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Association of Screening Lower Endoscopy With Colorectal Cancer Incidence and Mortality in Adults Older Than 75 Years

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IMPORTANCE Evidence indicates that screening for colorectal cancer (CRC) beginning at 50 years of age can detect early-stage CRC and premalignant neoplasms (eg, adenomas) and thus prevent CRC-related mortality. At present, the US Preventive Services Task Force recommends continuing CRC screening until 75 years of age and individualized decision-making for adults older than 75 years, while accounting for a patient's overall health and screening history. However, scant data exist to support these recommendations.

OBJECTIVE To examine the association of lower gastrointestinal tract screening endoscopy with the risk of CRC incidence and CRC-related mortality in older US adults.

DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study of health care professionals in the US included data from the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS) from January 1, 1988, through January 31, 2016, for the HPFS and June 30, 2016, for the NHS. Data were analyzed from May 8, 2019, to July 9, 2020.

EXPOSURES History of screening sigmoidoscopy or colonoscopy (routine/average risk or positive family history) to 75 years of age and after 75 years of age, assessed every 2 years.

MAIN OUTCOMES AND MEASURES Incidence of CRC and CRC-related mortality confirmed by National Death Index, medical records, and pathology reports.

RESULTS Among 56 374 participants who reached 75 years of age during follow-up (36.8% men and 63.2% women), 661 incident CRC cases and 323 CRC-related deaths were documented. Screening endoscopy after 75 years of age was associated with reduced risk of CRC incidence (multivariable hazard ratio [HR], 0.61; 95% CI, 0.51-0.74) and CRC-related mortality (HR, 0.60; 95% CI, 0.46-0.78), regardless of screening history. The HR comparing screening with nonscreening after 75 years of age was 0.67 (95% CI, 0.50-0.89) for CRC incidence and 0.58 (95% CI, 0.38-0.87) for CRC-related mortality among participants who underwent screening endoscopy before 75 years of age, and 0.51 (95% CI, 0.37-0.70) for CRC incidence and 0.63 (95% CI, 0.43-0.93) for CRC-related mortality among participants without a screening history. However, screening endoscopy after 75 years of age was not associated with risk reduction in CRC death among participants with cardiovascular disease (HR, 1.18; 95% CI, 0.59-2.35) or significant comorbidities (HR, 1.17; 95% CI, 0.57-2.43).

CONCLUSIONS AND RELEVANCE In this cohort study, endoscopy among individuals older than 75 years was associated with lower risk of CRC incidence and CRC-related mortality. These data support continuation of screening after 75 years of age among individuals without significant comorbidities.

Editorial

Supplemental content

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Colorectal cancer (CRC) is the second most common cause of cancer-related death in the US. In 2020, nearly 148 000 new cases of CRC and 53 200 CRC-related deaths were estimated to occur.[1] Previous studies have demonstrated that screening for CRC starting at 50 years of age for adults at average risk can accurately detect early-stage CRC and adenomatous polyps and thus prevent CRC mortality.[2,3]

However, uncertainty exists regarding the age at which screening can be discontinued. The US Preventive Services Task Force currently recommends continuing CRC screening until 75 years of age and recommends individualized screening decisions for adults aged 76 to 85 years by considering an individual's overall health and screening history.[4] Other guidelines do not recommend continued screening beyond the age of 75 years or when life expectancy is less than 10 years.[5-8] Each of these recommendations for older adults is based on modeling studies.[9-13] However, the effectiveness of screening in reducing CRC incidence and related mortality in an older population has not been established. Randomized clinical trials evaluating the efficacy of CRC screening have excluded individuals older than 75 years.[3,14,15] A previous analysis using the Medicare database[16] found a modest benefit of screening colonoscopy in reducing the risk of CRC in individuals aged 70 to 74 years and a smaller benefit in individuals aged 75 to 79 years, but the effect on CRC-related death was not evaluated. To address this gap in evidence, we conducted a prospective analysis of the association between lower gastrointestinal tract endoscopy for screening at different ages, including adults older than 75 years, and the risk of incident CRC and mortality. We also examined whether the associations differed according to screening history, family history of CRC, and comorbidities.

Key Points

Question Does screening still confer a benefit in reducing the risk of colorectal cancer (CRC) and related deaths in adults older than 75 years?

Findings In 2 large prospective cohorts including 56 374 men and women who reached 75 years of age during follow-up, screening lower endoscopy after 75 years of age regardless of screening history was associated with a reduced risk of CRC incidence and related mortality. However, screening endoscopy was not associated with a benefit for CRC-related mortality among individuals with a history of cardiovascular disease or multiple cardiovascular risk factors.

Meaning These findings provide empirical evidence supporting the continuation of screening endoscopy among many adults older than 75 years for prevention of CRC incidence and death, especially those who do not have significant comorbidities.

Methods

Study Population

We used data from 2 prospective cohorts of US adults: the Nurses' Health Study (NHS), which included 121 701 female registered nurses aged 30 to 55 years at enrollment in 1976, and the Health Professionals Follow-up Study (HPFS), which included 51 529 male clinicians aged 40 to 75 years at enrollment in 1986. Participants have been mailed questionnaires every 2 years since inception querying demographics, lifestyle factors, medical history, and disease outcomes, with a follow-up rate of greater than 90% of available person-time. Every 4 years, a validated semiquantitative food frequency questionnaire was used to assess habitual dietary intake. The study was approved by institutional review boards of Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health and those of participating registries as required. Return of the questionnaires was considered to imply written informed consent. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Assessment of Screening Lower Endoscopy

Details of endoscopy assessment are provided in the eMethods in the Supplement. In both the NHS and the HPFS, beginning in 1988 and continuing through 2014, participants were asked as part of biennial questionnaires whether they had undergone either sigmoidoscopy or colonoscopy in the past 2 years and, if so, the reason for the investigation. We defined a screening endoscopy as any lower gastrointestinal tract endoscopy for asymptomatic or routine screening or because of a family history of CRC, but not for symptoms such as visible blood, occult fecal blood, abdominal pain, diarrhea/constipation, or a positive barium enema finding or for follow-up of prior polyps and virtual colonography.

Ascertainment of CRC and Death

We requested permission from the participants who reported diagnoses of CRC in each biennial questionnaire and obtained medical records or pathology reports. We also identified lethal CRC cases through family members or the postal system or sought these from the National Death Index, tumor registries, and death certificates.[17,18] Medical records and death certificates were reviewed by cohort investigators blinded to exposure information to confirm CRC diagnosis, including anatomical location (details included in the eMethods in the Supplement). The primary cause of death was assigned according to the *International Classification of Diseases, Ninth Revision* codes 153 to 154 for CRC death.

Statistical Analysis

Data were analyzed from May 8, 2019, to July 9, 2020. A detailed description of statistical analysis is provided in the eMethods in the Supplement. We followed up participants from the 1988 baseline questionnaire through January 31, 2014, for HPFS and June 30, 2014, for NHS; for mortality, the end of follow-up was January 31, 2016, for HPFS and June 30, 2016, for NHS. We excluded participants with a baseline history of cancer (except for nonmelanoma skin cancer), inflammatory bowel disease, colorectal polyps, and missing information on diet and major lifestyle factors (eFigure in the Supplement). For the incidence analysis, we examined screening endoscopy findings reported on the biennial questionnaire before the diagnosis of CRC, death

Table 1. Age- and Sex-Adjusted Characteristics of Participants According to Screening Lower Endoscopy at 75 Years or Younger and Older Than 75 Years From Nurses' Health Study and Health Professionals Follow-up Study

	Screening lower endoscopy by age group[a]			
	≤75 y		>75 y	
Characteristic	No	Yes	No	Yes
Person-years	1 390 821	906 153	246 717	138 592
Age, mean (SD), y	62.7 (10.8)	68.7 (8.8)	79.6 (3.5)	82.0 (4.1)
Sex				
Male	33.9	47.3	36.2	47.7
Female	66.1	52.7	63.8	52.3
Family history of colorectal cancer	11.9	22.2	18.4	25.5
BMI, mean (SD)	25.5 (4.1)	25.3 (3.8)	25.4 (3.8)	25.3 (3.6)
Alcohol consumption, mean (SD), g/d	7.9 (11.6)	7.9 (10.6)	7.8 (10.9)	7.9 (10.7)
Physical activity, mean (SD), MET-h/wk	19.9 (19.5)	22.5 (20)	20.9 (17.7)	22.4 (18.2)
Past smoker	45.0	47.4	51.3	51.2
Current smoker	9.7	5.7	3.8	2.7
Multivitamin use	54.2	63.3	70.4	74.4
Aspirin use	31.1	32.8	37.1	38.1
Other NSAID use	21.1	26.0	23.4	23.5
Hypertension	45.4	48.5	70.3	70.5
Hypercholesterolemia	49.6	59.0	68.4	71.3
Diabetes	8.7	8.4	14.7	13.7
Cardiovascular disease	11.1	9.9	24.1	21.7
Routine physical examination	63.8	76.6	71.7	76.5
Total energy intake, mean (SD), kcal/d	1818 (500)	1813 (477)	1790 (479)	1780 (465)
Calcium intake, mean (SD), mg/d	957 (357)	1028 (355)	1085 (374)	1137 (377)
Folate intake, mean (SD), μg/d	472 (213)	520 (212)	566 (208)	593 (208)
Red/processed meat intake, mean (SD), serving/d	0.9 (0.5)	0.8 (0.5)	0.8 (0.5)	0.7 (0.4)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); MET-h, metabolic equivalent task hours; NSAID, nonsteroidal anti-inflammatory drug.

[a] Unless otherwise indicated, data are expressed as the percentage of participants. Values were updated during follow-up and standardized to the distribution of age and sex of the study population, with the exception of age and sex themselves.

due to any cause, or the end of follow-up, whichever came first. For the mortality analysis, we stopped updating the screening endoscopy status at the date of diagnosis of CRC and censored participants at the time of death due to any cause or the last follow-up cycle, whichever came first. We used Cox proportional hazards regression models to calculate hazard ratios (HRs) and 95% CIs, stratified by age, sex, and calendar year of the questionnaire cycle and adjusted for CRC risk factors in the multivariable analysis.

We updated history of screening endoscopy as a time-varying variable to account for changes during follow-up, and participants were considered screened for the subsequent follow-up once they reported having had screening endoscopy in any of the questionnaires. We examined screening endoscopy according to endoscopy that occurred at 75 years or younger and after 75 years of age. For analyses of screening endoscopy after 75 years of age, we included participants who reached the age of 75 years during follow-up without being diagnosed with CRC. We specifically examined whether the associations of screening endoscopy after 75 years of age with CRC incidence and mortality differed according to screening history. We also conducted subgroup analyses according to the presence or absence of family history of CRC, personal history of cardiovascular disease, and other comorbidities. Statistical analyses were conducted using SAS, version 9.4 (SAS Institute, Inc). All *P* values were 2 sided, and $P < .05$ indicated statistical significance.

Results

A total of 56 374 participants reached 75 years of age during follow-up (36.8% men and 63.2% women). The age- and sex-adjusted characteristics of participants throughout the study period according to screening endoscopy at 75 years or younger and older than 75 years are shown in **Table 1.** Participants who underwent screening endoscopy either at 75 years or younger or at older than 75 years, compared with those without screening endoscopy, were more likely to be male (≤75 years, 47.3% vs 33.9%; >75 years, 47.7% vs 36.2%) and older (mean [SD] age for ≤75 years, 68.7 [8.8] vs 62.7 [10.8] years; mean [SD] age for >75 years, 82.0 [4.1] vs 79.6 [3.5] years), to have a family history of CRC (≤75 years, 22.2% vs 11.9%; >75 years, 25.5% vs 18.4%), and to undergo routine physical examinations (≤75 years, 76.6% vs 63.8%; >75 years, 76.5% vs 71.7%). Participants who underwent screening endoscopy also tended to be more physically active (mean [SD] for ≤75 years, 22.5 [20.0] vs 19.9 [19.5] metabolic equivalent task hours per week; >75 years, 22.4 [18.2] vs 20.9 [17.7] metabolic equivalent task hours per week) and to use multivitamins (≤75 years, 63.3% vs 54.2%; >75 years, 74.4% vs 70.4%). There was a higher prevalence of hypertension (≤75 years, 48.5% vs 45.4%; >75 years, 70.5% vs 70.3%) and hypercholesterolemia (≤75 years, 59.0% vs 49.6%; >75 years, 71.3% vs 68.4%) but a lower prevalence of cardiovascular disease (≤75 years, 9.9% vs 11.1%; >75 years, 21.7% vs

Table 2. Screening Lower Endoscopy at 75 Years or Younger and at Older Than 75 Years and Risk of CRC and CRC-Related Mortality

Outcome	Screening lower endoscopy	
	No	Yes
Before or at 75 y		
CRC		
No. of cases	1516	732
No. of person-years	1 390 821	906 153
HR (95% CI)[a]		
Age-adjusted	1 [Reference]	0.60 (0.54-0.66)
Multivariable-adjusted	1 [Reference]	0.61 (0.55-0.67)
CRC-related mortality		
No. of cases	573	298
No. of person-years	1 437 293	1 004 554
HR (95% CI)[a]		
Age-adjusted	1 [Reference]	0.53 (0.45-0.61)
Multivariable-adjusted	1 [Reference]	0.54 (0.47-0.63)
After age 75 y		
CRC		
No. of cases	489	172
No. of person-years	246 717	138 592
HR (95% CI)[a]		
Age-adjusted	1 [Reference]	0.58 (0.48-0.70)
Multivariable-adjusted	1 [Reference]	0.61 (0.51-0.74)
CRC-related mortality		
No. of cases	212	111
No. of person-years	289 036	169 639
HR (95% CI)[a]		
Age-adjusted	1 [Reference]	0.63 (0.49-0.80)
Multivariable-adjusted	1 [Reference]	0.60 (0.46-0.78)

Abbreviations: CRC, colorectal cancer; HR, hazard ratio.

[a] Cox proportional hazards regression models were stratified by age, questionnaire cycle, and cohort, and multivariable models were further adjusted for family history of CRC, body mass index, physical activity, smoking, alcohol consumption, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, and intake of total calories, calcium, folate, or red and processed meat. We adjusted additionally for postmenopausal hormone use in women. The model for endoscopy after 75 years of age was further adjusted for screening endoscopy before or at 75 years of age.

24.1%) in the screened population compared with the unscreened population.

Screening at 75 Years or Younger

Among 127 992 participants (79 640 women and 48 352 men), we documented 2248 incident CRC cases and 871 CRC-related deaths during 26 and 28 years, respectively, encompassing 2 296 974 and 2 441 847 person-years of follow-up, respectively. The incidence rate difference between no screening and screening was 28.2 per 100 000 person-years for CRC incidence and 10.2 per 100 000 person-years for CRC-related mortality (**Table 2**). Screening endoscopy at 75 years or younger was associated with a significantly reduced risk of CRC incidence and related mortality. The multivariable-adjusted models comparing participants who had undergone screening endoscopy at 75 years or younger with those who had not yielded HRs of 0.61 (95% CI, 0.55-0.67) for incident CRC and 0.54 (95% CI, 0.47-0.63) for CRC-related mortality.

Screening at Older Than 75 Years and According to Screening History

Among the 56 374 participants (35 603 women and 20 771 men) who had reached age 75 years during follow-up without being diagnosed with CRC, we documented 661 incident CRC cases and 323 CRC-related deaths, encompassing 385 309 and 458 675 person-years of follow-up, respectively. The incidence rate difference between no screening and screening was 74.1 per 100 000 person-years for CRC incidence and 7.9 per 100 000 person-years for CRC mortality. With further adjustment for screening history, screening endoscopy at older than 75 years remained significantly associated with a reduced risk of CRC incidence (HR, 0.61; 95% CI, 0.51-0.74) and related mortality (HR, 0.60; 95% CI, 0.46-0.78). The associations were not significantly different from those for screening endoscopy at 75 years or younger (P = .97 for heterogeneity for CRC incidence; P = .51 for heterogeneity for mortality). Additional adjustment for attendance at routine physicals as an indicator of use of health care resources did not materially alter the associations.

We conducted stratified analyses of those who underwent screening endoscopy at older than 75 years according to an individual's screening history (**Table 3**). We found that the associations of screening endoscopy at older than 75 years with CRC incidence and mortality did not significantly differ according to screening history (P = .07 and P = .99 for interaction, respectively). Among participants who had undergone screening endoscopy at 75 years or younger, continuation of screening after 75 years of age yielded a risk reduction for incident CRC (HR, 0.67; 95% CI, 0.50-0.89) and CRC-related mortality (HR, 0.58; 95% CI, 0.38-0.87) compared with those who stopped screening after 75 years of age. Likewise, among participants who had never undergone screening endoscopy at 75 years or younger, the HRs comparing screening vs nonscreening after 75 years of age were 0.51 (95% CI, 0.37-0.70) for incident CRC and 0.63 (95% CI, 0.43-0.93) for CRC-related mortality.

Additional Subgroups

In subgroup analyses (**Figure**), having a history of cardiovascular disease at 75 years of age or 3 or more comorbidities, including cardiovascular disease (myocardial infarction or stroke), hypertension, hypercholesterolemia, and diabetes, tended to mitigate the benefits of continuing screening endoscopy after 75 years of age in risk reduction for CRC-related mortality, although the interactions were not statistically significant. The multivariable HRs of CRC-related death comparing continuation of screening endoscopy after 75 years of age, independent of screening history, were 1.18 (95% CI, 0.59-2.35) among participants with cardiovascular disease and 1.17 (95% CI, 0.57-2.43) for those with 3 or more comorbidities. Having a family history of CRC did not modify the benefits of screening after 75 years of age.

The associations were consistent among men and women (eTable 1 in the Supplement). Screening colonoscopy and sig-

moidoscopy at older than 75 years were both associated with reduced risk of CRC incidence (HRs, 0.63 [95% CI, 0.51-0.79] and 0.57 [95% CI, 0.43-0.77], respectively) and related mortality (HRs, 0.64 [95% CI, 0.48-0.85] and 0.51 [95% CI, 0.33-0.79], respectively) (eTable 2 in the Supplement). When stratified according to anatomical subsites of CRC, screening endoscopy, regardless of whether it was performed at 75 years or younger or at older than 75 years, was more strongly associated with reduced risk of developing distal colon and rectal cancer (eTable 3 in the Supplement). For example, the multivariable HRs for incident CRC among participants who underwent screening endoscopy at older than 75 years, compared with those who did not, were 0.76 (95% CI, 0.59-0.98) for proximal colon cancer, 0.50 (95% CI, 0.34-0.75) for distal colon cancer, and 0.38 (95% CI, 0.22-0.64) for rectal cancer (P = .02 for heterogeneity).

Sensitivity Analyses

Based on our prospective design, we examined the association of screening endoscopy reported before the diagnosis of CRC in our primary analyses. Thus, a neglect of CRC cases reported on the same questionnaire cycle as a report of screening endoscopy may overestimate the benefit of screening. In sensitivity analysis with 2-year lagged exposure, the associations of screening endoscopy with incident CRC were slightly attenuated but remained significant (HR, 0.66; 95% CI, 0.59-0.72), and those with CRC mortality did not materially change (HR, 0.54; 95% CI, 0.46-0.63) (eTable 4 in the Supplement). When we further included endoscopy for occult fecal blood and follow-up of virtual colonography in the screening endoscopy group, associations between screening endoscopy at older than 75 years and incident CRC were similar (HR, 0.65; 95% CI, 0.54-0.78), whereas those with CRC mortality became attenuated (HR, 0.77; 95% CI, 0.60- 0.99) (eTable 5 in the Supplement). We did not detect substantial differences in the associations with CRC-related death when we further classified screening endoscopy according to additional age groups (≤60, 61-70, 71-75, and >75 years) (eTable 6 in the Supplement). Finally, screening endoscopy at older than 75 years was associated with modest increases in the risk of non-CRC-related mortality and all-cause mortality in age-adjusted analyses (eTable 7 and eTable 8 in the Supplement), which were no longer significant after accounting for other CRC risk factors.

Table 3. Screening Lower Endoscopy at Older Than 75 Years and Risk of CRC and CRC-Related Mortality According to Screening Endoscopy at 75 Years or Younger[a]

Outcome	Screening lower endoscopy after 75 y	
	No	Yes
Screening before or at 75 y		
CRC		
No. of cases	137	90
No. of person-years	91 881	76 573
HR (95% CI)[b]		
Age-adjusted	1 [Reference]	0.68 (0.51-0.90)
Multivariable-adjusted	1 [Reference]	0.67 (0.50-0.89)
CRC-related mortality		
No. of cases	58	51
No. of person-years	112 437	96 069
HR (95% CI)[b]		
Age-adjusted	1 [Reference]	0.63 (0.42-0.93)
Multivariable-adjusted	1 [Reference]	0.58 (0.38-0.87)
No screening before or at 75 y		
CRC		
No. of cases	286	51
No. of person-years	118 782	40 134
HR (95% CI)[b]		
Age-adjusted	1 [Reference]	0.50 (0.36-0.68)
Multivariable-adjusted	1 [Reference]	0.51 (0.37-0.70)
CRC-related mortality		
No. of cases	124	42
No. of person-years	133 781	46 940
HR (95% CI)[b]		
Age-adjusted	1 [Reference]	0.72 (0.50-1.05)
Multivariable-adjusted	1 [Reference]	0.63 (0.43-0.93)

Abbreviations: CRC, colorectal cancer; HR, hazard ratio.

[a] The numbers in these strata do not sum to the total number of participants older than 75 years in Table 2 owing to exclusion of participants with missing screening endoscopy history data before or at 75 years of age.

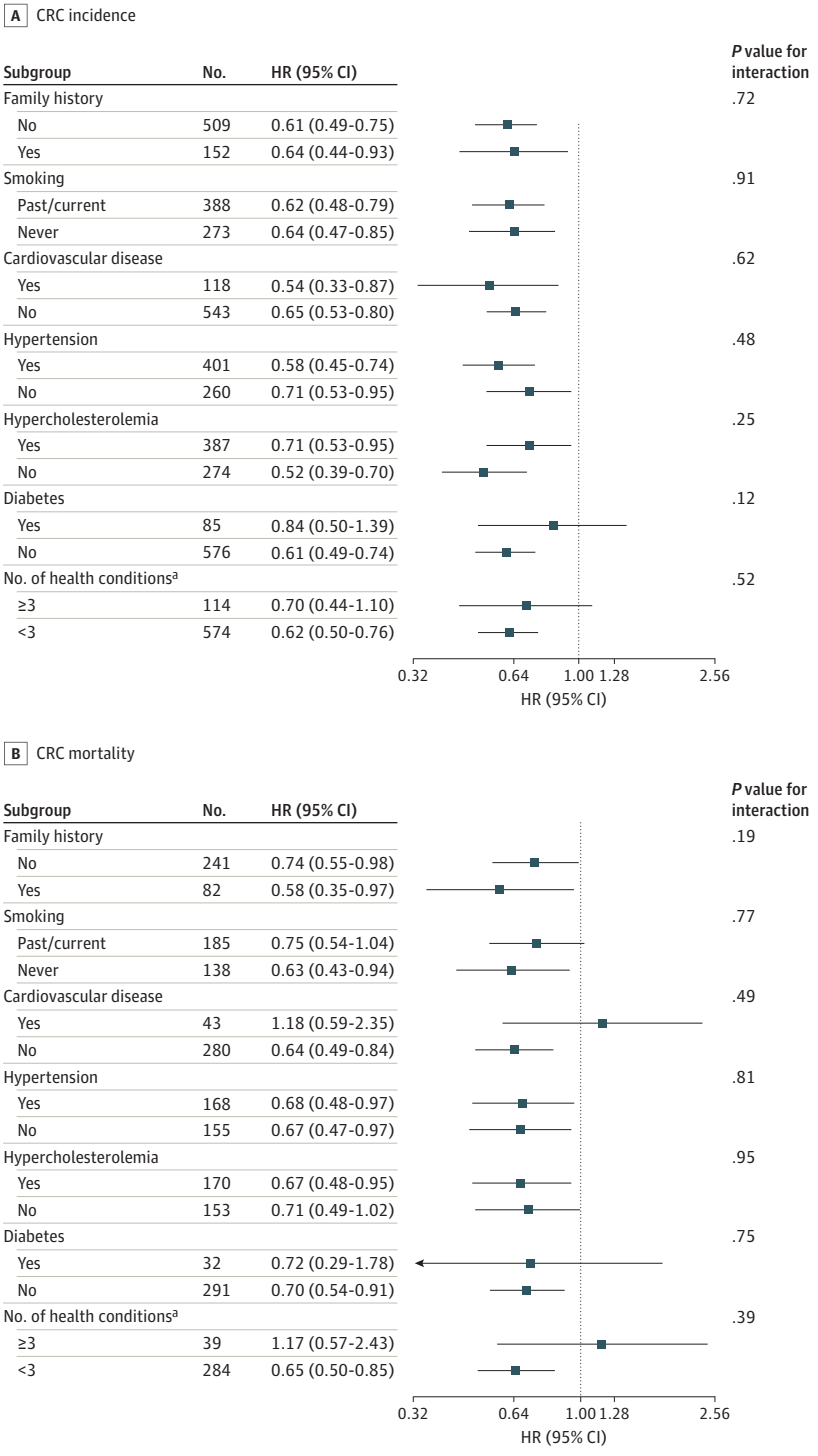
[b] Cox proportional hazards regression models were stratified by age, questionnaire cycle, and cohort, and multivariable models were further adjusted for family history of CRC, body mass index, physical activity, smoking, alcohol consumption, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, and intake of total calories, calcium, folate, or red and processed meat. We adjusted additionally for postmenopausal hormone use in women.

Discussion

In 2 large, prospective cohort studies in the US, we found that continuation of screening lower endoscopy after 75 years of age, regardless of screening history, was associated with reduced risk of CRC incidence and mortality. Screening endoscopy after 75 years of age was primarily associated with a lower incidence of distal colon and rectal cancer. Moreover, screening endoscopy after 75 years of age yielded a greater risk reduction for CRC death among certain subgroups of population, such as those without cardiovascular disease or with fewer comorbidities. In contrast, screening endoscopy was not associated with a benefit for CRC mortality among individuals with a history of cardiovascular disease or more comorbidities. These findings provide novel empirical evidence supporting both the initiation and continuation of screening endoscopy among many adults after 75 years of age for prevention of CRC incidence and related mortality, especially those without significant comorbidities.

Our study extends the previous findings of a study by Nishihara et al[19] in these cohorts, which showed that screening endoscopy was associated with a significantly reduced risk of CRC incidence and mortality among individuals with a median age younger than 60 years. Our results are also in line with prior evidence supporting CRC screening beyond 75 years of age.[11,20-22] Modeling studies have applied the microsimulation screening analysis-colon model to estimate the harms and

Figure. Screening Lower Endoscopy After 75 Years of Age and Risk of Colorectal Cancer (CRC) Incidence and Mortality in Subgroups of Family History of CRC, Cardiovascular Disease, and Cardiovascular Risk Factors



Hazard ratios (HRs) were calculated from Cox proportional hazards regression models that were stratified by age, questionnaire cycle, and cohort and further adjusted for family history of CRC, body mass index, physical activity, smoking, alcohol consumption, aspirin use, use of other nonsteroidal anti-inflammatory drugs, multivitamin use, prior screening endoscopy, and intake of total calories, calcium, folate, or red and processed meat. We additionally adjusted for menopausal hormone use in women.

[a] Includes cardiovascular disease (myocardial infarction or stroke), hypertension, hypercholesterolemia, and diabetes. Covariates at 75 years of age were used in these analyses.

benefits to determine the optimal age to stop CRC screening. For example, focusing on cost-effectiveness of screening endoscopy, it was demonstrated that screening should be considered in older adults who have not undergone previous screening to 86 years of age with no comorbidities, 83 years of age for those with moderate comorbidities, and 80 years of age for those with severe comorbidities.[11] Screening also appeared more cost-effective at older ages among those with a less intensive screening history, a high baseline risk for CRC, and fewer comorbidities.[20] A recent study[21,22] based on harm-benefit balance suggested that the optimal stop age for CRC screening ranged from 66 years for unhealthy individuals with

perfect screening history to 90 years for healthy individuals without prior screening. A previous analysis using a Medicare observational database[16] estimated that screening colonoscopy resulted in a modest, nonsignificant benefit in the reduction of 8-year risk for CRC, from 3.0% to 2.8%, for individuals aged 75 to 79 years. However, that study did not include patients who underwent screening at younger than 75 years and did not evaluate sigmoidoscopy or CRC mortality. We found that screening after 75 years of age showed no significant difference in the association with CRC incidence and death among people who had been screened at younger than 75 years compared with those who had not. These data suggest that among individuals older than 75 years without significant comorbidities, screening should be initiated for those who have never been screened and should be continued for those who had been screened previously.

Several factors might have affected the benefits of screening endoscopy for older adults. The baseline risk of colorectal neoplasia increases with age, leading to a greater percentage of older individuals who are likely to be effectively protected through early treatment or removal of precancerous polyps. On the other hand, comorbidities and risk of death due to competing diseases at an advanced age may offset the gains in life expectancy due to screening.[10,23] In addition, the benefits of endoscopy in older adults may be compromised owing to lower procedural completion rates, a higher risk of inadequate bowel preparation, and higher complication rates such as perforation, bleeding, and cardiovascular/pulmonary adverse events.[24-26] Nevertheless, the effects of screening endoscopy among older adults have not been adequately evaluated using empirical data. Given the difficulty of conducting randomized clinical trials of screening among older adults with sufficient follow-up, our data provide an important contribution in addressing this question.

Our results provide valuable information about the potential effects of screening endoscopy in individuals aged 75 years and older. We believe these could be complemented by future studies to inform guidelines on the age to discontinue routine screening for CRC. The absolute benefit of screening after 75 years of age could be estimated if the prevalence of screening use in the general population of older adults from national survey data was available. Studies on lesion detection rates during such a screening test can also provide a basis from which to infer long-term outcomes. Furthermore, for screening recommendations in older adults, the option to pursue other screening tests (eg, fecal immunochemical testing for stool DNA) should also be considered given the risk of procedural complications associated with colonoscopy. Ultimately, from a societal perspective, the recommendation to continue screening after 75 years of age and the chosen method will have to account for the cost-effectiveness and potential trade-offs, particularly under conditions of limited resources.

Strengths and Limitations

This study has several strengths. First, the biennial collection of endoscopy data with more than 28 years of follow-up allowed us to capture changes in the endoscopy status through adulthood and accurately assess the associations with subsequent risk of CRC incidence and related mortality, even among participants older than 75 years. Second, as indicated in our validation studies, the accuracy of the classification according to endoscopy status was high, because all participants were health care professionals. Third, the prospectively and repeatedly collected detailed information on lifestyle factors reduced the potential for residual confounding and recall bias.

Because the screening information was collected through biennial questionnaires, we did not know the exact date of screening examinations and were not able to identify screening-detected CRC accurately. Previous trials[3] have shown that the cumulative incidence of CRC in screening groups did not decrease until after 3 years after the intervention. However, in our study, the associations did not materially change in the sensitivity analysis adopting a 2-year lag in the assessment of screening before CRC diagnosis, indicating the robustness of our findings for the long-term benefits of screening.

We acknowledge other limitations to the study. Constrained by the relatively small number of incident cases in respective subgroups, we did not investigate whether the associations of screening endoscopy after 75 years of age with CRC incidence and mortality differed according to a history of other comorbidities, such as congestive heart failure or chronic kidney failure. In addition, as with other observational studies, we cannot eliminate the possibility of unmeasured confounding. Finally, our cohorts included mostly White health care professionals; studies in other racial/ethnic groups are needed to consider potential racial/ethnic disparities in CRC incidence and mortality.

Conclusions

In this prospective cohort study, continuation of screening endoscopy after 75 years of age was associated with a lower risk of CRC incidence and mortality, primarily distal CRC. The benefit was independent of screening history but may be modified by underlying health conditions such as a history of cardiovascular disease. Our findings provide evidence for patients, physicians, and policy makers to make informed decisions about CRC screening in an older population.

ARTICLE INFORMATION

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