

## Protective association of colonoscopy against proximal and distal colon cancer and patterns in interval cancer

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**Background:** The protective effect of colonoscopy against proximal colorectal cancer is variable and depends on the detection and complete removal of precancerous polyps.

**Objective:** To estimate the efficacy of colonoscopy in a medical center with open-access screening colonoscopy since 1998.

**Design:** Nested case-control study with incidence density sampling.

**Setting:** University-affiliated Veterans Affairs Medical Center.

**Patients:** Colorectal cancer (CRC) cases and control subjects selected from screening age patients matched by age, gender, and date of first primary care visit.

**Main Outcome Measurement:** Colonoscopy preceding the CRC diagnosis date.

**Results:** A total of 20.2% of CRC cases had a colonoscopy in the preceding 10 years compared with 49.0% of control subjects (adjusted odds ratio [aOR], 0.20; 95% confidence interval [CI], 0.11-0.34). Colonoscopy was strongly associated with decreased odds of both distal CRC (aOR, 0.16; 95% CI, 0.07-0.34) and proximal CRC (aOR, 0.26; 95% CI, 0.11-0.58). The fraction of cases attributed to interval cancers was 10.5%. Missed lesions predominantly localized to the cecum and rectum, and recurrent lesions clustered in the hepatic flexure. Cecal intubation rate was 93% (98% in adequately prepped patients), and the adenoma detection rate was 45.2% in the control group.

**Limitations:** Single-center, retrospective case-control design.

**Conclusion:** In an open access colonoscopy program characterized by a high cecal intubation rate and adenoma detection rate, colonoscopy was strongly associated with reduced odds of both distal and proximal CRC. Among interval cancers, missed lesions clustered in the cecum and rectum and recurrent lesions in the hepatic flexure. (Gastrointest Endosc 2015;82:529-37.)

*Abbreviations:* ADR, adenoma detection rate; CPRS, computerized patient record system; CRC, colorectal cancer; PCCRC, "postcolonoscopy" colorectal cancer; PCP, primary care provider; SFVAMC, San Francisco Veterans Administration Medical Center; VHA, Veterans Health Administration.

*DISCLOSURE:* The following author received research support for this study from the National Institutes of Health (K23 CA157929): M. Somsouk. All authors disclosed no financial relationships relevant to this publication.

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<http://dx.doi.org/10.1016/j.gie.2015.01.053>

Received June 12, 2014. Accepted January 27, 2015.

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Despite continued reductions in the rates of colorectal cancer (CRC) incidence and death, CRC remains the third most common noncutaneous cancer diagnosed in both men and women and the third leading cause of cancer-related death.<sup>1</sup> The decreasing CRC incidence over time has been attributed to increased patient participation in CRC screening programs,<sup>1</sup> which is recommended for average-risk adults age 50 years and older.<sup>2</sup> Fecal occult blood testing,<sup>3,4</sup> flexible sigmoidoscopy,<sup>5-9</sup> and colonoscopy<sup>7,10-14</sup> have all been shown to reduce CRC incidence and mortality; however, the protective effect of colonoscopy against the incidence of CRC in the proximal colon has not been consistently demonstrated.<sup>7,15-17</sup> Cancers arising after a prior colonoscopy, termed “postcolonoscopy” CRC (PCCRC),<sup>18</sup> account for 0.6% to 9% of CRCs in the literature.<sup>18-22</sup> In addition to proximal colon location, the risk of developing PCCRC has been associated with the quality of the index examination,<sup>23</sup> patient factors,<sup>21,23</sup> tumor biology,<sup>7</sup> and procedural factors, such as endoscopist subspecialty, cecal intubation rate, and adenoma detection rate (ADR).<sup>17-20,22,24,25</sup> Recent studies indicate that most PCCRCs are attributable to procedural factors, such as missed lesions, inadequate examinations, or incomplete resection.<sup>26,27</sup>

The San Francisco Veterans Administration Medical Center (SFVAMC) instituted an open-access screening colonoscopy program in 1998, after participating in the Veterans Affairs Cooperative Study Group 380.<sup>28</sup> Providers are able to request a screening colonoscopy by placing an electronic consult through the Veterans Health Administration (VHA) computerized patient record system (CPRS). Patients are scheduled for the procedure and given instruction for preprocedure preparation over the phone by trained nursing staff. Since 1999, an automated clinical computerized reminder was implemented throughout the VHA to ensure each individual member would have up-to-date health maintenance information.<sup>29</sup> The SFVAMC required resolution of the computerized reminder for CRC screening in approximately 2001. Although before 1998 some colonoscopies performed at the SFVAMC were screening colonoscopies (9% in 1996; 17% in 1997), the number steadily increased between 1998 and 2006, peaking in 2006 with 49% of procedures performed for a screening indication. Since 2006, screening colonoscopies have comprised 35% to 40% of our colonoscopy examinations.

In this study, we sought to evaluate whether colonoscopy use is associated with a reduced odds of both proximal and distal CRC. In addition, we sought to examine the potential factors contributing to interval cancers in a healthcare system where screening colonoscopy is rigorously applied.

## METHODS

### Study design

This was a nested case-control study with incidence density sampling of CRC cases and control subjects at

the SFVAMC between 1998 and 2011. Fourteen colonoscopists (13 board-certified gastroenterologists, 1 board-certified colorectal surgeon) performed colonoscopies at our institution during this time frame. This research was approved by the University of California San Francisco Institutional Review Board and the San Francisco VA Clinical Research Office on March 24, 2006 (11-05427).

### Data sources

Cases were identified using the SFVAMC cancer registry, which collects and reviews all diagnoses of cancer from the catchment area and reports to the Surveillance Epidemiology and End Results Program. Patient-level data on cases and control subjects were gathered from the VHA CPRS. CPRS, released in 1996, is the graphic user interface for the Veterans Health Information Systems and Technology Architecture, or Vista, integrated electronic medical record system and is used throughout the VHA for all aspects of patient care and treatment.<sup>29,30</sup> CPRS allows healthcare providers to review and update all electronic medical records for patients enrolled in the local facility or community-based outpatient clinics, including problem lists, inpatient and outpatient progress notes, medications, orders, consults, lab results, radiology results, procedure and pathology results, operative reports, and discharge summaries. CPRS documentation is also available on the Vista intranet, referred to as VistaWeb, which is a read-only intranet web portal that combines patient records from multiple VHA facilities. CPRS supports clinical decision-making and includes a clinical reminders package, which targets patients of a particular age, diagnosis, or other site-defined criteria for preventive health care and management of chronic conditions, ensuring that timely clinical interventions are initiated at the point of care.<sup>31</sup>

Clinical reminders were mandated nationally in the VHA in 1999.<sup>29</sup> The requirement to resolve computerized reminders for CRC screening at the SFVAMC began in 2001. Clearance of clinical reminders is audited internally on a yearly basis. Only performance of CRC screening (via colonoscopy, sigmoidoscopy, barium enema, or fecal occult blood testing) is able to resolve the clinical reminder, except in cases of a current cancer diagnosis or short life expectancy. Therefore, exposure to colonoscopy or other CRC screening could be reliably ascertained by reviewing the medical records.

### Identification of case subjects

Case subjects included members 50 years of age or older who were found on pathology (by either colonoscopy or on surgical specimen) to have an adenocarcinoma of the colon or rectum between 1998 and 2011 and who had been seen by a primary care provider (PCP) at least 6 months before diagnosis. Patients were excluded if they were diagnosed with CRC within 6 months of their first primary care visit. These “acute referrals” were not considered cases in this study because they did not have

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