

Association of smoking and flat adenomas: results from an asymptomatic population screened with a high-definition colonoscope

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Background: Flat adenomas represent a morphologically distinct class of polyps that may be difficult to detect, and little is known regarding risk factors for these lesions. Identification of risk factors for these lesions may aid in colorectal cancer (CRC) screening, because patients at risk for these lesions may require special imaging techniques. Smoking, an important risk factor for CRC, may be associated with molecular changes that increase the risk for flat adenomas.

Objective: The aim of this study was to examine the association between smoking and flat adenomas.

Design: Prospective cross-sectional study.

Setting: University hospital endoscopy center.

Patients: We enrolled asymptomatic patients presenting for CRC screening.

Interventions: We screened patients with a high-definition (1080i signal) wide-angle (170° field of view) Olympus 180-series colonoscope. We collected demographics, medication use, family history of CRC, diet history, and smoking history.

Main Outcome Measurements: Polyp morphology, assessed by using the Japanese Research Society Classification (JRSC).

Results: A total of 600 patients were enrolled. We observed that smoking was associated with having a flat adenoma of any size (adjusted odds ratio [OR], 2.53; 95% CI, 1.60-4.00), having only flat adenomas that were ≥ 6 mm in diameter (adjusted OR, 3.84; 95% CI, 2.02-7.32), as well as flat advanced adenomas (adjusted OR, 2.81; 95% CI, 1.08-7.30).

Limitations: The study design may not account for some confounding variables and provides no information regarding smoking status at the time of initiation of flat adenomas.

Conclusion: Smoking was associated with flat adenomas in our population. Our findings may explain the earlier onset of CRC in smokers as well as the advanced stage with which they present, with compared with nonsmokers. Smokers may require screening with high-definition colonoscopes to detect flat adenomas. (Gastrointest Endosc 2010;71:1234-40.)

Abbreviations: COX2, cyclooxygenase-2; CRC, colorectal cancer; IQR, interquartile range; JRSC, Japanese Research Society Classification; MMR, mismatch repair; NSAIDs, nonsteroidal anti-inflammatory drugs; OR, odds ratio.

DISCLOSURE: All authors disclosed no financial relationships relevant to this publication. (Research support for this study was provided by the Stony Brook University General Clinical Research Center [grant #MO1RR10710].)

See CME section; p. 1274

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doi:10.1016/j.gie.2009.12.012

Received September 11, 2009. Accepted December 7, 2009.

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Presented as an abstract at the American Gastroenterological Association's Digestive Disease Week Topic Forum (Important Clinical Issues Regarding Polyps and Colorectal Cancer), San Diego, California, May 19, 2008 (Gastroenterology 2008;134(Suppl 1):A60-A61).

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Flat nonpolypoid adenomas were initially described by Muto et al¹ more than 20 years ago and are considered to be more aggressive than their polypoid counterparts. This is supported by many reports in the Japanese-language literature^{2,3} and with more variation in Western published reports.⁴⁻¹⁰ Yashiro et al¹¹ provided molecular evidence to suggest that de novo cancers may arise from these morphologically distinct lesions. Although screening colonoscopy has been shown to decrease mortality and incidence of colorectal cancer (CRC),¹² there are emerging data suggesting that the magnitude of protection may be higher for the left side of the colon than the right side of the colon¹³; flat lesions may play a role in explaining missed colorectal cancers on the right side of the colon.

Little is known regarding the risk factors for these flat lesions, which may account for over one-half of all adenomas detected with a high-definition colonoscope.¹⁴ Information regarding risk factors for flat adenomas would aid in screening, because patients with important risk factors may require the use of new technologies, such as high-definition colonoscopy.^{14,15} In addition, special techniques may be needed for their removal.¹⁶⁻¹⁸

Smoking has been shown to be an important risk factor for colorectal neoplasia in several screening studies^{19,20} as well as population-based studies.²¹⁻²⁵ Recent American College of Gastroenterology guidelines state that in addition to age and a family history of CRC, smoking may warrant special consideration, such as an earlier age for screening.²⁶ Smokers may be at risk for an increased frequency of mutations in the mismatch repair (MMR) enzymes²⁷ associated with microsatellite instability.²⁸ Ogawa et al²⁹ have observed that microsatellite instability is higher in nonpolypoid cancers than in polypoid tumors. Microsatellite instability may also be associated with serrated lesions.³⁰ In addition, BRAF³¹ and K-*ras* have been associated with smoking as well as with nonpolypoid lesions³²⁻³⁴ and serrated lesions.³⁵ Therefore, smokers may be at higher risk for flat colorectal neoplasia.

The aim of the present study was to investigate smoking as a risk factor for flat adenomas in an average-risk population undergoing screening colonoscopy.

METHODS

Subjects

The present study was a prospective cross-sectional examination with a target population of consecutive asymptomatic patients presenting to Stony Brook University Medical Center between November 2006 and October 2007 for screening colonoscopy. The study was approved by our Institutional Review Board, and written informed consents were obtained. Patients were excluded if they had GI symptoms (hematochezia, change in bowel habits, or abdominal pain), an colonic neoplasia, colon resection, inflammatory bowel disease, or earlier endoscopy (colonoscopy or sigmoidoscopy) within the past 10 years.

Capsule Summary

What is already known on this topic

- Flat adenomas represent a morphologically distinct class of polyps that can be difficult to detect.

What this study adds to our knowledge

- In 600 asymptomatic patients presenting for cancer screening colonoscopy, smoking was associated with the presence of flat adenomas.

Data, which included demographics, known colorectal cancer risk factors, and medications, were entered into a 2-page standard form by a nurse who used a structured script for all queries based on validated questionnaires.^{36,37} A Spanish-language questionnaire was used by a Spanish-speaking clinician. Heights and weights were obtained by the nurse on the day of endoscopy. Body mass index (BMI) was calculated by dividing the weight (kg) by the square of height (m). Obesity was defined as a BMI ≥ 30 .

Patients were asked about current or past cigarette use, the number of packs per day, the number of years they had smoked, the year of cessation for those who had quit, and any changes in their past smoking patterns. As outlined above, this information was ascertained by using a standard script.³⁷ These figures were used to calculate exposure in pack-years. We defined 3 smoking categories¹⁹: (1) nonsmokers; (2) heavy exposure: ≥ 10 pack-years and still smoking or quit within the past 10 years; and (3) low exposure: < 10 pack-years or those who quit > 10 years earlier. For the main analyses, we compared nonsmokers with the heavy exposure group based on our previous studies.^{19,38} A family history of colorectal and other cancers was recorded and included the relationship to the patient as well as age at diagnosis. Patients were queried about a history of diabetes and cholecystectomy. Information was collected about medications, including past or current use of insulin, statins, aspirin use, nonsteroidal anti-inflammatory drugs (NSAIDs)/cyclooxygenase-2 (COX2) inhibitors, multivitamins (including vitamin D), folic acid, hormone replacement therapy, and calcium supplementation. Patients reported alcohol (glasses of red/white wine, shots/drinks liquor, cans/bottles beer) consumed per week.

Patients also completed a 10-question dietary survey based on modified questions from the Behavioral Risk Factor Surveillance System State Questionnaire.³⁶ The patients were queried about the average number of red meat, fish, chicken, fiber, whole-grain product, tomato-based food, salad, fruit, and vegetable servings per week over the past 5 years. Finally, participants were asked about weekly exercise and baseline activity level.

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