Post-Colonoscopy Cancer: Giving Feedback to the Endoscopist

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60 yo woman, screening colonoscopy: normal. Recommended next screening colonoscopy in 10 years. But 3 years later, she develops anemia.
How to solve the problem?

Sum of errors

Post-colonoscopy cancer
Research has established that people do not develop true understanding of a complex subject by listening passively to explanations.

True understanding comes only when learners actively construct their own understanding (mental representations) via a process of mentally building on their prior thinking and knowledge…

Feedback

Timely

Targeted

Actionable

Constructive

Targeted

Actionable

Constructive

Timely
Goals

- Identify non-observable ('hidden') causes of PCCRC
- Determine potential solutions to prevent such PCCRCs using expert decisions frameworks
- Develop effective strategies for quality assurance in colonoscopy. Special attention paid to education
'Unpacking' the problem...
Case

60 yo male, screening CS, during insertion suspicion flat lesion? Next recommended CS in 10 years

2 years later: pT1 tumor
Step 1. Is this a PCCRC?

Step 2. What type of PCCRC?

**Definition:** Cancer occurring after a colonoscopy in which no cancer is diagnosed.
Step 3. What is the most likely explanation?

- Initial colonoscopy
  - Interval from previous procedure > 4 years?
    - No
      - AA* same bowel segment?
        - Yes
          - Lesion resected?
            - Yes
              - Likely incomplete resection of previously identified lesion
            - No
              - Detected lesion not resected
    - Yes
      - Likely new cancer

*The modifying statement: deviation from the planned management pathway can be added where applicable
*≥10mm and/or villous histology and/or HGD

Rutter et al, Gastroenterology 2018
How to give feedback to the endoscopist?

A. Longer withdrawal time/ better technique?
B. Repeat CS with careful inspection and use of IEE techniques to target the suspect area?
C. Overall ADR?
D. Ability to detect NPCRNs?
How does non-polypoid (flat and depressed) colorectal neoplasm tie to PCCRC?
Japan Polyp Study: LST-NG is an important contributor to PCCRC

Randomised comparison of post-polypectomy surveillance intervals following a two-round baseline colonoscopy: the Japan Polyp Study Workgroup

>50% of advanced neoplasms during 3 year follow up were LST-NGs; 70% in proximal colon
Risk factors for metachronous advanced neoplasms

Watch out!

Matsuda et al, JPS, Gut 2020

<table>
<thead>
<tr>
<th>Risk factors at baseline</th>
<th>OR (95%CI)</th>
</tr>
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<tbody>
<tr>
<td>Multiple adenomas</td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>2.8 (1.4-5.9)</td>
</tr>
<tr>
<td>3-4</td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td></td>
</tr>
<tr>
<td>Morphology Flat (&lt;10mm)</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>3 (1.01-12.1)</td>
</tr>
<tr>
<td>Present</td>
<td>6.6 (2.1-17.6)</td>
</tr>
<tr>
<td>Family history - FDR with CRC</td>
<td>2.4 (1.1-5.4)</td>
</tr>
<tr>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>Large, proximal SSL</td>
<td>No risk factor</td>
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</table>
### High yield of synchronous/metachronous CRNs in patients with NPCRN/LST

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Method</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Zhan et al, BMC Gastroenterol 2015 (Germany)</td>
<td>802 patients</td>
<td>Follow up of patients referred for EMR of LSTs &gt; 20 mm</td>
<td>Frequent co-occurrence of HGD (67.2%) in large flat colonic polyps (&gt;20 mm) and synchronous polyps</td>
</tr>
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<td>Bick et al, Gastrointest Endosc 2016 (US)</td>
<td>728 patients with large LSTs</td>
<td>Prospective cohort, follow up</td>
<td>High yield of synchronous lesions in referred patients with large LSTs (traditional adenomas or SSL)</td>
</tr>
<tr>
<td>McGill et al, CGH 2017 (US)</td>
<td>4454 patients referred for CS</td>
<td>Prospective cohort, follow-up</td>
<td>Patients with NPCRN more often had advanced neoplasms at baseline (63% vs. 25%) and were more often diagnosed with advanced neoplasms (RR: 1.6, 95% CI 1.05–2.6) during the first surveillance CS than patients with polyoid CRNs</td>
</tr>
<tr>
<td>Torella et al, Arq Gastroenterol 2019 (Argentina)</td>
<td>70 patients with large LSTs</td>
<td>Follow-up of patients referred for resection of LSTs &gt; 20 mm</td>
<td>Increased risk (38.5%) of synchronous colorectal lesions in patients referred for endoscopic mucosal resection of large LSTs (traditional adenomas or SSL)</td>
</tr>
<tr>
<td>Bogie et al, UEGJ 2020 (NL)</td>
<td>8120 patients, 151 had LSTs at baseline</td>
<td>Prospective cohort, follow-up</td>
<td>LST patients more often developed metachronous CRNs (71.6% vs. 54.2%, P=0.04) and CRNs with HGD/SMI than large polyoid CRN patients (36.4% vs. 15.8%, P &lt; 0.001).</td>
</tr>
</tbody>
</table>
Systematic training on detection & resection of NP-CRN reduced PCCRC rate

Before training: 2 PCCRC per 1000 colonoscopies
After training: 0.8 PCCRC per 1000 colonoscopies (45% missed lesions)

van de Wetering et al, Gastrointest Endosc 2017
Learning-curve for the detection of NPC RN is steep

Figure 1: Learning curve for detection of non-polypoid neoplasms over time among four endoscopists. Detection rates are plotted as percentage of patients with at least one non-polypoid colorectal neoplasm found per sequential 200-colonoscopy blocks since training. 

McGill et al, Gut 2014

Sanduleanu et al, Gastroint Endosc 2016
What do you see?

color difference
absent innominate grooves
spontaneous bleeding
cloud-like appearance
Color difference
Absent innominate grooves

Courtesy of HM Chiu, NTUH
What do we know about LSTs?

Meta-analysis
2949 studies
48 included

Overall:
8.5% (6.5%–10.5%)
contain SMI

Risk of SMI differs by endoscopic subtype

Meta-analysis, Bogie et al, Endoscopy 2017
Case

50 yo healthy male
Normal screening colonoscopy.
Next recommended CS in 10 years but... 5 years later he develops anemia and colonoscopy shows cancer.

IHC: MMR deficient tumor

5 years later pT2 adenocarcinoma in the proximal colon

Lynch syndrome
How to give feedback to the endoscopist?

A. Awareness/education on hereditary CRC
B. Take a detailed family history
C. Knowledge base on genetic diagnosis
D. Instruct the patient to report new cancer cases in his family; clinical risk re-evaluation after 3-5 years?
E. Highest quality in performance of CS surveillance
A. Lynch syndrome: MMR deficient/MSI, fast-growing, often nonpolypoid and proximally located.

- MMR deficient neoplasms are often:
  - Flat
  - Proximally located

B. Sporadic CRC: MMR proficient/MSS, slow-growing, often polypoid and distally located.

Edelstein et al, CGH 2011
Rondagh et al, Endoscopy 2013
Macroscopic appearance of PCCRC

Early stage PCCRCs are more often flat than prevalent CRCs
OR 1.7, 95% CI 1.2-2.4

leClercq et al, Gut 2014
Specific features for Lynch tumors?
- Poor differentiation
- Inflammatory Crohn-like infiltrates
- Mucinous differentiation
- Signet-ring cells
- Medullary differentiation

Histology of PCCRCs

Poorly differentiated adenocarcinoma
Most likely explanation of PCCRC

10% of PCCRCs in high-risk* groups

43% of PCCRCs in high-risk# groups

Retrospective analysis
Single center
2015-2016
48 PCCRCs

Retrospective analysis
Single center
2010-2017
107 PCCRCs

*High-risk: Genetic syndromes IBD

Beaton et al, Endoscopy 2021

**High-risk:
Hereditary CRC, IBD, post colon resection for CRC, multiple complex polyps

Anderson R et al, Gastroenterology 2020
What’s the take-home message for the endoscopist?

A. Education
B. Education
C. Education
D. Education
Key points

❖ A significant proportion of PCCRCs are attributable to missed nonpolypoid colorectal neoplasms (LSTs nongranular) and high-risk conditions for CRC (hereditary CRC, IBD, post colon resection for CRC). Efforts are underway to train this know-how using the novel concepts of education science.

❖ In-depth analysis of PCCRC cases can be performed using expert decisions framework. This approach helps to design targeted interventions and provide feedback to the community.
Thank you