Colorectal Cancer Surveillance in Inflammatory Bowel Disease

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Disclosures

- No disclosures or conflicts of interest
Objectives: Colorectal Cancer Surveillance in IBD

- Describe current approach for colorectal (CRC) surveillance in inflammatory bowel disease (IBD)
- Outline classification scheme for describing IBD-associated dysplastic lesions
- Discuss role of chromoendoscopy in evaluation and detection of dysplasia
- Highlight optimal endoscopic surveillance techniques and management strategies in clinical practice
Burden of Colorectal Neoplasia in IBD

- Colitis-associated colorectal neoplasia, including dysplasia and malignancy, linked to IBD
  - Initially described by Crohn & Rosenberg (1925)

- IBD-associated colorectal cancer (CRC)
  - 1-2% of CRC cases in general population
  - 10-15% of all deaths among IBD patients
  - IBD is third highest risk factor for CRC behind genetic causes

- Distinct from sporadic CRC
  - Molecular, endoscopic and histologic features
  - Associated with increased mortality

References:
Risk of Colorectal Cancer in IBD

- Patients with long-standing IBD have higher risk for development of CRC than the general population

- 2.4-fold increased risk in UC and similar for Crohn’s colitis (relative to general populations)

- 1.5 to 2 times increased risk in IBD population compared with general population in North America

Risks for Colorectal Cancer in IBD

- Ulcerative colitis or Crohn’s colitis
- IBD Duration > 8-10 years
- Early age at onset of colitis
- Extensive colitis or backwash ileitis
- Histologic disease activity
- Family history of colon cancer
- Dysplasia at surveillance
- Primary sclerosing cholangitis (PSC)
- Pseudopolyps
PSC

Pseudopolyps
Factors that Decrease CRC Risk in IBD

- Colectomy (prophylactic)

- Surveillance colonoscopy with appropriate lesion resection and timely surgical intervention

- Chemoprevention (observational data)
  - 5-ASAs: potential chemopreventive effect
  - UDCA & folate- data inconclusive
  - Thiopurines/Anti-TNFs- data not supportive but effective for IBD management

Endoscopic CRC Surveillance: Random Biopsies


- 4-Quadrant Random Biopsies (n=32) from all colon segments (every 10 cm) to identify invisible dysplasia
  - Samples <0.1% of the surface mucosa

- Approximately 1 dysplasia detected per 1000 biopsies
- Approximately 9% of patients with dysplasia diagnosed

Farraye FA et al. Gastroenterology 2010; 138: 738-45
Farraye FA et al. Gastroenterology 2010; 138: 746-74 774 e1-4
High Rates of Interval CRC in Colitic IBD

Pathway Toward CRC in IBD

INFLAMMATION

**

DYSPLASIA

**

CANCER

DEATH
Current Approach to Colorectal Cancer Surveillance in IBD
Colorectal Dysplasia in IBD

- Most dysplasia is endoscopically visible

- Random biopsies to detect flat dysplasia
  - Poor sensitivity with significant risk of missed lesions

- Recent international consensus guidelines (SCENIC): major change in practice of colonoscopy surveillance and dysplasia management
  - Key recommendations & chromoendoscopy (CE) technique

SCENIC: Key Recommendations

- High definition (HD) white-light colonoscopy favored over standard definition for surveillance colonoscopy

- Narrow band imaging (NBI) not a replacement for HD white-light colonoscopy

- Chromoendoscopy used as an adjunct to HD-colonoscopy (conditional recommendation; strong recommendation with standard definition)

Narrow Band Not Superior to White Light

- HD-NBI not superior to HD-white light endoscopy (WLE) in detecting dysplasia

- Two studies on performance of surveillance colonoscopy with a HD colonoscope to compare NBI with WLE

- NBI versus WLE did not yield significant differences in dysplasia detection

van den Broek FJ et al. Endoscopy 2011;43:108-15
<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>Patients with dysplasia/all patients</th>
<th>RR (95% CI)</th>
<th>Absolute risk increase (95% CI)</th>
<th>No. of visible dysplastic lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiesslich 20</td>
<td>Randomized parallel-group</td>
<td>13/84; 6/81</td>
<td>2.1 (0.8-5.2)</td>
<td>8% (-2% to 18%)</td>
<td>32; 10</td>
</tr>
<tr>
<td>Kiesslich 21</td>
<td>Randomized parallel-group</td>
<td>11/80; 4/73</td>
<td>2.5 (0.8-7.5)</td>
<td>8% (-1% to 17%)</td>
<td>19; 2</td>
</tr>
<tr>
<td>Marion 24</td>
<td>Prospective tandem</td>
<td>22/102; 12/102</td>
<td>1.8 (0.96-3.5)</td>
<td>10% (0% to 20%)</td>
<td>35; 13</td>
</tr>
<tr>
<td>Rutter 23</td>
<td>Prospective tandem</td>
<td>7/100; 2/100</td>
<td>3.5 (0.8-16.4)</td>
<td>5% (-1% to 11%)</td>
<td>9; 2</td>
</tr>
<tr>
<td>Matsumoto 25</td>
<td>Prospective tandem</td>
<td>12/57; 12/57</td>
<td>1.0 (0.5-2.0)</td>
<td>0% (-2% to 2%)</td>
<td>18; 8</td>
</tr>
<tr>
<td>Hlavaty 26</td>
<td>Prospective tandem and additional cohort</td>
<td>4/30; 2/45</td>
<td>3.0 (0.6-15.4)</td>
<td>9% (-5% to 23%)</td>
<td>6; 2</td>
</tr>
<tr>
<td>Gunther 27</td>
<td>Retrospective two-group</td>
<td>2/50; 0/50</td>
<td>5.0 (0.3-101.6)</td>
<td>4% (-3% to 11%)</td>
<td>2; 0</td>
</tr>
<tr>
<td>Chiorean 22</td>
<td>Prospective tandem</td>
<td>No per-patient data given (N = 63)</td>
<td></td>
<td></td>
<td>41; 18</td>
</tr>
</tbody>
</table>

**SCENIC meta-analysis**

- **RR**, Relative risk; **CI**, confidence interval; SCENIC, Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendations.
Advanced Endoscopic Techniques for Studying Colonic Mucosa in IBD

- Various modalities to assess mucosal healing, microscopic inflammation, dysplasia or neoplasia
  - Chromoendoscopy*
  - Narrow band imaging
  - Confocal laser endomicroscopy
  - i-SCAN
  - Autofluorescence imaging
  - Fujinon Intelligent Color Enhancement

- *Chromoendoscopy superior to white-light endoscopy for detection of dysplasia or neoplasia detection and assessment of mucosal healing or inflammation

Chromoendoscopy with Targeted Biopsy Yields Over WLE

- Increase in dysplasia detection/patient: 7% (95% CI 3.3-10.3%)
- Likelihood of any dysplasia detection: OR 8.9 (95% CI 3.4-23)
- Likelihood of flat dysplasia detection: OR 5.2 (95% CI 1.7-15.9)
- To find another patient with >1 dysplasia: NNT 14.3 (range 9.7-30.3)

Soetinko R et al. Gastroenterology 2013;144(7):1349-52
CE More Effective in Dysplasia Detection

- Prospective longitudinal study from Mt Sinai Medical Center (2005-2011) of 68 IBD patients comparing standard colonoscopy versus CE in detecting dysplasia
  - N=68 (UC 55, CD 13), median followup 27.8 mo

- Each patient had: Random biopsies, Targeted white light examination (WLE), and CE

- Odds for detecting dysplasia (primary outcome)

CE More Effective in Dysplasia Detection

- 208 exams conducted, 44 dysplastic lesions, 24 pts
  - 6 by random biopsy, 11 by WLE, 27 by CE
  - 10 referred for colectomy: No carcinomas found

- Any time during study, CE (OR 5.4, 95% CI 2.9-9.9) and targeted WLE (OR 2.3, 95% CI 1.0-5.3) more likely than random biopsy to detect dysplasia

- CE was superior to WLE (OR 2.4, 95% CI 1.4-4.0)

- Patients identified with dysplasia more likely to need colectomy (HR 12.1, 95% CI 3.2-46.2)
CE More Effective in Dysplasia Detection

- **Conclusions**: CE was superior to random biopsy or WLE analyses in detecting dysplasia in IBD patients.

- Negative CE examination was best indicator of a dysplasia-free outcome.

- Positive CE result was associated with earlier referral for colectomy.

Nontargeted Biopsies

- SCENIC makes no recommendation on performance of random biopsies
  - 60% of panel members disagreed on this practice when using high-definition white-light colonoscopy with chromoendoscopy

Targeted Biopsies Superior

- Identify a greater proportion of patients with neoplasia than random biopsies

Classification of Colorectal Dysplasia in IBD
SCENIC: Terms & Characterization

- AVOID
  - DALM (Dysplasia-Associated Lesion or Mass)
  - Adenoma-like
  - Non-Adenoma-like

- ADVOCATE TERMS
  - Endoscopically resectable
  - Nonendoscopically resectable
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visible dysplasia</td>
<td>Dysplasia identified on targeted biopsies from a lesion visualized at colonoscopy</td>
</tr>
<tr>
<td>Polypoid</td>
<td>Lesion protruding from the mucosa into the lumen ≥ 2.5 mm</td>
</tr>
<tr>
<td>Pedunculated</td>
<td>Lesion attached to the mucosa by a stalk</td>
</tr>
<tr>
<td>Sessile</td>
<td>Lesion not attached to the mucosa by a stalk: entire base is contiguous with the mucosa</td>
</tr>
<tr>
<td>Nonpolypoid</td>
<td>Lesion with little (&lt;2.5 mm) or no protrusion above the mucosa</td>
</tr>
<tr>
<td>Superficial elevated</td>
<td>Lesion with protrusion but &lt;2.5 mm above the lumen (less than the height of the closed cup of a biopsy forceps)</td>
</tr>
<tr>
<td>Flat</td>
<td>Lesion without protrusion above the mucosa</td>
</tr>
<tr>
<td>Depressed</td>
<td>Lesion with at least a portion depressed below the level of the mucosa</td>
</tr>
<tr>
<td>General descriptors</td>
<td></td>
</tr>
<tr>
<td>Ulcerated</td>
<td>Ulceration (fibrinous-appearing base with depth) within the lesion</td>
</tr>
<tr>
<td>Border</td>
<td></td>
</tr>
<tr>
<td>Distinct border</td>
<td>Lesion’s border is discrete and can be distinguished from surrounding mucosa</td>
</tr>
<tr>
<td>Indistinct border</td>
<td>Lesion’s border is not discrete and cannot be distinguished from surrounding mucosa</td>
</tr>
<tr>
<td>Invisible dysplasia</td>
<td>Dysplasia identified on random (non-targeted) biopsies of colon mucosa without a visible lesion</td>
</tr>
</tbody>
</table>
SCENIC: Terms & Characterization
NONPOLYPOID COLORECTAL LESIONS IN IBD
Chromoendoscopy
SCENIC: Chromoendoscopy Technique

- Chromoendoscopy (CE) is currently the only technique included IBD surveillance guidelines
## Chromoendoscopy: Dye Preparation

<table>
<thead>
<tr>
<th>Technique</th>
<th>Purpose</th>
<th>Delivery</th>
<th>Methylene Blue Dilution (1%, 10mL ampule)</th>
<th>Indigo Carmine Dilution (0.8%, 5mL ampule)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panchromoendoscopy</td>
<td>Lesion Detection</td>
<td>Water jet channel using auxiliary foot pump or biopsy channel using spray catheter</td>
<td>1 ampule + 240 mL sterile water (0.04%)</td>
<td>2 ampules + 250 mL sterile water (0.03%)</td>
</tr>
<tr>
<td>Targeted Chromoendoscopy</td>
<td>Lesion characterization and border delineation</td>
<td>Syringe spray through biopsy channel</td>
<td>1 ampule + 40 mL sterile water (0.2%)</td>
<td>1 ampule + 25 mL sterile water (0.13%)</td>
</tr>
</tbody>
</table>
Chromoendoscopy: Technique

- Dilute dye sprayed through water jet during withdrawal
- Concentrated dye sprayed through accessory channel to detail suspicious lesions
- Lesions examined closely to characterize & determine borders
- Biopsies targeted to abnormal-appearing areas
Chromoendoscopy

- Superficial lesions with well-defined borders: potentially endoscopically resectable

- Resectable lesion
  - Remove en-bloc if possible
  - Biopsy adjacent mucosa

- Unresectable lesion
  - Biopsy and tattoo
Chromoendoscopy: Keys

- Avoid active disease

- Excellent bowel preparation required

- Wash residue during insertion

- Begin chromoendoscopy in cecum
  - Apply dye in a circumferential technique during withdrawal. Direct spray to the antigravity side.
Chromoendoscopy: Keys

- Suction excess solution after about 1 minute to aid mucosal visualization

- Assess 20-30-cm segments sequentially
  - Reinsert endoscope to the proximal extent of each segment followed by slow withdrawal and mucosal visualization

- Targeted dye spray for suspicious lesions:
Chromoendoscopy Challenges

- Time-consuming procedure
- Preparation/supplies
- Limitations: Poor preparation or active colitis
- No minimum competence requirement
- Effect on outcomes (cancer/mortality) require further study
Management of Colorectal Dysplasia in IBD
SCENIC: Visible Dysplasia

ENDOSCOPICALLY RESECTABLE

- SURVEILLANCE COLONOSCOPY rather than colectomy after removal of endoscopically resectable dysplasia (polypoid or nonpolypoid)
  - Data limited on management of non-polypoid endoscopically visible dysplasia; surveillance suggested; conditional recommendation

NONENDOSCOPICALLY RESECTABLE

- Refer to surgery or advanced colonoscopist
SCENIC: Invisible Dysplasia

- Confirm with GI pathologist

- Referral to endoscopist with expertise in IBD surveillance using chromoendoscopy with high-definition colonoscopy
Algorithm of pancolonic chromoendoscopy and targeted biopsy, and management of detected superficial colorectal lesions

The disease should be in remission. Excellent bowel preparation is a prerequisite. Residual debris and fluid should be washed and suctioned. White-light is used for insertion to the cecum.

Pancolonic chromoendoscopy: indigo carmine (IC): ~ 0.03% spray starts at the cecum

Lesions in the setting of chronic ulcerative colitis or crohn’s colitis

Within colitic area?

Yes

Superficial lesions (endoscopically resectable)

No

Sporadic lesion. Consider biopsy of adjacent mucosa

No

Biopsy to confirm dysplasia/cancer. Tattoo

Non-polypoid:
1. Superficial elevated
2. Flat
3. Depressed

Polypoid:
1. Pedunculated
2. Sessile

Yes

Standard management

Surgery

GASTROENTEROLOGY 2013;144:1349 -1352
Concentrated IC ~ 0.13%

Detailed viewing to determine the border, and, if possible, to assess the likely pathology: pseudopolyp, hyperplastic, sessile serrated adenoma, adenoma/dysplasia (low- and high-grade), or invasive carcinoma

No indication to resect: pseudopolyps or hyperplastic polyps

Resectable: pedunculated, or sessile, superficial elevated, flat or small depressed lesion that is circumscribed and without features of submucosal invasion

Unresectable: lesions with ill-defined border, features of submucosal invasive cancer, or large depression; or technically not feasible
Mucosal inflammation and multiple pseudopolyps may affect the interpretation of chromoendoscopy. Random biopsy is still justified in these circumstances.

* The resection of circumscribed nonpolypoid lesion is colonic IBD requires a high level of expertise - referral may be necessary.
** The pathology of LGD may require confirmation by a gastrointestinal pathologist.
*** Repeat resection may be considered for small residual lesions.
Objectives: Colorectal Cancer Surveillance in IBD

- Describe burden of colorectal cancer (CRC) & current approach for CRC surveillance in IBD
- Outline classification scheme for describing IBD-associated dysplastic lesions
- Discuss role of chromoendoscopy in evaluation and detection of dysplasia
- Highlight optimal endoscopic surveillance techniques and management strategies in clinical practice
Case 1

- 60 year old female with long-standing ulcerative pancolitis now in remission on 5-ASA therapy presents for second opinion regarding flat dysplasia found on random right colon biopsies. Chromoendoscopy revealed a large depressed lesion in the right colon with ill-defined borders that appeared technically difficult to resect, and biopsy of the lesion showed high-grade dysplasia as confirmed by a second GI pathologist.
Case 1

The recommended next step for this patient is:

A) No immediate action is required. Repeat surveillance colonoscopy in 1 year.
B) Repeat colonoscopy in 3 months.
C) Repeat colonoscopy with chromoendoscopy in 6 months.
D) Refer to colorectal surgeon to discuss proctocolectomy.
Case 1

The recommended next step for this patient is:

A) No immediate action is required. Repeat surveillance colonoscopy in 1 year.
B) Repeat colonoscopy in 3 months.
C) Repeat colonoscopy with chromoendoscopy in 6 months.
D) Refer to colorectal surgeon to discuss proctocolectomy.
Case 2

A 56 year old male with chronic ulcerative pancolitis for 31 years presents for surveillance colonoscopy. You would like to perform the procedure using chromoendoscopy. Patient-related factors that may limit your ability to perform this technique include *all but which* of the following?
Case 2: Answer

A) Presence of active colon inflammation
B) Presence of pseudopolyps
C) History of Primary Sclerosing Cholangitis
D) Poor bowel preparation
Case 2

A) Presence of active colon inflammation
B) Presence of pseudopolyps
C) History of Primary Sclerosing Cholangitis
D) Poor bowel preparation
Thank You