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Can We Avoid Colonoscopies in Lynch Syndrome?

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COLON

This summary reviews van Liere D, de Boer N, van Leerdam M et al. Fecal Immunochemical Test to Detect Colorectal Neoplasia in Lynch Syndrome: A Prospective Multicenter Study. Am J Gastroenterol 2025;120(3): 632-641.

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STRUCTURED ABSTRACT

Question: Can the fecal immunochemical test (FIT) extend colonoscopy surveillance intervals?

Design: Prospective multicenter observational study.

Setting: Five hospitals in the Netherlands.

Patients: Lynch syndrome patients with a pathogenic germline variant in *MLH1, MSH2/EPCAM, MSH6,* or *PMS2* due for surveillance colonoscopy (typically every 2 years starting at age 25 per Dutch guidelines). They excluded those with extended/total colectomy, incomplete colonoscopies, colonoscopies with inadequate bowel preparation quality or withdrawal <6 minutes, and colonoscopies with any mucosal inflammation/infection or polypectomy without

pathology report. They also excluded those who used bowel preparation within 7 days before FIT.

Exposure or Interventions: FIT (SENTiFIT—fecal occult blood [FOB] gold test (Sentinel Diagnostics, Milan, Italy) administered 3 months before surveillance colonoscopy

Outcomes: Colonoscopic findings of various types of any relevant neoplasia (colorectal cancer [CRC], advanced polyps, non-advanced polyps), advanced neoplasia (CRC, advanced polyps), or CRC + advanced adenoma compared to a control of no neoplasia or non-advanced serrated lesions.

Data Analysis: Descriptive analysis of baseline characteristics. Diagnostic performance of FIT measured by sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and area under the curve. Number needed to diagnose any neoplasia.

Funding: Dutch Digestive Foundation.

Results: Of 217 Lynch syndrome (LS) patients, 35 (16%) had *MLH1*, 56 *MSH2/EPCAM*, 70 *MSH6*, and 56 *PMS2* variants. Median age was 51, 15% had personal history of CRC, and 185 (85%) did not have any prior colon resection. Thirty-two percent had any neoplasia, 5 (2.3%) had advanced adenoma(s) all by size ≥10 mm, 4 had advanced serrated lesions (three-quarters by size ≥10 mm), and 4 (1.8%) had CRC, all of which were stage I or II. Two of the CRCs were found on index colonoscopy, and 2 after a delayed colonoscopy surveillance interval of 5-6 years. The advanced polyps were distributed throughout the colon.

At a FIT threshold of 2.5 ug Hgb/g feces, FIT had 26% sensitivity, 91% specificity, and 72% NPV for any relevant neoplasia, and 69% sensitivity, 91% specificity, and 97.1% for advanced neoplasia. At a threshold of 4.1 ug Hgb/g feces, FIT had 21% sensitivity, 94% specificity, and 71% NPV for any relevant neoplasia, 69% sensitivity, 94% specificity, and 97% NPV for advanced neoplasia, and 89% sensitivity , 94% specificity, and 99% NPV for CRC + advanced adenoma. For every 100 FIT tests at the 4.1 threshold, 11 patients would test positive but 2 with advanced neoplasia would be missed.

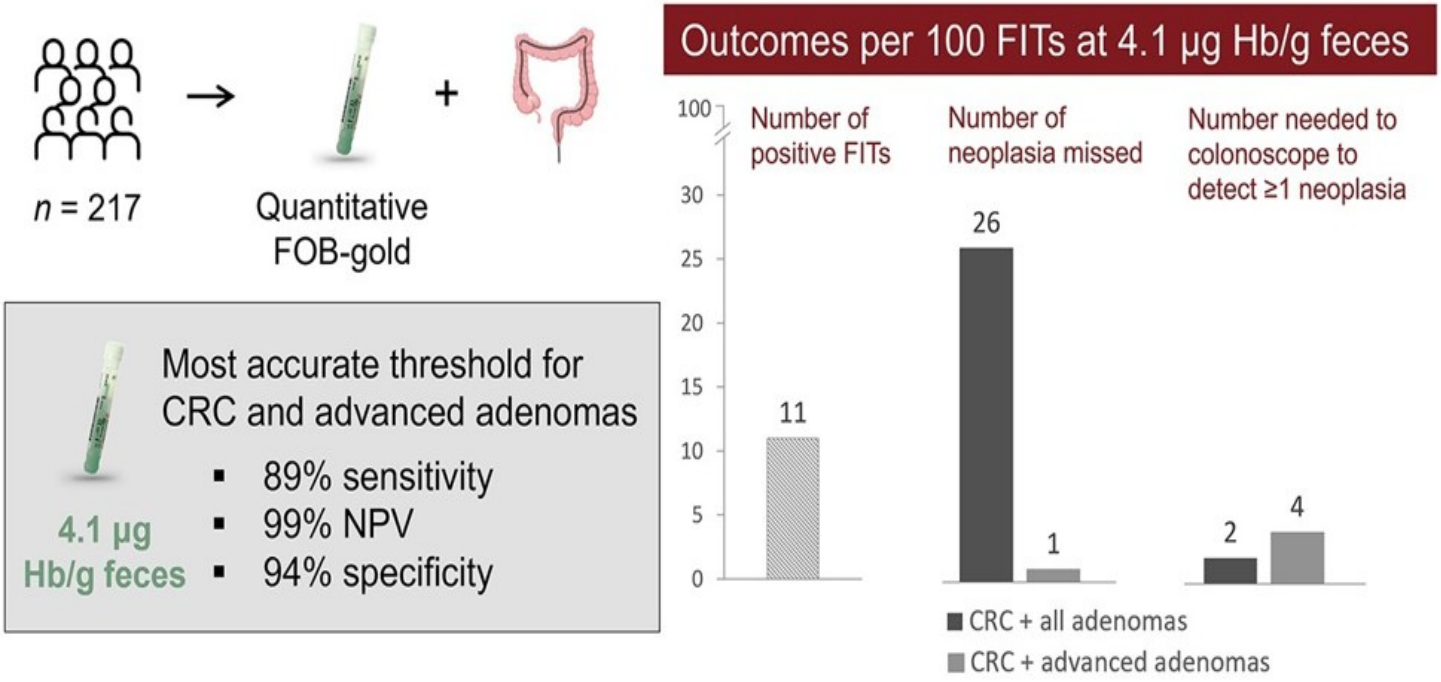

Figure 1. Visual abstract for FIT for surveillance in Lynch syndrome.

CRC, colorectal cancer; FIT, fecal immunochemical test; FOB, fecal occult blood; NPV, negative predictive value.

COMMENTARY

Why Is This Important?

Similar to other chronic diseases/diagnoses (polyposis syndromes, inflammatory bowel disease) that warrant frequent colonoscopy, the cumulative colonoscopic burden on both the affected individual patient and the healthcare system is significant, particularly in resource-limited settings. FIT continues to be explored as an inexpensive, non-invasive method to decrease colonoscopic burden and/or prioritize colonoscopy for those who benefit most in both average-risk and elevated-risk populations.[1,2] LS patients have one of the heaviest colonoscopic burdens, often requiring them annually.[3]

Key Study Findings

At the 4.1 ug Hgb/g feces threshold, FIT had a reasonable diagnostic accuracy for detection of colorectal cancer or advanced adenoma, although sensitivity was worse when the addition of sessile

For every 100 FIT tests, we would miss 2 LS patients with advanced neoplasia (cancer or advanced polyp). This is an intriguing study that raises the possibility that FIT, or alternative non-invasive tests, could be used as an adjunct to screening/surveillance colonoscopy in some respect for LS patients in the future.

Caution

In the United States, FIT is not commonly standardized or calibrated to specific fecal hemoglobin concentrations, thus cannot be readily used in daily practice at this current time. Even with proper calibration there are medicolegal implications of delaying gold-standard colonoscopy in the absence of more definitive evidence to change our national guidelines.[3]

My Practice

I personally am not yet comfortable extending surveillance intervals longer than recommended by National Comprehensive Cancer Network guidelines.[3] In terms of how we can make an impact on the burden of colonoscopy as providers, the bowel preparation process is often the most cumbersome step in the process. In addition to split bowel preparation, I favor prescribing low-volume or tablet bowel preparation products which is commonly covered by most insurances. Gummy bears (other than red/purple colors) are also considered a clear liquid and can help with the hunger during fasting.

In addition, we should not lose sight of the ultimate goal- prevention and risk reduction of colorectal cancer. I typically prescribe/recommend aspirin prophylaxis in LS of all genotypes. This is recommended by National Comprehensive Cancer Network guidelines (notably was not standard in Dutch guidelines for this study),[3] because it has been shown to substantially decrease colorectal cancer incidence over the course of decades.[4] Whether this itself is enough to extend surveillance intervals in select LS patients remains to be seen.

For Future Research

There are many future avenues with potential to decrease colonoscopic burden among LS patients. Given the high incidence of colorectal cancers, which does vary by affected gene, we will need to study a larger number of patients for each LS genotype powered for a wide range of risk profiles such as aspirin usage, personal history of CRC (most did not have prior CRC in this study) which portends higher metachronous CRC risk,[5] and family history of CRC. In addition, multitarget stool DNA tests have higher diagnostic accuracy than traditional FIT with broad payer coverage, and may have a larger impact in this high-risk population.

Conflict of Interest

The author has no conflicts of interest.

Abbreviations

CRC, colorectal cancer; FIT, fecal immunochemical test; FOB, fecal occult blood; LS, Lynch syndrome; NPV, negative predictive value; PPV, positive predictive value.

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