Colonoscopic findings in first-degree relatives of patients with colorectal cancer: a population-based screening program

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Background: A screening colonoscopy is recommended in first-degree relatives (FDRs) of colorectal cancer patients; few prospective, controlled studies have evaluated colorectal findings in a population-based screening program.

Objective: To evaluate the prevalence of colorectal neoplasia (adenomas and adenocarcinomas) in this increased-risk population, to compare it with that of average-risk individuals, and to identify features that might allow risk stratification for neoplasia among FDRs.

Design: Cross-sectional study.

Setting: Population-based screening program in Trentino, Italy.

Patients: FDRs of colorectal cancer patients between 45 and 75 years of age with no history of hereditary colorectal cancer syndromes or inflammatory bowel disease.

Controls: Average-risk individuals undergoing screening colonoscopy.

Intervention: Screening colonoscopy.

Results: Neoplasia was found in 33.4% of 1252 FDRs and in 30.3% of 765 controls; advanced neoplasia was found in 11.3% of FDRs and in 6.3% of controls. Odds ratios (ORs) from the multivariate logistic regression analysis adjusted for age, sex, cecal intubation rates, and colon cleansing showed an increased risk of advanced neoplasia (OR 2.41; 95% CI, 1.69-3.43; $P < .0001$) in FDRs. Age older than 56 years (OR 1.83; 95% CI, 1.15-2.99; $P = .013$) and male sex (OR 2.17; 95% CI, 1.39-3.10; $P < .001$) are independent predictors of advanced neoplasia.

Limitations: Italian subjects living in the same geographic area; of 4301 FDRs, 2521 were excluded.

Conclusions: The increased risk of advanced neoplasia supports the current recommendation for colonoscopic screening in this group; age and sex may assist in risk stratification of these individuals. (Gastrointest Endosc 2011;73: 527-34.)

Abbreviations: APSS, Azienda Provinciale per i Servizi Sanitari; BMI, body mass index; CRC, colorectal carcinoma; FDR, first-degree relative; FH, family history; OR, odds ratio; SIO, Sistema Informatico Ospedaliero.

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Colorectal cancer (CRC) is one of the most common types of cancer in developed countries. In Italy, 38,000 new cases were diagnosed in 2002.[1] Approximately 20% to 25% of cases of CRCs occur in patients with a family history (FH) of CRC. Apart from the 2 defined genetic syndromes, familial adenomatous polyposis and hereditary nonpolyposis CRC, an approximately 2- to 4-fold increased risk of colorectal neoplasia (adenomas and adenocarcinomas) was found in first-degree relatives (FDRs) of patients with CRC compared with individuals without an FH of CRC.[2] The results of many published studies are questionable because of a retrospective design or an unsatisfactory control group, and few studies[3] have prospectively evaluated the risk of the disease among the FDRs of CRC patients. Many studies focused on the risk of CRC, but only a few of them addressed the risk of finding adenomas in this population. Colorectal adenomas are precursors of most cancers. There is a particular risk of advanced adenomas (adenomas ≥10 mm and/or villous component and/or high-grade dysplasia) progressing to invasive cancer; a 2.6% to 5.7% annual transition rate was calculated.[4] A screening colonoscopy with removal of detected polyps leads to a substantial decrease in the incidence[5] and mortality rate[6] of CRC in average-risk individuals. A decrease in the incidence and mortality was also observed in individuals with an FH of CRC undergoing screening colonoscopy.[7]

A screening colonoscopy at an earlier age and/or performed more frequently than in average-risk individuals is endorsed by many authoritative groups in this population, especially in individuals with more than 1 FDR affected or receiving a diagnosis at age 60 or younger.[8-10]

The Screening dei Familiari A Rischio di Cancro Colorettale (SFACC) screening program is a colonoscopy-based program for FDRs of CRC patients. In our previous study, we evaluated factors that influence the use of screening colonoscopies in our population.[11] In this study, we describe colorectal findings among FDRs undergoing a screening colonoscopy and compare them with findings of average-risk subjects undergoing a colonoscopy as a primary screening tool (first objective). Our secondary objective was to identify features that might allow the use of risk stratification for colorectal neoplasia among this increased-risk group.

Take-home Message

- An increased risk of advanced colorectal neoplasia was found in a population-based screening program among first-degree relatives compared with average-risk individuals. The risk of advanced neoplasia increases with age or if the relative is male. Demographic characteristics such as age and sex may provide useful insight into familial risk stratification and may assist in customizing screening strategies.

METHODS

Screening program setting

In 2005, the health authorities of the Trentino region in Italy established a screening program for FDRs of patients with CRC. The Trentino publicly funded health-care system (the Italian term is Azienda Provinciale per i Servizi Sanitari [APSS]) has a catchment area of 500,000 inhabitants. Trained gastroenterologists from public endoscopic practices took part in the screening program. This study was approved by the APSS Institutional Review Board. FDRs provided written informed consent to participate in the screening program.

Screening design

As previously reported,[11] starting in December 2005, FHs from patients with newly diagnosed CRC were prospectively collected. All new cases of CRC were ascertained by a pathological diagnosis. These data were obtained from 2 databases: (1) the TESI database (Tesi Imaging, Milano, Italy), in which gastroenterologists store data on endoscopic procedures, demographics, and clinical, endoscopic, and pathological diagnosis and (2) the Sistema Informatico Ospedaliero (SIO) database, in which clinical information including procedures, laboratory tests, and hospital discharge reports on residents is stored. Health and demographic information on all FDRs was obtained during in-person consultation between the physician and the index patient; in cases in which the index patient had died, family data were collected from an FDR. In the other cases in which it was not possible to contact the living index patients, a letter was mailed to their general practitioners. They were asked to provide the FH on a special form and to mail it back to the Screening dei Familiari a Rischio di Cancro Colorettale coordinating center.[11] Inclusion criteria were (1) FDRs either between the ages of 45 and 75 years or 10 years younger than the youngest patient with CRC in the family and (2) FDRs residing in the APSS catchment area. Exclusion criteria were (1) having undergone a colonoscopy or barium enema in the 5 years before the study and (2) a history of hereditary CRC syndromes, inflammatory bowel diseases, and/or severe comorbidities. Data on the FDRs' health status and previous endoscopies collected from the index patients were compared with information contained in the TESI and SIO databases. Eligible subjects were contacted by letter and phone call to set up an appointment with a gastroenterologist, as described.[11] Data on body mass index (BMI) and smoking habits were collected during the visit. A colonoscopy was performed free of charge within 2 months.

Control group

Control subjects were chosen from consecutive, average-risk, asymptomatic individuals residing in the