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Characteristics of Missed or Interval Colorectal Cancer and Patient Survival: A Population-Based Study

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BACKGROUND & AIMS: Colorectal cancers (CRCs) diagnosed within a few years after an index colonoscopy can arise from missed lesions or the development of a new tumor. We investigated the proportion, characteristics, and factors that predict interval CRCs that develop within 6–60 months of colonoscopy. **METHODS:** We performed a population-based cohort study of Utah residents who underwent colonoscopy examinations from 1995 through 2009 at Intermountain Healthcare or the University of Utah Health System, which provide care to more than 85% of state residents. Colonoscopy results were linked with cancer histories from the Utah Population Database to identify patients who underwent colonoscopy 6–60 months before a diagnosis of CRC (interval cancer). Logistic regression was performed to identify risk factors associated with interval cancers. **RESULTS:** Of 126,851 patients who underwent colonoscopies, 2659 were diagnosed with CRC; 6% of these CRCs (159 of 2659) developed within 6 to 60 months of a colonoscopy. Sex and age were not associated with interval CRCs. A higher percentage of patients with interval CRC were found to have adenomas at their index colonoscopy (57.2%), compared with patients found to have CRC detected at colonoscopy (36%) or patients who did not develop cancer (26%) ($P < .001$). Interval CRCs tended to be earlier-stage tumors than those detected at index colonoscopy, and to be proximally located (odds ratio, 2.24; $P < .001$). Patients with interval CRC were more likely to have a family history of CRC (odds ratio, 2.27; $P = .008$) and had a lower risk of death than patients found to have CRC at their index colonoscopy (hazard ratio, 0.63; $P < .001$). **CONCLUSIONS:** In a population-based study in Utah, 6% of all patients with CRC had interval cancers (cancer that developed within 6 to 60 months of a colonoscopy). Interval CRCs were associated with the proximal colon, earlier-stage cancer, lower risk of death, higher rate of adenoma, and family history of CRC. These findings indicate that interval colorectal tumors may arise as the result of distinct biologic features and/or suboptimal management of polyps at colonoscopy.

Keywords: Colon Cancer; Detection; Screening; Missed or Interval Cancer.

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Colorectal cancer (CRC) is the third most common cancer in the United States and the second leading cause of cancer-related mortality in men and women.[1] Adenomatous polyps are accepted as the precursor lesion for most colorectal cancer. Colonoscopy can detect and remove precursor lesions and diagnose patients at an earlier stage of cancer. Colonoscopy is the preferred option for CRC screening in the United States.[2] It is hypothesized that most CRCs diagnosed within a few years (3–5 y) after an index colonoscopy are owing to missed lesions or new interval cancer development. In the literature, these tumors variously have been referred to as missed, interval, or postcolonoscopy CRC. Controversy exists around the effectiveness of colonoscopy for preventing CRC and the risk of interval cancers after screening colonoscopy.

The few large population-based studies that have evaluated the risk and predictors of interval CRCs at colonoscopy have reported rates as high as 14%.[3] Six population-based studies, 2 from Canada,[4,5] 1 from Germany,[6] 1 from The Netherlands,[7] a US study limited to the Medicare population,[8] and an analysis of 3 chemoprevention polyp trials,[9] have

Abbreviations used in this paper: **CI, confidence interval; CRC, colorectal cancer; EMR, electronic medical record; FAP, familial adenomatous polyposis; HR, hazard ratio; IHC, Intermountain Healthcare; OR, odds ratio; UPDB, Utah Population Database; UUHSC, University of Utah Health Sciences.**

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described the development of colorectal cancer after colonoscopy with rates ranging between 2.9% and 7.9%. An additional study limited to a single Veterans Affairs medical center also reported an interval CRC rate of 5.1%.[10]

Most of these previous reports came from countries with health care systems that differ from those of the United States Studies completed solely in Veterans[11] or Medicare[8] populations also may not be generalizable to the US population and routine clinical practice.

In this study we assessed the proportion, characteristics, and predictors of interval CRCs occurring within 5 years of colonoscopy in a large population-based study from Utah, reflecting usual clinical care in the United States.

Materials and Methods

Design

This study was approved by the Institutional Review Boards of the University of Utah and Intermountain Healthcare (IHC), and by the Resource for Genetic and Epidemiologic Research (http://www.research.utah.edu/rge/), an administrative oversight board created to govern access to the Utah Population Database (UPDB).

We performed a population-based retrospective cohort study of residents in the state of Utah, between 50 and 80 years of age, who underwent colonoscopy between February 15, 1995, and January 31, 2009, at IHC and/or the University of Utah Health Sciences (UUHSC) clinical facilities. By using the UPDB, de-identified medical information on these patients was merged with cancer histories from the Utah Cancer Registry.

Description of Databases

This investigation took advantage of unique Utah databases. The study required patient-level data integration between IHC, the UUHSC, and the UPDB. The UPDB combines genealogies with data from statewide resources, including the Utah Cancer Registry, statewide inpatient discharge and ambulatory surgery records, driver's license data, as well as birth and death certificates. This resource also has been linked to the demographic records from the UUHSC[12] and IHC.[13] In combination, the UUHSC and IHC together provide care to more than 85% of the Utah population. Previous demographic and genetic analyses have shown that the population recorded in the Utah Population Database is genetically representative of US white and northern European populations with a low level of inbreeding.[14] Of particular interest for this study was the inclusion of the Utah Cancer Registry records as part of the UPDB. The Utah Cancer Registry is a statewide cancer registry established in 1966, and since 1973 it has been part of the Surveillance, Epidemiology, and End Results network of the National Cancer Institute registries. State law requires that all cancer diagnosis be notified to the Utah Cancer Registry.

Linkage of Electronic Medical Record Data to the UPDB

These linked resources have been used to assess colonoscopy screening rates in high-risk individuals[15] as well as recent studies on preeclampsia,[16] spontaneous preterm delivery,[17] cancer in twins,[18] heritability of inflammatory bowel disease,[19] and effects of family conditions on later-life mortality.[20]

Study Definition

Colonoscopy procedure information was extracted from the Intermountain Healthcare and University of Utah Health Sciences electronic medical records (EMRs) using Current Procedural Teminology codes 45378, 45379, 45380, 45383, 45384, or 45385. A diagnosis of colorectal cancer in patients undergoing colonoscopy was identified through the Utah Cancer Registry. We defined interval CRCs as cases in which a colonoscopy was performed between 6 and 60 months (primary definition) or 6 and 36 months (secondary definition) before CRC diagnosis and detected CRCs as those diagnosed within 6 months of a colonoscopy as outlined in Figure 1. Both of these definitions have been used in multiple prior studies to determine the CRC miss rate at the index procedures.[3,5,6,8,10] This is based on the assumption that CRCs suspected/detected on a colonoscopy would be diagnosed within 6 months of the index procedure. A period of 36–60 months was used in this analysis to define interval cancers because this window is the estimated mean sojourn time (the duration of the preclinical screen-detectable period) for CRC. Polypectomy and resultant adenomas and villous adenomas (defined as those

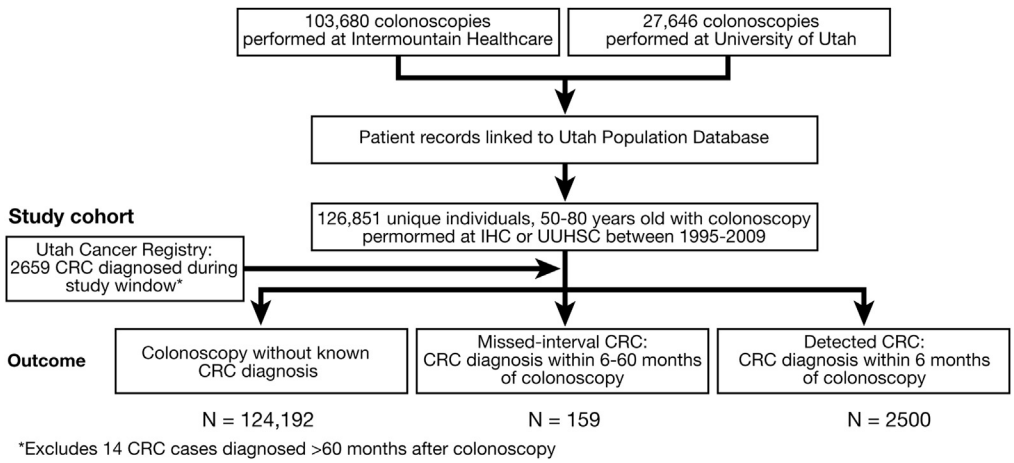

Figure 1. Study flow diagram.