Colonoscopy surveillance; international cohort studies

Ernst J. Kuipers
Colonoscopic Polypectomy and Long-Term Prevention of Colorectal-Cancer Deaths

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Figure 2. Cumulative Mortality from Colorectal Cancer in the General Population, as Compared with the Adenoma and Nonadenoma Cohorts.

Zauber AG, et al. NEJM 2012, Feb 23
The incidence of interval cancer after screening colonoscopy depends on adenoma detection rates.

ORs for interval cancer with ADR < 20% vs ADR > 20%: 10.9 – 12.5

Kaminski M et al. NEJM 2010
## Risk of interval cancer after colonoscopy in relation to ADR

<table>
<thead>
<tr>
<th>Patient underwent colonoscopy in setting with ADR</th>
<th>RR for interval cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;30%</td>
<td>1.0</td>
</tr>
<tr>
<td>15 – 30%</td>
<td>1.90 (0.83 – 4.39)</td>
</tr>
<tr>
<td>&lt;15%</td>
<td>3.61 (1.33 – 9.81)</td>
</tr>
</tbody>
</table>
Interval cancers after colonoscopy; a pooled multi-cohort analysis

Table 3  Description of CRC cases by study

<table>
<thead>
<tr>
<th>Study (N)</th>
<th>APPS (837)</th>
<th>CPPS (913)</th>
<th>AFT (1086)</th>
<th>PPT (2024)</th>
<th>WBF (1304)</th>
<th>NPS (939)</th>
<th>VA (871)</th>
<th>UDCA (1193)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC, N (%/N study)</td>
<td>5 (0.6)</td>
<td>8 (0.9)</td>
<td>6 (0.6)</td>
<td>13 (0.6)</td>
<td>8 (0.6)</td>
<td>3 (0.3)*</td>
<td>8 (0.9)</td>
<td>7 (0.6)</td>
<td>58 (0.6)</td>
</tr>
<tr>
<td>Cancer/1000 person-years follow-up</td>
<td>1.52</td>
<td>2.24</td>
<td>1.77</td>
<td>1.52</td>
<td>1.77</td>
<td>1.14*</td>
<td></td>
<td>2.14</td>
<td>1.69</td>
</tr>
<tr>
<td>Stage I or II CRC N</td>
<td>5</td>
<td>6</td>
<td>5</td>
<td>8</td>
<td>8</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>Right sided N (%)</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>29</td>
</tr>
<tr>
<td>Died CRC N (%)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>9</td>
</tr>
</tbody>
</table>

*Does not include two cancers detected after the first 3 years of this study during a longer period of clinical follow-up as reported elsewhere. 15

AFT, Aspirin Folate Trial; APPS, Antioxidant Polyp Prevention Study; CPPS, Calcium Polyp Prevention Study; CRC, colorectal cancer; NPS, National Polyp Study; PPT, Polyp Prevention Trial; UDCA, Ursodoxycyclic Acid Study; VA, Veterans Affairs Cooperative Study; WBF, Wheat Bran Fiber Study.

Table 4  Association of proposed explanation for interval cancer and location of interval cancer

<table>
<thead>
<tr>
<th>Proposed explanation for interval cancer</th>
<th>Median time from baseline colonoscopy (years)</th>
<th>Location of interval cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Right (N=29)*</td>
</tr>
<tr>
<td>Missed (N=30)</td>
<td>2.3</td>
<td>19 (65.5)</td>
</tr>
<tr>
<td>Incomplete removal (N=11)</td>
<td>2.9</td>
<td>4 (13.8)</td>
</tr>
<tr>
<td>New (N=14)</td>
<td>3.5</td>
<td>4 (13.8)</td>
</tr>
<tr>
<td>Failed biopsy detection (N=3)</td>
<td>2.0</td>
<td>2 (6.9)</td>
</tr>
</tbody>
</table>

*Right colon defined as proximal to the splenic flexure.
Adherence to colonoscopy surveillance; a community-based cohort

- 2990 adenoma patients, median follow-up 48 months
Colonoscopy surveillance; a community-based cohort

• 2990 adenoma patients, median follow-up 48 months

• Diagnosis during surveillance:
  – 7% of patients diagnosed with advanced adenoma
  – 32% diagnosed with non-advanced adenoma
  – 61% no neoplastic lesion

Van Heijningen EM et al. Gastroenterol 2013; 144:1410-8
Colonoscopy surveillance; a community-based cohort

- 2990 adenoma patients, median follow-up 48 months

- Risk factors for advanced neoplasia during surveillance:
  - Adenoma size $\geq 10$ mm (OR 1.7; 1.2 – 3.3)
  - Adenoma number (OR 1.6 – 3.3 for 2 - $\geq 5$ adenomas)
  - Proximal location (OR 1.6; 1.2 – 2.3)
  - Villous histology (OR 2.0; 1.2 – 3.2)
  - Incomplete baseline colonoscopy (OR 3.2; 1.2 – 8.5)
  - Insufficient bowel prep (OR 3.4; 1.6 – 7.4)

Van Heijningen EM et al. Gastroenterol 2013; 144:1410-8
Colonoscopy surveillance

• The optimal surveillance interval depends on

  – Baseline findings
    • number and size of neoplastic lesions

  – Quality of the baseline exam
    • bowel prep
    • detection
    • removal
US and European adenoma surveillance guidelines

**US guideline**
- Lower risk; 1-2 small ads w LGD
- Higher risk; 3-10 ads and/or at least 1 large and/or villous histology or HGD
- Highest risk; >10 ads

**European guideline**
- Low risk; 1-2 small ads
- Intermediate risk; 3-4 small ads or at least 1 large
- High risk; >4 small ads or >2 ads with at least one large

- 5-10 yr
- 3 yr
- < 3 yr
- 5 yr or no surveillance
- 3 yr
- 1 yr

AsiaPacific colonoscopy surveillance recommendations

<table>
<thead>
<tr>
<th>Baseline colonoscopy: most advanced finding(s)</th>
<th>Recommended surveillance interval (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No polyps</td>
<td>10</td>
</tr>
<tr>
<td>Small (&lt;10 mm) hyperplastic polyps in rectum and sigmoid</td>
<td>10</td>
</tr>
<tr>
<td>1–2 small (&lt;10 mm) tubular adenomas</td>
<td>5–10</td>
</tr>
<tr>
<td>3–10 tubular adenomas</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10 adenomas</td>
<td>&lt;3</td>
</tr>
<tr>
<td>One or more tubular adenomas ≥10 mm</td>
<td>3</td>
</tr>
<tr>
<td>One or more villous adenomas</td>
<td>3</td>
</tr>
<tr>
<td>Adenoma with high-grade dysplasia</td>
<td>3</td>
</tr>
<tr>
<td>Serrated lesions</td>
<td>3</td>
</tr>
<tr>
<td>Sessile serrated polyp(s) &lt;10 mm with no dysplasia</td>
<td>5</td>
</tr>
<tr>
<td>Sessile serrated polyp(s) ≥10 mm OR</td>
<td>3</td>
</tr>
<tr>
<td>Sessile serrated polyp with dysplasia OR</td>
<td>3</td>
</tr>
<tr>
<td>Traditional serrated adenoma</td>
<td>1</td>
</tr>
<tr>
<td>Serrated polyposis syndrome</td>
<td>1</td>
</tr>
</tbody>
</table>

The impact of colonoscopy surveillance on CRC incidence in the UK

<table>
<thead>
<tr>
<th>N surveillance colonoscopies</th>
<th>N patients</th>
<th>N CRCs</th>
<th>Multivariable HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>51.942</td>
<td>121</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>29.503</td>
<td>51</td>
<td>0.57 (0.40 – 0.80)</td>
</tr>
<tr>
<td>2</td>
<td>12.663</td>
<td>22</td>
<td>0.51 (0.31 – 0.84)</td>
</tr>
<tr>
<td>≥3</td>
<td>6.296</td>
<td>16</td>
<td>0.54 (0.29 – 0.99)</td>
</tr>
</tbody>
</table>

The impact of colonoscopy surveillance on CRC incidence in the UK

High-risk subgroup:
- Suboptimal colonoscopy
- Proximal polyps
- High-grade or >20 mm lesion
Netherlands: 100,000 additional colonoscopies required for FIT-based program

Total population 17 million, target population (55 – 75 yr) 3.5 million
Annual number of German men undergoing colonoscopy screening

Brenner H et al. Gastroenterology 2015
European Polyp Surveillance (EPoS) trials

EPoS I
1-2 non-advanced adenomas
13,700 patients

NS
5 yr
10 yr

EPoS II
3-10 non-advanced, or ≥1 advanced adenoma
13,700 patients

3 yr
5 yr
10 yr

EPoS III
Serrated polyps ≥10 mm, or ≥5 mm prox
No sample size

NS
5 yr
10 yr

## Surveillance recommendations after treatment for treatment for CRC

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>II–III</td>
<td>I–IV: colon/rectum*</td>
<td>I–III</td>
</tr>
<tr>
<td>History and/ or physical exam</td>
<td>Every 3–6 mo. for 5 yrs</td>
<td>Every 3–6 mo. for 2 yrs</td>
<td>Every 3–6 mo. for 3 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Every 6 mo. in yrs 3–5</td>
<td>Every 6–12 mo. in yrs 4–5</td>
</tr>
<tr>
<td>Serum CEA test</td>
<td>Every 3–6 mo. for 5 yrs</td>
<td>Every 3–6 mo. for 2 yrs</td>
<td>Every 3–6 mo. for 3 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Every 6 mo. in yrs 3–5</td>
<td>Every 6mo in yrs 3–5</td>
</tr>
<tr>
<td>Chest CT</td>
<td>Annually, or every 6–12 mo. for high-risk pts, for 3 yrs</td>
<td>Every 6–12 mo. for 3 yrs</td>
<td>Every 3–6 mo. for 2 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Every 6–12 mo. for 3 yrs</td>
<td>Every 6–12 mo. in yrs 3–5</td>
</tr>
<tr>
<td>Abdominal CT</td>
<td>Annually, or every 6–12 mo. for high-risk pts, for 3 yrs</td>
<td>Every 6–12 mo. for 3 yrs</td>
<td>Every 3–6 mo. for 2 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Every 3–6 mo. for 3 yrs</td>
<td>Every 6–12 mo. in yrs 3–5</td>
</tr>
<tr>
<td>Pelvic CT</td>
<td>Annually or every 6–12 mo. for high-risk pts, for up to 3 yrs, or up to 5 yrs for pts with rectal cancer</td>
<td>Annually for 5 yrs</td>
<td>Every 3–6 mo. for 2 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NA</td>
<td>Every 6–12 mo. in yrs 3–5</td>
</tr>
<tr>
<td>Liver CEUS</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Can substitute for abdominal CT</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>At 1yr; every 5 yrs thereafter</td>
<td>At 1 yr</td>
<td>At 1 and 4 yrs, then every 5 yrs; annually if advanced adenoma is detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>At 1 yr; every 3–5 yrs thereafter</td>
<td>At 1 and 4 yrs, then every 5 yrs; annually if advanced adenoma is detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NA</td>
<td>At 1 yr; then every 5 yrs</td>
</tr>
</tbody>
</table>

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Conclusions (1)

- Adenoma patients are at increased risk for recurrent neoplasia
- Colonoscopy surveillance can reduce CRC incidence and mortality
- This in particular pertains to patients with advanced neoplasia
Conclusions (2)

- Most data on neoplasia recurrence and impact of surveillance come from historical series with lower than current quality standards.
- Surveillance puts significant burden on resources, with for many patients lower impact than the baseline exam.
- The optimal surveillance schedule remains to be determined, also taking current quality standards into account.