NORMAL COLONOSCOPY IN FIT +VE PERSONS: DILEMMAS

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Disclosure

- Olympus: Educational & research grants, consultancy
- Pentax: Educational & research grants
- Cook: Educational grants & research grants
- Boston Scientific: Educational grants, consultancy
- ERBE: Educational grants
- Medtronics: Educational grants
- Astra: Research grants
- CDX diagnostics: Consultancy
Colonoscopy is the gold standard test to detect CRC
Faecal Immunochemical Test (FIT)

Screening

Symptomatic
Clinical value and diagnostic performance of FIT depends on the cut off levels and test population

Direct comparison of sensitivity & specificity for advanced neoplasm* of 9 quantitative FITs

- A) 
  - Sensitivity [%]**
  - Specificity [%]**

- B) 
  - at thresholds recommended by manufacturer (range: 2-17 µg Hb/g feces) (A)
  - at uniform threshold (15 µg Hb/g feces) (B)

- C) 
  - Very similar sensitivity
  - at thresholds adjusted to yield same specificity (93%) (C)

*Colorectal cancer or advanced adenoma; **Each dot represents one FIT

Gastroenterology
Accuracy of FIT for Colorectal Cancer: systematic review and meta-analysis

a) Sensitivity 0.79 (CI, 0.69 - 0.86)
b) Specificity 0.94 (CI, 0.92 - 0.95)
c) Positive likelihood ratio 13.10 (CI, 10.49 to 16.35)
d) Negative likelihood ratio 0.23 (CI, 0.15 to 0.33)
e) Diagnostic accuracy 95% (CI 93-97%)

Sensitivity improves with lower cut-off

0.89 [CI, 0.80-0.95] at a cut-off value less than 20 μg/g

0.70 [CI, 0.55-0.81] at cut-off values of 20 to 50 μg/g

However, corresponding specificity is lower

Screening colonoscopy & Interval cancer

- A good quality screening colonoscopy has a reduced risk of CRC, duration effect 10 years
- However one of the risk factors for interval cancer is a +ve FOBT indication for the initial colonoscopy

Interval cancers in a FOBT-based colorectal cancer population screening programme: implications for stage, gender and tumour site

R J C Steele,¹,² P McClements,³ C Watling,³ G Libby,² D Weller,⁴ D H Brewster,³ R Black,³ F A Carey,⁵ C G Fraser²


- Three regions in Scotland, pilot roll out, age 50-69
- 2 yearly G-FOBT (in total 3 rounds of screening)
- Uptake ~ 55%: 618-447-389 cancers detected

- Rest of Scotland- Non screened population: 2416-2196-2094 cancers detected
Interval cancers in a FOBT-based colorectal cancer population screening programme: implications for stage, gender and tumour site

R J C Steele,¹ ² P McClements,³ C Watling,³ G Libby,² D Weller,⁴ D H Brewster,³ R Black,³ F A Carey,⁵ C G Fraser²


<table>
<thead>
<tr>
<th></th>
<th>Round 1, % (n)</th>
<th>Round 2, % (n)</th>
<th>Round 3, % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen-detected</td>
<td>56.6 (351)</td>
<td>46.5 (208)</td>
<td>35.7 (139)</td>
</tr>
<tr>
<td>Interval</td>
<td>31.2 (193)</td>
<td>47.7 (213)</td>
<td>58.9 (229)</td>
</tr>
<tr>
<td>Missed</td>
<td>0.3 (2)</td>
<td>0.9 (4)</td>
<td>0.5 (2)</td>
</tr>
<tr>
<td>Miscellaneous*</td>
<td>10.7 (66)</td>
<td>4.9 (22)</td>
<td>4.9 (19)</td>
</tr>
<tr>
<td>Not on SCR</td>
<td>2 (6)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Miscellaneous cancers include cancers diagnosed in those with an evaluable result who did not undergo colonoscopy.
SCR, Scottish Cancer Registry.
Long-term risk of colorectal cancer after negative colonoscopy in a Danish gFOBT screening cohort

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2 Copenhagen University Hospital Herlev, Herlev, Denmark
3 Department of Pathology, Vejle Hospital, Vejle, Denmark

166,277 FOBT screening (feasibility study in 2 counties) compared to rest of 1,240,348 Danish citizens of same age (50-74 yrs)

14 CRC out of 771 +ve FOBT followed by –ve colonoscopy, 1.8%, 8 years FU

Persons with +ve FOBT followed by –ve colonoscopy had the same long-term CRC risk compared to unscreened population (average risk)

Int J Cancer 2017;141:503-511
In the scenario of organized FOBT-based screening programs, around 20 – 30% of individuals have a positive test followed by a negative colonoscopy.

Colorectal cancer after negative colonoscopy in fecal immunochemical test-positive participants from a colorectal cancer screening program

Authors
Liseth Rivero-Sánchez¹, Jaume Grau², Josep María Augé³, Lorena Moreno⁴, Angels Pozo², Anna Serradesanferm², Mireia Díaz⁴, Sabela Carballal¹, Ariadna Sánchez¹, Leticia Moreira¹, Francesc Balaguer¹, Maria Pellisé¹, Antoni Castells¹, on behalf of the PROCOLON group

Endoscopy International Open 2018; 06: E1140–E1148
1st round CRC screening 2010-12, 50-69 yrs, F 54%

130,206, 40% acceptance, 5.8% +ve

Cut-off ≥20µgHb/g faeces

2659 FIT +ve persons underwent colonoscopy

Experienced endoscopists, Olympus SD/HD,

4L PEG split bowel prep, 6 minutes withdrawal time

811 (30.5%) –ve colonoscopy

Observational study with structured telephone interview
PCCRC 0.4%  
3/700
• The vast majority >95% did not present with any significant pathology on FU to account for +ve FIT
• Although FIT selects high risk individuals, the low PCCRC 0.4% reinforces the colonoscopy quality factor
Yield of repeat colonoscopy in asymptomatic individuals with a positive fecal immunochemical test and recent colonoscopy

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Seoul, Korea

Gastrointest Endosc 2019
Jan 2013 - July 2017
OC sensor, ≥20µgHb/g faeces
Retrospective study

Participants with FITs and clinical data (n=52,376)

Positive results from FIT (F-Hb≥100 ng Hb/mL) (n=3,229)

Without colonoscopy (n=867)

With colonoscopy (n=2,362)

Potential participants (n=2,362)

- Previous history of CRC or colorectal surgery (n=28)
- Inflammatory bowel disease (n=25)
- Poor bowel preparation (n=51)
- Incomplete data (n=30)

n=134

Negative results from FIT (F-Hb<100 ng Hb/mL) (n=49,147)

Without colonoscopy (n=42,622)

With colonoscopy (n=6,525)

Eligible participants (n=6,525)

- Previous history of CRC or colorectal surgery (n=116)
- Inflammatory bowel disease (n=47)
- Poor bowel preparation (n=140)
- Incomplete data (n=87)
n=390

Eligible participants (n=2,228)

n=390

Eligible participants (n=6,135)
<table>
<thead>
<tr>
<th></th>
<th>FIT-positive participants (n = 2228)</th>
<th></th>
<th>FIT-negative participants (n = 6135)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;3 years (n = 514)</td>
<td>3-10 years (n = 427)</td>
<td>&gt;10 years or no colonoscopy (n = 1287)</td>
<td>&lt;3 years (n = 1365)</td>
</tr>
<tr>
<td>Age, y</td>
<td>64.1 ± 8.0</td>
<td>64.0 ± 8.2</td>
<td>64.6 ± 8.6</td>
<td>.343</td>
</tr>
<tr>
<td>Male sex</td>
<td>304 (59.1)</td>
<td>228 (53.4)</td>
<td>664 (51.6)</td>
<td>.015</td>
</tr>
<tr>
<td>Current or ex-smoker</td>
<td>185/409 (45.2)</td>
<td>142/354 (40.1)</td>
<td>390/993 (39.3)</td>
<td>.114</td>
</tr>
<tr>
<td>Family history of CRC</td>
<td>52 (10.1)</td>
<td>33 (7.7)</td>
<td>55 (4.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Obesity (BMI ≥25 kg/m²)</td>
<td>147/367 (40.1)</td>
<td>97/311 (31.2)</td>
<td>318/905 (35.1)</td>
<td>.052</td>
</tr>
<tr>
<td>Hypertension</td>
<td>206 (40.1)</td>
<td>168 (39.3)</td>
<td>539 (41.9)</td>
<td>.584</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>74 (14.4)</td>
<td>66 (15.5)</td>
<td>209 (16.2)</td>
<td>.618</td>
</tr>
<tr>
<td>Colorectal neoplasia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any CRN</td>
<td>283 (55.1)</td>
<td>240 (56.2)</td>
<td>843 (65.5)</td>
<td>.001</td>
</tr>
<tr>
<td>ACRN</td>
<td>56 (10.9)</td>
<td>54 (12.6)</td>
<td>335 (26.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CRC</td>
<td>11 (2.1)</td>
<td>7 (1.6)</td>
<td>93 (7.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intramucosal cancer</td>
<td>2 (18.2)</td>
<td>1 (14.3)</td>
<td>24 (25.8)</td>
<td>.576</td>
</tr>
<tr>
<td>I- II</td>
<td>4 (36.4)</td>
<td>2 (28.6)</td>
<td>38 (40.9)</td>
<td>.576</td>
</tr>
<tr>
<td>III - IV</td>
<td>3 (27.3)</td>
<td>4 (57.1)</td>
<td>25 (26.9)</td>
<td>.576</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (18.2)</td>
<td>0 (.0)</td>
<td>6 (6.5)</td>
<td>.576</td>
</tr>
</tbody>
</table>
Offer repeat colonoscopy for FIT +ve <3 years

Recall bias of participants regarding private colonoscopy
Family history higher in shorter colonoscopy intervals
No quality control on colonoscopy / endoscopist
False +ve FIT

- Drugs: PPI, NSAID?
- Small bowel / UGI pathology
- Anorectal lesions
- Menstruation
- Physiological blood loss (0.5-1.5ml / day)

Rockey DC. NEJM 1999; 341: 38 – 46
Quality of Colonoscopy
Quality in screening colonoscopy: position statement of the European Society of Gastrointestinal Endoscopy (ESGE)

Rembacken B et al. Quality in screening... Endoscopy 2012; 44: 957–968

Authors
B. Rembacken¹, C. Hassan², J. F. Riemann³, A. Chilton⁴, M. Rutter⁵, J.-M. Dumonceau⁶, M. Omar⁷, T. Ponchon⁸

Institutions
Institutions are listed at the end of article.

Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative

Kaminski Michal F et al. Performance measures for... Endoscopy 2017; 49
What would you do in clinical practice?

• Consider patient factors
  – Bowel prep, drugs, test compliance

• Investigate colonoscopy factors
  – Endoscopist KPI, equipment, accessories

• Selective investigations to R/O other causes
  – CT/MRI/UGI endoscopy

• Consider repeating colonoscopy
Conclusion

- FIT diagnostic accuracy is 95%
- 1/3rd have negative colonoscopy
- PCCRC is rare in high quality screening
- Quality in screening colonoscopy is the key

- Repeat colonoscopy if patient factors and/or colonoscopy quality compromised