Chromoendoscopy - Should It Be Standard of Care in IBD?

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What is the point of surveillance anyway?

“Detection of dysplasia is the immediate goal of surveillance colonoscopy”

“The purpose of colonoscopic surveillance in IBD is to identify dysplasia and intervene to prevent its progression.”

“Simply stated, the goals of any cancer surveillance program in UC are to prevent cancer and to save lives.”

1Laine et al. Gastrointest Endosc. 2015;81:489-501
2Ulmann T. AGA Perspective 2015 vol 11.
3Kornbluth et al. Am J Gastroenterol 2010;105:500
What is “STANDARD OF CARE”?

The Modern Definition
(Hall v. Hilburn; McCourt v. Abernathy; Johnston v. St. Francis Medical Center)
That which a minimally competent physician in the same field would do under similar circumstances.¹

However, clinical practice guidelines are being used more frequently as support for the standard of care; but their acceptance and uses are continually changing and decided on a case-by-case basis.¹


What is chromoendoscopy?
• Topical application of stains or pigments (typically methylene blue or indigo carmine in IBD) to the mucosal surface to highlight characteristics of the epithelium.
• Facilitates visualization and detection of dysplastic lesions that can be difficult to distinguish from non-dysplastic mucosa.
• The equipment needed for chromoendoscopy is widely available.
• Interpretation of the findings is not always straightforward; impact on clinical outcomes has not been established in large controlled trials.
68 yo with pan UC x 18 years for surveillance colonoscopy

White light, high definition

White light, high definition, indigo carmine

Where do the guidelines stand?

Crohn's and Colitis Foundation of America

The Committee endorses the incorporation of chromoendoscopy into surveillance colonoscopy for appropriately trained endoscopists.

Where do the guidelines stand?

Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice Parameters Committee

After 8 – 10 years of colitis, annual or biannual surveillance colonoscopy with multiple biopsies at regular intervals should be performed (Evidence B).

Where do the guidelines stand?

Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice Parameters Committee

….. the natural history of dysplastic lesions found by chromoendoscopy and not seen with routine white light colonoscopy is unknown. At present, therefore, the recommendation to routinely use chromoendoscopy-enhanced surveillance in low-risk patients awaits additional information regarding longer-term follow-up. Given the increased yield of chromoendoscopy, it may be of value in follow-up of the “higher-risk” patient.
Where do the guidelines stand?

British Society of Gastroenterology guidelines

4. Pancolonic dye spraying with targeted biopsy of abnormal areas is recommended. **Recommendation grade: A.** If chromoendoscopy is not used, the strategy of random biopsy outlined in the 2002 guideline should be followed. **Recommendation grade: C**


Where do the guidelines stand?

European Crohn's and Colitis Organisation

Statement 9L: Chromoendoscopy with targeted biopsies is the surveillance procedure of choice for appropriately trained endoscopists [EL1b, RG B]. Alternatively, random biopsies (quadrant biopsies every 10 cm) and targeted biopsies of any visible lesion should be performed if white light endoscopy is used [EL3, RG B]

Where do the guidelines stand?

**SCENIC international consensus**

**Statement 2:** When performing surveillance with standard-definition colonoscopy, chromoendoscopy is recommended rather than white-light colonoscopy. (85% agreement; strong recommendation; moderate-quality evidence)

**Statement 3:** When performing surveillance with high-definition colonoscopy, chromoendoscopy is *suggested* rather than white-light colonoscopy. (84% agreement; conditional recommendation; low-quality evidence)

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**2013 Meta-Analysis Chromoendoscopy (CE) with targeted biopsy vs WLE with random biopsies**

- 6 unique studies; 665 patients
- The pooled incremental yield of CE over WLE for the detection of any grade of dysplasia per patient was 7% (95% CI: 3.3%–10.3%)
- NNT to detect one extra patient with dysplasia was 14.3 (95% CI: 9.7–30.3).
- CE resulted
  - 9-fold increased likelihood of detecting any dysplasia - pooled odds ratio was 8.9 (95% CI 3.4 –23.0).
  - 5-fold greater likelihood of detecting non-polypoid dysplasia - the pooled odds ratio was 5.2 (95% CI 1.7–15.9).
  - 93% lower likelihood to miss dysplasia - pooled odds ratio was 0.07 (95% CI 0.03–0.21)

Lane L. et al. Gastrointest Endosc. 2015;81:489-501
Lane L. et al. Gastroenterology. 2015;148:639-651
Meta-analysis including 5111 colorectal lesions in 3418 patients. Pooled sensitivity 89.0% (95% CI: 85.2-91.9) Pooled specificity of 85.7% (95% CI: 81.3-89.2)²


Neoplastic
Has not been validated for characterization of dysplasia in colitis
58 yo with pan UC x 19 yrs

47 yo with a 26 yr history of pan UC.

Path: Patchy minimal chronic active colitis

When in doubt, BIOPSY
Arguments Against Chromoendoscopy

- Agree that chromoendoscopy is the most sensitive method for detection of dysplasia in colitis
- Agree that it is reasonable to use chromoendoscopy in high risk patients such as those with prior dysplasia or primary sclerosing cholangitis with colitis.
- Have common reservations

**Table 1. Challenges in Chromoendoscopy for Colitis Surveillance**

<table>
<thead>
<tr>
<th>Operator barriers</th>
<th>To be discussed</th>
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</thead>
<tbody>
<tr>
<td>Training of fellows, gastroenterologists, nurses, and staff</td>
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<td>Unknown learning curve</td>
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<td>Identifying clinically relevant lesions</td>
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<td>Pathologist interobserver variability in identifying and grading dysplasia</td>
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<td>Varying endoscopists’ skill in managing or resecting found dysplasia</td>
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<tr>
<td>Operational barriers</td>
<td>Applies to all surveillance colonoscopy</td>
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<td>Availability of dye, equipment</td>
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<td>Billing and reimbursement</td>
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<td>Time requirement</td>
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<td>Prep quality</td>
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<td>Confounding of findings by inflammation</td>
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<td>Patients’ willingness to undergo repeated, timely exams</td>
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<tr>
<td>Knowledge barriers</td>
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<td>Uncertain natural history of dysplasia detected by CE</td>
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<tr>
<td>Lack of well-defined population at risk</td>
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<td>Lack of risk stratification</td>
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<td>Uncertain implications of prior surveillance findings for management</td>
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<td>Uncertainty of appropriate surveillance intervals</td>
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**Can you learn chromoendoscopy (CE)?**

**YES**

- 6 endoscopists (Mayo Clinic sites); no previous experience in the use of CE in IBD
- Reviewed WL and CE images of neoplastic and non-neoplastic colonic mucosa
- 75 patients with long-standing UC had surveillance colonoscopy with white light endoscopy (WLE) followed by CE.
- 77 polypoid abnormalities identified by WLE; an additional 79 polypoid abnormalities identified by CE.
- 10 dysplastic lesions were identified by WLE and an additional 12 lesions by CE

Withdrawal time decreased with experience

Median (25th, 75th percentile) withdrawal time
- < 5 procedures = 31 min (15–36)
- 5-14 procedures = 18 min (13–27)
- >15 procedures = 19 min (18–22)

Excellent agreement among in interpretation of lesions detected by CE

Chromoendoscopy Learning Resources


Chromoendoscopy videos:
https://www.youtube.com/watch?v=OARkbgwlObI
https://www.youtube.com/watch?v=uGR4gjxfFjg
https://www.youtube.com/watch?v=gcN_FkXhR-M

ASGE On-line Learning Center
http://asge.extendmed.com/index.php

Table 1  Seven guidelines (SURFACE) for chromoendoscopy in ulcerative colitis

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| (1) | **Strict patient selection.**  
Patients with histologically proven ulcerative colitis and at least eight years' duration in clinical remission. Avoid patients with active disease. |
| (2) | **Unmask the mucosal surface.**  
Excellent bowel preparation is needed. Remove mucus and remaining fluid in the colon when necessary. |
| (3) | **Reduce peristaltic waves.**  
When drawing back the endoscope, a spasmolytic agent should be used (if necessary). |
| (4) | **Full length staining of the colon.**  
Perform full length staining of the colon (prechromoendoscopy) in ulcerative colitis rather than local staining. |
| (5) | **Augmented detection with dyes.**  
Intravital staining with 0.4% indigo carmine or 0.1% methylene blue should be used to unmask flat lesions more frequently than with conventional colonoscopy. |
| (6) | **Crypt architecture analysis.**  
All lesions should be analysed according to the pit pattern classification. Whereas pit pattern types I-II suggest the presence of non-malignant lesions, staining patterns III-V suggest the presence of intraepithelial neoplasias and carcinomas. |
| (7) | **Endoscopic targeted biopsies.**  
Perform targeted biopsies of all mucosal alterations, particularly of circumscript lesions with staining patterns indicative of intraepithelial neoplasias and carcinomas (pit pattern III-V). |

Gut 2004;53:165–167
What do I do?

1 gram indigo carmine in 1 liter wash water (0.1% solution)

Prospective studies have used 0.1-0.4% IC or 0.1% MB.

Take Home Points

- Chromoendoscopy is the most sensitive method for the detection of dysplasia.
- More and more guidelines/consensus statements suggest or recommend chromoendoscopy
- Chromoendoscopy is not difficult to learn (see the resources provided)
- Recognize pit patterns, when in doubt, biopsy.
- Read the SCENIC guidelines
- Only you, the practicing gastroenterologist can determine what is the standard of care