Index colonoscopy-related risk factors for postcolonoscopy colorectal cancers

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Background and Aims: Postcolonoscopy colorectal cancers (PCCRCs) are defined as those detected ≤10 years after an index colonoscopy negative for cancer, but modifiable risk factors are not well established in large, community-based populations.

Methods: We evaluated risk factors from the index colonoscopy for PCCRCs diagnosed 1 to 10 years after an index colonoscopy using a case-control design. Odds ratios (OR) and 95% confidence intervals (CI) were adjusted for potential confounders.

Results: A proximal polyp ≥10 mm (OR, 8.18; 95% CI, 4.59-14.60), distal polyp ≥10 mm (OR, 3.30; 95% CI, 1.65-6.58), adenoma with (OR, 3.23; 95% CI, 1.83-5.68) and without advanced histology (OR, 1.87; 95% CI, 1.37-2.55), and an incomplete colonoscopy (OR, 5.52; 95% CI, 2.98-10.21) were associated with PCCRC. Risk factors for early versus late cancers (12-36 months vs >36 months to 10 years after examination) included incomplete polyp excision in the colonic segment of the subsequent cancer (OR, 4.76; 95% CI, 2.35-9.65); failure to examine the segment (OR, 2.42; 95% CI, 1.27-4.60); and a polyp ≥10 mm in the segment (OR, 2.38; 95% CI, 1.53-3.70). A total of 559 of 1206 patients with PCCRC (46.4%) had 1 or more risk factors that were significant for PCCRC (incomplete examination, large polyp, or any adenoma).

Conclusions: In a large community-based study with comprehensive capture of PCCRCs, almost half of PCCRCs had potentially modifiable factors related to polyp surveillance or removal and examination completeness. These represent potential high-yield targets to further increase the effectiveness of colorectal cancer screening. (Gastrointest Endosc 2019;89:168-76.)

INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of death from cancer in the United States.[1] Screening reduces mortality through detection and treatment of early-stage CRC and removal of precancerous adenomatous polyps (adenomas).[2] The United States Preventive Services Task Force endorses multiple CRC screening approaches[2,3]; however, the effectiveness of each hinges on colonoscopy because it is either the follow-up or the primary test. Yet colonoscopy has limitations. Postcolonoscopy CRCs (PCCRCs) are defined as those diagnosed after a colonoscopy in which no cancer is detected[4]; the term is sometimes used interchangeably with interval

Abbreviations: CI, confidence interval; CRC, colorectal cancer; KPNC, Kaiser Permanente Northern California; KPSC, Kaiser Permanente Southern California; PCCRC, postcolonoscopy colorectal cancers; SD, standard deviation.

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cancer, although the proposed definition for the latter has evolved to CRC diagnosed after a screening or surveillance examination in which no cancer is detected and before the date of the next recommended examination.[5,6]

Frequency estimates of PCCRC vary based on the length of follow-up after colonoscopy.[4-9] Among previous studies evaluating an interval of 6 to 36 months after colonoscopy, PCCRCs comprised 3.7% (95% confidence interval (CI), 2.8%-4.9%) of all CRCs diagnosed,[8] and among studies of cancers diagnosed 6 months to 10 years after colonoscopy, 1.8% to 9.0% were PCCRCs.[7]

There are 3 plausible explanations for PCCRC: neoplasia missed at colonoscopy due to factors such as poor bowel preparation, incomplete examination, and difficult-to-see flat polyps or polyps behind folds; incomplete colonoscopic resection of detected neoplasia that progresses to cancer; and development of new neoplasia after colonoscopy.[7] Risk from the first 2 proposed mechanisms could be reduced by improving colonoscopy quality. Consistent with this hypothesis is physician adenoma detection rate, a colonoscopy quality metric reflecting the percentage of a physician's screening colonoscopies in which an adenoma is detected, has been shown to be inversely related to the risk of PCCRC and PCCRC-related mortality.[10-14]

Several risk factors for PCCRC, including procedure-related factors, have been suggested,[4,5,7,8] including incomplete resection of precancerous polyps and missed lesions at the index colonoscopy.[15-22] However, most studies had few cancer cases (<200 cases)[15-18,20-22]; were conducted only on patients with previous adenomas or polypectomy[15,16,18,19]; or only included cancers detected within 5 years after colonoscopy, potentially missing slower developing lesions.[15-19,21,22] To our knowledge, no studies have comprehensively examined factors specific to the quality and findings of the index colonoscopy in a large community-based population in an integrated health care setting with long-term follow-up.

This study examined the index colonoscopy predictors of PCCRC diagnosed >1 year and up to 10 years after examination.

METHODS

Study setting

The study was performed among health-plan members of 2 large, integrated health care delivery organizations: Kaiser Permanente Northern California (KPNC) and Southern California (KPSC). These systems serve over 7 million people in urban, suburban, and semi-rural regions throughout California. Health-plan membership is diverse and similar in socioeconomic characteristics to the underlying demographics of the region.[23-25]

The study was approved by the institutional review boards of KPNC and KPSC. The authors had sole responsibility for the study design, data collection, decision to submit the manuscript for publication, and drafting of the manuscript. This study was conducted within the National Cancer Institute-funded Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) consortium (U54 CA163262), which conducts multisite, coordinated, transdisciplinary research to evaluate and improve cancer-screening processes. The funding source had no role in the conception, design, analysis, decision to publish, or conduct of the study.

Study design

A case-control study design was used to examine the association between factors related to a colonoscopy that was negative for colorectal cancer (index colonoscopy) and the risk of PCCRC in the following 1 to 10 years. A secondary analysis examined factors associated with early (arising >12 months and ≤36 months after examination) versus late PCCRCs (arising >36 months to 10 years after) among patients with PCCRC. This analysis allowed for the evaluation of index colonoscopy-related factors specific to the colonic segment where the PCCRC was subsequently diagnosed (ie, whether the colonic segment was examined, a polyp was found in the segment, and the polyp was completely excised).

Exposure variables

Index colonoscopy-related factors included bowel preparation adequacy; extent of the examination; polyp presence, largest size, location, and completeness of excision; and adenoma presence and advanced histology status. Inadequate bowel preparation was described as fair, poor, suboptimal, inadequate, or unsatisfactory; adequate bowel preparation was described as satisfactory, good, very good, excellent, or optimal. An incomplete colonoscopy was defined as a colonoscopy that did not reach the cecum. If the adequacy of the bowel preparation or extent of the examination was not described, it was assumed the preparation was adequate and the examination was complete for the main analyses. An index colonoscopy with any polyp included those with 1 or more polyps removed; the size of the largest polyp and its colonic segment location were noted if recorded. A proximal polyp was a polyp in the cecum, ascending colon, hepatic flexure, or transverse colon; a distal polyp was a polyp in the splenic flexure, descending colon, sigmoid colon, or rectum. Incomplete polyp excision was a polyp described as incompletely excised. A PCCRC was considered to have arisen in a colonic segment in which a previous polyp had been removed if the segment matched the segment of the subsequently diagnosed PCCRC. The presence of an adenoma and its advanced histology status (defined as a villous or tubulovillous adenoma) were identified using Systematized Nomenclature of Medicine (SNOMED) codes from pathology reports. Adenoma data were inconsistently available at KPSC associated with the transition from paper

TABLE 1. Characteristics of cases and controls

	Cases, n (%)	Controls, n (%)	Total, n (%)
Total	1206	634	1840
Age at index colonoscopy			
50-64 years	407 (33.8)	176 (27.8)	583 (31.7)
65-90 years	799 (66.3)	458 (72.2)	1257 (68.3)
Mean (SD)	68.5 (9.1)	69.9 (8.6)	68.9 (9.0)
Sex			
Female	590 (48.9)	293 (46.2)	883 (48.0)
Male	616 (51.1)	341 (53.8)	957 (52.0)
Race/ethnicity			
Non-Hispanic white	824 (68.3)	444 (70.0)	1268 (68.9)
Hispanic	125 (10.4)	68 (10.7)	193 (10.5)
Black	118 (9.8)	53 (8.4)	171 (9.3)
Asian/Pacific Islander	80 (6.6)	60 (9.5)	140 (7.6)
Other/unknown	59 (4.9)	9 (1.4)	68 (3.7)
Family history of colorectal cancer			
No	991 (82.2)	512 (80.8)	1503 (81.7)
Yes	215 (17.8)	122 (19.2)	337 (18.3)
Index colonoscopy time interval			
1993-1998	213 (17.7)	32 (5.1)	245 (13.3)
1999-2001	221 (18.3)	96 (15.1)	317 (17.2)
2002-2004	280 (23.2)	145 (22.9)	425 (23.1)
2005-2007	356 (29.5)	239 (37.7)	595 (32.3)
2008-2012	136 (11.3)	122 (19.2)	258 (14.0)
Median year	2004	2005	2004
Time from index colonoscopy to diagnosis/reference date			
>12 months to ≤36 months	441 (36.6)	247 (39.0)	688 (37.4)
>36 months to 10 years	765 (63.4)	387 (61.0)	1152 (62.6)
Mean (SD)	4.1 (2.1)	4.3 (2.5)	4.2 (2.2)
Health-plan region			
KPNC	827 (68.6)	488 (77.0)	1315 (71.5)
KPSC	379 (31.4)	146 (23.0)	525 (28.5)

SD, Standard deviation; *KPNC*, Kaiser Permanente Northern California; *KPSC*, Kaiser Permanente Southern California.

to electronic medical records during the study interval; therefore, we elected not to use KPSC adenoma data. Validation studies have confirmed high levels of sensitivity for capture of colonoscopies compared with manual procedure logs (99%) and assignment of adenoma status (100%).[26]

Case and control definitions

PCCRC cases (n = 1206) included KPNC (n = 827) and KPSC (n = 379) health-plan members who had an index colonoscopy negative for CRC and were subsequently diagnosed with CRC (colorectal adenocarcinoma) between 1998 and 2010 for KPNC and between 2005 and 2012 for KPSC, with the diagnosis occurring >12 months and up to 10 years after the colonoscopy. CRCs diagnosed within 12 months after the colonoscopy were considered detected cancers and not included in the PCCRC definition.

Controls (n = 634) were KPNC (n = 488) and KPSC (n = 146) health-plan members who had an index colonoscopy negative for CRC and were without a CRC diagnosis at the time of their selection as controls between 2002 and 2012, which was >1 year and up to 10 years after their colonoscopy. For efficiency, controls were cancer-free patients who were controls in a concurrent large case-control study examining the impact of screening colonoscopy on CRC mortality.[27,28] In that study, controls were matched to fatal cases on birth year (±1 year), sex, health-plan enrollment duration before diagnosis (±1 year), and geographic region; controls were assigned their original matched case's CRC diagnosis date as their own

TABLE 2. Characteristics of the index colonoscopy examinations for cases and controls

	Cases, n (%)	Controls, n (%)	Total, n (%)	*P* value
Total	1206	634	1840	
Adequacy of bowel preparation				
Adequate	851 (70.6)	526 (83.0)	1377 (74.8)	
Inadequate	138 (11.4)	67 (10.6)	205 (11.1)	
Unknown	217 (18.0)	41 (6.5)	258 (14.0)	<.001
Extent of examination				
Complete	1049 (87.0)	565 (89.1)	1614 (87.7)	
Incomplete	107 (8.9)	14 (2.2)	121 (6.6)	
Unknown	50 (4.2)	55 (8.7)	105 (5.7)	<.001
Polyp, by size				
No polyp	434 (36.0)	358 (56.5)	792 (43.0)	
<10 mm	393 (32.6)	215 (33.9)	608 (33.0)	
≥10 mm	268 (22.2)	32 (5.1)	300 (16.3)	
Unknown size	111 (9.2)	29 (4.6)	140 (7.6)	<.001
Polyp, by location				
No polyp	434 (36.0)	358 (56.5)	792 (43.0)	
Proximal	132 (11.0)	74 (11.7)	206 (11.2)	
Distal	170 (14.1)	102 (16.1)	272 (14.8)	
Proximal and distal	221 (18.3)	73 (11.5)	294 (16.0)	
Unknown location	249 (20.7)	27 (4.3)	276 (15.0)	<.001
KPNC data only	827	488	13,315	
Adenoma, by histology				
No adenoma	432 (52.2)	276 (56.6)	708 (53.8)	
No advanced histology	267 (32.3)	111 (22.8)	378 (28.8)	
Advanced histology	106 (12.8)	20 (4.1)	126 (9.6)	
Unknown histology	22 (2.7)	81 (16.6)	103 (7.8)	<.001
Index colonoscopy indication				
Screening	202 (24.4)	111 (22.8)	313 (23.8)	
Surveillance	153 (18.5)	70 (14.3)	223 (17.0)	
Diagnostic	452 (54.7)	229 (46.9)	681 (51.8)	
Unknown	20 (2.4)	78 (16.0)	98 (7.5)	<.001
Physician adenoma detection rate				
Quartile 1: <19%	177 (21.4)	97 (19.9)	274 (20.8)	
Quartile 2: 19% to <25%	168 (20.3)	95 (19.5)	263 (20.0)	
Quartile 3: 25% to <32%	172 (20.8)	105 (21.5)	277 (21.1)	
Quartile 4: 32% to 61%	190 (23.0)	91 (18.7)	281 (21.4)	
Unknown	120 (14.5)	100 (20.5)	220 (16.7)	.04
Median	0.257	0.253	0.255	

(*continued on the next page*)

reference date.[28] For the current study, risk estimates were adjusted for age, sex, and time from index colonoscopy to cancer diagnosis/reference date, among other factors, as detailed in the analysis.

Exclusion criteria included receipt of the index colonoscopy before age 50 years or after age 90 years; a history of CRC, other GI cancers, inflammatory bowel disease, Lynch syndrome, or familial adenomatous polyposis; or a missing index colonoscopy report.

Data sources

Electronic records were sourced for patient sex, age, race/ethnicity, colonoscopy procedures and pathology findings, family history of CRC, and previous diagnoses of

TABLE 2. Continued

	Cases, n (%)	Controls, n (%)	Total, n (%)	*P* value
Physician experience				
Quartile 1: <14 years	206 (24.9)	108 (22.1)	314 (23.9)	
Quartile 2: 14 to <20 years	177 (21.4)	91 (18.7)	268 (20.4)	
Quartile 3: 20 to <28 years	195 (23.6)	109 (22.3)	304 (23.1)	
Quartile 4: 28 to 47 years	178 (21.5)	96 (19.7)	274 (20.8)	
Unknown	71 (8.6)	84 (17.2)	155 (11.8)	<.001
Median	19	20	19	

Adequate bowel preparation was defined as a preparation listed in the index colonoscopy report as satisfactory, good, very good, excellent, or optimal. Inadequate bowel preparation was defined as a preparation listed in the index colonoscopy procedure report as fair, poor, suboptimal, inadequate, or unsatisfactory. Complete colonoscopy was defined as to the cecum or terminal ileum. Index colonoscopy indication (screening, surveillance, or diagnostic) was ascertained using a validated algorithm, physician adenoma detection rate was for the year of the index colonoscopy, and physician experience was defined as years from medical school graduation to the index colonoscopy.

CRC, inflammatory bowel disease, other gastrointestinal cancers, Lynch syndrome, and familial adenomatous polyposis. Endoscopy procedures were identified using Current Procedural Terminology codes.[29] Cancer diagnoses were obtained from the KPNC and KPSC cancer registries, which report to the Surveillance, Epidemiology and End Results (SEER) registry, and maintain a >97% population-based completeness standard as verified by random audits. Additional retrospective audits and death clearance processes have historically captured approximately 1% to 2% additional cases. Electronic data sources were complemented by manual chart abstractions of all colonoscopy reports in the 10-year interval before PCCRC diagnosis for cases, and for controls, a comparable 10-year look-back period before their reference date (date of diagnosis in the matching case from the previous case-control study).

Data analysis

Population characteristics and the frequency of index colonoscopy-related factors were compared using chi-squared tests and t tests. Multivariable logistic regression was used to evaluate the association between colonoscopy-related factors and PCCRC. For the base model, odds ratios (ORs) and 95% confidence intervals (CIs) were adjusted for age (50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-90 years), sex (male, female), race/ethnicity (non-Hispanic white, Hispanic, black, Asian/Pacific Islander, other/unknown), family history of colorectal cancer (yes, no), year of index colonoscopy (1993-1998, 1999-2001, 2002-2004, 2005-2007, 2008-2012), time from index colonoscopy to the cancer diagnosis/reference date, medical region (KPNC, KPSC), extent of examination (complete or incomplete), and adequacy of the bowel preparation (adequate or inadequate). Because of the strong collinearity between the polyp- and adenoma-related factors, these were evaluated in separate multivariable models. Model 1 added polyp detection to the base model as a 2-level variable (yes, no). Model 2 added polyp detection/size/location to the base model as a 5-level variable (no polyp, distal polyp <10 mm, distal polyp ≥10 mm, proximal polyp <10 mm, and proximal polyp ≥10 mm). Model 3 added adenoma/histology to the base model as a 3-level variable (no adenoma, adenoma without advanced histology, and adenoma with advanced histology), and only KPNC data were used for model 3. For extent of examination, we examined the potential modifying effect of sex by including an interaction term in the model. In sensitivity analyses, we evaluated the influence of excluding 75 patients who had >1 colonoscopy in the year before the index colonoscopy, and separately, 295 patients whose colonoscopy report was missing bowel preparation data (n = 258) and/or extent of the examination (n = 105). Also, in an analysis restricted to KPNC data, we separately added to the base model (described above) the following index colonoscopy indication (ie, screening, surveillance, or diagnostic) ascertained using a validated algorithm,[30] physician adenoma detection rate (quartiles) for the year of the index colonoscopy, and physician experience defined as years from medical school graduation to the index colonoscopy.

Multivariable logistic regression was performed to evaluate the association among colonoscopy-related factors specific to the colonic segment in which the PCCRC was subsequently diagnosed, and early PCCRC (case-only analysis); late PCCRC served as the reference group. The risk factors evaluated included whether the colonic segment in which the PCCRC was subsequently diagnosed was examined at the index colonoscopy, whether a polyp was found in the segment (no polyp, polyp <10 mm, or polyp ≥10 mm), and whether the polyp was completely excised. The base model adjusted for age, sex, race/ethnicity, family history of colorectal cancer, year of the index colonoscopy, and medical region. All analyses were performed using SAS version 9.3 and Stata version 14.2 for Windows (StataCorp, College Station, Tex).

RESULTS

Participant characteristics

The mean (± standard deviation [SD]) age of study participants was 68.9 ± 9.0 years, 52.0% were male,

TABLE 3. Association between index colonoscopy quality and examination findings and postcolonoscopy colorectal cancer (PCCRC)

Model	At index colonoscopy	Cases, n (%)	Controls, n (%)	OR (95% CI)
	Total	1206	634	
1	No polyp	434 (36.0)	358 (56.5)	1.00 (reference)
	Polyp	772 (64.0)	276 (43.5)	2.68 (2.15-3.34)
	Complete examination	1099 (91.1)	620 (97.8)	1.00 (reference)
	Incomplete examination	107 (8.9)	14 (2.2)	5.52 (2.98-10.21)
	Adequate bowel preparation	1068 (88.6)	567 (89.4)	1.00 (reference)
	Inadequate bowel preparation	138 (11.4)	67 (10.6)	1.11 (0.78-1.57)
	Total	917		581
2	No polyp	434 (47.3)	358 (61.2)	1.00 (reference)
	Distal polyp, <10 mm	97 (10.6)	80 (13.8)	1.06 (0.73-1.53)
	Distal polyp, ≥10 mm	59 (6.4)	12 (2.1)	3.30 (1.65-6.58)
	Proximal polyp, <10 mm	176 (19.2)	115 (19.8)	1.32 (0.97-1.81)
	Proximal polyp, ≥10 mm	151 (16.5)	16 (2.8)	8.18 (4.59-14.60)
	Total (KPNC only)	805		407
3	No adenoma	432 (53.7)	276 (67.8)	1.00 (reference)
	Adenoma, no advanced histology	267 (33.2)	111 (27.3)	1.87 (1.37-2.55)
	Adenoma, advanced histology	106 (13.2)	20 (4.9)	3.23 (1.83-5.68)

Odds ratios (OR) and 95% confidence intervals (CI) were adjusted for age, sex, race/ethnicity, family history of colorectal cancer, year of index colonoscopy, time from index colonoscopy to the cancer diagnosis/reference date, medical region, extent of examination, and adequacy of the bowel preparation (base model). In model 1, polyp detection was added to the base model. In model 2, polyp detection/size/location was added to the base model. In model 3, adenoma/histology was added to the base model and only Kaiser Permanente Northern California (KPNC) data were used because histology status was not available from Kaiser Permanente Southern California. Adequate bowel preparation was defined as a preparation listed in the index colonoscopy report as satisfactory, good, very good, excellent, or optimal. Inadequate bowel preparation was defined as a preparation listed in the index colonoscopy procedure report as fair, poor, suboptimal, inadequate, or unsatisfactory. Complete colonoscopy was defined as to the cecum or terminal ileum. Adenoma with advanced histology was defined as a villous or tubulovillous adenoma. Colonoscopies detecting both proximal and distal polyps were categorized as proximal for these analyses.

68.9% were non-Hispanic white, and 71.5% were KPNC health-plan members (Table 1). Cases and controls had similar ages (mean ± SD: 68.5 ± 9.1 vs 69.9 ± 8.6, respectively) and average time intervals from index colonoscopy to cancer diagnosis or reference date (mean ± SD: 4.1 ± 2.1 vs 4.3 ± 2.5 years, respectively) (Table 1). Among the cases, 36.6% of PCCRCs arose >12 months to ≤36 months after the index colonoscopy.

Quality and finding characteristics of the index colonoscopy examinations

Inadequate bowel preparation was noted in 11.4% of cases and 10.6% of controls; 14.0% of procedures did not report the adequacy of the bowel preparation. Incomplete colonoscopies were reported in 8.9% of cases and 2.2% of controls; 5.7% of procedures did not report the extent of the examination. The detection of any polyp was more common among cases than controls (64.0% vs 43.5%), as well as any polyp ≥10 mm (22.2% vs 5.1%; 7.6% unknown size). Adenomas were also more common among KPNC cases compared with controls (47.8% vs 43.4%), and 12.8% of cases had adenomas with advanced histology compared with 4.1% for controls, with 7.8% having unknown histology (Table 2).

Index colonoscopy-related risk factors for PCCRC

In adjusted analyses (Table 3), the detection of any polyp (OR, 2.68; 95% CI, 2.15-3.34) and an incomplete colonoscopy (OR, 5.52; 95% CI, 2.98-10.21) were both significantly associated with PCCRC, whereas inadequate bowel preparation was not (OR, 1.11; 95% CI, 0.78-1.57) (model 1). ORs for incomplete examination and inadequate bowel preparation were comparable for models 2 and 3, and are therefore not reported. There was no significant difference between women (OR, 6.22; 95% CI, 2.77-13.96) and men (OR, 4.89; 95% CI, 1.87-12.77) (P interaction = .82) in the association between an incomplete colonoscopy and PCCRC.

Compared with no polyps, a proximal polyp ≥10 mm (OR, 8.18; 95% CI, 4.59-14.60) and a distal polyp ≥10 mm (OR, 3.30; 95% CI, 1.65-6.58) were significantly associated with PCCRC (model 2). A proximal polyp <10 mm (OR, 1.32; 95% CI, 0.97-1.81) and a distal polyp <10 mm (OR, 1.06; 95% CI, 0.73-1.53) were not significantly associated with PCCRC.

Compared with no adenoma, an adenoma with advanced histology (OR, 3.23; 95% CI, 1.83-5.68) and without advanced histology (OR, 1.87; 95% CI, 1.37-2.55) were both significantly associated with PCCRC (model 3, Table 3).

TABLE 4. Association between early versus late postcolonoscopy colorectal cancer (PCCRC) and index colonoscopy quality and examination findings

Model	At index colonoscopy	Early PCCRC, n (%)	Late PCCRC, n (%)	OR (95% CI)
	Total	441	765	
1	Colonic segment* examined			
	Yes	401 (93.5)	720 (97.0)	1.00 (reference)
	No	28 (6.5)	22 (3.0)	2.42 (1.27-4.60)
2	Polyp detected at colonic segment*			
	No	314 (71.2)	579 (75.7)	1.00 (reference)
	Yes	127 (28.8)	186 (24.3)	1.27 (0.94-1.72)
3	Polyp detected at colonic segment*			
	No	314 (71.2)	579 (75.7)	1.00 (reference)
	Yes, <10 mm	61 (13.8)	133 (17.4)	0.85 (0.59-1.24)
	Yes, ≥10 mm	66 (15.0)	53 (6.9)	2.38 (1.53-3.70)
4	Polyp excision at colonic segment*			
	No polyp	303 (73.0)	558 (77.0)	1.00 (reference)
	Complete excision	77 (18.6)	154 (21.2)	0.95 (0.67-1.34)
	Incomplete excision	35 (8.4)	13 (1.8)	4.76 (2.35-9.65)

Odds ratios (OR) and 95% confidence intervals (CI) were adjusted for age, sex, race/ethnicity, family history of colorectal cancer, year of index colonoscopy, and medical region.
*Colonic segment refers to the segment of the colon where the PCCRC was subsequently found.

Among 1206 cases, 559 (46.4%) had 1 or more of the risk factors that were significant for PCCRC (incomplete examination, large polyp, or any adenoma); among 634 controls, 155 (24.5%) had 1 or more risk factors.

In sensitivity analyses, the main risk estimates were not substantially changed by excluding 75 cases with one or more colonoscopies in the year before the index colonoscopy (Supplementary Table 1, available online at www.giejournal.org), or by excluding 295 patients with missing information on the adequacy of bowel preparation and/or completeness of the examination (Supplementary Table 2, available online at www.giejournal.org). Also, compared with screening colonoscopies, diagnostic colonoscopies were associated with a higher risk of PCCRC, physician adenoma detection rates were inversely associated with PCCRC, and physician experience was not a significant factor (Supplementary Table 3, available online at www.giejournal.org).

Index colonoscopy-related risk factors for early versus late PCCRCs

In comparison with cases with a late PCCRC, an incomplete polyp excision in the colonic segment where the PCCRC was found (OR, 4.76; 95% CI, 2.35-9.65), a polyp ≥10 mm in the segment (OR, 2.38; 95% CI, 1.53-3.70), and failure to examine the segment (OR, 2.42; 95% CI, 1.27-4.60) during the index colonoscopy were all significantly associated with early PCCRC (Table 4). A polyp <10 mm at the segment was not significantly associated with PCCRC (OR, 0.85; 95% CI, 0.59-1.24). Among 48 cases who had an incomplete polyp excision at the colonic segment where cancer was subsequently diagnosed, 4 (8.3%) were re-examined within 12 months to evaluate the post-polypectomy site; 2 (4.2%) refused recommended surgical follow-up; 12 (25.0%) had follow-up at or shortly after recommended intervals, but the intervals ranged between >1 and 5 years after the examination; and 30 (62.5%) did not follow up until the time of cancer diagnosis.

DISCUSSION

In a large community-based integrated health care setting with up to 10 years of follow-up, index colonoscopy-related factors significantly associated with PCCRC were any colonic polyp ≥10 mm in size, an incomplete examination, and any adenoma. Inadequate bowel preparation and polyps <10 mm in size were not significantly associated with PCCRC. Also, incomplete polyp excision in the colonic segment where the PCCRC was subsequently found, a polyp ≥10 mm in the segment, and failure to examine the segment were significantly associated with early PCCRC, whereas a polyp <10 mm in that segment was not significantly associated with early PCCRC.

Several potential clinical and endoscopy-related risk factors for PCCRC and interval cancer have been suggested,[4,5,8] including higher and lower comorbidity score[31-34]; older age[31,32,35]; female sex[20,31,33]; colonoscopy as follow-up to a positive fecal test[20]; prior diverticular disease or history of abdominal/pelvic surgery[32,33,35]; tumor molecular characteristics such as microsatellite

instability and CpG island methylator positive phenotype;[36] family history of colorectal cancer[22]; colonoscopy performed by a non-gastroenterologist[31,34,35,37] or in a non-academic or non-inpatient setting[31,32]; and colonoscopy performed by an examiner with a high incomplete colonoscopy rate,[31] low polypectomy rate,[31,32] or low annual colonoscopy volume.[32] Also, some previous studies have implicated incomplete resection and missed lesions at colonoscopy as risk factors,[15-18] whereas case-control and cohort studies have implicated incomplete resection and incomplete examinations.[19-22] The current study extends the findings of previous studies by demonstrating an association between factors related to missed and incompletely excised lesions at the index colonoscopy and PCCRC and early PCCRC in an extremely large community-based population, including >2% of the United States population, in an integrated health care setting with comprehensive capture of cancers and detailed medical records, with non-cancer controls, and among patients followed for up to 10 years after examination.

The presence of a large polyp at the index colonoscopy was strongly associated with PCCRC. Large polyps are more likely to require piecemeal excision, increasing the chance of incomplete resection, which can result in progression of the residual lesion to cancer. In a study of 269 patients who had 346 neoplastic polyps removed, 10.1% were incompletely resected, and the incomplete resection rate was higher for polyps 10 to 20 mm in size than for smaller polyps (17.3% vs 6.8%).[38] Moreover, 20.4% of polyps removed piecemeal were incompletely resected.[38] In another study, after piecemeal excision of sessile adenomas >20 mm in size in which all adenomatous tissue was believed to have been removed, the adenoma recurrence rate 6 months after excision was 46.0%.[39] Lesion location was also a significant predictor of PCCRC. A large lesion in the proximal colon was a stronger risk factor than a large lesion in the distal colon. Proximal lesions are more likely to be flat or depressed, making them harder to detect and potentially more difficult to resect, and some may progress more rapidly to colorectal cancer.[4,7]

Another factor strongly associated with PCCRC was incomplete colonoscopy. Failure to intubate the cecum and complete a full structural examination contributes to PCCRC through the mechanism of missed lesions.[7] In a previous study, patients whose colonoscopy was performed by endoscopists with cecal intubation rates of ≥95% had a 27% lower risk of PCCRC than patients whose examiners had cecal intubation rates of <80%.[31] The current study's findings are consistent with a smaller German study of 78 patients with PCCRCs versus 433 patients with CRC detected at screening, in which incomplete examination was associated with a 2.6-fold higher odds of PCCRC.[20] The German study noted the PCCRC risk varied by sex; women with an incomplete examination had a >4-fold increased odds of PCCRC, whereas for men, incomplete examination was not significantly associated with PCCRC.[20] Other studies have suggested female sex is a risk factor for PCCRC,[20,31,33] and incomplete examination may be a contributing factor.[7,40] However, the current, much larger study did not find a significantly stronger association in women compared with men.

Adenomas with and without advanced histology at the index colonoscopy were also significantly associated with PCCRC. These findings are consistent with a previous study in which patients with an adenoma at colonoscopy had higher odds of PCCRC (OR, 1.89; 95% CI, 1.29-2.77), compared with patients without an adenoma, whereas those with a villous adenoma had >8-fold higher odds (OR, 8.40; 95% CI, 5.57-12.66).[22]

We also found that failing to completely excise a polyp in the colonic segment where the PCCRC was subsequently diagnosed conferred a more than 4-fold increase in the odds of an early-arising PCCRC, compared with a late-arising PCCRC, whereas failure to examine the relevant colonic segment, and having a polyp ≥10 mm in size in the relevant segment, each conferred over a 2-fold increase in odds. These findings are consistent with the assumption that missed or incompletely excised lesions are more likely to progress to cancer faster than new lesions developing de novo.

Study strengths include the large number of PCCRC cases, the use of non-cancer controls from the same underlying population to minimize selection bias, adjustment of OR estimates for important potential confounders, and the integrated health care setting, which provided a stable community-based population with comprehensive clinical information in linked databases enabling accurate exposure and outcome ascertainment that eliminated potential bias associated with differential recall between cases and controls.

Study limitations include the possibility of residual confounding inherent in observational studies. The use of controls selected for another concurrent study increased feasibility/efficiency, but precluded matching on time from index colonoscopy to cancer diagnosis/reference date; however, the time distributions among cases and controls were similar, and inclusion as a covariate did not alter the main estimates and conclusions. The lack of adenoma data from KPSC limited the extent to which we were able to examine physician adenoma detection rate as a risk factor. The study design precluded calculations of exact attributable risk estimates, although the 46.4% of PCCRC cases with at least 1 significant risk factor supports the stated conclusions. In future studies, evaluating PCCRC by adherence to surveillance interval recommendations would be informative.

CONCLUSIONS

In a large community-based integrated health care setting, factors related to missed and incompletely resected neoplasia at the index colonoscopy were significantly associated with PCCRC and early PCCRC. These

findings suggest that improvements in the performance of colonoscopy, particularly related to ensuring complete examinations and excision of polyps, may substantially reduce the burden of PCCRC.

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REFERENCES

1. Centers for Disease Control and Prevention. Colorectal Cancer Statistics. Available at: http://www.cdc.gov/cancer/colorectal/statistics/index.htm. Accessed March 2016.
2. U.S. Preventive Services Task Force. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2008;149:627-37.
3. US Preventive Services Task Force; Bibbins-Domingo K, Grossman DC, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. JAMA 2016;315:2564-75.
4. le Clercq CM, Sanduleanu S. Interval colorectal cancers: what and why. Curr Gastroenterol Rep 2014;16:375.
5. Sanduleanu S, le Clercq CM, Dekker E, et al. Definition and taxonomy of interval colorectal cancers: a proposal for standardising nomenclature. Gut 2015;64:1257-67.
6. Rutter MD, Beintaris I, Valori R, et al. World Endoscopy Organization consensus statements on post-colonoscopy and post-imaging colorectal cancer. Gastroenterology 2018;155:909-25.
7. Adler J, Robertson DJ. Interval colorectal cancer after colonoscopy: exploring explanations and solutions. Am J Gastroenterol 2015;110:1657-64; quiz 1665.
8. Singh S, Singh PP, Murad MH, et al. Prevalence, risk factors, and outcomes of interval colorectal cancers: a systematic review and meta-analysis. Am J Gastroenterol 2014;109:1375-89.
9. Rex DK, Bond JH, Feld AD. Medical-legal risks of incident cancers after clearing colonoscopy. Am J Gastroenterol 2001;96:952-7.
10. Corley DA, Jensen CD, Marks AR, et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med 2014;370:1298-306.
11. Kaminski MF, Regula J, Kraszewska E, et al. Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med 2010;362:1795-803.
12. Rogal SS, Pinsky PF, Schoen RE. Relationship between detection of adenomas by flexible sigmoidoscopy and interval distal colorectal cancer. Clin Gastroenterol Hepatol 2013;11:73-8.
13. Kaminski MF, Anderson J, Valori R, et al. Leadership training to improve adenoma detection rate in screening colonoscopy: a randomised trial. Gut 2016;65:616-24.
14. Kaminski MF, Wieszczy P, Rupinski M, et al. Increased rate of adenoma detection associates with reduced risk of colorectal cancer and death. Gastroenterology 2017;153:98-105.
15. Pabby A, Schoen RE, Weissfeld JL, et al. Analysis of colorectal cancer occurrence during surveillance colonoscopy in the dietary Polyp Prevention Trial. Gastrointest Endosc 2005;61:385-91.
16. Robertson DJ, Lieberman DA, Winawer SJ, et al. Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. Gut 2014;63:949-56.
17. le Clercq CM, Bouwens MW, Rondagh EJ, et al. Postcolonoscopy colorectal cancers are preventable: a population-based study. Gut 2014;63:957-63.
18. Huang Y, Gong W, Su B, et al. Risk and cause of interval colorectal cancer after colonoscopic polypectomy. Digestion 2012;86:148-54.
19. Belderbos TD, Pullens HJ, Leenders M, et al. Risk of post-colonoscopy colorectal cancer due to incomplete adenoma resection: a nationwide, population-based cohort study. United European Gastroenterol J 2017;5:440-7.
20. Brenner H, Chang-Claude J, Seiler CM, et al. Interval cancers after negative colonoscopy: population-based case-control study. Gut 2012;61:1576-82.
21. Farrar WD, Sawhney MS, Nelson DB, et al. Colorectal cancers found after a complete colonoscopy. Clin Gastroenterol Hepatol 2006;4:1259-64.
22. Samadder NJ, Curtin K, Tuohy TM, et al. Characteristics of missed or interval colorectal cancer and patient survival: a population-based study. Gastroenterology 2014;146:950-60.
23. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. Am J Public Health 1992;82:703-10.
24. Gordon NP. How Does the Adult Kaiser Permanente Membership in Northern California Compared with the Larger Community? 2006. Available at: http://www.dor.kaiser.org/dor/mhsnet/public/kpnc_community.htm. Accessed March 10, 2017.
25. Koebnick C, Langer-Gould AM, Gould MK, et al. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. Perm J 2012;16:37-41.
26. Corley DA, Jensen CD, Marks AR, et al. Physician adenoma detection rate variability and subsequent colorectal cancer risk following a negative colonoscopy. Gastroenterology 2013;144(5 Suppl 1):S2-3.
27. Goodman M, Fletcher RH, Doria-Rose VP, et al. Observational methods to assess the effectiveness of screening colonoscopy in reducing right colon cancer mortality risk: SCOLAR. J Comp Eff Res 2015;4:541-51.
28. Doubeni CA, Corley DA, Quinn VP, et al. Effectiveness of screening colonoscopy in reducing the risk of death from right and left colon cancer: a large community-based study. Gut 2018;67:291-8.
29. American Medical Association. CPT 2011 Professional Edition. American Medical Association Press; 2010.
30. Lee JK, Jensen CD, Lee A, et al. Development and validation of an algorithm for classifying colonoscopy indication. Gastrointest Endosc 2015;81:575-82.e574.
31. Baxter NN, Sutradhar R, Forbes SS, et al. Analysis of administrative data finds endoscopist quality measures associated with postcolonoscopy colorectal cancer. Gastroenterology 2011;140:65-72.
32. Cooper GS, Xu F, Barnholtz Sloan JS, et al. Prevalence and predictors of interval colorectal cancers in Medicare beneficiaries. Cancer 2012;118:3044-52.
33. Erichsen R, Baron JA, Stoffel EM, et al. Characteristics and survival of interval and sporadic colorectal cancer patients: a nationwide population-based cohort study. Am J Gastroenterol 2013;108:1332-40.
34. Singh H, Nugent Z, Demers AA, et al. Rate and predictors of early/missed colorectal cancers after colonoscopy in Manitoba: a population-based study. Am J Gastroenterol 2010;105:2588-96.
35. Bressler B, Paszat LF, Chen Z, et al. Rates of new or missed colorectal cancers after colonoscopy and their risk factors: a population-based analysis. Gastroenterology 2007;132:96-102.
36. Nishihara R, Wu K, Lochhead P, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med 2013;369:1095-105.
37. Haseman JH, Lemmel GT, Rahmani EY, et al. Failure of colonoscopy to detect colorectal cancer: evaluation of 47 cases in 20 hospitals. Gastrointest Endosc 1997;45:451-5.
38. Pohl H, Srivastava A, Bensen SP, et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology 2013;144:74-80.e71.
39. Zlatanic J, Waye JD, Kim PS, et al. Large sessile colonic adenomas: use of argon plasma coagulator to supplement piecemeal snare polypectomy. Gastrointest Endosc 1999;49:731-5.
40. Chutkan R. Colonoscopy issues related to women. Gastrointest Endosc Clin N Am 2006;16:153-63.

SUPPLEMENTARY TABLE 1. Association between index colonoscopy quality and examination findings and postcolonoscopy colorectal cancer (PCCRC): among those without a colonoscopy in the year before the index colonoscopy

Model	At index colonoscopy	Cases, n (%)	Controls, n (%)	OR (95% CI)
	Total	1147	618	
1	No polyp	421 (36.7)	346 (56.0)	1.00 (reference)
	Polyp	726 (63.3)	272 (44.0)	2.53 (2.02-3.16)
	Complete examination	1050 (91.5)	604 (97.7)	1.00 (reference)
	Incomplete examination	97 (8.5)	14 (2.3)	5.02 (2.70-9.34)
	Adequate bowel preparation	1021 (89.0)	554 (89.6)	1.00 (reference)
	Inadequate bowel preparation	126 (11.0)	64 (10.4)	1.06 (0.74-1.52)
	Total	869		565
2	No polyp	421 (48.4)	346 (61.2)	1.00 (reference)
	Distal polyp, <10 mm	92 (10.6)	78 (13.8)	1.00 (0.69-1.46)
	Distal, polyp, ≥10 mm	55 (6.3)	12 (2.1)	2.96 (1.48-5.91)
	Proximal polyp <10 mm	164 (18.9)	113 (20.0)	1.25 (0.91-1.72)
	Proximal polyp, ≥10 mm	137 (15.8)	16 (2.8)	7.19 (4.01-12.90)
	Total (KPNC only)	754		394
3	No adenoma	410 (54.4)	266 (67.5)	1.00 (reference)
	Adenoma, no advanced histology	252 (33.4)	109 (27.7)	1.86 (1.36-2.56)
	Adenoma, advanced histology	92 (12.2)	19 (4.8)	2.84 (1.57-5.13)

Odds ratios (OR) and 95% confidence intervals (CI) were adjusted for age (50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-90 years), sex, race/ethnicity, family history of colorectal cancer, year of index colonoscopy (1993-1998, 1999-2001, 2002-2004, 2005-2007, 2008-2012), time from index colonoscopy to the cancer diagnosis/reference date, medical region, bowel preparation adequacy, and extent of examination. In model 1, polyp detection was added to the base model. In model 2, polyp detection/size/location was added to the base model. In model 3, adenoma/histology was added to the base model, and only Kaiser Permanente Northern California (KPNC) data were used because histology status was not available from Kaiser Permanente Southern California. Inadequate bowel preparation was defined as a preparation listed in the index colonoscopy procedure report as fair, poor, suboptimal, inadequate, or unsatisfactory. Adenoma with advanced histology was defined as a villous or tubulovillous adenoma. Colonoscopies detecting both proximal and distal polyps were categorized as proximal for these analyses.

SUPPLEMENTARY TABLE 2. Association between index colonoscopy quality and examination findings and postcolonoscopy colorectal cancer (PCCRC): among those without missing data for bowel preparation adequacy or extent of examination

Model	At index colonoscopy	Cases, n (%)	Controls, n (%)	OR (95% CI)
	Total	967	578	
1	No polyp	357 (36.9)	314 (54.3)	1.00 (reference)
	Polyp	610 (63.1)	264 (45.7)	2.38 (1.88-3.01)
	Complete examination	880 (91.0)	564 (97.6)	1.00 (reference)
	Incomplete examination	87 (9.0)	14 (2.4)	5.21 (2.78-9.76)
	Adequate bowel preparation	831 (85.9)	513 (88.8)	1.00 (reference)
	Inadequate bowel preparation	136 (14.1)	65 (11.2)	1.30 (0.92-1.85)
	Total	753		532
2	No polyp	357 (47.4)	314 (59.0)	1.00 (reference)
	Distal polyp, <10 mm	76 (10.1)	77 (14.5)	0.87 (0.58-1.29)
	Distal, polyp, ≥10 mm	49 (6.5)	12 (2.3)	3.12 (1.54-6.32)
	Proximal polyp, <10 mm	143 (19.0)	113 (21.2)	1.15 (0.83-1.61)
	Proximal polyp, ≥10 mm	128 (17.0)	16 (3.0)	7.64 (4.23-13.82)
	Total (KPNC only)	656		369
3	No adenoma	342 (53.7)	249 (67.5)	1.00 (reference)
	Adenoma, no advanced histology	226 (34.5)	103 (27.9)	2.06 (1.47, 2.88)
	Adenoma, advanced histology	88 (13.4)	17 (4.6)	3.43 (1.85, 6.39)

Odds ratios (OR) and 95% confidence intervals (CI) were adjusted for age (50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-90 years), sex, race/ethnicity, family history of colorectal cancer, year of index colonoscopy (1993-1998, 1999-2001, 2002-2004, 2005-2007, 2008-2012), time from index colonoscopy to the cancer diagnosis/reference date, medical region, bowel preparation adequacy, and extent of examination. In model 1, polyp detection was added to the base model. In model 2, polyp detection/size/location was added to the base model. In model 3, adenoma/histology was added to the base model, and only Kaiser Permanente Northern California (KPNC) data were used because histology status was not available from Kaiser Permanente Southern California. Inadequate bowel preparation was defined as a preparation listed in the index colonoscopy procedure report as fair, poor, suboptimal, inadequate, or unsatisfactory. Adenoma with advanced histology was defined as a villous or tubulovillous adenoma. Colonoscopies detecting both proximal and distal polyps were categorized as proximal for these analyses.

SUPPLEMENTARY TABLE 3. Association between colonoscopy indication, physician adenoma detection rate, and physician experience and postcolonoscopy colorectal cancer (PCCRC): among KPNC cases and controls

Model	At index colonoscopy	Cases, n (%)	Controls, n (%)	OR (95% CI)
1	Index colonoscopy indication			
	Screening	202 (25.0)	111 (27.1)	1.00 (reference)
	Surveillance	153 (19.0)	70 (17.1)	1.44 (0.94, 2.20)
	Diagnostic	452 (56.0)	229 (55.9)	1.52 (1.09, 2.14)
2	Physician adenoma detection rate			
	Quartile 1: <19%	177 (25.0)	97 (25.0)	1.00 (reference)
	Quartile 2: 19% to <25%	168 (23.8)	95 (24.5)	0.75 (0.50, 1.13)
	Quartile 3: 25% to <32%	172 (24.3)	105 (27.1)	0.56 (0.37, 0.85)
	Quartile 4: 32% to 61%	190 (26.9)	91 (23.5)	0.52 (0.34, 0.80)
3	Physician experience			
	Quartile 1: <14 years	206 (27.2)	108 (26.7)	1.00 (reference)
	Quartile 2: 14 to <20 years	177 (23.4)	91 (22.5)	0.85 (0.57, 1.26)
	Quartile 3: 20 to <28 years	195 (25.8)	109 (27.0)	1.21 (0.83, 1.78)
	Quartile 4: 28 to 47 years	178 (23.5)	96 (23.8)	1.22 (0.83, 1.80)

Odds ratios (OR) and 95% confidence intervals (CI) were adjusted for age (50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-90 years), sex, race/ethnicity, family history of colorectal cancer, year of index colonoscopy (1993-1998, 1999-2001, 2002-2004, 2005-2007, 2008-2012), time from index colonoscopy to the cancer diagnosis/reference date, medical region, bowel preparation adequacy, extent of examination, and polyp detection. In model 1, colonoscopy indication (screening, surveillance, or diagnostic) was added to the base model. In model 2, physician adenoma detection rate (for the year of the index colonoscopy, in quartiles) was added to the base model. In model 3, physician experience (years from medical school graduation to the index colonoscopy, in quartiles) was added to the base model. For each model, only Kaiser Permanente Northern California (KPNC) data were used.