Colorectal cancer mortality reduction is associated with having at least 1 colonoscopy within the previous 10 years among a population-wide cohort of screening age CME

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Background and Aims: Colonoscopy has been demonstrated to be effective in colorectal cancer (CRC) mortality reduction, although current screening guidelines have yet to be evaluated. We assessed the protective benefit of colonoscopy within the previous 10 years and whether this effect is maintained with age.

Methods: We used administrative data to compare risk of CRC death (CCD) across colonoscopy utilization among a population-wide cohort comprising individuals aged 60 to 80 years (N = 1,509,423). Baseline and time-dependent colonoscopy exposure models were assessed in the context of competing "other causes of death" (OCDs). Cumulative incidence of CCD and OCD across colonoscopy exposure, over follow-up, was estimated. Relative hazards were computed by age strata (60-69 years, 70-74 years, 75+ years) and proximal and distal cancer subsites.

Results: At least 1 colonoscopy during 10 years before baseline was estimated to provide a 51% reduced hazard of CCD (hazard ratio [HR] 0.49; 95% confidence interval [CI], 0.45-0.54) over the following 8 years. When colonoscopy was modeled as a time-dependent covariate, the risk of CCD was further diminished (multivariable-adjusted HR 0.36; 95% CI, 0.33-0.38). Stratified analyses suggested moderately attenuated CCD risk reduction among the oldest age group; however, consideration of OCDs suggest that this is related to competing risks. CCD risk reduction related to colonoscopy was lower for proximal cancers.

Conclusions: Colonoscopy within the previous 10 years provides substantial protective benefit for average-risk individuals over 60 years. CCD risk reduction may be maintained well beyond 74 years, a common upper age limit recommended by screening guidelines. (Gastrointest Endosc 2016;84:133-41.)

Colorectal cancer (CRC) is the second and third leading cause of cancer mortality for Canadian men and women, respectively, yet disease-specific mortality has been in decline over the past decade.[1] Although this reduction has been attributed to advances in treatment,[2] increased screening uptake is likely an important contributing factor.[3] Because of its high sensitivity and specificity and the ability to excise precancerous lesions during the

Abbreviations: CCD, colorectal cancer death; CIHI, Canadian Institute for Health Information; CRC, colorectal cancer; DAD, discharge abstract database; HR, hazard ratio; OCD, other causes of death; OCR, Ontario Cancer Registry; OHIP, Ontario Health Insurance Plan; SDS, Same Day Surgery database.

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procedure (ie, polypectomy), colonoscopy is considered the modality of choice for CRC screening in the United States.[4] Cancer detection at screening colonoscopy has been associated with lower rates of recurrence, longer disease-free survival, and lower mortality.[5]

Although colonoscopy utilization has been on the rise in North America[6-8] and some European countries,[9] there are no published results for CRC mortality from randomized controlled trials. Pooled results from 4 trials evaluating flexible sigmoidoscopy for screening have demonstrated reductions of approximately 20% and 30%, in CRC incidence and mortality, respectively. Those for the per-protocol analyses demonstrated a further increase in these reductions of 15%.[10] Meta-analysis of observational evidence has demonstrated screening colonoscopy to be even more efficacious in reducing the risk of these outcomes.[10] Case control[11-16] and cohort[17-19] studies evaluating all-indication colonoscopy have reported similarly strong effects, upholding the benefits of complete large-bowel endoscopy in CRC prevention, regardless of the indication for the procedure.

Recent clinical consensus on CRC screening recommends colonoscopy every 10 years for average-risk individuals.[4,20-22] However, none of the existing evidence has specifically evaluated this guideline, with prior observational studies comparing ever versus never colonoscopy exposure accrued over arbitrary intervals. The majority of observational studies on the efficacy of colonoscopy in CRC prevention have been case-control designs, the few longitudinal analyses of right-censored data having not considered findings in context of competing outcomes.[19,23] Ignoring competing causes of failure in survival analyses can result in biased estimation of covariate effects and cumulative incidence, potentially obscuring interpretation of colonoscopy benefit.

This study assessed the protective benefit of colonoscopy within the previous 10 years on the hazard of CRC death (CCD) in a population-wide Ontario cohort of screening age within a competing risks framework.

METHODS

Data sources

All data were sourced from Ontario, Canada administrative health databases. The Ontario Health Insurance Plan (OHIP) database contains billing claim records for all insured services performed by physicians in the province. The Ontario Cancer Registry (OCR), capturing diagnostic and mortality information on all new cases, except non-melanoma skin cancers, since 1964 has been validated as being of high quality.[24] The Canadian Institute for Health Information (CIHI) Discharge Abstract (CIHI-DAD) and Same Day Surgery (CIHI-SDS) databases collectively contain diagnostic, procedural, and vital status information on all persons who have been discharged from hospitals or outpatient surgery. The Registered Persons Database (RPDB) contains demographic information on all OHIP-insured individuals, comprising almost all Ontarians. Administrative databases were linked through the Institute for Clinical Evaluative Sciences (ICES). ICES operates under special mandate from the Ontario Ministry of Health and Long-Term Care, obviating the requirement for individual consent for use of administrative health data for approved research. Ethics approval was provided by the Sunnybrook Health Sciences Centre Research Institute Research Ethics Board in Toronto.

Study population

The study was conducted among an Ontario population-wide cohort comprising individuals aged 60 through 80 years on January 1, 2002 (ie, follow-up start) who had no prior diagnosis of CRC recorded in the OCR. Baseline exclusions included hospitalization for inflammatory bowel disease and radical colorectal surgery within the previous 10 years, identified in CIHI-DAD and CIHI-SDS databases, because these were deemed likely to constrain colonoscopy utilization and confound the association between colonoscopy use and death. Individuals with these criteria incident after January 1, 2002 but before CRC diagnosis were additionally excluded to avoid these sources of bias.

Study variables

Main exposure. The main exposure was all-indication colonoscopy, identified by using OHIP billing codes as described previously.[13,25] Colonoscopy exposure was ascertained from January 1, 1992, making this age range appropriate to study the effect of colonoscopy exposure among Ontarians aged 50 years and older, the recommended screening age in Canada,[20] the United States,[4,21] and Europe.[22] Extent of colonoscopy was evaluated by using 3 classifications. Our main exposure classification, complete colonoscopy, included endoscopy complete to the cecum, or terminal ileum. Two additional classifications included procedures terminating at least as far as the splenic and hepatic flexures. Colonoscopies terminating distal to these regions or of unspecified extent, and flexible sigmoidoscopy, did not qualify for positive exposure status.

Because OHIP has only recently implemented billing codes distinguishing between screening and diagnostic colonoscopies, we were unable to limit exposure to the former. As has been done elsewhere,[13] we attempted to minimize inclusion of CRC diagnostic colonoscopies by disregarding those performed after 6 months prior to a CRC diagnosis.

OUTCOME

The primary study outcome was CCD. All other causes of death were defined as *other cause* (OCD). Date of death was determined from date of last contact from the RPDB.