BRIEF COMMUNICATIONS

Long-Term Efficacy of Sigmoidoscopy in the Reduction of Colorectal Cancer Incidence

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Screening sigmoidoscopy is associated with a reduction in both the incidence and mortality of colorectal cancer. Although current guidelines recommend sigmoidoscopy screening every 5 years, the duration of risk reduction is not known. We conducted a population-based case–control study to examine the association between sigmoidoscopy screening and colorectal cancer incidence. We collected information on screening history and risk factors from case patients with distal (n = 1026) and proximal (n = 642) colorectal cancer and from 1294 control subjects from October 1998 through February 2002. Screening sigmoidoscopy was associated with a statistically significant reduction in the incidence of distal colorectal cancer (odds ratio [OR] = 0.24, 95% confidence interval [CI] = 0.17 to 0.33). These reductions were sustained for up to 16 years with little attenuation. We also observed strong inverse associations between cancer incidence and sigmoidoscopy in analyses that included subjects with symptom-related tests. Current recommendations regarding the frequency of sigmoidoscopy screening may be unnecessarily aggressive. [J Natl Cancer Inst 2003;95:622–5]

Sigmoidoscopy screening for colorectal cancer has been shown to be efficacious in reducing the mortality *(1–3)* and probably the incidence *(3–10)* of this common disease. Risk reductions for distal disease appear to be as much as 60%–80% for mortality and as much as 50%–70% for incidence. Although the optimum sigmoidoscopy screening interval for individuals at average risk of colorectal cancer is not known, current guidelines recommend a 5-year screening interval *(11–13)*. However, such a period may be overly aggressive, given that the duration of the progression from adenoma to carcinoma may be as long as 15 years *(14,15)*. Indeed, some have advocated once-in-a-lifetime sigmoidoscopy screening *(16,17)*. Here we evaluate the efficacy of sigmoidoscopy in relation to screening interval in a population-based case–control study of colorectal cancer.

We used an institutionally approved protocol to identify eligible case patients, which included all male and female residents of King, Snohomish, and Pierce counties (WA) who were newly diagnosed with invasive colorectal adenocarcinoma [International Classification of Diseases for Oncology codes C18.0, C18.2–.9, and C20.0–.9 *(18)*] from October 1998 through February 2002, as identified through the Puget Sound Surveillance, Epidemiology, and End Results (SEER) Program[1] registry, and who were aged 20–74 years at diagnosis. SEER reports include information on cancer stage and grade, the patient's first course of treatment, and demographics. All eligible subjects had a publicly available telephone number. Of the 2185 eligible case patients identified, 131 (6%) were deceased, 66 (3%) had physicians who refused permission to contact them, 22 (1%) could not be located, and 240 (11%) refused to participate, resulting in a final sample size of 1726 case patients (overall response rate of 79%).

Community-based control subjects were randomly selected according to the age and sex distribution of the case patients by using Washington State driver's license data for individuals aged 20–64 years and Health Care Financing Administration files for individuals older than 64 years. Of the 1891 potential control subjects identified, 38 (2%) had died, 19 (1%) could not be located, and 510 (27%) refused to participate. The final study sample included 1324 control subjects (overall response rate of 70%).

We used a structured 50-minute telephone interview to obtain information from the study subjects on known or suspected risk factors for colorectal cancer, including their screening histories prior to 1 year before diagnosis (for case patients) or before interview date (for control subjects). Information on screening tests (fecal occult blood test, sigmoidoscopy, and colonoscopy) included the date of (or subject's age at) first and last tests, number of tests, and the reason for the test; we also collected information about the subject's demographics, personal medical history, family history of cancer, medication use, and lifestyle factors such as level of physical activity, occupation, alcohol consumption, and diet.

Subjects were classified as having undergone colorectal cancer screening (i.e., screening-only sigmoidoscopy) if they had sigmoidoscopy without having had prior symptoms, regardless of their family history of colorectal cancer. We considered the associations between screening-only sigmoidoscopy and colorectal cancer incidence and between any sigmoidoscopy (including symptom-related) and colorectal cancer incidence. To eliminate the possibility of bias that might arise from the selection of individuals who were at reduced risk of colorectal cancer because they had had a previous screen that was negative *(19)*, subjects who had undergone more than one test were excluded from the analysis of the association between single-screen-only sigmoidoscopy and colorectal cancer incidence. It is possible, however, that some individuals who had multiple tests may have been at higher than average risk of disease due to the fact that they had frequent sigmoidoscopies because they were previously diagnosed with polyps, which are a precursor of colorectal cancer *(20)*. Our analyses included only those tests performed more than 1 year prior to diagnosis or interview date, to avoid the clustering of screening tests that may have occurred shortly before diagnosis *(21)*. Odds ratios (ORs) and 95% confidence intervals

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Journal of the National Cancer Institute, Vol. 95, No. 8,

(CIs) for the association between screening and colorectal cancer incidence were estimated from a logistic regression model. Covariates were age (in 5-year intervals), sex, family history of colorectal cancer, postmenopausal hormone use (females), level of education, smoking history, body mass index (BMI), and the number of previous tests (for individuals who had more than one sigmoidoscopy). We excluded case patients with missing information about the affected subsite within the colon (n = 10). We also excluded subjects with incomplete information on screening (case patients, n = 48; control subjects, n = 30). All statistical tests were two-sided.

The mean age was 60.6 years (range = 20–75 years) for case patients and 62.0 years (range = 20–75 years) for control subjects. Overall, case patients were more likely than control subjects to report having a family history of colorectal cancer (26% versus 15%), to have a higher BMI (mean BMI, 27.8 kg/m^2 versus 26.7 kg/m^2), and to be current or former smokers (62% versus 57%). Among the women in our study, case patients were less likely than control subjects to have used postmenopausal hormones (45% versus 50%). Among the case patients, 35% were diagnosed with localized disease, 50% were diagnosed with regional disease, and 15% were diagnosed with distant metastases. Among the control subjects, 50% reported ever having a sigmoidoscopy and 27% reported ever having a screening sigmoidoscopy.

Sigmoidoscopy was associated with a statistically significant and sustained reduction in the incidence of distal colorectal cancers. Compared with individuals who had never had a screening sigmoidoscopy ("Never any screening test"), those who had ever had a screening sigmoidoscopy ("Ever any screening test") had an OR for distal colorectal cancer of 0.24 (95% CI = 0.17 to 0.33) (Table 1). This OR was similar to the OR for distal colorectal cancer among those reporting a single screening sigmoidoscopy (OR = 0.30, 95% CI = 0.20 to 0.43). This association between screening sigmoidoscopy (whether single or multiple) and reduced incidence of distal colorectal cancer was observed for individuals who reported having a screening sigmoidoscopy during all time intervals examined within the past 16 years relative to diagnosis or interview. The OR for distal colorectal cancer was also statistically significant when we included individuals with symptom-related sigmoidoscopies (i.e., "any test") in the analysis (OR = 0.47, 95% CI = 0.37 to 0.60). There was little evidence that this inverse relative risk was attenuated with increasing time since last screening. There was also some evidence that ever having had a sigmoidoscopy was associated with a modest reduction in the risk of proximal lesions (OR = 0.83, 95% CI = 0.66 to 1.04), although the inverse association was inconsistent across screening intervals.

Results from studies that have examined the optimal screening interval for sigmoidoscopy are generally consistent with a longer screening interval than the current recommended interval of 5 years. Selby et al. *(2)* reported that mortality from rectosigmoid cancer was

Table 1. Association between colorectal cancer incidence and time since sigmoidoscopy by years before diagnosis*

Interval between sigmoidoscopy and cancer diagnosis, y†	Any test			Any screening test			Single screening test		
	No. of case patients	No. of control subjects	OR (95% CI)†	No. of case patients	No. of control subjects	OR (95% CI)†	No. of case patients	No. of control subjects	OR (95% CI)‡
Distal colon cancer									
Never‖	462	723	1.00 (referent)	860	979	1.00 (referent)	732	867	1.00 (referent)
Ever‖	125	423	0.47 (0.37 to 0.60)	47	226	0.24 (0.17 to 0.33)	38	155	0.30 (0.20 to 0.43)
2–3	32	120	0.42 (0.28 to 0.64)	11	83	0.15 (0.08 to 0.29)	7	47	0.19 (0.08 to 0.42)
4–5	15	106	0.24 (0.14 to 0.41)	9	57	0.20 (0.10 to 0.41)	7	41	0.23 (0.10 to 0.53)
6–7	13	51	0.39 (0.21 to 0.74)	8	25	0.33 (0.15 to 0.76)	7	22	0.33 (0.14 to 0.79)
8–10	17	52	0.53 (0.30 to 0.94)	9	31	0.34 (0.16 to 0.73)	9	22	0.53 (0.24 to 1.17)
11–15	20	35	0.91 (0.52 to 1.61)	6	11	0.58 (0.21 to 1.59)	5	7	0.78 (0.24 to 2.51)
16+	28	59	0.72 (0.45 to 1.16)	4	19	0.21 (0.07 to 0.63)	3	16	0.19 (0.05 to 0.66)
Proximal colon cancer									
Never‖	359	723	1.00 (referent)	507	979	1.00 (referent)	449	867	1.00 (referent)
Ever‖	170	423	0.83 (0.66 to 1.04)	99	226	0.89 (0.68 to 1.16)	70	155	0.92 (0.68 to 1.26)
2–3	51	120	0.89 (0.62 to 1.27)	33	83	0.82 (0.54 to 1.25)	23	47	1.02 (0.61 to 1.72)
4–5	29	106	0.56 (0.36 to 0.87)	19	57	0.67 (0.39 to 1.14)	14	41	0.69 (0.37 to 1.28)
6–7	18	51	0.73 (0.42 to 1.27)	10	25	0.80 (0.38 to 1.69)	6	22	0.53 (0.21 to 1.34)
8–10	28	52	1.13 (0.70 to 1.83)	12	31	0.85 (0.43 to 1.67)	8	22	0.82 (0.36 to 1.87)
11–15	16	35	0.96 (0.52 to 1.75)	11	11	2.08 (0.89 to 4.86)	7	7	2.05 (0.70 to 5.95)
16+	28	59	0.93 (0.58 to 1.49)	14	19	1.36 (0.67 to 2.75)	12	16	1.39 (0.65 to 2.99)

*OR = odds ratios obtained from logistic regression models; CI = confidence interval.

†Excludes subjects who had a sigmoidoscopy less than 0–1 years prior to diagnosis or reference date (for "Any test," 439 patients with distal colon cancer, 113 patients with proximal colon cancer, and 149 control subjects were excluded). The Year 0–1 category includes a substantial number of individuals for whom their sigmoidoscopy identified their cancer. The OR for sigmoidoscopy in the "Any test" group was 5.39 (95% CI = 4.12 to 7.06).

‡Adjusted for age (5-year intervals), sex, family history of colorectal cancer (present/absent), postmenopausal hormone use (women), level of education (less than high school, high school, some college, college graduate), body mass index (quartiles), and number of previous tests.

§Adjusted for age (5-year intervals), sex, family history of colorectal cancer (present/absent), postmenopausal hormone use (women), level of education (less than high school, high school, some college, college graduate), body mass index (quartiles).

‖Never = subjects who did not have a sigmoidoscopy test; ever = subjects who had the test more than 2 years before diagnosis or interview. There are fewer individuals in the "Never" category for the "Any test" analysis compared with the "Any screening test" analysis because the "Never any screening test" category includes 654 patients (398 case patients, 256 control subjects) who have had a diagnostic test although not a screening test, and thus are included in the "Never any test" category.

reduced by 60% among those who had a screen using a rigid sigmoidoscope for up to 10 years before they were diagnosed with colorectal cancer. The magnitude of the inverse association appeared to be similar for individuals whether they had a screen 9–10 years before the diagnosis of the fatal cancer or in the 2 years before diagnosis (intervals >10 years were not evaluated). In a large U.S. Department of Veterans Affairs population study, the incidence of colon cancer (both distal and proximal) and rectal cancer was reduced by approximately 50% among individuals who had either type of endoscopy for any reason; those reductions were sustained for 5–6 years *(3)*. In a small randomized controlled sigmoidoscopy trial, screening was found to reduce the incidence of distal colorectal cancer by 80% (95% CI = 3% to 95%) at 13 years, although this finding was based on only 10 cases in the control group and two cases in the screening group *(6)*. Results of a recent study *(4)* suggest that a 60% colorectal cancer risk reduction associated with sigmoidoscopy screening might be sustained for at least 10 years, especially for individuals with more advanced disease. However, that study was limited by its small sample size and by its use of individuals with cancers other than colorectal cancers as control subjects. Two studies *(1,10)* have also shown that sigmoidoscopy screening is associated with some reduction in the risks of proximal as well as distal cancers. Presumably, all of these risk reductions are attributable to the identification of adenomas, which are the precursor lesions for colorectal cancer *(14)*, and their removal at a follow-up colonoscopy *(15)*. This is difficult to directly assess in our study, however, because adenoma removal is associated with both case patient status (because of their association with cancer risk) and control subject status (because their removal should reduce risk) *(21)*. Our interview did ascertain the respondent's polyp history, including the type of polyp and the date of the polypectomy, but the validity of self-reported polyp type is low, and we cannot be certain that adenomas were more frequently removed than other, more indolent lesions, such as hyperplastic polyps. Not surprisingly though, 98% of polypectomies in control subjects were the result of a preceding sigmoidoscopy.

Our study had some limitations. First, we relied on self reports of screening history. However, several studies *(22–25)* have found that, in general, colon cancer screening procedures are validly reported by individuals. In one recent study comparing self reports with medical records *(24)*, sigmoidoscopy was found to have a sensitivity of 95% and a specificity of 92%. Second, the proportion of individuals who used colorectal cancer screening in our study was slightly lower than that reported for participants in The Centers for Disease Control and Prevention's Behavioral Risk Factors Surveillance System (BRFSS) survey, a random digit dialing telephone survey *(26)*. However, because response rates in the BRFSS were only approximately 60%, the enrolled comparison group may be healthier and therefore more likely to seek screening than the general population. We believe it likely that the screening practices of our control subjects were more representative of the screening practices of the general population. Finally, although this was a large study, the sample size was limited in some screening duration categories.

Despite the evidence for the efficacy of screening in reducing colorectal cancer incidence and mortality, screening for this disease is underutilized. Currently, 34% of U.S. adults older than 50 years have had a sigmoidoscopy or a colonoscopy within the past 5 years *(26)*. Although the efficacy of colonoscopy must be greater than that of sigmoidoscopy *(27)*, the acceptability *(28, 29)*, cost-effectiveness *(30,31)*, and more widespread delivery of sigmoidoscopy argues in favor of this approach for screening. The findings from our study support the recommendation of a sigmoidoscopy (with colonoscopic follow-up) every 10 years. This approach, if more widely used, could substantially reduce the incidence of mortality from colorectal cancer. If the current proportion of U.S. adults older than 50 years who have a sigmoidoscopy every 10 years doubled, the incidence of distal colorectal cancer would be reduced by approximately 19 000 cases annually.

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NOTES

[1]*Editors's note:* SEER is a set of geographically defined, population-based central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

Supported by Public Health Service grant U01 CA074794 (to the Seattle Colorectal Cancer Family Registry) from the National Cancer Institute, National Institutes of Health, Department of Health and Human Services, and through cooperative agreements with members of the Colon Cancer Family Registry and principal investigators.

We thank Noel Weiss for advice and consultation at various stages of this project, and Ric Johnston and John Hampton for statistical advice and programming.

Manuscript received July 5, 2002; revised November 4, 2002; accepted January 30, 2003.