Impact of family history of CRC on the prevention of early-onset CRC: a multicenter study

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Background

The incidence of colorectal cancer (CRC) in people under 50 years old is increasing without a clear established cause.
Background

The Cause for this increase remains uncertain. In EOCRC a ≈13% (range: 9–26%) carry germline pathogenic variants in known cancer predisposition genes and ≈28% (range: 13–33%) have a family history of CRC.
Background

Individuals with a family history (FH) of CRC are known to have an increased risk of this cancer.

<table>
<thead>
<tr>
<th>Family Risk of colorectal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC in <strong>at least 2 FDR</strong> diagnosed at any ages</td>
</tr>
<tr>
<td>CCR or an <strong>advanced adenoma</strong> in <strong>at least 2 FDR</strong> diagnosed at any ages</td>
</tr>
<tr>
<td>CCR in <strong>at least 1 FDR</strong> &lt; 50 years old</td>
</tr>
<tr>
<td>CCR or an <strong>advanced adenoma</strong> in at least <strong>1 FDR</strong> &lt; 60 years old</td>
</tr>
</tbody>
</table>

Starting colonoscopy surveillance at the age of 40 years old or 10 years before the age of the diagnosis of the youngest relative

Van Leerdam et al, Endoscopy 2019; 51: 1082–1093
Roos et al, Clinical Gastroenterology and Hepatology 2019;17:2657–2667
The component potentially preventable by early screening for FH in early-onset CRC is still uncertain, and a recent study conducted in the USA suggests that up to 16% of cases could be potentially prevented if current US screening guidelines were followed.

N: 713
- 79.4% No family history or hereditary syndrome
- 9% Family history (FH)
- 7% Hereditary syndrome (HS)
- 4.6% HS + FH

Potentially prevented: colonoscopy performed >5 years earlier
Early diagnosis: Colonoscopy performed >1 year earlier

Stanich et al, Gastroenterology 2021;160:1850–1852
Aims

We sought to explore the proportion of preventable EOCRC due to family history of CRC following the ESGE guidelines in Europe
Patients and Methods

A retrospective, descriptive, multicenter European study

→ Including: patients with CRC diagnosed before the age of 50.
→ Excluding: hereditary syndromes, inflammatory bowel disease or other histological diagnoses

Database was collected with patients from: January 2010 to December 2020.

Personal and family history of CRC, age at diagnosis, and molecular studies that have ruled out the hereditary component were recorded.

Following the statistical analysis of Stanich et al, we assumed:

• Potentially prevented CRC: colonoscopy carried out 5 years or more before the patient’s diagnosis age.
• Earlier diagnosis CCR: screening that would have started 1 year to 4 years before the CRC diagnosis

Descriptive statistics were used.
## Results

### Patients’ Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Mean age of CRC diagnosis (+/−SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Whole cohort</strong></td>
<td>903 (100%)</td>
<td>41.8 (±6.51)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>448/903 (49.6%)</td>
<td>41.37 (±6.60)</td>
</tr>
<tr>
<td>Male</td>
<td>455/903 (50.3%)</td>
<td>42.29 (±6.41)</td>
</tr>
<tr>
<td><strong>Location of CRC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right colon</td>
<td>217 (25%)</td>
<td></td>
</tr>
<tr>
<td>Left colon</td>
<td>317 (36%)</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>342 (39%)</td>
<td></td>
</tr>
<tr>
<td><strong>TNM Stage at diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>138 (15%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>180 (21%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>295 (35%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>238 (28%)</td>
<td></td>
</tr>
<tr>
<td><strong>Family History of CRC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>275 (30.4%)</td>
<td>41.5 (±6.49)</td>
</tr>
<tr>
<td>No</td>
<td>628 (69.6%)</td>
<td>41.95 (±6.53)</td>
</tr>
<tr>
<td>≥ 1 FDR</td>
<td>155 (17%)</td>
<td>42.4 (±6.15)</td>
</tr>
<tr>
<td>≥ 1 FDR &lt; 50 years old</td>
<td>35 (3.8%)</td>
<td>39.7 (±7.3)</td>
</tr>
<tr>
<td>≥ 1 FDR &lt; 60 years old</td>
<td>66 (7.5%)</td>
<td>41.1 (±6.5)</td>
</tr>
<tr>
<td>≥ 2 FDR</td>
<td>33 (3.6%)</td>
<td>43.3 (±5.5)</td>
</tr>
</tbody>
</table>
Results

ESGE Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Total</th>
<th>Mean Age at diagnosis (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 FDR &lt;50 years old</td>
<td>27 (2.8%)</td>
<td>39.7 (±7.56)</td>
</tr>
<tr>
<td>≥ 2 FDRs</td>
<td>23 (2.5%)</td>
<td>44 (±4.59)</td>
</tr>
<tr>
<td>Both criteria (1 FDR &lt;50 years old and 2 or more FDRs)</td>
<td>8 (0.8%)</td>
<td>41 (±7.59)</td>
</tr>
<tr>
<td>Total ESGE criteria</td>
<td>57 (6.3%)</td>
<td>41.59 (±6.7)</td>
</tr>
</tbody>
</table>

6% MET THE ESGE FAMILY CRITERIA

Mean age at cancer diagnosis was 41 years old
Results

Impact on prevention

Difference (in years) between the age at diagnosis of CRC and the recommended starting age according to:

- Potentially prevented CRC
- Earlier diagnosis CCR
- No earlier diagnosis/prevention possible

THE ESGE GUIDELINE

Starting 10 years earlier that the youngest CRC relative

THE ESGE GUIDELINE adding starting 10 years earlier

31.5%

28.9%

21%

55.2%
Conclusions

- Up to 6% of patients with EOCRC have a 1 FDR <50 years old or 2 or more FDRs with CRC.

- Applying the ESGE guidelines, a prevention could have been made in only 30% of these cases. Performing the screening colonoscopy 10 years before the diagnosis of the youngest relative with CRC, this percentage increases to 55.2%.

- Therefore, this group of patients with early-onset CRC could be prevented if the current surveillance guidelines were applied correctly.

- Differences in the clinical definition of significant family history of CRC and advanced adenomas may explain the difference with previous studies.

- The ESGE recommendation should include starting earlier if relatives with CRC are younger than 50 years old.

- Effort is needed to increase the uptake of early screening in cases with FH or CRC.
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Thank you!

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