Colon Cancer Surveillance & Chemoprevention in IBD

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What is the risk of colon Cancer in the U.S. Population?

U.S.  148,810 cases / year
     49,960 deaths / year

148K per year / 307 million = 0.048%

Colorectal cancer rates 10 times higher:

N. America, W. Europe  VS  Africa, Asia
What is the Risk of Colon Cancer in Patients with IBD?

Best data from Manitoba

Population based

Reporting is a legal requirement

6027 IBD patients in database

5529 matched controls

Follow-up to 41.7 years for UC

Bernstein CN. Cancer 2001; 91(4): 854-92
What is the Risk of Colon Cancer in Patients with IBD?

• 1% of all cases of colorectal cancer occur in IBD patients nevertheless…

• IBD patients are one of the highest risk groups for colorectal cancer.

Choi PM Gut 1994; 35: 950-4
What is the Risk of Colon Cancer in Patients with IBD?

Ulcerative Colitis

Increased Relative Risk = 2.75

Crohn’s Disease

Increased Relative Risk = 2.64

(Crohn’s: small bowel ca IRR = 17.4)

Bernstein CN. Cancer 201; 91(4): 854-92
Do UC and Crohn’s Have Similar Risks for Colon Ca?

Yes

- Both depend on the extent and duration of colorectal disease
- The more extensive and longer the disease, the more the risk
Colorectal Ca in IBD Variables

- Extent
- Duration
- Family history of Colorectal Ca
- More severe inflammation
- Primary Sclerosing Cholangitis
- Early age at onset

Colorectal Ca in IBD

Variables

- **Extent:** Longstanding UC
  - Pan-colonic risk: 19 times higher
  - Left-sided risk: 4 times higher

Colorectal Ca in IBD
Variables

- **Extent**
- **Duration**
  - For extensive ulcerative colitis
    - After 20 years  8 %
    - After 30 years  18 %

Colorectal Ca in IBD
Variables

• Duration
• Extent
• Family history of Colorectal Ca
  – 147 UC cases, 150 controls
  – Cancer in 1\textsuperscript{st} Degree relatives:
    • 14.3\% cases; 6.7\% controls
  – Odds ratio is 2.33, $p=0.03$

Nuako KW  Gastroenterology 1998; 115: 1079-83
Colorectal Ca in IBD Variables

- Duration
- Extent
- Family history of Colorectal Ca

- More severe inflammation
  - St Marks, London
  - Case (68) : Control (136) study
  - Inflammation severity & cancer risk
  - Odds Ratio 4.7, p<0.001

Rutter M Gastroenterology 2004; 126: 451-59
Colorectal Ca in IBD Variables

- Duration
- Extent
- Family history of Colorectal Ca
- More severe inflammation

- Primary Sclerosing Cholangitis
  - Meta-analysis, 11 studies
  - Risk of colon Ca in PSC + UC
  - Odds ratio 4.09  95% CI [2.89, 5.76]

Soetikno RM  Gastrointes Endos 2002; 56: 48-54
Colorectal Ca in IBD Variables

- Duration
- Extent
- Family history of Colorectal Ca
- More severe inflammation
- Primary Sclerosing Cholangitis

- Early age at onset
  - Sweden. 91 pt with UC + colorectal CA
  - For each 10 year increase in age at onset
  - Cancer risk decreased by half
    - Odds Ratio 0.51 95%CI [0.46, 0.56]

Ekblom A  NEJM  1990; 323: 1228-1233
Predictive and Protective Factors for CRC in UC

188 cases (UC+CRC) and 188 controls UC

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Pseudopolyps</td>
<td>2.5</td>
<td>1.4-4.6</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>1 or 2 colonoscopies</td>
<td>0.4</td>
<td>0.2-0.7</td>
<td>&lt;.05</td>
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<tr>
<td>Smoking</td>
<td>0.5</td>
<td>0.2-0.9</td>
<td>&lt;.05</td>
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<tr>
<td>Steroid use &gt; 1 yr</td>
<td>0.4</td>
<td>0.2-0.8</td>
<td>&lt;.05</td>
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<tr>
<td>Aspirin</td>
<td>0.3</td>
<td>0.1-0.8</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>0.1</td>
<td>.03-.05</td>
<td>&lt;.05</td>
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<tr>
<td>5-ASA for 1-5 years</td>
<td>0.4</td>
<td>0.2-0.8</td>
<td>&lt;.05</td>
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</tbody>
</table>

Velayos FS Gastroenterology 2006; 130: 1941-9
5-ASA Effect on Colorectal Ca and Dysplasia in UC: Meta-analysis

Any Cancer or dysplasia

Number in each study

Adjusted odds ratio

Velayos FS  Am J Gastro 2005; 100: 1345-53
## 5-ASA Effect on Colorectal Ca and Dysplasia in UC: Meta-analysis

18 UC = Ca matched with 30 UC controls

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th># Cases</th>
<th># Controls</th>
<th>Odds Ratio</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Mesalazine</td>
<td>None</td>
<td>3</td>
<td>1</td>
<td></td>
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<tr>
<td></td>
<td>&lt;4.5 kg</td>
<td>14</td>
<td>15</td>
<td>0.311</td>
<td>0.047</td>
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<tr>
<td></td>
<td>&gt;4.5kg</td>
<td>1</td>
<td>14</td>
<td>0.024</td>
<td></td>
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<tr>
<td>Folic Acid</td>
<td>None</td>
<td>15</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ever</td>
<td>3</td>
<td>18</td>
<td>0.11</td>
<td>0.002</td>
</tr>
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</table>

**Immune Modulator Effect on Colorectal Ca and Dysplasia in UC**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Drug</th>
<th># Patients</th>
<th>Rx Time</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Matula</td>
<td>2005</td>
<td>6-MP</td>
<td>315</td>
<td>8 years</td>
<td>No Effect</td>
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<tr>
<td>Rutter</td>
<td>2004</td>
<td>AZA/6-MP</td>
<td>68</td>
<td>8 years</td>
<td>Non-significant</td>
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<tr>
<td>Lashner</td>
<td>1989</td>
<td>15</td>
<td>98</td>
<td>&gt; 1 year</td>
<td>No Effect</td>
</tr>
</tbody>
</table>
Ursodeoxycholic Acid: Prevention of Colon Neoplasia in UC + PSC

52 patients
UCDA
28-20 mg/kg/day

Pardi DE Gastro 2003; 124: 889-893
High Dose Urso for PSC

- UCDA 28-20 mg/kg/day 76 pt  
  versus  
- Placebo 74 pt
- Liver biopsy prior to Rx & after 5 years
- Study terminated after 6 years—futility
- Risk 2.1x greater with UCDA for:  
  - Death, transplant, minimal listing criteria  
    • P=0.038

Lindor KD Hepatology May 20, 2009 epub
Do Biologics Reduce the Risk of Colon Ca in IBD?

- Plausible
- Not much data so far
  - 1 recent study
Colectomy Rates After Rx with Infliximab vs Placebo

- ACT-1, ACT-2, and extension study
- 728 patients; 87% with 52 wk follow-up
  - Infliximab 484 pt; Placebo 244 pt.
- Colectomy: 10% Infliximab, 17% placebo
  - P=0.02
- Colorectal Ca: Infliximab 1, Placebo 0
- Colon Dysplasia: Infliximab 2, Placebo 1

Sandborn WJ  Gastroenterology 2009 epub
Colonoscopic Surveillance for Dysplasia in IBD

- Initial screening after 8-10 years
- $\geq 33$ biopsies for 90% sensitivity
- 4 quadrant random biopsies each 10 cm
- If initial exam is negative, repeat each 1-2 years
- For PSC begin screening at the time of diagnosis, repeat yearly

Itzkowitz SH. Inflam Bowel Dis 2005; 11: 314-21
Chromoendoscopy Targeted Biopsies

102 patients
Each had:
- Standard exam
- Targeted biopsies
- Methylene blue

Marion JF Am J Gastro 2008; 103: 2342-9
Colectomy for Colon Cancer Risk in IBD: Indications

Absolute

- Flat high-grade dysplasia
- Multifocal flat low-grade dysplasia
- Flat dysplasia plus PSC
- Adenoma-like polyp, DALM, that can’t be removed endoscopically

Colectomy for Colon Cancer Risk in IBD: Indications

Controversial

• Pan-colonic Disease for > 8-10 years
• Unifocal flat low-grade dysplasia
Cancer Prevention and Surveillance in IBD: Summary

Prevention
- Minimize inflammation

Surveillance
- Target high risk patients
- Surveillance colonoscopy