Published in final edited form as:
Am J Gastroenterol. 2012 August ; 107(8): 1213–1219. doi:10.1038/ajg.2012.167.

Colorectal endoscopy, advanced adenomas, and sessile serrated polyps: implications for proximal colon cancer

Andrea N. Burnett-Hartman[1,2], **Polly A. Newcomb**[1,2], **Amanda I. Phipps**[1,2], **Michael N. Passarelli**[1,2], **William M. Grady**[1,3], **Melissa P. Upton**[3], **Lee-Ching Zhu**[4], and **John D. Potter**[1,2]

[1]Fred Hutchinson Cancer Research Center, Seattle, Washington

[2]School of Public Health, University of Washington, Seattle, Washington

[3]School of Medicine, University of Washington, Seattle, Washington

[4]Group Health, Seattle, Washington

Abstract

OBJECTIVES—Colonoscopy is associated with a decreased risk of colorectal cancer but may be more effective in reducing the risk of distal than proximal malignancies. To gain insight into the differences between proximal and distal colon endoscopic performance, we conducted a case-control study of advanced adenomas, the primary targets of colorectal endoscopy screening, and sessile serrated polyps (SSPs), newly recognized precursor lesions for a colorectal cancer subset that occurs most often in the proximal colon.

METHODS—The Group Health-based study population included: 213 advanced adenoma cases, 172 SSP cases, and 1,704 controls ages 50–79, who received an index colonoscopy from 1998–2007. All participants completed a structured questionnaire covering endoscopy history. Participants with polyps underwent a standard pathology review to confirm the diagnosis and reclassify a subset as advanced adenomas or SSPs. Logistic regression analyses were conducted to estimate adjusted odds ratios (OR) and 95% confidence intervals (CI) for the association between endoscopy and advanced adenomas and SSPs separately; site-specific analyses were completed.

RESULTS—Previous endoscopy was associated with decreased risk of advanced adenomas in both the rectum/distal colon (OR=0.38; 95% CI: 0.26–0.56) and proximal colon (OR=0.31; 95% CI: 0.19–0.52), but there was no statistically significant association between prior endoscopy and SSPs (OR=0.80; 95%CI: 0.56–1.13).

CONCLUSIONS—Our results support the hypothesis that the effect of endoscopy differs between advanced adenomas and SSPs. This may have implications for proximal colon cancer

Corresponding author: Andrea N. Burnett-Hartman, 1100 Fairview Ave. N, M4-B402, Seattle, WA 98109, aburnett@fhcrc.org, phone: 206-667-2126, fax: 206-667-5977.

Guarantor of the article: Andrea N. Burnett-Hartman

Potential competing interests: None

Specific author contributions:
Burnett-Hartman –study concept and design, acquisition of data, analyses and interpretation, statistical analysis, drafting manuscript, final approval
Newcomb – study concept and design, obtained funding, drafting of manuscript, final approval
Phipps – study design and analyses, final approval
Passarelli- study design and analyses, final approval
Grady – critical revision of manuscript for important intellectual content, final approval
Upton – acquisition of data, interpretation of data, final approval
Zhu – acquisition of data, interpretation of data, final approval
Potter – study concept and design, obtained funding, interpretation of data, final approval

prevention and be due to the failure of endoscopy to detect/remove SSPs, or the hypothesized rapid development of SSPs.

Introduction

Colorectal cancer screening is associated with decreased colorectal cancer incidence and mortality; yet it does not prevent all occurrences (1–5). In particular, proximal colon carcinomas may be less affected by screening (4–12). Sigmoidoscopy and colonoscopy are endoscopic procedures used for colorectal cancer screening and primary prevention, but the extent of the colon examined by the respective procedures is different. Sigmoidoscopy examines the rectum and distal portion of the colon, whereas colonoscopy visualizes the rectum and the entire colon.

Given these differences, it was generally assumed that colonoscopy would prevent cancer in the distal and proximal portions of the colon, whereas sigmoidoscopy might prevent only distal disease (13, 14). The results of several observational studies and clinical trials call into question this assumption, suggesting that both sigmoidoscopy and colonoscopy are associated with substantially decreased risks of rectal and distal colon cancer, but they may not modify the risk of proximal colon cancer (4–10). Other studies show reductions in both distal and proximal colon cancer associated with colonoscopy, but report larger effects in the distal colon (11, 12)

Biologic differences between proximal and distal colon polyps and/or cancer, differences in the quality of the colon preparation between the proximal and distal colon, and insufficient endoscopist training have been suggested as possible reasons for the decreased efficacy of endoscopy in the proximal colon (15–17). However, to date there are no published studies examining the association between prior endoscopy and the risk of different types of colorectal cancer precursor lesions. Because different precursor lesions probably represent divergent biologic pathways to colorectal cancer (15), evaluating their association with prior endoscopic exams may shed light on the reasons for reduced efficacy of endoscopy in the proximal colon.

Approximately 75% of colorectal cancers arise from adenomatous polyps (adenomas) and are in the adenoma-carcinoma pathway to colorectal cancer (18). The adenoma-carcinoma pathway usually involves *APC* mutation as an early event, followed by an accumulation of genetic mutations that activate oncogenes and inhibit tumor suppressor genes, which then drive the progression of the adenoma to adenocarcinoma (19). Because of the strong evidence linking adenomas to the risk of subsequent colorectal cancer, the primary targets for colorectal endoscopic procedures are adenomas (13). Detection and removal of adenomas can avert progression of these precursor lesions from pre-malignant to malignant disease, thereby preventing cancer. Most colorectal adenomas, however, will not progress to cancer (20). Large adenomas (≥ 10mm in diameter) and adenomas with villous histological components (microscopic finger-like projections) have higher rates of progression to cancer than do small adenomas (21, 22) The detection of adenomas with these characteristics, which have been termed advanced adenomas, thus is particularly important for the prevention of colorectal cancer. Advanced adenomas may be used as an indicator of increased risk of colorectal cancer resulting in recommendations to shorten the cancer surveillance interval from 10 years to 3–5 years (13).

Recent research suggests that, in addition to advanced adenomatous polyps, other colorectal polyps play a significant role in colorectal cancer development. In particular, certain serrated polyps may be precursors for colorectal cancers that develop via a “serrated polyp pathway” (23–27). Serrated polyps are distinct from conventional adenomas and represent a heterogeneous group of polyps with varying histology and malignant potential. Until

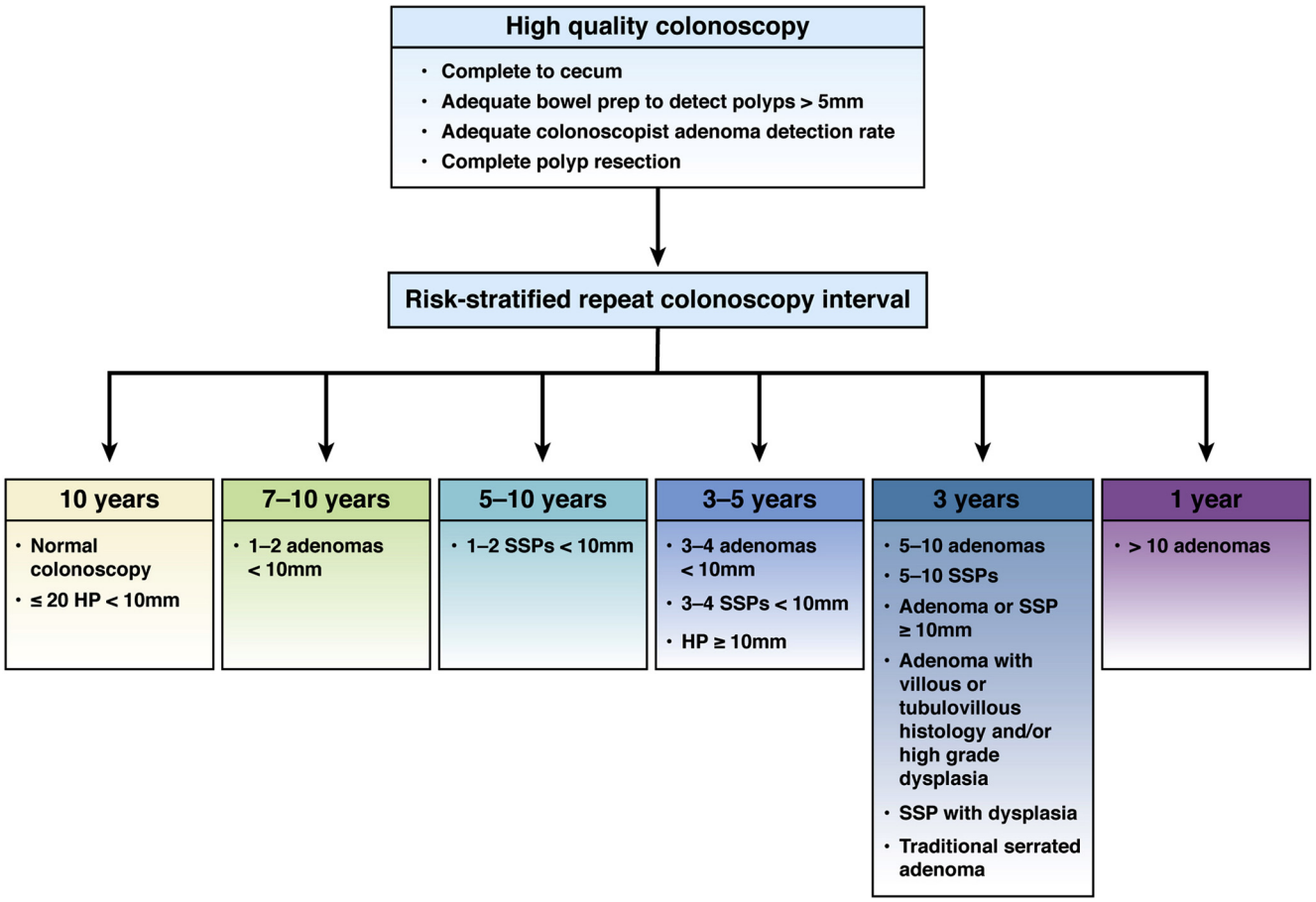

Figure 1. Recommendations for follow-up after colonoscopy and polypectomy. Recommendations for post-colonoscopy follow-up in average risk adults are depicted. After high-quality colonoscopy defined by examination complete to cecum adequate to detect polyps >5 mm, performed by a colonoscopist with adequate ADR with complete polyp resection, risk-stratified repeat colonoscopy intervals are provided. SSP, sessile serrated polyp/sessile serrated adenoma/sessile serrated lesion.

We specifically searched for articles evaluating factors that might increase risk among individuals with 1–2 adenomas <10 mm. In a pooled analysis of individuals with 1–2 small adenomas in 7 prospective polyp surveillance studies, an increased risk for metachronous advanced neoplasia was found for those with a history of polyps (absolute risk, 11.5%) or concurrent distal and proximal small adenomas (absolute risk, 11.0%).[24] However, most studies contributing to this pooled analysis were randomized trials of strategies to reduce polyp recurrence, and were performed before the era of modern colonoscopy, impacting relevance to current practice in which baseline adenoma detection may have improved due to focus on optimizing bowel preparation and ADRs. In a separate study that included an analysis of 4496 patients with 1–2 nonadvanced adenomas, risk for incident CRC was similar among those with proximal only vs distal only adenomas (RR, 1.5; 95% CI, 0.7–2.8).[18] More research is needed to determine whether subsets of individuals with low-risk adenoma, such as those with advanced age, young-onset adenoma, proximal adenoma, male sex, or other factors might benefit from shorter duration of follow-up.

We considered a recommendation of 10 years alone rather than a range of 7- to 10-year follow-up after removal of 1–2 adenomas <10 mm in size, given that evidence supports that these patients are at lower than average risk for CRC. The 7- to 10-year range was chosen because of ongoing uncertainty regarding whether the observed lower than average risk for CRC could be reduced further by exposure to surveillance,[17] and also because we cannot rule out the possibility that exposure to surveillance colonoscopy in some studies contributed to the low risk of CRC observed in these patients.[16,18] We anticipate that ongoing work may clarify whether surveillance colonoscopy can improve outcomes in patients with 1–2 small adenomas, and also whether characteristics (such as size <6 mm) may help guide the choice between recommending a shorter 7-year vs a longer 10-year surveillance interval.

The Task Force recognizes that many patients with 1–2 nonadvanced adenomas <10 mm will have had a prior

This information is intended to be shared with the patient post-pathology report.

American Society for Gastrointestinal Endoscopy

Stay on top of your health!

(Insert Logo)

We would like to share the results of your recent colonoscopy.

- **Exam results:**

  ☐ **Normal – No polyps**

  ☐ **Polyps removed: _____**
  (number of polyps removed)

- **Type of polyp(s) removed:**

  ☐ **Adenomatous --** a benign, precancerous growth.

  ☐ **Hyperplastic --** a benign growth with no potential to develop into cancer.

  ☐ **Other --** _____

- **Follow-up exam**

  Your doctor recommends a follow-up colonoscopy in _____ years from your recent exam date _____.
  (date of colonoscopy)

- A report of your colonoscopy results and the recommended follow-up colonoscopy date will also be sent to your referring physician:

  _____
  (name of referring physician)

- Ask the doctor who performed your colonoscopy if they send screening reminders when it is time for another colonoscopy. If not, take care to note the date of your next exam so that you stay on schedule with your preventative care. **Keep this document with your personal medical records at home.**

-more-

This information is intended to be shared with the patient post-pathology report.

WHY FOLLOW-UP EXAMS ARE IMPORTANT

- Removal of an adenomatous polyp prevents cancer from developing at that spot, but you are at risk to develop new polyps at other locations in your colon. Close follow-up is recommended.
- Finding a polyp is common. Over the age of 50, 25% of men and 15% of women will have an adenomatous polyp found on colonoscopy.
- The presence of a polyp only means that you are at risk for colon cancer. It DOES NOT mean that you will get cancer, however, continued follow-up with your doctor is important to minimize the risk of developing colon cancer in the future.

TALK TO YOUR FAMILY MEMBERS

- Because adenomatous polyps and colon cancer run in families, it is extremely important that you notify your parents, children and siblings if you have a polyp or cancer discovered during your colonoscopy.
  - o Your family members should speak with their doctors about having a screening colonoscopy.
  - o It is important that they indicate the type of polyp or cancer found during your exam AND your age at time of diagnosis.
- If you have had an adenomatous polyp removed in the past and change doctors, make sure that your new doctor knows about the polyp history to determine an appropriate screening schedule.

Notes from doctor's visit or phone call:

_____

_____

For more information about colon cancer, colon cancer screening, or colonoscopy, visit www.Screen4ColonCancer.org.

Doctor's Contact Information:

Name: _____

Address: _____

Phone: _____