Are PCCRC More Lethal than Detected CRC?

A Canadian Perspective
Mechanisms

Late detection = more advanced disease

Missed neoplasia

Incomplete resection

Aggressive tumour biology

New neoplasia
### Table 2  Stage at diagnosis of study cohort (2007–20 subgroup)

<table>
<thead>
<tr>
<th>Stage at diagnosis</th>
<th>All patients (n=20 055)</th>
<th>DETECTED (n=12 930)</th>
<th>PCCRC (n=1331)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missing</td>
<td>2575 (12.8%)</td>
<td>1399 (10.8%)</td>
<td>247 (18.6%)</td>
</tr>
<tr>
<td>0/I*</td>
<td>4032 (20.1%)</td>
<td>3244 (25.1%)</td>
<td>328 (24.6%)</td>
</tr>
<tr>
<td>II</td>
<td>4804 (24.0%)</td>
<td>3278 (25.4%)</td>
<td>264 (19.8%)</td>
</tr>
<tr>
<td>III</td>
<td>5164 (25.7%)</td>
<td>3519 (27.2%)</td>
<td>306 (23.0%)</td>
</tr>
<tr>
<td>IV</td>
<td>3480 (17.4%)</td>
<td>1490 (11.5%)</td>
<td>186 (14.0%)</td>
</tr>
</tbody>
</table>

**Disease Stage?**

Majority of studies demonstrate PCCRC present at *earlier* stages

Govindarajan et al.: greater stage IV disease among PCCRC
Challenges

Rarity of outcome
Small samples

Lead time bias
Immortal time bias

Limitations of administrative data
Clinical and Molecular Characteristics of Post-Colonoscopy Colorectal Cancer: A Population-based Study

Elena M. Stoffel,1,2 Rune Erichsen,2 Trine Frøslev,2 Lars Pedersen,2 Mogens Vyberg,3 Erika Koeppé,1 Seth D. Crockett,5 Stanley R. Hamilton,4 Henrik T. Sørensen,2 and John A. Baron5

1Department of Internal Medicine, University of Michigan Health System, Ann Arbor, Michigan; 2Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark; 3Institute of Pathology, Department of Clinical Medicine, Aalborg University Hospital, Aalborg, Denmark; 4Division of Pathology and Laboratory Medicine, The University of Texas, MD Anderson Cancer Center, Houston, Texas; and 5Department of Internal Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

See Covering the Cover synopsis on page 777; see editorial on page 793.

Keywords: Colorectal Neoplasm; Colon Cancer; Interval Cancer; Surveillance.
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16% misclassification

- Index exam was flexible sigmoidoscopy
- Patient had a CRC diagnosis
- Pathology review did not confirm CRC
PRIMARY AIM

Evaluate patient, procedural, and endoscopist characteristics associated with PCCRC

SECONDARY AIM

Compare long term outcomes between PCCRC and detected CRC
Clinical and endoscopist factors associated with post-colonoscopy colorectal cancer in a population-based sample

Fahima Dossa\textsuperscript{1,2} | Rinku Sutrads\textsuperscript{2,3,4} | Refik Saskin\textsuperscript{2,3} | Eugene Hsieh\textsuperscript{5} | Pauline Henry\textsuperscript{6} | Devon P. Richardson\textsuperscript{7} | Pierre-Anthony Leake\textsuperscript{8} | Shawn S. Forbes\textsuperscript{9} | Lawrence F. Paszat\textsuperscript{2,3,10} | Linda Rabeneck\textsuperscript{2,3,11,12} | Nancy N. Baxter\textsuperscript{2,3,13,14}

COLORECTAL DISEASE. 2021; 23:635-645
Clinical and endoscopist factors associated with post-colonoscopy colorectal cancer in a population-based sample

Design
Population-based study

Population
Patients diagnosed with CRC between 2000-2005

Colonoscopy complete to cancer location

Exclusions: pre-existing CRC, IBD, colonic resection

Definitions
Detected CRC: colonoscopy claim submitted between 0 and 180 days prior to diagnosis

PCCRC: colonoscopy claim submitted between 181 days to 36 months prior to diagnosis
Diagnostic Confirmation

1. Institution Assignment
   - Location of surgery
   - Cancer-related admission
   - Colonoscopy location

2. Random Sampling and Matching
   - Institution-based sampling frame
   - 500 PCCRC matched to detected CRC from same institution

3. Chart review
   - Reviewed colonoscopy reports and admission notes
Survival Analysis

Secondary outcome: overall survival

Time zero: date of diagnosis

Kaplan Meier survival analysis

Cox PHM: covariates included age, sex, tumour location
Diagnostic Confirmation

8% met administrative definition of PCCRC

Detected CRC: 95% confirmed

PCCRC: 84% confirmed

Reasons for misclassification:
- Flexible sigmoidoscopy
- PCCRC classified as detected and vice versa
- Insufficient information for classification
# Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Detected (n=412)</th>
<th>PCCRC (n=367)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>67.3</td>
<td>71.6</td>
</tr>
<tr>
<td>FEMALE SEX</td>
<td>38.8%</td>
<td>48.0%</td>
</tr>
<tr>
<td>SYMPTOMS</td>
<td>75.0%</td>
<td>63.5%</td>
</tr>
<tr>
<td>COMPLETE SCOPE</td>
<td>76.2%</td>
<td>86.4%</td>
</tr>
<tr>
<td>PROXIMAL TUMOUR</td>
<td>32.8%</td>
<td>54.2%</td>
</tr>
</tbody>
</table>
Overall Survival

Unadjusted 5-year OS:
- 49.7% PCCRC
- 61.2% Detected

![Graph showing survival probability over time with two lines representing detected and PCCRC cancers. The Log-rank test p-value is 0.003.]

<table>
<thead>
<tr>
<th>Time to death (years)</th>
<th>Number at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Detected cancers</td>
</tr>
<tr>
<td>0</td>
<td>412</td>
</tr>
<tr>
<td>1</td>
<td>330</td>
</tr>
<tr>
<td>2</td>
<td>275</td>
</tr>
<tr>
<td>3</td>
<td>228</td>
</tr>
<tr>
<td>4</td>
<td>207</td>
</tr>
<tr>
<td>5</td>
<td>192</td>
</tr>
</tbody>
</table>
Multivariable analysis

Adjusted for age, sex, tumour location

HR: 1.12
[95%CI: 0.92-1.32]

No statistically significant difference in overall survival
Tumour Location?
<table>
<thead>
<tr>
<th>Context</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excluded high risk patients</td>
<td>Prior CRC, IBD, colorectal surgery</td>
</tr>
<tr>
<td>Colonoscopy to site of cancer</td>
<td>Requirement for inclusion</td>
</tr>
<tr>
<td>Diagnostic confirmation</td>
<td>Chart review to decrease misclassification</td>
</tr>
<tr>
<td>Causal pathways</td>
<td>Did not adjust for tumour stage</td>
</tr>
</tbody>
</table>

Other features of this study that may explain why results differ from studies demonstrating survival differences
Mechanisms

- Late detection = more advanced disease
- Aggressive tumour biology

Missed neoplasia

Incomplete resection

New neoplasia
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A Canadian Perspective

FAHIMA DOSSA, MD PHD(C)
DEPARTMENT OF SURGERY
INSTITUTE OF HEALTH POLICY, MANAGEMENT, AND EVALUATION
UNIVERSITY OF TORONTO

FAHIMA.DOSSA@MAIL.UTORONTO.CA
@FDOSSTA