Ulcerative colitis patients with low grade dysplasia should undergo frequent surveillance colonoscopies (and not immediate colectomy)...

David T. Rubin, MD, FACP, AGAF
Associate Professor of Medicine
Co-Director, Inflammatory Bowel Disease Center
University of Chicago Medical Center
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Sometimes

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Why do we do surveillance colonoscopy in UC?

• Prevention of colorectal cancer
• Prevention of death from colorectal cancer
• Because the guidelines tell us to
  – Based on consensus
  – Based on “best” evidence
    • Concepts of field effect
    • Accepted limitations to detection ability in historical approach
Low Grade Dysplasia in ulcerative colitis
Yesterday....

• “Invisible”

• Low-grade dysplasia → subsequent high-grade dysplasia or cancer in 29% - 54% of patients\textsuperscript{1-3}

• Concurrent adenocarcinoma ~19\%\textsuperscript{2-4}

• Distinction not made between flat dysplasia and polypoid dysplasia

\textsuperscript{1}Connell WR et al. Gastroenterology. 1994;107:934-944.

Progression of LGD to Advanced Neoplasia: NYC
Worst Case Scenario?

• 46 patients with UC and flat LGD

• 7 cases of colorectal CA

• Rate of progression \textbf{53\% at 5 years} (point estimate)

• Unifocal LGD same risk as multifocal or recurrent LGD

• 2 patients with an interval NEGATIVE colonoscopy who subsequently had Duke’s C CRC

Ullman T et al., Gastroenterology 2003;125.
Time to Cancer Post–Dysplasia Diagnosis: UK

Kaplan-Meier Method

Probability of Remaining Cancer-Free

Years
0 1 2 3 4 5 6 7 8 9 10

High-grade dysplasia
Low-grade dysplasia

Follow-up of Neoplasia in UC: Chicago

Raised and flat dysplasia in all patients

Progression to HGP/CRC

n=41

Raised dysplasia only
Flat dysplasia

Pekow, et al. Inflamm Bowel Dis, in press.
Chromoendoscopy suggests we are missing dysplasia frequently...

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<tr>
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So where are all the occult cancers?

• We are missing them…?
• They don’t exist
  – Dysplasia found in the current age has a different predictive value than in the previous era
  – LGD doesn’t progress to cancer
  – Current therapies reduce the risk of cancer progression

What happens to dysplasia found on chromoendoscopy?

• Kiesslich (zoom scope)
  – No follow-up
• Kiesslich (confocal laser endomicroscopy)
  – No follow-up
• Hurlstone (zoom scope)
  – No follow-up
• Rutter
  – No follow-up
• Marion\(^1\)
  – Follow-up with colectomy specimens
  – 5 of original 102 had colectomy due to unresectable LGD.
  – No CRC.

\(^1\)Marion J, et al. Am J Gastroenterol, 2008;103:2342
Follow-Up Chromoendoscopy in IBD: a Long-Term, Prospective, Endoscopic Trial (New York)

- 102 patients, 59 had exams in this follow-up

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<td>A: standard surveillance colonoscopy with 4 random biopsies every 10 cm</td>
<td>LGD n=1</td>
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<td>B: targeted biopsy or removal of lesions visible under white light THEN Method C</td>
<td>polypoid LGD n=4, all were resected</td>
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<td>C: methylene blue dye spray segmentally applied throughout the colon with biopsy or removal any pit-pattern abnormality or lesion revealed by the dye spray.</td>
<td>LGD n=7, 6 were resected, one was deemed unresectable.</td>
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- 5 of original 102 had colectomy due to unresectable LGD. **No CRC.**


In fact, cancer rates are lower than we thought previously.... An updated meta-analysis

- 48 studies included in the meta-analysis
- Included both population based and referral centers
- Included 131,743 persons-years of follow up
- Overall cumulative risk at 10, 20 and 20+ years is 1%, 3% and 7%
- Rate higher in referral centers and those with extensive disease

Lutgens MW, et al. DDW 2008: #194
Not all LGD is the same!
Biologically or prognostically

Macroscopic classification of dysplasia illustrated in a hypothetical case of ulcerative colitis with partial colonic involvement. Dysplasia is shown in black, normal colon in yellow, diseased colon in red.

Itzkowitz S. and Harpaz N. Gastroenterology 126:1634, 2004

We can SEE neoplasia in IBD most of the time (U.K., Chicago)

• “Invisible”: indistinguishable from surrounding inflamed or quiescent mucosa
• “Visible”
  – Polypoid “adenoma-like” lesion
  – Irregular borders “spreading” lesion, not endoscopically resectable (DALM)
  – Mass
  – Stricture
• Optical colonoscopy sensitivity (retrospective studies1,2):
  – Per lesion sensitivity: 61.6%-77.3%
  – Per patient sensitivity: 78.3%-89.3%

Modeling dysplasia detection: how does more accurate biopsies affect the 33 biopsy rule??

- Enhanced endoscopy can detect much smaller dysplastic fields.
- The proportion of negative biopsies is inversely predictive of the size of the dysplastic field.
- If we can detect dysplasia more accurately, the predictive value is different!
- Such “dysplastic fields” have “unknown (perhaps much lower) colorectal cancer risk.”


Patients don’t want colectomy for LGD... even if the 19% number is accurate (which it probably isn’t)

- Patient survey: Dartmouth and Univ of Chicago (n=199)
- 60% of patients would refuse colectomy if their risk of synchronous colon cancer was 20% (as reported with flat LGD)
- The refusers would only agree to colectomy if their risk of synchronous colon cancer was on average 73%

Siegel CA, et al. Submitted 2009
Balancing risks and benefits of colectomy for LGD

• Colectomy adversely affects quality of life when you’ve been in remission (average 6 stools per day)

• Risk of colectomy
  – Anesthesia mortality (1/100,000)
  – Colectomy mortality <1%
  – Small bowel obstruction 28%
  – Dehydration 14%


The paradigm shift in our approach to IBD dysplasia...

• If we can see it, we should be able to follow it

• The results:
  – new information about the natural history of CRC in UC
  – new information about the predictive value of neoplastic lesions
  – fewer colectomies
  – happier patients
  – unhappy surgeons?
Who should NOT be followed?
Considerations

Higher Risk
• Unresectable lesion
• PSC
• Uncontrolled inflammation in addition to dysplasia
• Pseudopolyposis

The Patient who won’t let you
• Poor prep
• Non-compliant
• No follow-up

Rubin’s Rules for Following LGD

• Surveillance must be performed correctly: clean prep, careful exam, adequate biopsies
• Confirm the diagnosis – review of histopathology
• Discuss the controversy with your patient
• Get a second opinion
• Polypoid dysplasia (without flat dysplasia) completely removed can be followed with increased surveillance intensity (3 months *1 then q6 months *2…)
• *Repeated dysplasia, higher grade lesions or increased sphincter tone (yours) should trigger colectomy
• If you live in NYC, all bets are off....
Times have Changed....

Take the colon out!

Follow with care!