Original Study

Interval Colorectal Cancer After Colonoscopy

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Abstract

Interval colon cancers represent a small but important subgroup of colon cancers. Although some might occur in part because of genetic predisposition others are due to other risk factors such as age, history of neoplasia, and limitations in the examination. Understanding these predisposing characteristics might allow customized or improved screening or surveillance strategies.

Background: As more patients are screened for colorectal cancer a small but significant number of interval cancers develop after colonoscopy for colorectal cancer screening. **Materials and Methods:** We reviewed records of 75,314 adult patients who underwent colonoscopy for screening or diagnostic purposes between 1998 and 2006 inclusively, and identified 77 who developed interval cancers within the next 5 years. We reviewed their original endoscopic findings to determine the clinical and endoscopic factors that might predict a greater risk for future cancers. **Results:** Patients aged $\geq$ 60 years had a higher risk of an interval neoplasm ($P < .0001$). Interval cancers were more common on the right side of the colon and in the hepatic flexure (both $P < .0001$). We did not observe an increased rate of interval cancers in patients with poor preparation ($P = .799$); however, examination completion rates did affect the rate of interval cancers ($P = .016$). **Conclusion:** Better identification of higher risk patients and assurance of follow-up examinations might increase the percentage of colon cancers discovered at an early stage. Special attention to careful examination of the right colon is key.

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Introduction

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of death from cancer in the United States.[1,2] The 5-year survival rate is 90% if the disease is localized at the time of diagnosis, but this rate decreases to 68% if it is spread regionally, and further decreases to 10% if distant metastases have developed.[1] The relatively slow progression from a benign but detectable adenoma to invasive cancer provides the opportunity to devise a screening and treatment strategy that detects and removes neoplastic tissues while they are still treatable. Most deaths from CRCs can be prevented with regular colonoscopy coupled with the removal of polyps.[2-4]

Currently, the preferred strategy dictates that individuals older than the age of 50 should have a colonoscopy every 10 years, with high-risk patients screened more frequently.[5] Adenomas can be reduced by 76% to 90%, with a significant reduction in CRC mortality, in patients who undergo a clearing colonoscopy.[5,6] However, this strategy is not perfect, because cancers are observed during the time interval between the initial colonoscopy and the recommended follow-up examination, which are called 'interval cancers.' These can be the result of a rapidly growing tumor which becomes established after the initial examination or there could be a cancerous or precancerous lesion that was not appreciated or removed during the initial examination. Studies have found miss rates of 5% to 16.8% for polyps, with smaller polyps being missed more often, and advanced adenomas being missed in 5.4% of colonoscopies.[7-9] Population- or clinical registry-based studies suggest that interval colon cancers account for 3% to 9% of cancer patients but will increase as screening programs extend to more people.[10-12] We began monitoring our patient population for interval cancers as part of an institutional quality management program and to improve our understanding of the characteristics of the patients, and the procedures. As a provider center we had access to clinical data not available in registry programs, allowing us to identify factors that could potentially affect the interval cancer rate. Thus, we report a single-institution experience which has the advantage of having more specific clinical data and a heterogeneous patient population including post-neoplasia surveillance patients, which is representative of practice in the United States.

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Materials and Methods

We used our endoscopy unit's electronic endoscopic report writer, ProVation MD (ProVation Medical, Minneapolis, MN) to identify all individuals who had a colonoscopy between January 1, 1998 and December 31, 2006 at Massachusetts General Hospital. Individuals younger than the age of 18, those with a history of inflammatory bowel disease, or whose endoscopic examination was a flexible sigmoidoscopy were excluded from this population. A total of 86,005 colonoscopies were performed on 75,314 patients (reference cohort). Patients with suspected Lynch syndrome, other genetic predispositions, or polyposis were not excluded.

Using a retrospective review of our institution's electronic health record and diagnosis data from our pathology department, we then identified patients who had a colonoscopy during this time period in which colon cancer was not observed, all polyps were removed, and the physician determined that the patient was free of neoplasia. Seventy-seven of these patients subsequently had at least 1 more colonoscopy in the next 5 years, which resulted in the pathological diagnosis of colon cancer, whom we considered to have an interval CRC.

For both patient groups (reference and interval cancer patients), we collected demographic information such as age and sex, and characteristics of both of the colonoscopies performed. Data on indications for the examination, quality of the bowel preparation, examination completeness (defined as whether the endoscopist reached the cecum, terminal ileum, ileocecal valve, or surgical stoma) and examination findings were collected and compared between the 2 patient groups. For the reference group, we collected data on all colonoscopies, because not all patients returned for a follow-up examination during our study period or had a diagnosis of cancer. For the interval cancer patients, we collected data on only the characteristics of the examination before the diagnosis of CRC ("index examination"), and the information (size, location, stage) of the interval cancers.

During the study period, patient preparation was a polyethylene glycol solution administered the day before the procedure. The procedures were performed in a hospital endoscopy unit and one community-based unit by one of 52 faculty gastroenterologists or 6 general surgeons. Approximately 20% of the procedures were performed by or with gastroenterology fellows under the direct supervision of faculty endoscopists.

All data were collected and analyzed using Microsoft Excel 2003 software (Microsoft Corporation, Redmond, WA). We performed χ^2 tests to obtain P values for our comparative analyses, and Student t tests for the comparison of 2 means. Significance was set at 0.05, except for multiple comparisons, for which we applied the Bonferroni correction (the significance for these tests is noted within the tables).[13] The study was approved by our institutional review board.

Results

Of the 86,005 colonoscopies performed during our study period, 77 of these examinations resulted in an instance of interval cancer (0.090%). If the interval window was shortened to 3 years, there were 37 cases (0.043%). In a review of examinations that were indicated for cancer screening and/or family history of colon cancer or polyps, we found 27 interval cancer cases out of a total of 36,992 examinations (0.073%). In a review of only screening examinations, we found only 17 interval cancers, out of a total of 24,096 screening examinations during the study period (0.071%). During this period, 2509 patients of this reference group had 1 or more diagnoses of CRC. Using our definition of interval cancer, the 77 interval cancer patients who developed cancer within 5 years of the first examination represented 3.07% of all of our CRC patients. When the interval period was decreased to 3 years, the percent of interval cancers was reduced to 37 cases (1.5%).

The demographic data for both of the reference interval cancer groups are summarized in Table 1. The reference group ranged in age from 18 to 102 years, with a mean age of 59.7 years, and the sex distribution was 49.3% male. The interval cancer patients' ages ranged from 40 to 87 years with a mean age of 68.9 years, and the sex distribution was 54.5% male. The difference in sex distribution between the 2 groups was not statistically significant ($P = .423$); however, the mean age of our interval cancer group (68.4 years) was significantly older than the reference group (59.7 years; $P < .0001$). Our interval cancer group also had a greater rate of patients aged 60 years or older at the time of the examination (81.8%), compared with only 49.2% in the reference group ($P < .0001$).

We examined the characteristics of the colonoscopies performed (Table 2). The percentages of screening indications (family history of polyps and/or cancer, screening for polyps or malignant neoplasm) were not different among the reference groups ($P = .575$ and $P = .171$, respectively). Conversely, the interval cancer group had a larger percent (34.0%) of examinations that were indicated for surveillance purposes (personal history of CRC, malignant neoplasm, or polyps), compared with only 21.7% in the reference group, which was significant ($P = .002$) even when the Bonferroni correction was applied (significance for this group was set at $P < .010$). Last, diagnostic indications such as anemia and diarrhea, hematochezia/melena/occult blood and other were not significantly different between the 2 groups.

We also collected data on the quality of bowel preparations and examination completeness. We had data on bowel preparation

Table 1 Patient Demographic Characteristics

	Reference Group	Interval Cancer Group	*P*
Number of Patients	75,314	77	
Total Number of Examinations	86,005	77	
Sex, n (%)			
Female	37,641 (50.7)	35 (45.5)	.423
Male	36,639 (49.3)	42 (54.5)	
Total Patient, n	74,280	77	
Age, Years			
Mean	59.7	68.4	<.0001
95% CI	(59.6-59.8)	(66.0-70.8)	
SD	13.1	10.5	
Median	59	68	
Range	(18-102)	(40-87)	
Patients Aged ≥60 Years, n (%)	42,284 (49.2)	63 (81.8)	<.0001