Evaluation of a risk index for advanced proximal neoplasia of the colon

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Background: A clinical risk index that uses distal colorectal findings at flexible sigmoidoscopy (FS) in conjunction with easily determined risk factors for advanced proximal neoplasia (APN) may be useful for tailoring or prioritizing screening with colonoscopy.

Objective: To conduct an external evaluation of a previously published risk index in a large, well-characterized cohort.

Design: Cross-sectional.

Setting: Teaching hospital and colorectal cancer screening center.

Patients: A total of 5139 asymptomatic persons aged 50 to 74 (54.9% women) with a mean age (± SD) of 58.3 (± 6.2) years.

Interventions: Between 2003 and 2011, all participants underwent a complete screening colonoscopy and removal of all polyps.

Main Outcome Measurements: Participants were classified as low, intermediate, or high risk for APN, based on their composite risk index scores. The concordance or c-statistic was used to measure discriminating ability of the risk index.

Results: A total of 167 persons (3.2%) had APN. The prevalence of those with APN among low-, intermediate-, and high-risk categories was 2.1%, 2.9%, and 6.5%, respectively. High-risk individuals were 3.2 times more likely to have APN compared with those in the low-risk category. The index did not discriminate well between those in the low- and intermediate-risk categories. The c-statistic for the overall index was 0.62 (95% confidence interval, 0.58-0.66).

Limitations: Distal colorectal findings were derived from colonoscopies and not FS itself.

Conclusion: The risk index discriminated between those at low risk and those at high risk, but it had limited ability to discriminate between low- and intermediate-risk categories for prevalent APN. Information on other risk factors may be needed to tailor, or prioritize, access to screening colonoscopy. (Gastrointest Endosc 2015;81:1427-32.)

Abbreviations: AN, advanced neoplasia; APN, advanced proximal neoplasia; BMI, body mass index; CRC, colorectal cancer; FS, flexible sigmoidoscopy; SSA, sessile serrated adenoma.

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Colorectal cancer (CRC) is one of the most common cancers in women and men worldwide.[1,2] Approximately 136,830 new cases of CRC were diagnosed in the United States in 2014.[3] The U.S. Preventive Services Task Force recommends screening for persons at average risk of CRC with an annual fecal occult blood test, periodic flexible sigmoidoscopy (FS), or colonoscopy.[4] FS, a less-invasive procedure than colonoscopy, can identify asymptomatic persons who should undergo examination of the proximal colon via colonoscopy to detect those harboring advanced proximal neoplasia (APN) who are at an increased risk of CRC.[5] A clinical risk index that uses several risk factors for CRC including distal colorectal findings may provide a useful approach for tailoring screening and recommending screening colonoscopy to those who could most benefit from the procedure.

Several risk indices or prediction tools for advanced neoplasia (AN) or APN of the colon have been developed.[6-15] These indices have encompassed several risk factors for CRC including age, sex, body mass index (BMI), smoking status, alcohol use, dietary information, and physical activity. However, the risk index developed by Imperiale et al[6] has garnered the most attention and has been evaluated independently elsewhere.[16] The objective of this research was to conduct an evaluation of the risk index developed by Imperiale et al[6] among a large and well-characterized cohort of asymptomatic individuals undergoing screening colonoscopy.

METHODS

The risk index

The risk index for APN developed by Imperiale et al[6] included the risk factors age, sex, and most advanced distal colorectal findings. Points assigned to categories for each risk factor were summed to derive an overall score ranging from 0 to 7. Those with scores of 0 or 1 are assigned a low-risk category, those with scores of 2 or 3 an intermediate-risk category, and those with scores of 4 through 7 a high-risk category for APN. The risk index was developed in a derivation cohort (n = 1994) and evaluated in a validation cohort (n = 1031).[6] Imperiale et al[6] did not collect information on those with family histories of CRC and thus did not exclude these participants from the cohort.

Study approval

The study protocol was approved by the research ethics boards at Sunnybrook Health Sciences Centre and Women's College Hospital in Toronto and the Conjoint Health Research Ethics Board at the University of Calgary.

Participants

From 2003 to 2008, we prospectively enrolled asymptomatic persons aged 50 to 74 years referred for outpatient colonoscopy to undergo a complete colonoscopy and endoscopic removal of all polyps at Women's College Hospital in Toronto. In Calgary, by using the same inclusion criteria, participants were enrolled from 2009 to 2011 at the Alberta Health Service's Colon Cancer Screening Centre. Participants were excluded if they (1) were not between the ages of 50 and 74 years; (2) had a history of colon surgery; (3) had documented ulcerative colitis, colon polyps, and/or colon cancer; (4) had experienced rectal bleeding in the previous 6 months on more than one occasion; (5) had a marked change in bowel habits in the previous 6 months; (6) had lower abdominal pain that would normally require medical attention in the previous 6 months; (7) had a history of sigmoidoscopy, colonoscopy, or barium enema within the previous 10 years; or (8) had a medically significant concurrent disease that would preclude the safe performance of colonoscopy as judged by the principal investigator.

Study protocol

Eligible persons, who provided consent, completed a baseline questionnaire that covered demographic information, history of colon examinations (sigmoidoscopy, colonoscopy, and barium enema), medical history, prior surgeries, smoking history, alcohol consumption, physical activity, nonsteroidal anti-inflammatory drug use, and family history of cancer.

In the main analysis, we used the risk index of Imperiale et al[6] with updated definitions (Table 1) to incorporate information on sessile serrated adenomas (SSAs). Participants were classified based on their most advanced finding at colonoscopy. APN was defined as a tubular, villous ($\geq$25% villous component), or traditional serrated adenoma with high-grade dysplasia or diameter $\geq$10 mm; an SSA with high-grade or low-grade dysplasia or diameter $\geq$10 mm;[17] or an invasive cancer occurring proximal to the distal colon (defined as the rectum, sigmoid colon, and descending colon). Distal findings were categorized by using the following hierarchy: none, hyperplastic, nonadvanced neoplasia, and advanced neoplasia or cancer. Nonadvanced neoplasia was defined as tubular adenoma or traditional serrated adenoma with low-grade dysplasia or diameter $<$10 mm or SSA with no dysplasia $<$10 mm in size. Advanced neoplasia or cancer was defined by using the same criteria as for APN but occurring in the distal colon.

We conducted 3 additional analyses to explore the performance of the risk index when we (1) excluded those with family histories of CRC, (2) excluded all participants with SSAs, and (3) attempted to classify SSAs as they would have been during the development of the risk index. In the latter case, SSAs with dysplasia or a diameter $\geq$10 mm were classified as AN (risk score of 3), whereas nonadvanced SSAs were classified as hyperplastic (risk score of 1).