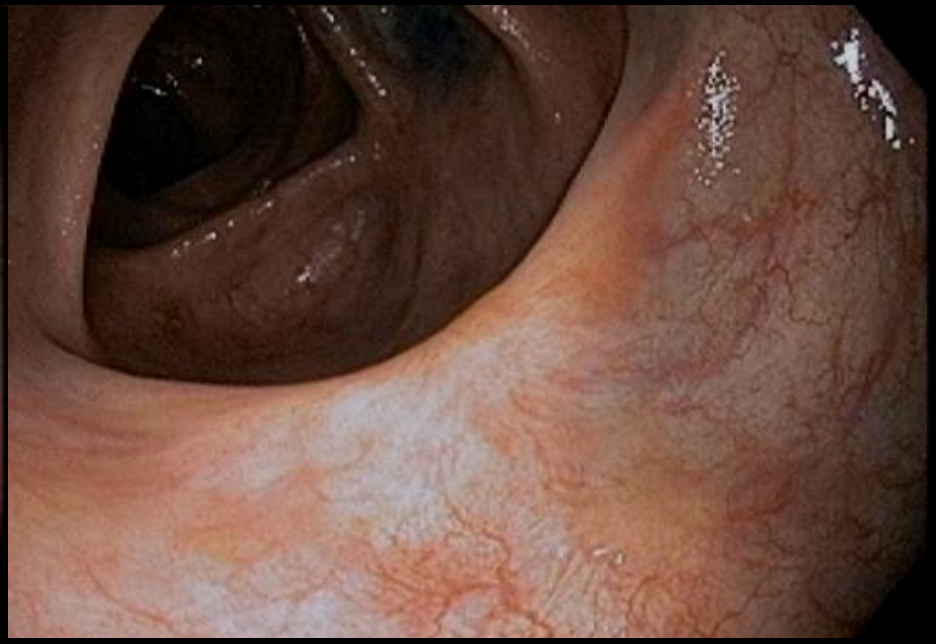




Courtesy: Roy Soetikno, MD

3 Months Later





Problems:

1. EMR on non-polypoid lesions can be extremely difficult in IBD
2. Saline lifts may not work
3. Lesions difficult to capture with snare
4. When in doubt: tattoo and refer!

Summary: Surveillance 2015

- Pancolonic chromoendoscopy with targeted biopsy of visible lesions is preferred
- Random biopsies may be unnecessary (and not cost effective)
- Well demarcated lesions (polypoid or nonpolypoid) without features of submucosal invasion should be resected endoscopically
  - Biopsy margins to confirm complete resection
  - Tattoo

- Real question: can the entire dysplastic lesion be removed?
- Always Consider:
  - Patient preferences / risk tolerance
  - Your ability / comfort with EMR
  - Surgical risks
  - Willingness to undergo close surveillance

Areas for Future Study, Debate, Education

- MC, RCT of HD vs. HD/Chromo
- Role of random biopsies
- Role of newer generation electonic enhancements (NBI, FICE,etc)
- Natural hx and optimal mgmt of non-polypoid lesions
- Training of endoscopists in lesion identification
- Should resection of dysplasia be left to advanced endoscopists?

…And More Questions

- Will detection of more/early dysplasia reduced CRC incidence and mortality?
- Will it lead to increased or reduced number of surveillance exams?
- More complications from lesion resection?
- False patient reassurance of risk?
  - More patients declining surgery…higher risk later?

Barrett's Esophagus

1998

- Risk of cancer: 1:200/yr
- Standard def scopes
- Belief: dysplasia invisible
- Random bx q2 cm to detect invisible dysplasi
- HGD: surgery
- Cost-effectiveness of surveillance debated

2015

- Risk of cancer: 1:800/yr
- High def scopes
- Belief: >90% of HGD visible
- Targeted biopsies of visual abnormalities
- NBI shown to enhance dysplasia detection
- Role of random bx debated
- HGD: endoscopic resection
- Cost-effectiveness of surveillance debated