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Long-Term Colorectal-Cancer Incidence and Mortality after Lower Endoscopy

Reiko Nishihara, Ph.D., Kana Wu, M.D., Ph.D., Paul Lochhead, M.B., Ch.B., Teppei Morikawa, M.D., Ph.D., Xiaoyun Liao, M.D., Ph.D., Zhi Rong Qian, M.D., Ph.D., Kentaro Inamura, M.D., Ph.D., Sun A. Kim, M.D., Ph.D., Aya Kuchiba, Ph.D., Mai Yamauchi, Ph.D., Yu Imamura, M.D., Ph.D., Walter C. Willett, M.D., Dr.P.H., Bernard A. Rosner, Ph.D., Charles S. Fuchs, M.D., M.P.H., Edward Giovannucci, M.D., Sc.D., M.P.H., Shuji Ogino, M.D., Ph.D., and Andrew T. Chan, M.D., M.P.H.

ABSTRACT

BACKGROUND

Colonoscopy and sigmoidoscopy provide protection against colorectal cancer, but the magnitude and duration of protection, particularly against cancer of the proximal colon, remain uncertain.

METHODS

We examined the association of the use of lower endoscopy (updated biennially from 1988 through 2008) with colorectal-cancer incidence (through June 2010) and colorectal-cancer mortality (through June 2012) among participants in the Nurses' Health Study and the Health Professionals Follow-up Study.

RESULTS

Among 88,902 participants followed over a period of 22 years, we documented 1815 incident colorectal cancers and 474 deaths from colorectal cancer. With endoscopy as compared with no endoscopy, multivariate hazard ratios for colorectal cancer were 0.57 (95% confidence interval [CI], 0.45 to 0.72) after polypectomy, 0.60 (95% CI, 0.53 to 0.68) after negative sigmoidoscopy, and 0.44 (95% CI, 0.38 to 0.52) after negative colonoscopy. Negative colonoscopy was associated with a reduced incidence of proximal colon cancer (multivariate hazard ratio, 0.73; 95% CI, 0.57 to 0.92). Multivariate hazard ratios for death from colorectal cancer were 0.59 (95% CI, 0.45 to 0.76) after screening sigmoidoscopy and 0.32 (95% CI, 0.24 to 0.45) after screening colonoscopy. Reduced mortality from proximal colon cancer was observed after screening colonoscopy (multivariate hazard ratio, 0.47; 95% CI, 0.29 to 0.76) but not after sigmoidoscopy. As compared with colorectal cancers diagnosed in patients more than 5 years after colonoscopy or without any prior endoscopy, those diagnosed in patients within 5 years after colonoscopy were more likely to be characterized by the CpG island methylator phenotype (CIMP) (multivariate odds ratio, 2.19; 95% CI, 1.14 to 4.21) and microsatellite instability (multivariate odds ratio, 2.10; 95% CI, 1.10 to 4.02).

CONCLUSIONS

Colonoscopy and sigmoidoscopy were associated with a reduced incidence of cancer of the distal colorectum; colonoscopy was also associated with a modest reduction in the incidence of proximal colon cancer. Screening colonoscopy and sigmoidoscopy were associated with reduced colorectal-cancer mortality; only colonoscopy was associated with reduced mortality from proximal colon cancer. Colorectal cancer diagnosed within 5 years after colonoscopy was more likely than cancer diagnosed after that period or without prior endoscopy to have CIMP and microsatellite instability. (Funded by the National Institutes of Health and others.)

From the Department of Medical Oncology, Dana–Farber Cancer Institute and Harvard Medical School (R.N., P.L., T.M., X.L., Z.R.Q., K.I., S.A.K., A.K., M.Y., Y.I., C.S.F., S.O.); the Departments of Nutrition (R.N., K.W., A.K., W.C.W., E.G.), Epidemiology (W.C.W., E.G., S.O.), and Biostatistics (B.A.R.), Harvard School of Public Health; the Channing Division of Network Medicine, Department of Medicine (K.W., W.C.W., B.A.R., C.S.F., E.G., A.T.C.), and Department of Pathology (S.O.), Brigham and Women's Hospital and Harvard Medical School; and the Division of Gastroenterology, Massachusetts General Hospital (A.T.C.) — all in Boston; the Gastrointestinal Research Group, Institute of Medical Sciences, University of Aberdeen, Aberdeen, United Kingdom (P.L.); the Department of Pathology, University of Tokyo Hospital, Tokyo (T.M.); and Laboratory of Human Carcinogenesis, National Cancer Institute, National Institutes of Health, Bethesda, MD (K.I.). Address reprint requests to Dr. Chan at the Division of Gastroenterology, Massachusetts General Hospital, 55 Fruit St., GRJ-825C, Boston, MA 02114, or at achan@partners.org.

Drs. Nishihara, Wu, Lochhead, and Morikawa and Drs. Ogino and Chan contributed equally to this article.

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Table 1. Age-Adjusted Demographic and Clinical Characteristics According to Status with Respect to Lower Endoscopy and Polypectomy in 1998.*

Characteristic	Men				Women			
	No Lower Endoscopy (N=14,287)	Polypectomy (N=1259)	Negative Sigmoidoscopy (N=8091)	Negative Colonoscopy (N=3578)	No Lower Endoscopy (N=31,423)	Polypectomy (N=1481)	Negative Sigmoidoscopy (N=16,748)	Negative Colonoscopy (N=3957)
Age (yr)	62.5±8.9	68.3±8.8	64.8±9.1	65.8±9.0	63.4±7.1	66.4±6.7	65.0±6.9	64.3±6.8
Body-mass index†	25.9±3.4	26.2±3.3	25.7±3.3	25.8±3.2	25.4±4.5	25.7±4.5	25.1±4.2	25.2±4.3
History of colorectal cancer in first-degree relative (%)	9	25	13	19	10	33	17	29
Smoking status (%)								
Never smoked	46	40	47	46	45	40	46	44
Former smoker	47	53	48	49	43	50	46	48
Current smoker	7	6	5	5	12	10	7	8
Weekly physical activity level (METs)‡	32.9±28.6	31.0±28.0	33.3±28.4	32.7±26.7	17.5±16.9	16.5±14.7	17.4±16.4	17.3±16.1
Red-meat intake (servings/day)	1.2±0.9	1.1±0.8	1.1±0.8	1.1±0.8	0.9±0.4	0.9±0.4	0.9±0.4	0.9±0.4
Folate intake (μg/day)	532±226	540±222	558±230	562±231	432±164	431±149	456±167	448±164
Calcium intake (mg/day)	918±346	903±331	934±342	936±340	965±327	994±332	1031±342	1019±342
Total caloric intake (kcal/day)	2004±543	1961±546	1954±523	1967±520	1716±415	1715±395	1719±408	1716±411
Alcohol intake (g/day)	10.8±13.6	11.8±14.1	10.3±12.3	10.9±12.8	5.7±8.5	6.1±8.8	5.7±8.3	5.8±8.3
Current multivitamin use (%)	56	57	60	61	58	56	64	65
Regular use of aspirin (%)§	55	57	57	57	41	40	43	44
Nonsteroidal antiinflammatory drug use (%)¶	17	19	19	19	31	33	35	34
Cholesterol-lowering drug use (%)¶	12	18	17	17	14	19	17	17
History of postmenopausal hormone use (%)	NA	NA	NA	NA	67	78	80	81

* Plus–minus values are means ±SD. Values were standardized to the age distribution of the study population, except for the values for age. Data were for the midpoint of the follow-up period (1998) for the Health Professionals Follow-up Study for men and the Nurses' Health Study for women. Polypectomy was defined as removal of an adenoma. Percentages do not always sum to 100 owing to rounding. NA denotes not applicable.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Metabolic equivalents (METs) are defined for each type of physical activity as a multiple of the number of metabolic equivalents for sitting quietly for 1 hour. For example, a participant who walked at a rate of 3.0 miles per hour for 1 hour once per week would have a MET score of 3.3.
§ Regular aspirin use was defined as current use of two or more aspirin tablets per week for the Nurses' Health Study and use of aspirin at least two times per week for the Health Professionals Follow-up Study.
¶ Drug use was defined as current, regular use of the agent.