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Clinical and Endoscopist Factors Associated with Post-Colonoscopy Colorectal Cancer in a Population-Based Sample

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Abstract

Background: Factors associated with verified post-colonoscopy colorectal cancers (PCCRC) have not been well defined and survival for these patients is not well described. We aimed to assess the association of patient, tumour, and endoscopist characteristics with PCCRC.

Methods: Using population-based data, we identified individuals diagnosed with CRC from Jan. 1, 2000 to Dec. 31, 2005, who underwent a colonoscopy within 3 years prior to diagnosis.

Detected cancers were those diagnosed ≤ 6 months following colonoscopy; PCCRC were diagnosed > 6 months to ≤ 3 years following colonoscopy. Post-colonoscopy and detected cancers were verified through chart review using a hospital-based simple random sampling frame. We used multivariable conditional logistic regression to determine the association of patient, tumour, and endoscopist factors with PCCRC and compared overall survival using Cox proportional hazard models.

Results: Using the random sampling frame, we identified 498 patients with PCCRC and 498 with detected CRC; we obtained records and confirmed 367 patients with PCCRC and 412 with detected cancers. In multivariable analysis, patient age (OR 1.01; 95%CI: 1.00-1.03) and tumour location (distal vs. proximal OR 0.36; 95%CI: 0.25-0.53) were associated with PCCRC; endoscopist quality measures were not significantly associated with PCCRC. We did not find significant differences in overall survival between PCCRC and detected cancers (HR 1.12; 95%CI: 0.92-1.32).

Conclusion: Although endoscopic quality measures are important for CRC prevention, endoscopist factors were not associated with PCCRC. This study highlights the need for further research into the role of tumour biology in PCCRC development.

What does this paper add to the literature?

Previous studies of factors associated with post-colonoscopy colorectal cancer using administrative databases are limited by risk for outcome misclassification. In this population-based study, we used chart review to verify diagnoses of post-colonoscopy and detected cancers and show that endoscopic quality measures are not significantly associated with PCCRC.

Word count: 47/50

Introduction

While colonoscopy is an effective tool for prevention, detection, and diagnosis of colorectal cancer (CRC), some patients are found to have cancer a short time after non-diagnostic colonoscopy. Reported rates of post-colonoscopy CRC (PCCRC) range from 0.96%¹ to 12.1%² of patients who undergo non-diagnostic colonoscopy.

Quality of colonoscopy has been implicated as a major contributor to the occurrence of PCCRC. Previous studies have linked endoscopist factors, including specialty,³⁻⁶ colonoscopy completion rate,^{3,7} polypectomy rate,^{3,6} adenoma detection rate,^{8,9} endoscopy case volume,^{2,6} and mean withdrawal time,^{10,11} and factors associated with adequacy of examination for a given patient, such as completeness,¹² preparation quality,¹³ and history of diverticular disease,^{5,6,14-16} with the occurrence of PCCRC. However, not all PCCRC result from inadequate endoscopic performance. Patient factors, including age,^{2,3,5,16-19} sex,^{2,3,12,14,16} race,^{6,20} and comorbidities^{2,3,6,14-16} are known to be associated with PCCRC. Additionally, some CRC develop rapidly, bypassing the gradual progression from adenoma to carcinoma. Biological differences between cancers of patients presenting with PCCRC and detected CRC (i.e. screen-detected or found on diagnostic colonoscopy without previous short-interval non-diagnostic colonoscopy) have been demonstrated in several cohort studies.^{3,9,17,21-32}

Research on risk factors for PCCRC is challenging. Many studies use administrative data to classify patients as having PCCRC, without confirmation by medical record review.³² This is an important limitation, as misattribution may be substantial – in a chart review of 101 Danish patients identified as having PCCRC based on administrative data,¹⁷ 16% of cases did not have PCCRC on chart review. Studies that confirm PCCRC through chart review tend to be small and do not have a population-based sampling frame, limiting generalizability.^{10,12,15,25} To address this, the aim of our study was to evaluate patient, procedural, and endoscopist characteristics associated with PCCRC in a population-based sample of patients with confirmed post-colonoscopy and detected CRC, and to compare long-term outcomes between these groups.

Methods

Overview

We conducted a population-based study in Ontario, Canada using data from linked administrative databases and primary chart abstraction. Administrative data were obtained from ICES, an independent, non-profit research institute that houses health data for residents of Ontario who receive healthcare through the province's universal, publicly funded healthcare program. The Research Ethics Board at St. Michael's Hospital, Toronto, Canada reviewed the study protocol and ethics approval was obtained for chart review from all involved institutions.

Administrative Data Cohort

We identified all patients in Ontario who developed incident CRC between January 1, 2000 and December 31, 2005 using the Ontario Cancer Registry (OCR). The OCR contains information on all new cases of cancer diagnosed in the province since 1964 and is over 95% complete.³³ Cancer site was determined using ICD-9/ICD-10 codes (**Supplemental Table 1**). Using physician claims data captured in the Ontario Health Insurance Plan (OHIP) database, we limited our cohort to patients who underwent colonoscopy at least up to the site of the cancer in the 36 months prior to CRC diagnosis (**Supplemental Table 1**). We excluded patients with pre-existing diagnoses of CRC or inflammatory bowel disease, and those who had undergone colonic resection prior to CRC diagnosis, through linkage to the Canadian Institutes for Health Information Discharge Abstract Database and Same Day Surgery databases.

Definitions

Consistent with previous work,^{3,5} we selected 6 months as the cut-point for defining PCCRC in our administrative data cohort. This definition assumes virtually all cancers diagnosed

at colonoscopy are registered in the OCR within 6 months following the procedure. Patients for whom physicians submitted claims for colonoscopy between 0-180 days prior to the recorded CRC diagnosis date were defined as having **detected CRC**; patients for whom claims for colonoscopy were submitted between 181 days to 36 months before the date of CRC diagnosis were defined as having **PCCRC**. For patients with multiple colonoscopies in the 36 months preceding CRC diagnosis, we used the date of the earliest complete colonoscopy as the index colonoscopy and used this date to classify the patient as having a post-colonoscopy or detected CRC.

Diagnostic Confirmation and Matching

To ensure accurate classification of patients from our administrative data cohort, we performed confirmatory chart review. Because patients could have had a colonoscopy at any facility in the province, to facilitate chart review, we developed an institution-based sampling frame. We first used administrative data to determine the date and location of all colonoscopies up to 36 months prior to CRC diagnosis and all colon resections from 3 months prior to diagnosis to 6 months after diagnosis (**Supplemental Table 1**). For patients who did not undergo colon resection, we determined the date of cancer-related hospital admissions from the 3 months prior to CRC diagnosis to 3 months after diagnosis. We then assigned each patient to an institution based on, in order of preference, location of surgery, location of cancer-related hospital admission, or location of colonoscopy. We took a simple random sample of patients belonging to these 87 institutions until as close to 500 PCCRC patients were included. After this process, a total of 498 patients with PCCRC were identified from 49 institutions. From the same institutions, we identified all patients in our cohort with detected CRC, and 1 randomly selected patient with detected CRC was matched to each PCCRC patient based on year of diagnosis. All further analyses were limited to the matched sample.

At the 49 included institutions, we reviewed colonoscopy reports and records pertaining to CRC admissions for all included patients to confirm the diagnosis of CRC. When CRC could not be confirmed, patients were excluded. Colonoscopy reports were also used to confirm if a cancer was detected or not detected at colonoscopy. Only patients correctly assigned to PCCRC (cases) and detected CRC (controls) categories were included in further analyses.

Patient Factors

We obtained demographic information for included patients from the Registered Persons Database, a roster of all OHIP beneficiaries. Data from both the OCR and chart abstraction were used to determine whether the site of cancer was proximal (proximal to the splenic flexure), distal (splenic flexure and distal bowel), or not otherwise specified. We abstracted information on indication for colonoscopy, family history of CRC, and quality of bowel preparation (poor, not poor, and not reported) from colonoscopy reports. For some patients, we reviewed charts at multiple institutions.

Endoscopist Factors

We determined endoscopist characteristics using previously published methods.³ Briefly, we determined the endoscopist who performed each index colonoscopy using OHIP claims data. The self-designated specialty for the endoscopist (gastroenterologist, general surgeon, or other) was ascertained from the Ontario Physicians Human Resources Data Center. For each index colonoscopy, we determined the endoscopist's procedure volume (log-transformed number of colonoscopies performed), polypectomy rate (proportion of colonoscopies with an accompanying claim for removal of a polyp >3mm in size, categorized as <10%, 11-20%, 21-30%, >30%), and completion rate (proportion of total colonoscopies with a billing code indicating the colonoscope visualized the cecum or terminal ileum, categorized as <80%, 80-89%, 90-94%, ≥95%) for the 2 years preceding the index procedure using OHIP data (**Supplementary Table 1**). This approach allowed endoscopist performance characteristics to change over time.

Statistical Analysis

We compared patient and endoscopist factors between post-colonoscopy and detected CRC groups using Cochran-Mantel-Haenszel tests for categorical variables and t-tests for continuous variables, including only those patients with diagnoses confirmed through chart review. To identify patient and endoscopist factors associated with PCCRC, we constructed a conditional logistic regression model, accounting for matched pairs. We developed secondary models stratified by site of cancer (proximal and distal). As a sensitivity analysis, we constructed similar models restricted to matched pairs with similar tumour locations (proximal, distal, not otherwise specified).

In a secondary analysis, we compared overall survival between PCCRC and detected CRC patients using Kaplan-Meier survival curves and the log-rank test. Time to death was defined as time from CRC diagnosis until date of death. Patients who had not died were censored

on March 31, 2016, the last date of follow-up available at the time of the analysis. Univariable and multivariable Cox proportional hazards models, accounting for matched pairs, were used to determine the unadjusted and adjusted associations between exposure group and mortality. Multivariable models were adjusted for patient age (continuous), sex (male, female), and tumour location (proximal, distal, not otherwise specified). Tumour stage was not adjusted for as it was considered to potentially fall along the causal pathway.

Data were analyzed using SAS Enterprise Guide 6.1 (SAS Institute, Cary, NC). All statistical tests were two-sided, and p-values <0.05 were considered statistically significant.

Results

We identified 21,692 patients diagnosed with CRC who underwent a colonoscopy in the 3-year period before cancer diagnosis (**Figure 1**), 1,752 (8%) of whom met administrative criteria for PCCRC. Using the random sampling frame, 498 patients with PCCRC and 498 patients with detected CRC were identified.

Reports were found for 439 patients with PCCRC and, of these, 367 (84%) patients had diagnoses of PCCRC confirmed on chart review. Reports were found for 434 patients with detected CRC, among whom 412 (95%) patients had diagnoses confirmed on chart review. Among the 94 misclassified patients, reasons for misclassification included: the intended procedure was a flexible sigmoidoscopy rather than colonoscopy (n=43, 46%), misclassification of PCCRC as detected CRC and vice-versa (n=24, 25%), and insufficient information to classify the cancer as detected or undetected (n=27, 29%). Median follow-up for patients with confirmed post-colonoscopy and detected CRC was 6.5 years.

Patient and Endoscopist Characteristics

Of the 367 patients with confirmed PCCRC, 27.9% were diagnosed within 1 year of colonoscopy, 36.7% between 1 and 2 years after colonoscopy, and 35.4% between 2 and 3 years after colonoscopy.

When compared to patients with detected CRC, patients with PCCRC were older (71.58 ± 11.45 years vs. 67.31 ± 12.28 years, $p < 0.001$), more likely to be female (48.0% vs. 38.8%, $p = 0.01$), and more likely to have proximal cancers (54.2% vs. 32.8%, $p < 0.001$) (**Table 1**). Patients with detected CRC were more likely to have symptoms than those with PCCRC (75.0% vs. 63.5%, $p = 0.002$).

Index colonoscopies for patients with confirmed post-colonoscopy and detected CRC were performed by 313 endoscopists. A greater proportion of patients with PCCRC underwent colonoscopy by an endoscopist who was not a gastroenterologist or general surgeon than patients with detected CRC (17.4% vs. 11.2%, $p=0.01$) (**Table 1**). Polypectomy rates, colonoscopy completion rates, and procedure volumes of endoscopists were similar between groups. Preparation quality was not reported for 87.4% of colonoscopies.

Factors Associated with PCCRC

In multivariable analysis among patients with confirmed PCCRC and detected cancers, factors independently associated with PCCRC were patient age (OR 1.01; 95%CI: 1.00-1.03), endoscopist specialty (general surgeon vs. gastroenterologist OR 0.66; 95%CI: 0.49-0.88), and proximal tumour location (distal vs. proximal OR 0.36; 95%CI: 0.25-0.53) (**Table 2**). Endoscopist quality measures, including polypectomy rate, colonoscopy completeness rate, and procedure volumes, were not significantly associated with PCCRC.

When stratified by tumour location, age (OR 1.04; 95%CI: 1.01-1.06) and endoscopist specialty (general surgeon vs. gastroenterologist OR 0.37; 95%CI: 0.20-0.70) were independently associated with PCCRC in the distal, but not proximal, colon (**Table 2**). Additionally, endoscopist colonoscopy volumes appeared associated with PCCRC in the distal colon, though this did not reach statistical significance (OR 0.77; 95%CI: 0.58-1.02); this relationship was not seen for proximal tumours.

In sensitivity analysis restricted to 137 pairs of patients with matching tumour location, age was the only factor independently associated with PCCRC (OR 1.03; 95%CI: 1.00-1.06) (**Table 3**).

Overall Survival

Unadjusted 5-year overall survival was worse in patients with PCCRC (49.7% in patients with PCCRC vs. 61.2% in patients with detected CRC, $p=0.003$) (**Figure 2**). However, after adjusting for age, sex, and tumour location, there was no significant difference in overall survival between groups (HR 1.12; 95%CI: 0.92-1.32).

Discussion

In this large, population-based sample of patients with confirmed post-colonoscopy and detected CRC, the most consistent characteristics associated with PCCRC were older patient age and proximal tumour location. Importantly, we found that when colonoscopy reached at least the

location of the cancer, administrative data measures of endoscopist quality, including completion rate, polypectomy rate, and colonoscopy volume, were not consistently associated with PCCRC. This was particularly true for proximal tumours. Additionally, after adjustment for covariates, we did not find differences in overall survival between patients with PCCRC and detected cancers.

Many studies have found associations between measures of endoscopist quality and development of PCCRC,^{1,3,8,15,34-37} supporting the need to optimize colonoscopy performance to reduce the rate of missed cancers. Our study, however, did not find consistent relationships between endoscopist quality and PCCRC development. To be considered a PCCRC, we required that patients had a colonoscopy complete to the site of their CRC. Additionally, to enable feasible chart review, we used a hospital-based sampling frame and thus not all endoscopists in the province were included. These details may explain the lack of association between endoscopist completion rate/measures of endoscopist quality and PCCRC. However, our findings suggest that PCCRC development is unlikely to be completely explained by factors related to colonoscopy quality.

Although quality is important for appropriate detection of CRC and its precursors, even if high-quality colonoscopy is performed, PCCRC can develop – some CRC develop rapidly, and others do not have easily identifiable pre-malignant precursors,³⁸ suggesting tumour biology may play an important role in PCCRC development. There is support in the literature for such a relationship, particularly for CRC developing through the mismatch repair (MMR) pathway. Similar to PCCRC, tumours developing through the MMR pathway are more likely to be found in proximal locations and in older patients. These cancers may grow more quickly than tumours from the classic chromosomal instability pathway, without the slow progression from adenoma to carcinoma.³⁹⁻⁴¹ Several studies have evaluated the role of MMR deficiency and missed cancers. In a large study evaluating the relationship between MMR status and PCCRC,¹⁷ which included 725 patients with PCCRC and 9,640 patients with incident cancers identified during diagnostic colonoscopy, patients with PCCRC were more likely to have proximal tumours and were older than patients with detected CRC. After adjustment for age, sex, and cancer location, patients with PCCRC were more likely to have MMR deficient tumours than those with detected cancers (OR 1.28; 95%CI: 1.02-1.62). Other studies examining the association between microsatellite instability (MSI) status and PCCRC have consistently found significant associations, with odds ratios ranging from 2.10 to 4.20.^{22,25,29,42} Taken together, these studies

suggest that at least some PCCRC may be attributable to tumours with altered molecular biology,⁴³ specifically arising from the MMR pathway, and indicate that such tumours may be more challenging to detect and/or prevent with colonoscopy.

With long follow-up and adjustment for age, sex, and tumour location, we found patients with PCCRC did not have worse overall survival than patients with detected cancer. This was a surprising finding - in a population-based study conducted in Hong Kong examining 854 patients with PCCRC and 10,005 with detected cancers, PCCRC was independently associated with cancer-specific mortality (hazard ratio [HR] 1.32; 95%CI: 1.18-1.49).⁴⁴ Additionally, a case-control study in England, adjusting for age, sex, comorbidity, and deprivation, also demonstrated poorer overall survival among patients with PCCRC (HR 1.17; 95%CI: 1.10-1.24).² However, the degree of association between PCCRC and survival has varied between studies. Notably, several studies have demonstrated similar survival among patients with PCCRC and detected cancers. In a Danish population-based study of 982 patients with PCCRC and 35,704 patients who did not undergo colonoscopy prior to the diagnostic procedure, the adjusted 2-5 year mortality rate ratio was 1.0 (95%CI: 0.88-1.20).¹⁴ Similarly, in a Korean population-based study that included 6,130 patients with PCCRC and 72,030 patients with detected cancers, both groups demonstrated similar unadjusted 5-year survival (78.0% versus 76.8%, respectively).¹⁸ Unadjusted five-year survival was also similar in a single-institution study of 51 patients with PCCRC matched to 112 patients with detected cancers (44% versus 41%, respectively).²⁹ Although one study, reported patients with PCCRC to have better overall survival than those with detected cancers (HR 0.63; 95%CI: 0.49-0.81),²⁷ a subsequent study from the same group that matched patients by age, sex, and hospital site, did not find differences in survival between groups.⁴² Poorer survival may be expected given the etiology of PCCRC; however, multiple studies report these cancers actually present at earlier stages than detected cancers.^{6,19,27} The poorer survival seen in some studies has, therefore, been partly attributed to lead time bias^{45,46}; once adjusted for, the survival difference between patients with PCCRC and detected cancers attenuates.⁴⁷

This study is population-based and thus results reflect the general population of patients diagnosed with CRC after undergoing colonoscopy in Ontario. Further, we have included only patients with confirmed PCCRC. There was substantial misclassification based on our administrative data definition. After chart review, we found 16% of patients identified as having

PCCRC and 5% of those identified as having a detected cancer based on administrative data were not confirmed. The study of 725 patients with PCCRC in Denmark found a similar proportion of patients with PCCRC misclassified based on administrative data; in this study, chart review of 101 patients with PCCRC treated at a single hospital demonstrated 16% did not have true PCCRC.¹⁷

Despite the strengths, our study has limitations. Although we used measures of endoscopist performance, we could not determine the quality of colonoscopy, colonoscopy withdrawal times, or trainee involvement, and bowel preparation was poorly reported. Additionally, we did not have access to CRC pathology, specifically, molecular characteristics (e.g. MMR status), nor could we identify or exclude patients with polyposis syndromes. We used a hospital-based sampling frame to facilitate chart review and this may have reduced the variability in endoscopist performance. However, we included patients undergoing colonoscopy at 98 sites by 313 endoscopists, and thus substantial variability in our represented endoscopists would be expected. Our study included only 367 patients with PCCRC and 412 patients with confirmed detected CRC and may have been underpowered to find small differences in endoscopy and endoscopist characteristics associated with PCCRC. We did not match our patients a priori based on tumour location and, as a result, our analysis of pairs matched on tumour location had a small sample size. The decision to not match patients based on tumour location was made so that the effect of tumour location could be taken into consideration and included in multivariable analyses, potentially giving us more information on factors involved in development of PCCRC. Tumour location was categorized as proximal or distal only, as further subcategorization would have led to small subgroups from which meaningful information could not be drawn; however, this categorization is consistent with previous literature in this area. Finally, survival data were limited to overall survival and we did not examine differences in recurrence or cancer-specific survival.

In conclusion, although multiple factors, including patient, endoscopist, and tumour factors, may contribute to PCCRC, in our population-based sample of 367 patients with PCCRC and 412 patients with detected cancer, only tumour location and patient age were significantly associated with PCCRC. We did not find measures of endoscopist quality to be consistently associated with PCCRC status. Future work on PCCRC should examine the contribution of tumour biology while accounting for differences in the quality of the index colonoscopy.

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Table and Figure Legend

Table 1. Description of cohort with patient and endoscopist characteristics, by confirmed detected or post-colonoscopy colorectal cancer (PCCRC)

Table 2. Multivariable analysis of patient, endoscopist and colonoscopy characteristics associated with diagnosis of PCCRC

Table 3. Multivariable analysis restricted to 137 matched pairs with similar tumor locations for factors associated with PCCRC

Figure 1. Study flow diagram

Figure 2. Unadjusted overall survival for patients with post-colonoscopy and detected colorectal cancers

Supplementary Table 1. Administrative codes used to identify patients and procedures.

Table 1. Description of cohort with patient and endoscopist characteristics, by confirmed detected or post-colonoscopy colorectal cancer (PCCRC)

Variable	Total n=779	Detected n=412	New/missed n=367	p-value
Patient Characteristics				
Age				

Mean $\pm$ SD	69.32 $\pm$ 12.08	67.31 $\pm$ 12.28	71.58 $\pm$ 11.45	<.001
Median (IQR)	71 (62-78)	68 (59-76)	73 (65-80)	<.001
Sex				0.01
Female	336 (43.1)	160 (38.8)	176 (48.0)	
Male	443 (56.9)	252 (61.2)	191 (52.0)	
Family History				0.006
Yes	199 (25.5)	124 (30.1)	75 (20.4)	
No	267 (34.3)	138 (33.5)	129 (35.1)	
Not reported	313 (40.2)	150 (36.4)	163 (44.4)	
Presence of Symptoms				0.002
Yes	542 (69.6)	309 (75.0)	233 (63.5)	
No	39 (5.0)	19 (4.6)	20 (5.4)	
Not reported	198 (25.4)	84 (20.4)	114 (31.1)	
<i>Endoscopist Characteristics</i>				
Endoscopist specialty				0.01
Gastroenterology	295 (37.9)	151 (36.7)	144 (39.2)	
General Surgery	374 (48.0)	215 (52.2)	159 (43.3)	
Other	110 (14.1)	46 (11.2)	64 (17.4)	
Polypectomy %				0.14
$\leq 10\%$	133 (17.1)	63 (15.3)	70 (19.1)	
11-20%	358 (46.0)	182 (44.2)	176 (48.0)	
21-30%	198 (25.4)	117 (28.4)	81 (22.1)	
$>30\%$	90 (11.6)	50 (12.1)	40 (10.9)	
Completeness %				0.45
$<80\%$	239 (30.7)	124 (30.1)	115 (31.3)	
80-89%	226 (29.0)	129 (31.3)	97 (26.4)	
90-94%	163 (20.9)	80 (19.4)	83 (22.6)	
95%+	151 (19.4)	79 (19.2)	72 (19.6)	
Volume median, (IQR)	396 (213-554)	397 (214-553)	396 (213-554)	0.63
Log (volume) median, (IQR)	6 (5-6)	6 (5-6)	6 (5-6)	0.63
<i>Procedure Characteristics</i>				
Colonoscopy Complete ¹				<.001

Yes	631 (81.0)	314 (76.2)	317 (86.4)	
No	148 (19.0)	98 (23.8)	50 (13.6)	
Colonoscopy preparation				0.17
Not Poor	62 (8.0)	36 (8.7)	26 (7.1)	
Poor	36 (4.6)	14 (3.4)	22 (6.0)	
Not reported	681 (87.4)	362 (87.9)	319 (86.9)	
CRC location				<.001
Proximal	334 (42.9)	135 (32.8)	199 (54.2)	
Distal	392 (50.3)	258 (62.6)	134 (36.5)	
NOS	53 (6.8)	19 (4.6)	34 (9.3)	
Year of diagnosis				0.93
2000	134 (17.2)	69 (16.7)	65 (17.7)	
2001	150 (19.3)	77 (18.7)	73 (19.9)	
2002	123 (15.8)	68 (16.5)	55 (15.0)	
2003	123 (15.8)	69 (16.7)	54 (14.7)	
2004	117 (15.0)	59 (14.3)	58 (15.8)	
2005	132 (16.9)	70 (17.0)	62 (16.9)	

Data presented in brackets represents proportions unless otherwise specified.

¹Determined from administrative data.

Abbreviations: SD, standard deviation; IQR, interquartile range; NOS, not otherwise specified.

Table 2. Multivariable analysis of patient, endoscopist and colonoscopy characteristics associated with diagnosis of PCCRC

	All patients (n = 779)		Proximal Cancer (n = 334; PCCRC, n= 199)		Distal Cancer (n = 392; PCCRC, n = 134)	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.01 (1.00-1.03)	0.05	1.01 (0.98-1.03)	0.67	1.04 (1.01-1.06)	<0.01
Sex						
Female	Referent		Referent		Referent	
Male	0.79 (0.58-1.07)	0.13	0.97 (0.63-1.49)	0.89	0.67 (0.43-1.05)	0.08
Family history						

None/not reported	Referent		Referent		Referent	
Yes	0.81 (0.54-1.20)	0.30	0.81 (0.47-1.41)	0.46	0.70 (0.40-1.24)	0.22
Presence of symptoms						
No	Referent		Referent		Referent	
Yes	0.62 (0.31-1.22)	0.17	1.09 (0.52-2.26)	0.82	0.30 (0.08-1.12)	0.07
Not reported	0.92 (0.45-1.88)	0.81	1.72 (0.61-4.83)	0.31	0.53 (0.14-1.99)	0.35
Endoscopist specialty						
Gastroenterology	Referent		Referent		Referent	
General surgery	0.66 (0.49-0.88)	<0.01	1.03 (0.66-1.62)	0.88	0.37 (0.20-0.70)	<0.01
Other	1.41 (0.83-2.39)	0.20	1.99 (0.80-4.94)	0.14	1.31 (0.59-2.92)	0.51
Endoscopist						
Polypectomy %						
≤10%	Referent		Referent		Referent	
11-20%	0.83 (0.58-1.19)	0.31	0.80 (0.42-1.52)	0.49	0.83 (0.48-1.46)	0.53
21-30%	0.77 (0.48-1.23)	0.28	0.44 (0.22-0.88)	0.02	0.96 (0.44-2.08)	0.92
>30%	1.07 (0.62-1.87)	0.80	0.66 (0.26-1.62)	0.36	1.09 (0.49-2.42)	0.84
Endoscopist						
Completeness %						
<80%	Referent		Referent		Referent	
80-89%	0.74 (0.46-1.20)	0.22	0.88 (0.50-1.54)	0.64	0.86 (0.46-1.61)	0.64
90-94%	1.09 (0.75-1.59)	0.66	1.29 (0.74-2.23)	0.36	1.12 (0.62-2.00)	0.71
95%+	0.99 (0.61-1.60)	0.96	1.03 (0.50-2.16)	0.93	0.89 (0.43-1.85)	0.76
Endoscopist						
colonoscopy log volume	0.97 (0.82-1.15)	0.73	1.15 (0.86-1.54)	0.34	0.77 (0.58-1.02)	0.06
Quality of preparation						
Not poor	Referent		Referent		Referent	
Poor	2.36 (0.91-6.17)	0.08	1.78 (0.35-8.92)	0.49	3.24 (0.74-14.23)	0.12
Not reported	1.31 (0.75-2.31)	0.35	1.09 (0.54-2.20)	0.82	1.78 (0.60-5.26)	0.30
Cancer location						
Proximal	Referent		-	-	-	-
Distal	0.36 (0.25-0.53)	<0.01	-	-	-	-
NOS	0.81 (0.46-1.42)	0.46	-	-	-	-

Abbreviations: NOS, not otherwise specified.

Table 3. Multivariable analysis restricted to 137 matched pairs with similar tumor locations for factors associated with PCCRC

	OR (95% CI)	p-value
Age	1.03 (1.00-1.06)	0.01
Sex		
Female	Referent	
Male	0.71 (0.39-1.32)	0.28
Family History		
No/Not reported	Referent	
Yes	1.17 (0.61-2.24)	0.63
Presence of Symptoms		
No	Referent	
Yes	0.29 (0.09-0.98)	0.06
Not reported	1.10 (0.28-4.31)	0.89
Endoscopist Specialty		
Gastroenterology	Referent	
General surgery	1.05 (0.46-2.36)	0.91
Other	1.22 (0.51-2.92)	0.65
Endoscopist Proportion Polypectomy		
≤10%	Referent	
11-20%	0.73 (0.30-1.78)	0.49
21-30%	0.40 (0.14-1.12)	0.08
>30%	0.78 (0.22-2.78)	0.71
Endoscopist Proportion Completeness		
<80%	Referent	
80-89%	0.52 (0.22-1.25)	0.15
90-94%	0.97 (0.38-2.46)	0.95
95%+	0.83 (0.33-2.06)	0.68
Endoscopist Colonoscopy Volume		
Log Volume	1.07 (0.75-1.52)	0.70
Quality of Preparation		
Not poor	Referent	
Poor	3.51 (0.50-24.66)	0.21

Figure 1. Study flow diagram. Adult patients with colorectal cancer were first identified. Following exclusions, those meeting administrative data definitions of PCCRC and detected CRC were identified. Patients who underwent colonoscopy within 6 months of the recorded CRC diagnosis date were defined as having detected CRC; those with colonoscopies between 6 months and 36 months before CRC diagnosis were defined as having PCCRC. For patients who underwent multiple colonoscopies in the 36 months preceding diagnosis, the earliest date of colonoscopy was used as the index colonoscopy for categorization.

Figure 2. Unadjusted overall survival for patients with post-colonoscopy and detected colorectal cancers

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