Advanced proximal neoplasia of the colon in average-risk adults

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Background: Estimating risk for advanced proximal neoplasia (APN) based on distal colon findings can help identify asymptomatic persons who should undergo examination of the proximal colon after flexible sigmoidoscopy (FS) screening.

Objective: We aimed to determine the risk of APN by most advanced distal finding among an average-risk screening population.

Design: Prospective, cross-sectional study.

Setting: Teaching hospital and colorectal cancer screening center.

Patients: A total of 4651 asymptomatic persons at average risk for colorectal cancer aged 50 to 74 years (54.4% women [n = 2529] with a mean [± standard deviation] age of 58.4 ± 6.2 years).

Interventions: All participants underwent a complete colonoscopy, including endoscopic removal of all polyps.

Main Outcome Measurements: We explored associations between several risk factors and APN. Logistic regression was used to identify independent predictors of APN.

Results: A total of 142 persons (3.1%) had APN, of whom 85 (1.8%) had isolated APN (with no distal findings). APN was associated with older age, a BMI >27 kg/m^2, smoking, distal advanced adenoma and/or cancer, and distal non-advanced tubular adenoma. Those with a distal advanced neoplasm were more than twice as likely to have APN compared with those without distal lesions.

Limitations: Distal findings used to estimate risk of APN were derived from colonoscopy rather than FS itself.

Conclusion: In persons at average risk for colorectal cancer, the prevalence of isolated APN was low (1.8%). Use of distal findings to predict APN may not be the most effective strategy. However, incorporating factors such as age (>65 years), sex, BMI (>27 kg/m^2), and smoking status, in addition to distal findings, should be considered for tailoring colonoscopy recommendations. Further evaluation of risk stratification approaches in other asymptomatic screening populations is warranted. (Gastrointest Endosc 2014;80:660-7.)

(footnotes appear on last page of article)

Colorectal cancer (CRC) is the second most common cancer in women and the third in men worldwide.[1,2] Evidence from randomized controlled trials has shown that screening with fecal occult blood testing can reduce CRC mortality by at least 16%.[3,4] In 2001, the Canadian Task Force on Preventive Health Care recommended annual or biennial CRC screening with a guaiac-based fecal occult blood test or periodic flexible sigmoidoscopy (FS) for Canadians aged 50 years or older.[5] Although several organized screening programs in Canada, including Ontario's ColonCancerCheck Program, have implemented guaiac-based fecal occult blood test or fecal immunochemical test screening,[6] and colonoscopy is the preferred strategy in the United States,[7] further assessment of the feasibility of FS, a less invasive procedure than colonoscopy is warranted. Of the 4 randomized controlled trials of FS,[8-11] 3 show a reduction in CRC mortality,[9-11] and a recent meta-analysis of these trials shows a 28% reduction in CRC mortality (intention to treat analysis) with no evidence of heterogeneity.[12] FS can identify asymptomatic persons

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who should undergo examination of the proximal colon by using colonoscopy because those harboring advanced proximal neoplasia (APN) are at an increased risk of CRC.[13] However, FS is, by nature, ineffective in the identification of proximal lesions in the absence of distal neoplasia.

Several studies have reported on findings at colonoscopy in asymptomatic populations.[14-19] However, most of these studies included persons with family histories of CRC,[14-17] and some did not exclude those who had colonoscopies in the previous 10 years to approximate a true average-risk screening population.[16,18] In addition, none took into account the more recently recognized serrated neoplasia pathway.[20] We conducted a prospective, cross-sectional study of average-risk adults who underwent screening colonoscopy to determine the risk of APN in individuals with distal colorectal adenomas and distal high-risk lesions compared with those without. Further, we examined potential clinical risk factors for APN including age, sex, body mass index (BMI), smoking history, alcohol consumption, and nonsteroidal anti-inflammatory drug (NSAID) use.

Take-home Message

- In persons at average risk for colorectal cancer, the prevalence of advanced proximal neoplasia (APN) and isolated APN is low (3.1% and 1.8%, respectively).
- Incorporating factors such as age, sex, body mass index, and smoking status, in addition to distal findings, may be useful in prioritizing access to screening colonoscopy. Further evaluation of this approach in other screening populations is warranted.

METHODS

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. A similar approach to the Veterans Affairs Cooperative Study 380[14,21] was followed in regard to study protocol and data collection methods.

Participants

From 2003 to 2008, we prospectively enrolled 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, 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; (8) had a medically significant concurrent disease that would preclude the safe performance of colonoscopy as judged by the principal investigator; or (9) refused to participate in the study.

Study protocol

Eligible persons who provided consent completed a baseline questionnaire that covered demographic information, history of colon examinations (sigmoidoscopy, colonoscopy, barium enema), medical history, prior surgeries, smoking history, alcohol consumption, physical activity, NSAID use, and family history of cancer. Smoking history, alcohol consumption, and NSAID use (frequency and duration) were ascertained as previously described in detail.[21] The participants underwent a physical examination, and vital signs were recorded.

Before colonoscopy, participants were given instructions for bowel preparation by the endoscopist. The day before the procedure, the participants underwent bowel preparation. Informed consent for the procedure was obtained separately from study consent. At colonoscopy, the total duration of the procedure and withdrawal time; adequacy of bowel preparation (good, fair, poor); farthest extent reached; and the number, size, shape, location, and removal method of all polyps were recorded in a standardized fashion. The size of all polypoid lesions was measured by using open biopsy forceps, the blades of which measured 7 mm across when opened. If colonoscopy could not be completed, the procedure was repeated, and the results are included.

For the Toronto participants, a central pathology interpretation of all biopsied lesions was completed by the designated study pathologist (E.H.). For the Calgary participants, interpretation was completed by several pathologists. Participants were classified based on their most advanced finding. Diagnostic criteria were based on the World Health Organization Classification of Tumours of the Digestive System.[22] Criteria for diagnosing sessile serrated adenomas were based on seminal pathology articles in the literature.[20,23]

An APN was defined as a tubular adenoma, villous adenoma ($\geq$25% villous component), or traditional serrated adenoma $\geq$10 mm or with high-grade dysplasia, sessile serrated adenoma $\geq$10 mm or with high-grade or low-grade dysplasia, or invasive cancer occurring proximal to the distal colon (defined as the rectum, sigmoid colon, descending colon, and splenic flexure). Distal findings were recorded by using the following hierarchy: normal, hyperplastic, non-advanced tubular adenoma, and advanced adenoma and/or cancer. Non-advanced tubular adenoma