

Trends in Colorectal Cancer Incidence Rates in the United States by Tumor Location and Stage, 1992–2008

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Abstract

Background: Results from case-control studies outside the United States have been conflicted about the efficacy of colonoscopy for reducing cancer risk in the right colon. To contribute to this discourse from an alternative perspective, we analyzed high-quality surveillance data to report on recent trends in population-based colorectal cancer incidence rates by tumor location in the United States.

Methods: Data from cancer registries in the Surveillance, Epidemiology, and End Results Program were analyzed to examine colorectal cancer incidence trends from 1992 through 2008 among individuals aged ≥ 50 years ($n = 267,072$). Joinpoint regression analysis was used to quantify annual percent change in age-standardized rates by tumor location and disease stage.

Results: Incidence rates for right-sided colon tumors decreased annually by 2.6% (95% CI: 2.0–3.2) since 1999 in men and 2.3% (CI: 1.6–3.0) since 2000 in women, after remaining stable during the previous seven/eight years. Incidence rates for left-sided tumors were generally decreasing from 1992 to 2008 in both sexes. Beginning in 1999/2000, substantial, almost identical annual declines occurred for late-stage disease in both the right and left colon: 3.9% (CI: 3.1–4.8) and 4.2% (CI: 3.5–4.9), respectively, in men; and 3.3% (CI: 2.5–4.1) and 3.3% (CI: 2.8–3.8) in women.

Conclusion: Large declines in the incidence of right-sided colon tumors among individuals 50 years and older began around 2000.

Impact: Increased colonoscopy utilization during the past decade may have contributed to a reduction in risk for cancers in both the right and left colorectum in the United States. *Cancer Epidemiol Biomarkers Prev*; 21(3): 411–6. ©2012 AACR.

Introduction

It has been estimated that up to two-thirds of all colorectal cancers (CRC) are preventable by colonoscopy (1, 2), and the rapid declines in population-based CRC incidence rates in the United States since 1998 have been predominantly attributed to an increase in colonoscopy utilization (3, 4). Colonoscopy use increased very gradually during the 1990s (5, 6), then accelerated rapidly from a prevalence of 20% in 2000 to 48% in 2008 among Americans 50 years and older, according to the National Health Interview Survey (7). One of the drivers of this increase was the expansion of Medicare coverage to include colonoscopy as a screening option for high-risk individuals in 1998 and for all beneficiaries in 2001 (8–10).

Approximately 42% of CRC patients in the United States are diagnosed with a malignancy in the right, or

proximal, colon, which spans from the cecum through the transverse colon up to the splenic flexure (11). Of the 3 most common screening modalities in the United States, only colonoscopy and high-quality fecal occult blood test (FOBT) have the potential to detect precancerous polyps in the right colon, though FOBT primarily identifies cancer (12). Several case-control studies conducted in Canada and Germany in recent years found that colonoscopy has little or no benefit for the prevention of right-sided lesions (13–16). In contrast, Brenner and colleagues have reported a 56% reduction in right-sided colon cancer risk associated with a colonoscopy in the previous 10 years (17). Although colonoscopy is likely less effective in the right than in the left colon for many reasons, including differences in tumor biology and bowel characteristics (18), it is counterintuitive that this screening option offers no protection against right-sided malignancies because the colonoscope allows visualization and removal of polyps in the right colon, and polypectomy has been shown to decrease cancer risk (19).

Descriptive studies are unique in their ability to monitor changes in disease patterns in relation to public health interventions at the population level, and have also been valuable in supporting findings of analytic studies. We attempted to shed light on the relationship between colonoscopy utilization and cancer risk in the right colon by

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analyzing population-based incidence trends for CRC by tumor location and stage at diagnosis among patients 50 years and older during the recent increase in colonoscopy uptake in the United States.

Methods

Data

We obtained invasive CRC cases diagnosed in adults 50 years and older between 1992 and 2008 from the 13 oldest cancer registries in the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (11). The states, metropolitan areas, and other registries that comprise the SEER 13 database, which covers approximately 14% of the U.S. population, are Atlanta, Connecticut, Detroit, rural Georgia, Hawaii, Iowa, Los Angeles, New Mexico, San Francisco-Oakland, San Jose-Monterey, Seattle-Puget Sound, Utah, and the Alaska Native Tumor Registry. We restricted our analysis to individuals 50 years and older because guidelines recommend that CRC screening begin at age 50 among asymptomatic, average-risk adults (12).

Statistical analysis

We calculated age-adjusted CRC incidence rates (using the 2000 U.S. standard population), expressed per 100,000 persons, by anatomic subsite, stage at diagnosis, and sex using SEER*Stat software version 7.0.4 (20). Tumor location within the colorectum was designated right-sided (C18.0 and C18.2–C18.4, corresponding to cecum, ascend-

ing colon, hepatic flexure, and transverse colon) or left-sided (C18.5–C18.7, C19.9, and C20.9, corresponding to splenic flexure, descending colon, sigmoid colon, recto-sigmoid junction, and rectum) according to the *International Classification of Diseases for Oncology*, 3rd edition (ICD-03; ref. 21). Stage at diagnosis was grouped into early (local), late (regional and distant combined), or unstaged disease according to SEER Summary Stage guidelines (22). We then evaluated incidence trends from 1992 to 2008 using the Joinpoint Regression Program, version 3.5.0 (23), allowing a maximum of 2 joinpoints. The joinpoint model uses a sequence of permutation tests to select the optimal number of "joinpoints"—that is, points in time in which the trend changes in direction or magnitude. The slope of the line segment between joinpoints is described as the annual percent change, the statistical significance for which is set at the $\alpha = 0.05$ level.

Results

There were 112,589 cases of cancer diagnosed in the right colon and 154,483 cases diagnosed in the left colon among patients 50 years and older in the 13 oldest SEER areas during 1992 to 2008. The likelihood of a right-sided tumor location was higher in women (47%) than in men (37%). After remaining stable during the 1990s, overall incidence rates of right-sided colon cancer decreased similarly in men and women in the 2000s, by 2.6% per year (95% CI: 2.0–3.2) in men and by 2.3% per year (CI: 1.6–3.0) in women (Fig. 1, Table 1). These declines were

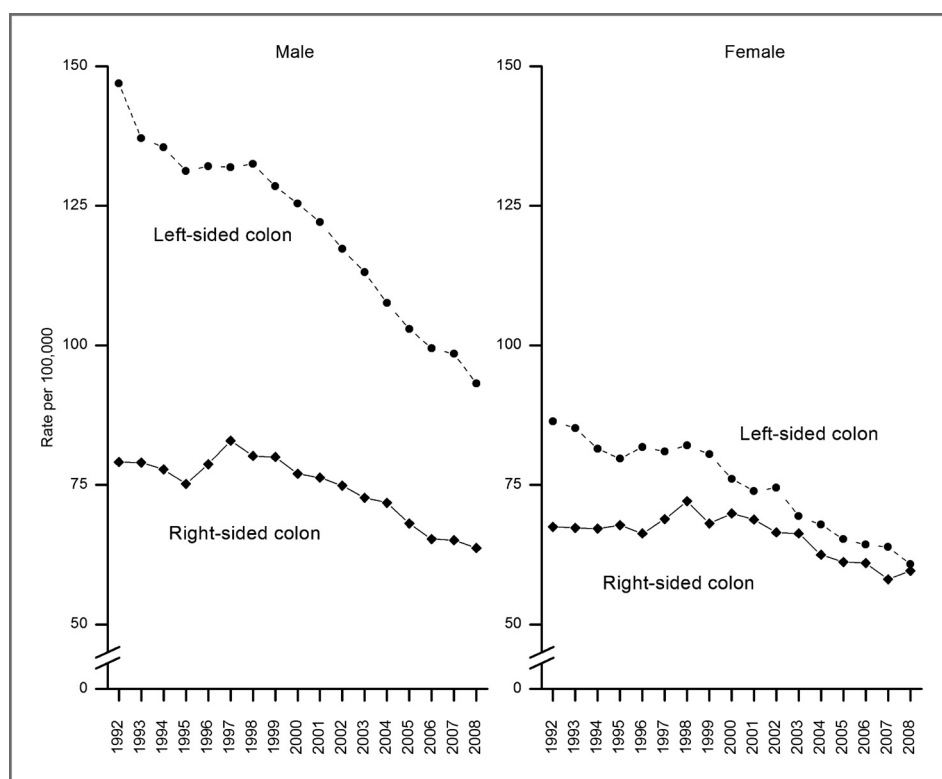


Figure 1. Trends in colorectal cancer incidence rates among adults 50 years and older by tumor location, 1992–2008.

Table 1. Trends in colorectal cancer incidence rates among adults 50 years and older by tumor location and stage, 1992–2008

Sex	Location	Stage	N	Trend 1		Trend 2		Trend 3	
				Years	APC	Years	APC	Years	APC
Male	Right side	All	49,849	1992–1999	0.5	1999–2008	–2.6 ^a		
		Early	19,161	1992–1998	1.9 ^a	1998–2008	–0.9 ^a		
		Late	29,131	1992–2000	–0.3	2000–2008	–3.9 ^a		
		Unstaged	1,557	1992–2008	–3.8 ^a				
	Left side	All	84,589	1992–1995	–3.5 ^a	1995–1998	0.9	1998–2008	–3.5 ^a
		Early	38,308	1992–1995	–4.1 ^a	1995–1999	1.4	1999–2008	–3.2 ^a
		Late	42,285	1992–2000	–1.6 ^a	2000–2008	–4.2 ^a		
		Unstaged	3,996	1992–2008	–4.7 ^a				
Female	Right side	All	62,740	1992–2000	0.6	2000–2008	–2.3 ^a		
		Early	23,576	1992–2001	2.1 ^a	2001–2008	–1.0		
		Late	36,885	1992–2000	–0.2	2000–2008	–3.3 ^a		
		Unstaged	2,279	1992–2008	–4.2 ^a				
	Left side	All	69,894	1992–1995	–2.6 ^a	1995–1998	0.7	1998–2008	–2.9 ^a
		Early	30,822	1992–1999	–0.3	1999–2008	–2.4 ^a		
		Late	35,147	1992–1999	–1.2 ^a	1999–2008	–3.3 ^a		
		Unstaged	3,925	1992–2008	–3.8 ^a				

Abbreviation: APC, annual percent change.

^aThe APC is significantly different from zero ($P \leq 0.05$).

primarily driven by large decreases in the incidence of late-stage disease, by 3.9% per year (CI: 3.1–4.8) in men and by 3.3% per year (CI: 2.5–4.1) in women. Incidence rates for early stage cancers in the right colon increased significantly during the 1990s by about 2% per year in both men and women, then moderately declined (not statistically significant in women).

The overall incidence of left-sided colorectal tumors was generally decreasing during 1992 to 2008 at annual rates of 3.5% in men and 2.6% to 2.9% in women, though an interruption occurred from 1995 to 1998 in both sexes (Table 1). Moderate declines during the 1990s for late-stage disease in the left colon almost tripled during the 2000s, from 1.6% (CI: 0.8–2.3) to 4.2% (CI: 3.5–4.9) per year in men and from 1.2% (CI: 0.5–2.0) to 3.3% (CI: 2.8–3.8) per year in women. Incidence rates for unknown stage showed declining annual trends of 4% to 5% throughout the study period, regardless of tumor location. Notably, between 1992–1999 and 2000–2008, the proportion of late-stage tumors decreased from 61% to 57% in the right colon, but remained relatively unchanged in the left colon and rectum (51%–50%).

Discussion

Our study found that incidence rates for right-sided colon cancer in individuals 50 years and older began declining in 1999/2000 after remaining stable in the previous decade. In contrast, rates of left-sided CRC have been generally decreasing since 1992. Although the proportion of right-sided tumors was higher in women than

in men, incidence patterns by tumor location and stage were generally similar across gender. The rapid declines for late-stage disease beginning in 2000 were strikingly similar for right- and left-sided tumors in both magnitude and timing, and, as others have noted (24), likely reflect the influence of increased colonoscopy screening. Our results are consistent with previous analyses of CRC incidence trends by subsite (4, 24). However, we expanded upon earlier studies by examining these trends according to stage at diagnosis using the most current available data, further supporting findings that colonoscopy may be beneficial for reducing cancer risk in both the left and right colon (1, 17, 25, 26).

The dissemination of colonoscopy as a screening tool for CRC began slowly in the early 1990s in the United States (5, 6). In 1998, the Medicare program, which insures more than 90% of Americans aged 65 years and older, began reimbursement for colonoscopy screening in individuals at high-risk for CRC; in 2001, coverage was expanded to include beneficiaries at average risk, spurring an acceleration in colonoscopy utilization (8–10). According to data obtained from the National Health Interview Survey, colonoscopy rates (a colonoscopy reported in the previous 10 years) among individuals aged 50 years and older almost doubled between 2000 and 2005, from 20% to 39%; by 2008 prevalence had reached 48% (7). In contrast, use of other screening tests (FOBT, barium enema, and sigmoidoscopy) has declined since 2001 (10). Temporal patterns of screening use are similar by sex, though reported testing is slightly higher

for men than for women. For example, in 2008, 50% of men and 47% of women reported recent use of colonoscopy, whereas sigmoidoscopy rates were 3% and 2%, respectively (7). Our study shows a decrease in incidence rates of right-sided colon cancers that coincides with the increase in colonoscopy uptake.

The large decrease we observed in late-stage disease in the right colon is consistent with the documented stage shift in the Medicare cohort that was confined to right-sided lesions and was strongly associated with the change in coverage for colonoscopy (5). Gross and colleagues postulated that the selective effect on the right colon reflected the surge of whole-colon screening in a population with previously stable sigmoidoscopy rates (5). In contrast to sigmoidoscopy, which is limited to cancer detection in the rectum and left colon, high-quality colonoscopy allows examination of the entire colorectum. We observed a stage shift of 4% (61% vs. 57%) in right-sided tumors and no change in left-sided tumors in the 1990s compared with the 2000s in the 13 SEER areas included in our study.

Changes in lifestyle factors may have contributed to the declines we observed for both right- and left-sided CRCs in the 2000s. Downturns in behaviors known to increase CRC risk, such as obesity (27), smoking (28), and consumption of red/processed meats (29) and alcohol (30), or increases in behaviors that decrease risk, such as physical activity (31), milk/calcium consumption (32), and/or use of menopausal hormone therapy (MHT; ref. 33) or non-steroidal anti-inflammatory drugs (NSAID; ref. 34), could initiate declines in incidence. Although it has been estimated that changes in risk factors accounted for 50% of the overall decline in CRC incidence from 1975 to 2000 (4), the contribution to more recent trends by anatomic subsite is unknown. The obesity epidemic may have attenuated effects on incidence resulting from reductions in smoking prevalence and increases in the use of NSAIDs and MHT over the past few decades. If lifestyle factors were primarily responsible for the decline, similar trends would likely be expected among unscreened populations. However, incidence rates for right-sided colon cancer have remained stable since 1992 in both men and women younger than 50 years, for whom screening is not recommended for persons at average risk (4, 35).

Our findings support those of a recent well-controlled, population-based study conducted in Germany by Brenner and colleagues that showed a 56% risk reduction for right-sided colon cancers associated with high-quality colonoscopy in the previous 10 years (17). In contrast to earlier cross-sectional studies that found no protection against right-sided lesions (14–16), Brenner and colleagues controlled for numerous CRC risk factors, including age and family history, both of which are associated with

right-sided lesions (36, 37), flat neoplasms that are more difficult to detect (38), and higher colonoscopy miss rates (36, 39). More recent case ascertainment (2003–2007) and high rates (91%) of colonoscopy completeness (intubation of cecum) in the Brenner study may have also contributed to the protection against right-sided tumors, as techniques and training for conducting colonoscopy have improved over time and completeness of intubation is associated with lower miss rates (17, 36). Completion rates in the United States are comparable, in the range of 90% to 95% (40, 41).

A number of factors potentially contribute to the lower sensitivity of colonoscopy for detecting lesions in the right versus the left colon. For example, nonpolypoid (flat or depressed) colorectal neoplasms are more prevalent in the right colon. These lesions are more likely to contain carcinoma, more challenging to detect, and more common in high-risk individuals (38, 42–44). In addition, adequate bowel cleansing, which is essential for full visualization of the colonic mucosa, is more difficult in the right colon (45). Older patients, who may have more challenges with bowel preparation, are at substantially higher risk for right-sided cancers (37, 44). Finally, complete endoscopic examination is more technically arduous for the right than the left colon. These factors likely contributed to conflicting study results for the efficacy of colonoscopy in the right colon and may have attenuated the declines in right-sided colon cancer incidence rates.

The conclusions that can be drawn from our study are limited by its ecologic nature. However, high-quality data from population-based SEER registries have often been used to reflect the influence of public health interventions on cancer incidence. Examples include the effect of aggressive mammography screening on population-based breast cancer incidence (46) and the impact of screening patterns on cervical cancer incidence (47, 48).

In summary, substantial declines in the incidence of both right- and left-sided CRCs, particularly for late-stage disease, occurred in the wake of increased colonoscopy utilization in the United States.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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