Post-Colonoscopy Colorectal Cancer: Current Status and Future Directions

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Disclosures

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Thank You

- Matt Rutter MD, PhD
- Evelien Dekker MD, PhD
- Doug Corley MD, PhD
- Silvia Sanduleanu MD, PhD
- PCCRC Expert Working Group
- WEO CRC Screening Committee
- WEO Members
- CHORD Research Team
Agenda

- Discuss the burden and importance of post-colonoscopy colorectal cancer (PCCRC)

- Understand how standardized nomenclature and methodology is critical for PCCRC studies

- Provide the latest evidence on PCCRC rates globally and the underlying cause of PCCRC

- Discuss future directions
Post-Colonoscopy Colorectal Cancer is a Global Concern

3-10% of all CRCs diagnosed worldwide are PCCRCs

Rutter M et al. Gastroenterology 2018
Post-Colonoscopy CRC is a Quality Issue

Quality Indicators for Colonoscopy and the Risk of Interval Cancer

Michal F. Kaminski, M.D., Jaroslaw Regula, M.D., Ewa Kraszewska, M.Sc., Marcin Polkowski, M.D., Urszula Wojciechowska, M.D., Joanna Didkowska, M.D., Maria Zwierko, M.D., Maciej Rupinski, M.D., Marek P. Nowacki, M.D., and Eugeniusz Butruk, M.D.

Adenoma Detection Rate and Risk of Colorectal Cancer and Death

Douglas A. Corley, M.D., Ph.D., Christopher D. Jensen, Ph.D., Amy R. Marks, M.P.H., Wei K. Zhao, M.P.H., Jeffrey K. Lee, M.D., Chyke A. Doubeni, M.D., M.P.H., Ann G. Zaber, Ph.D., Jolanda de Boer, M.B., Bruce H. Fireman, Ph.D., Joanne E. Schottinger, M.D., Virginia P. Quinn, Ph.D., Nirupa R. Ghai, Ph.D., Theodore R. Levin, M.D., and Charles P. Quesenberry, Ph.D.

Longer Withdrawal Time Is Associated With a Reduced Incidence of Interval Cancer After Screening Colonoscopy

Aasma Shaukat,1,2,3 Thomas S. Rector,3 Timothy R. Church,4 Frank A. Lederle,3 Adam S. Kim,5 Jeffery M. Rank,5 and John I. Allen6

Increased Rate of Adenoma Detection Associates With Reduced Risk of Colorectal Cancer and Death

Michal F. Kaminski,1,2,3,4* Paulina Wieszczy,1,2,4* Maciej Rupinski,1,2 Urszula Wojciechowska,5 Joanna Didkowska,3 Ewa Kraszewska,3 Jaroslaw Kobiela,2,6 Robert Franchyk,1,2 Maria Rupinska,1,2 Bartlomiej Kocot,5 Anna Chaber-Ciapinska,1,2 Jacek Pachlewski,1 Marcin Polkowski,1,2, and Jaroslaw Regula1,2
UK key performance indicators and quality assurance standards for colonoscopy

Colin J Rees,1,2,3 Siwan Thomas Gibson,4 Matt D Rutter,2,3,5 Phil Baragwanath,6 Rupert Pullan,7 Mark Feeney,7 Neil Haslam,8 on behalf of: the British Society of Gastroenterology, the Joint Advisory Group on GI Endoscopy, the Association of Coloproctology of Great Britain and Ireland
CONSENSUS STATEMENT

World Endoscopy Organization Consensus Statements on Post-Colonoscopy and Post-Imaging Colorectal Cancer

Post-Colonoscopy Colorectal Cancer Definition

Definition: Cancer occurring after a colonoscopy in which no cancer is diagnosed

Interval Type PCCRC
Detected before recommended screening or surveillance interval

Non-interval Type PCCRC
Detected at / after recommended screening or surveillance interval

Rutter M et al. Gastroenterology 2018
WEO Standardized PCCRC Rate Calculation

- Denominator = CRCs occurring within 3 years of a colonoscopy

- Rates calculated from year of colonoscopy
  - Detected CRC [TP] = CRC diagnosed within 6 month of the colonoscopy
  - PCCRC [FN] = CRC diagnosed 6-36 month after the colonoscopy

- PCCRC-3yr Rate = FN / [TP + FN]
Published PCCRC Rates using WEO Methodology
Pooled PCCRC Rate – WEO Methodology

### Precise Methodology

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burr 2019</td>
<td>7.39 (7.24, 7.53)</td>
<td>25.56</td>
</tr>
<tr>
<td>Cheung 2019</td>
<td>7.86 (7.36, 8.39)</td>
<td>24.56</td>
</tr>
<tr>
<td>Pedersen 2019</td>
<td>10.42 (9.96, 10.89)</td>
<td>24.75</td>
</tr>
<tr>
<td>Forsberg 2020</td>
<td>6.98 (6.63, 7.35)</td>
<td>25.11</td>
</tr>
<tr>
<td>Overall (I^2 = 98.17%, p = 0.00)</td>
<td>8.15 (6.92, 9.38)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

### Unadjusted Methodology

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breslau 2007</td>
<td>3.44 (3.13, 3.78)</td>
<td>11.20</td>
</tr>
<tr>
<td>Singh 2010</td>
<td>7.95 (7.20, 8.74)</td>
<td>10.61</td>
</tr>
<tr>
<td>Cooper 2014</td>
<td>7.25 (7.04, 7.46)</td>
<td>11.27</td>
</tr>
<tr>
<td>Gevindasen 2016</td>
<td>9.20 (8.89, 9.52)</td>
<td>11.19</td>
</tr>
<tr>
<td>Burr 2019</td>
<td>7.67 (7.53, 7.83)</td>
<td>11.30</td>
</tr>
<tr>
<td>Cheung 2019</td>
<td>7.86 (7.36, 8.39)</td>
<td>11.00</td>
</tr>
<tr>
<td>Macken 2019</td>
<td>7.40 (7.10, 7.71)</td>
<td>11.21</td>
</tr>
<tr>
<td>Pedersen 2019</td>
<td>8.95 (8.51, 9.42)</td>
<td>11.07</td>
</tr>
<tr>
<td>Forsberg 2020</td>
<td>7.22 (6.85, 7.59)</td>
<td>11.15</td>
</tr>
<tr>
<td>Overall (I^2 = 98.98%, p = 0.00)</td>
<td>7.43 (6.45, 8.42)</td>
<td>100.00</td>
</tr>
</tbody>
</table>
Chart Autopsy of PCCRC Cases – What’s the Cause?

Initial Colonoscopy

- Interval from prior colonoscopy >4 years?
  - Yes: Likely new cancer
  - No: Advanced adenoma in same segment?
    - Yes: Advanced adenoma resected?
      - Yes: Cecum intubated + adequate prep?
      - No: Incomplete resection
    - No: Advanced adenoma resected?
      - Yes: Detected lesion
      - No: Missed lesion

Rutter M et al. Gastroenterology 2018
Most Plausible Explanation of PCCRCs: UK Study

- Missed lesion, exam adequate: 27%
- Missed lesion, exam inadequate: 58%
- Detected lesion, not resected: 8%
- Incomplete resection: 7%
Most Plausible Explanation of PCCRCs: UK Study

- Missed lesion, exam inadequate: 25%
- Detected lesion, not resected: 9%
- Missed lesion, exam adequate: 66%

Beaton D et al. Endoscopy 2021
Most Plausible Explanation of PCCRCs: US Study

- Missed lesion, exam adequate: 73%
- Detected lesion, not resected: 6%
- Missed lesion, exam inadequate: 3%
- Incomplete resection: 18%

Leung L et al. DDW 2021 – PRELIMINARY DATA
Summary

- PCCRC rate is an important quality measure for colonoscopy services
- Standardization in nomenclature and methodology are critical for benchmarking
- PCCRC rate $\approx 8\%$ [95% CI: 6.9-9.4] or 1 out of 12 patients diagnosed with CRC
- Most common cause of PCCRC cases $< 4$ years $\rightarrow$ missed lesions ($\approx 80\%-90\%)$
Future Directions

- More studies are needed across the globe for PCCRC rate benchmarking - ideal target?
- What interventions are effective in reducing PCCRC rates?
- How do we drive down PCCRC rates in high-risk groups (e.g., Lynch, IBD)?
- What are the main drivers of PCCRC? More PCCRC audits are needed.
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