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Lower Endoscopy Reduces Colorectal Cancer Incidence in Older Individuals

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This article has an accompanying continuing medical education activity on page e15. Learning Objective: Upon completion of this CME activity, successful learners will be able to discuss the effectiveness of lower endoscopy for colorectal cancer (CRC) prevention in older individuals.

See Covering the Cover synopsis on page 596.

BACKGROUND & AIMS: In older individuals, there are unclear effects of lower endoscopy on incidence of colorectal cancer (CRC) and of colonoscopy on site of CRC. We investigated whether sigmoidoscopy or colonoscopy is associated with a decreased incidence of CRC in older individuals, and whether the effect of colonoscopy differs by anatomic location. **METHODS:** We performed a case-control study using linked US Veterans Affairs and Medicare data. Cases were veterans aged 75 years or older diagnosed with CRC in fiscal year 2007. Cases were matched for age and sex to 3 individuals without a CRC diagnosis (controls). We determined the number of cases and controls who received colonoscopies or sigmoidoscopies from fiscal year 1997 to a date 6 months before the diagnosis of CRC (for cases) or to a corresponding index date (for controls). The probability of exposure was modeled using generalized linear mixed equations, adjusted for potential confounders. For the analysis of CRC risk in different anatomic locations, the proximal colon was defined as proximal to the splenic flexure. **RESULTS:** We identified 623 cases and 1869 controls (mean age, 81 y; 98.7% male, 86.2% Caucasian). Among cases, 243 (39.0%) underwent any lower endoscopy (177 colonoscopies). Among controls, 978 (52.3%) underwent any lower endoscopy (758 colonoscopies). Cases were significantly less likely than controls to have undergone lower endoscopy within the preceding 10 years (adjusted odds ratio [aOR], 0.58; 95% confidence interval [CI], 0.48–0.69). This effect was significant for colonoscopy (aOR, 0.57; 95% CI, 0.47–0.70), but not sigmoidoscopy. Similar results were observed when a 5-year exposure window was applied. Colonoscopy was associated with a reduced risk of distal CRC (aOR, 0.45; 95% CI, 0.32–0.62) and proximal CRC (aOR, 0.65; 95% CI, 0.46–0.92). **CONCLUSIONS:** In a study of the US Veterans Affairs and Medicare databases, lower endoscopy in the preceding 10 years was associated with a significant reduction in CRC incidence among older veterans. Colonoscopy was associated with significant reductions in distal and proximal CRC.

Keywords: Colon Cancer; Early Detection; Prevention; Geriatric Medicine.

The prevention of colorectal cancer (CRC) in older adults must consider competing factors that operate in opposite directions. Specifically, older individuals have a higher prevalence of colorectal neoplasia, but experience diminished health and life expectancy, and increased risk for procedure-related harm.[1–3] There is evidence that the use of CRC screening tests is not well targeted to those elderly patients who are most likely to benefit.[4,5] A study of a large cohort of veterans 70 years or older showed that only 47% of patients with no comorbidity were tested, whereas 41% of patients with severe comorbidity and a 5-year mortality rate of 55% received a screening test regardless.[5] A survey of Veterans Affairs (VA) health care providers showed a significant prevalence of inappropriate CRC screening decisions based on patient age, comorbidity, and prior screening history.[6]

Much of the uncertainty regarding CRC prevention in older adults stems from the relative paucity of studies informing evidence-based decisions. Knowledge of the effectiveness of lower gastrointestinal (GI) endoscopic procedures to prevent CRC in geriatric populations is a fundamental component of these decisions, but has been understudied. This is particularly the case for colonoscopy,

Abbreviations used in this paper: **aOR, adjusted odds ratio; CI, confidence interval; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; DSS, Decision Support System; FY, fiscal year; GI, gastrointestinal; ICD-9-CM, 9th revision of the Clinical Modification of the International Classification of Diseases; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio; VA, Veterans Affairs.**

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which in the elderly is associated with increased risks related to bowel preparation, sedation, and the procedure itself.[7–10] In older studies that support the effectiveness of lower endoscopic procedures, the elderly constituted numerically modest subgroups, and it is not clear whether the findings can be generalized to older age groups.[11–13]

Complicating the issue further is an expanding body of literature showing that although colonoscopy effectively decreases overall CRC incidence and mortality, the protection is less for proximal CRC than for distal CRC.[14–17] Whether and to what extent this affects elderly patients is unclear, but is important to study: epidemiologic data have shown a rightward shift in the distribution of CRC, which may be related to the ageing of the population,[18] and right-sided CRC is associated more frequently with molecular features that increase with age, such as methylation and microsatellite instability.[19] Thus, the effect of colonoscopy according to colon location constitutes another important consideration when making CRC screening decisions in the older population.

The primary aim of our study was to determine whether exposure to a lower gastrointestinal endoscopic procedure (sigmoidoscopy or colonoscopy) is associated with a reduced CRC incidence in older individuals. A secondary aim was to determine whether the effect of colonoscopy differs according to CRC location within the colon.

Methods

The study was approved by the Institutional Review Board at Indiana University–Purdue University at Indianapolis, and by the Richard L. Roudebush VA Medical Center Research and Development Committee in Indianapolis, Indiana. We conducted a case-control study to determine the association of CRC with exposure to lower-GI endoscopic procedures (colonoscopy and sigmoidoscopy) in veterans who were diagnosed with CRC at age 75 or older.

Data Sources

The VA system is the largest integrated health care system in the United States, and its databases contain information on medical diagnoses and procedures performed at any VA facility. Data for this study were obtained from the following:

1. The VA Medical SAS data sets. The VA Medical SAS datasets, housed at the Austin Information Technology Center in Austin, Texas, are national administrative data that contain information on all VA inpatient stays and outpatient encounters occurring at VA facilities. The data include patient-level information on diagnoses, procedures, surgeries, dates, and other utilization information. Diagnoses are coded according to the 9th revision of the Clinical Modification of the International Classification of Diseases (ICD-9-CM). Procedures occurring in the inpatient setting also are coded according to the ICD-9-CM; procedures occurring in the outpatient setting are coded using the Current Procedural Terminology codes and the Healthcare Common Procedure Coding System codes.

2. The VA Decision Support System (DSS) Pharmacy National Data Extract. The DSS pharmacy data include all outpatient prescriptions dispensed within the VA. In these analyses, the DSS pharmacy data were used to identify exposure to aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) between fiscal year (FY) 2002 and CRC diagnosis date or the corresponding index date for controls.

3. Linked VA Centers for Medicare and Medicaid Services (CMS) data. Linked VA–CMS data were obtained from the VA Information Resource Center. The linked VA–CMS data include CMS data for any veteran who has obtained health care services from the VA since 1992, has enrolled in the VA, or has received compensation or pension benefits from the VA since 2000. Similar to the VA Medical SAS data sets, the VA–CMS data contain inpatient and outpatient data, including diagnoses, dates of procedures, and other health care use information. For these analyses, the VA–CMS data were used to identify procedures performed in non-VA facilities for which CMS was the primary payor.

Identification of Cases and Controls

Cases were defined as veterans age 75 and older with a first diagnosis of CRC at a VA facility in FY 2007. The diagnosis was based on at least one inpatient ICD-9-CM code for CRC and/or at least 2 outpatient diagnoses for CRC on different days (ICD-9-CM codes listed in Supplementary Table 1). The VA Central Cancer Registry data did not become available to investigators until about 3 years after our project was funded and initiated. Our CRC identification algorithm was developed and validated at the Roudebush VA Medical Center in Indianapolis. Several algorithms were developed to ascertain incident CRC cases in 2001–2006 using administrative data, with the facility's cancer registry as the gold standard for CRC case ascertainment. The best algorithm, which was based on 1 inpatient or 2 or more outpatient CRC diagnoses, had a sensitivity of 85.8%, a specificity of 99.9%, a positive predictive value of 71.3%, an area under the curve (c-statistic) of 0.93, and was the one used for the present study. By using those codes, CRC location was defined as proximal (cecum, ascending colon, transverse colon) or distal (splenic flexure, descending colon, sigmoid colon, rectum). For 140 cases, the cancer location was unspecified at the time of diagnosis and not subsequently specified by available coding within 3 months of the index date; these cases and corresponding controls were analyzed separately in the secondary analysis examining the effect of colonoscopy by location. Thirty-two cases with codes for both left- and right-sided CRC (likely representing synchronous cancers) were excluded from the secondary analysis examining the effect of colonoscopy by location. To ensure that the identified cases were incident cancers, those with evidence of CRC by diagnostic coding and those who underwent colorectal surgical resection (ICD surgical codes and Current Procedural Terminology codes listed in Supplementary Table 2) between FY 1997 and FY 2006 were excluded. Each case patient was matched to 3 controls according to age ($\pm$1 y) and sex.

Controls were defined as veterans aged 75 or older without evidence of a CRC diagnosis during the same time frame in either the VA or VA–CMS data. To ensure comparable exposure time with cases, controls were assigned a time reference point that corresponded to the date of CRC diagnosis in their matched