Surveillance for Colorectal Neoplasia in IBD: What to Do in 2014

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Teaching Objectives

• Identify the high risk patient by understanding the risk factors for developing colorectal neoplasia in IBD
• Review the natural history and management of dysplasia in 2014
• Contrast random vs. targeted biopsies and review guidelines for dysplasia surveillance in IBD patients
Increased Risk of CRC in UC

- Meta analysis of cohort studies that reported on the occurrence of CRC in patients with UC and/or CD
- Pooled SIR of CRC in all patients with IBD in population-based studies was 1.7 (95% CI, 1.2-2.2)
- Cumulative risks of CRC were 1%, 2%, and 5% after 10, 20, and greater than 20 years of disease duration
- High-risk groups were patients with extensive colitis and an IBD diagnosis before age 30 with SIR of 6.4 (95% CI, 2.4-17.5) and 7.2 (95% CI, 2.9-17.8)


Factors That Increase the Risk of CRC in IBD

- Duration of colitis
- Anatomic extent of disease
  - No increase in proctitis patients, intermediate risk in left sided UC and highest risk in in pan colitis
- Primary sclerosing cholangitis
- Family history of colorectal cancer
  - Highest risk if FDR with CRC < 50
- Age of IBD onset

Factors That Increase the Risk of CRC in IBD

• Previous dysplasia
• Severity of endoscopic and histologic inflammation
• Endoscopic findings
  – Strictures, pseudopolyps, foreshortened colon
• Male gender
  – Men: SIR 2.6, 95% CI, 2.2-3.0
  – Women: SIR 1.9, 95% CI, 1.5-2.3

**Histological inflammation is a Risk for Neoplasia in UC**

<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Patients</th>
<th>Risk (OR or HR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutter UK (2004)</td>
<td>Case-control</td>
<td>68 cases 136 controls</td>
<td>Histologic inflammation (retrospective) OR 4.69 (2.10 – 10.48)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
| Gupta NY (2007) | Cohort       | 418 pts 65 neoplasia 15 advanced neoplasia | Inflammation (pathology reports)  
advanced neoplasia  
any neoplasia  
any advanced neoplasia  
HR 2.2  
HR 1.3  
HR 2.4  
HR 2.0 | p<0.05  
p=0.03  
p=0.03  
p=0.01 |
| Rubin Chicago (2006) | Case-control | 59 cases 141 controls | Average Histologic Inflammation (re-graded) OR 4.9 (1.7-14.3)  
7.1 (1.7-29.8) | 0.004  
0.007 |

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Endoscopic Predictors of CRC Risk in UC

- Case Control Study (1988 through 2002) of patients with CRC (n=68) and controls (n=136)
- Multivariate Analysis
  - Macroscopically normal colon (OR 0.38; CI, 0.21-0.74)
  - Post inflammatory polyps (OR 2.29; CI, 1.28-4.11)
  - Strictures (OR 4.62; CI, 1.03-20.8)
- Five year risk of CRC following a normal colonoscopy was no different than that of matched general population controls


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Surveillance Colonoscopy in IBD

- No RCTs proving value of colonoscopy have ever been conducted but accepted as standard of care
- 149 patients with IBD-associated CRC from the Netherlands (1/90 to 7/06)
  - 100% five year survival of 23 patients enrolled in a surveillance program prior to CRC detection, compared with 74% in a non-surveillance group (p=0.042)
  - Of 30 CRC-related deaths during the study period only 1 patient was in the surveillance group compared to 29 in the non-surveillance group (p=0.047)
  - 52% of patients in the surveillance group had Stage 0-1 CRC, compared to 24% in the non-surveillance group (p=0.004)


Is Surveillance Cost Effective?

- Colonoscopy surveillance was determined to be cost effective for high risk groups of IBD patients
  - Any history of dysplasia
  - Extensive active colitis
  - PSC, strictures with the last 5 years
  - Family history of CRC before 50 years of age
- Chromoendoscopy is both more effective and less costly than WLE and becomes cost effective relative to no surveillance when performed at intervals of ≥ 7 years

IBD Surveillance Circa 2010

- Ideally perform surveillance colonoscopy when IBD is in remission
- Bowel prep must be ideal
- Screening after 8 years for all UC; at diagnosis for PSC
- Surveillance q 1-3 years for extensive and left sided colitis; yearly for PSC
- Representative biopsy specimens from each anatomic section of the colon should be obtained
- A minimum of 33 random biopsy specimens be taken in patients with pan colitis recommended


IBD Surveillance Circa 2010

- Colectomy for HGD in flat mucosa; data insufficient for LGD (colectomy for multifocal LGD)
- Adenoma like DALMs (endoscopically resectable polypoid dysplasia) can be managed with continued surveillance
- Non adenoma like DALMs (non-endoscopically resectable polypoid dysplasia) require colectomy
- Chromoendoscopy with targeted biopsies is recommended as an alternative to random biopsies for endoscopists who have expertise with this technique

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The Future of Endoscopic Surveillance

• White Light Endoscopy with HD scopes and ideal bowel preps
  – Low yield and high cost of random biopsies
• Narrow Band Imaging
• Confocal endomicroscopy
• Chromoendoscopy

Is Most Dysplasia in Ulcerative Colitis Visible at Colonoscopy?

- Most dysplastic lesions in ulcerative colitis are visible at colonoscopy
- From a clinical perspective, the endoscopic resectability of a lesion is more important than whether it is thought to be a sporadic adenoma or a dysplasia-associated lesion/mass


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**NBI is No More Effective than WLE for Dysplasia Detection in IBD**

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Number</th>
<th>NBI</th>
<th>WLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dekker et al (2007)</td>
<td>Tandem</td>
<td>42</td>
<td>8/11(^a) (73%)</td>
<td>7/11(^a) (64%)</td>
</tr>
<tr>
<td>Van den Broek, et al (2011)</td>
<td>Tandem</td>
<td>48</td>
<td>8/11(^a) (73%)</td>
<td>9/11(^a) (82%)</td>
</tr>
<tr>
<td>Ignjatovic et al (2012)</td>
<td>Parallel group</td>
<td>112</td>
<td>5/56(^b) (9%)</td>
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</tr>
</tbody>
</table>

\(^a\) Proportion of total dysplastic lesions detected overall.  \(^b\) Proportion of patients with at least one dysplastic lesion


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Confocal Endomicroscopy


Comparison between endomicroscopy and histopathology for intraepithelial neoplasia in CUC

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**Chromoendoscopy**

- Improves the detection of subtle colonic lesions, raising the sensitivity of the endoscopic examination
- Chromoendoscopy with or without a magnifying colonoscope can improve lesion characterization, increasing the specificity of the examination
- Crypt architecture can be categorized using the pit pattern, aiding differentiation between neoplastic and non-neoplastic changes, and enabling the performance of targeted biopsies
- Provides a more accurate diagnosis of the extent of disease and inflammatory activity

Chromoendoscopy: Which Dye?

- **Indigo carmine (0.1%-0.4%)**
  - Contrast stain neither reacts or is absorbed by the colonic mucosa
  - Pools in mucosal grooves allowing better definition of small or flat lesions as well as alterations in mucosal architecture
  - Can be washed off the mucosa

- **Methylene blue**
  - Vital dye taken up by colonic mucosa within 1-2 minutes staining noninflamed mucosa but is poorly taken up by dysplastic tissue or inflamed mucosa

- **No published studies comparing indigo carmine to methylene blue in patients with IBD**


Non Neoplastic Pattern

Neoplastic pattern

Chromoendoscopy Example

Dye spray catheter  Mucosa stained with methylene blue  Magnifying analysis and pit pattern


Controlled Studies on the Use of Chromoendoscopy in Patients with Ulcerative Colitis

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Dye / MB= methylene blue IC= Indigocarmine</th>
<th>Number of lesions</th>
<th>Difference (x-fold)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiesslich et al. (2003)</td>
<td>165</td>
<td>MB</td>
<td>42 (32 vs 10)</td>
<td>3.07</td>
</tr>
<tr>
<td>Hurlstone et al. (2004)</td>
<td>324</td>
<td>IC and magnification</td>
<td>93 (69 vs 24)</td>
<td>3.81</td>
</tr>
<tr>
<td>Rutter et al. (2004)</td>
<td>100</td>
<td>IC</td>
<td>7 (7 vs 0)</td>
<td>4.50</td>
</tr>
<tr>
<td>Kiesslich et al. (2007)</td>
<td>153</td>
<td>MB and Confocal Endomicroscopy</td>
<td>23 (19 vs 4)</td>
<td>4.75</td>
</tr>
<tr>
<td>Marion et al. (2008)</td>
<td>102</td>
<td>MB</td>
<td>20 (17 vs 9)</td>
<td>5.66</td>
</tr>
</tbody>
</table>

Chromoendoscopy Video
2013;144:1349-52.
The Future of Endoscopic Surveillance

• The paradigm for neoplasia surveillance in IBD is rapidly evolving with advancements in endoscopic imaging technology

• Random biopsies should be required only in areas of poorly visualized colonic mucosa, either due to mucosal inflammation or to poor bowel preparation

• Well-demarcated neoplastic lesions without features of submucosal invasion should be resected if possible endoscopically, and such patients should ideally continue in an endoscopic surveillance program


The Elephant in the Room

No definitive way to compensate for chromoendoscopy

What to Do in 2014

• All patients with ulcerative colitis and Crohn’s colitis should undergo a screening colonoscopy 8-10 years after onset of disease symptoms to stage extent of disease and evaluate for endoscopic features that confer an increased risk for IBD associated colorectal neoplasia

• Surveillance colonoscopy
  – Ulcerative colitis patients with left sided or extensive colitis (excluding patients with isolated proctitis)
  – Crohn’s colitis patients involving more than one segment of the colon or at least 1/3 of the colon

Shergill AK, Farraye FA. Towards a consensus on endoscopic surveillance of patients with colonic inflammatory bowel disease. GI Clinics North America. 2014, in press.
What to Do in 2014

• Patients with the highest risk of IBD associated colorectal neoplasia should undergo annual surveillance. Lower risk patients can undergo surveillance at less frequent intervals, every 2-5 years.

• Dye based chromoendoscopy (DBC) with targeted biopsies maximizes colorectal neoplasia detection during surveillance colonoscopy.
  – European and Australian guidelines agree that this is the surveillance method of choice.
  – Most US guidelines endorse DBC with targeted biopsy as an option for surveillance.

Shergill AK, Farraye FA. Towards a consensus on endoscopic surveillance of patients with colonic inflammatory bowel disease. GI Clinics North America. 2014, in press.

What to Do in 2014

• Use random biopsies as alternative to DBC or in patients with poor prep and/or multiple pseudopolyps.

• Endoscopically visible lesions that are well-circumscribed and amenable to endoscopic resection with no evidence of dysplasia in the surrounding flat mucosa or elsewhere in the colon are appropriate for continued colonoscopic surveillance.

Shergill AK, Farraye FA. Towards a consensus on endoscopic surveillance of patients with colonic inflammatory bowel disease. GI Clinics North America. 2014, in press.
International Consensus for Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients (SCENIC)
March 2014, San Francisco

Organizers: Loren Laine MD, Alan Barkun MD, Kenneth McQuaid MD, Roy Soetikno MD and Tonya Kaltenbach MD

Thank You