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Incidence, characteristics, and predictive factors of post-colonoscopy colorectal cancer

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Abstract

Background: Post-colonoscopy colorectal cancer (PCCRC) is colorectal cancer (CRC) diagnosed after a colonoscopy in which no cancer is found.

Objective: As PCCRC has become an important quality indicator, we determined its rates, characteristics, and index colonoscopy-related predictive factors.

Methods: We carried out a multicenter, observational, retrospective study between 2015 and 2018. Rates were calculated for PCCRC developing up to 10 years after colonoscopy. PCCRC was categorized according to the most plausible explanation using World Endoscopy Organization methodology. Our PCCRC population was compared to a control cohort without CRC matched 1:4 by sex, age, index colonoscopy date, indication, endoscopist, and hospital.

Results: One hundred seven PCCRC and 2508 detected CRC were diagnosed among 101,524 colonoscopy (0.1%), leading to rates of 0.4%, 2.2%, 3.1%, and 4.1% at 1, 3, 5, and 10 years, respectively. PCCRC was in right (42.4%), left (41.4%), and transverse (16.4%) colon with 31.5% at stage I, 24.7% stage II, 32.6% stage III, and 11.2% stage IV. Twenty point three percent were classified as incomplete resection,

5.4% as unresected lesions, 48.6% as missed lesions with adequate colonoscopy, and 25.7% as missed lesions with inadequate colonoscopy. The median time from colonoscopy to PCCRC was 42 months. Previous inadequate preparation (OR 3.05, 95%CI 1.73–5.36) and piecemeal polypectomy (OR 19.89, 95%CI 8.67–45.61) were independently associated with PCCRC.

Conclusions: In our population, 4.1% of CRC cases were PCCRC. Most of these lesions were in right colon and attributable to lesions not visualized despite adequate bowel cleansing. Previous inadequate cleansing and piecemeal polypectomy were associated with PCCRC.

KEYWORDS
colonoscopy, colorectal cancer, colorectal neoplasms, incidence

INTRODUCTION

Post-colonoscopy colorectal cancer (PCCRC) is defined as cancers appearing after a colonoscopy in which no cancer is diagnosed,[1–3] and a recent consensus by the World Endoscopy Organization (WEO) formulated recommendations on classification and rate calculation of these lesions.[4] Reported rates of PCCRC according to large population-based studies range between 2.9% and 14%.[5,6]

Potential reasons for PCCRC include missed lesions due to inadequate bowel preparation or incomplete colonoscopy, as well as endoscopist-dependent factors, such as short withdrawal time, a suboptimal inspection technique with a low adenoma detection rate (ADR), or incomplete polypectomy.[7] In this regard, patients attended by endoscopists with lower ADR have a higher risk of interval cancer.[8,9] However, index colonoscopy-related characteristics associated with the subsequent development of PCCRC have not been adequately investigated.

Most of these lesions could be avoided and indicate opportunities for improved colonoscopy performance, leading to PCCRC becoming an important quality indicator in endoscopy services. Therefore, we performed this multicenter observational retrospective study to assess the PCCRC rates in a regional group of secondary and tertiary centers, classify PCCRC according to the most plausible explanation following the WEO algorithm, and identify the index colonoscopy-related factors that lead to PCCRC using a case-control design.

Key Summary

Summarize the established knowledge on this subject

- The post-colonoscopy colorectal cancer (PCCRC) rate has become one of the main quality indicators for colonoscopy because it reflects its efficacy in detecting and preventing cancer.
- A recent World Endoscopy Organization (WEO) consensus statement offered recommendations on classification and rate calculation for benchmark services.

What are the significant and/or new findings of this study?

- We estimated a 3-year PCCRC rate of 2.2% over a 4-year period, attributed mostly to missed lesions despite an adequate index colonoscopy.
- Inadequate bowel preparation and piecemeal polypectomy at index colonoscopy were independently associated with subsequent PCCRC development.
- Our findings may help identify opportunities for improved colonoscopy performance and help other services initiate monitoring and review of their PCCRC cases and rates.

MATERIALS AND METHODS

Study design

We performed an observational, retrospective, multicenter study to identify and review the PCCRC cases at eight hospitals in the province of Alicante in Spain (Hospital General Universitario Dr. Balmis, Hospital Universitario del Vinalopó, Hospital General Universitario de Elche, Hospital General Universitario de Elda, Hospital Universitario de San Juan de Alicante, Hospital Universitario Vega Baja, Hospital Universitario Marina Baixa, and Hospital Universitario de Torrevieja). This study was approved by the institutional ethics committee. A waiver of informed consent was obtained given the study's observational nature.

Using the Pathology Department databases, we searched all biopsies tagged with International Classification of Diseases, 10th Revision (ICD-10) codes for malignant neoplasm of the colon (ICD-10 C18.0-C18.9), rectosigmoid (ICD-10 C19), and rectum (ICD-10 C20) and selected all colorectal adenocarcinomas diagnosed between January 2015 and December 2018. Neuroendocrine tumors or

squamous cell carcinomas of the anorectum and adenocarcinoma of the appendix were excluded.

Case and control selection

All CRC cases were matched with the Endoscopy Unit database and individually reviewed to identify which patients had an index colonoscopy negative for CRC in the preceding 6–120 months (10 years), which were selected as PCCRC cases. CRCs diagnosed at the colonoscopy or within 6 months were considered detected cancers[4] and not included as PCCRC. Patients with a personal history of CRC diagnosed with a new CRC in the same bowel segment were considered a recurrence and not included as PCCRC. In addition, patients with inflammatory bowel disease or hereditary CRC syndromes were excluded.

A case-control study design was used to examine the association between factors related to index colonoscopy and the risk of PCCRC in the subsequent 6 months to 10 years. Controls were patients who underwent a colonoscopy negative for CRC between 2005 and 2018 and were without a CRC diagnosis at the time of their selection as controls between 2021 and 2022. Controls were matched to cases for birth year (±1 year), sex, date of index colonoscopy (±1 year), endoscopist, indication (primary CRC screening, fecal immunochemical test (FIT) positive screening, post-polypectomy surveillance or symptoms), and center. Four matched controls were assigned for each PCCRC case.

Data collection

The clinical record and pathology, radiology, and endoscopy reports were reviewed to obtain the patient sex, age, index colonoscopy-related factors (date, endoscopist, indication, bowel preparation adequacy, extent of the examination, polyp presence, number, size, morphology,[10] location, method and completeness of excision), and pathology findings (adenomatous or serrated, villous component, grade of dysplasia). For each CRC, information on the size, location, histology, and TNM stage was collected.

An adequate colonoscopy was defined as a complete procedure with adequate bowel preparation. Inadequate bowel preparation was described as a Boston Bowel Preparation Scale (BBPS) score of 0–1 in any colonic segment; adequate bowel preparation was considered a BBPS score of 2–3 in every colonic segment. 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 that the preparation was adequate, and the examination was complete for the main analyses.

Endoscopists were classified according to their endoscopy volume. Physicians with full-time dedication to endoscopy were considered high-volume endoscopists, whereas other gastroenterologists with part-time dedication to endoscopy were considered low-volume endoscopists.

Non-advanced adenoma (NAA) was defined as tubular adenomas <10 mm with low-grade dysplasia. Advanced adenoma (AA) was defined as an adenoma ≥10 mm, containing ≥25% villous component, or high-grade dysplasia (HGD). A proximal polyp was a polyp in the cecum, ascending colon, hepatic flexure, or transverse colon. CRC was defined as an invasion of malignant cells through the muscularis mucosa. Normal colonoscopy referred to colonoscopy in which no neoplasia was found.

Outcome definitions

The primary outcome was to estimate the PCCRC rates at 1, 3, 5, and 10 years. The secondary outcomes were to identify the most plausible explanation for PCCRC according to the WEO algorithm and to determine which index colonoscopy characteristics are related to the development of PCCRC.

According to the WEO consensus,[4] true-positive colonoscopy was a colonoscopy in which CRC was detected during that procedure or within 6 months; false-negative colonoscopy was a colonoscopy in which no CRC was found but PCCRC was detected between 6 and 120 months after the procedure. The unadjusted PCCRC rate was calculated as the number of PCCRC cases divided by the total number of PCCRC cases plus the number of detected CRCs, expressed as a percentage (i.e., false-negative colonoscopies divided by true-positive colonoscopies + false-negative colonoscopies expressed as a percentage). If a case of CRC fit into both categories (PCCRC and detected cancer), it was accounted for in both groups. If a patient had more than one colonoscopy in the 120 months prior to the PCCRC diagnosis, only the closest false-negative colonoscopy was included.

Root-cause analysis

A root-cause analysis was performed for each PCCRC case following the algorithm proposed by the WEO[4] to classify PCCRC according to the most plausible explanation using the following categories: (A) Possible missed lesion, prior examination adequate; (B) Possible missed lesion, prior examination negative but inadequate; (C) Detected lesion, not resected; and (D) Likely incomplete resection of the previously identified lesion.

A case fit into category A if the patient had an adequate colonoscopy within the last 4 years that did not detect cancer and no AA was identified in the same bowel segment, category B was considered if the patient had an inadequate colonoscopy within the last 4 years that did not detect cancer where no AA was identified in the same bowel segment, category C if the patient had a colonoscopy within the last 4 years in which AA was identified but not resected in the same bowel segment, and category D if the patient had a colonoscopy within the

last 4 years in which AA was resected from the same bowel segment but there was no endoscopic/histological confirmation of complete resection. PCCRC appearing 4 years after the index colonoscopy was categorized as likely new cancer.

Data analysis

The patients' endoscopy reports were analyzed via the electronic institutional database (Endobase, Olympus Europe,). Categorical variables were described as numbers and frequencies (*n*, %), and quantitative variables as the mean and standard deviation (SD) or median and interquartile range (IQR) depending on their distribution. The parametric distribution of the quantitative variables was determined using the Kolmogorov-Smirnov test. In the univariate analysis, categorical variables were compared using chi-squared, and odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by multivariate logistic regression. All tests were two-sided. A *p*-value <0.05 was considered significant. All analyses were performed using IBM SPSS Statistics 24 (SPSS Inc.).

RESULTS

PCCRC rates

During the 4-year study period, from January 2015 to December 2018, we detected 107 PCCRC cases and 2508 detected CRCs out of 101,524 colonoscopies (0.1%). Of these PCCRC cases, 11 were diagnosed within 6 and 12 months after the false-negative colonoscopy, 56 within 6 and 36 months, 81 within 6 months and 5 years, and 107 within 6 months and 10 years. These results led to the following rates (Figure 1): 1-year PCCRC rate of 0.4% (95% CI 0.2–0.6), 3-year PCCRC rate of 2.2% (95% CI 1.6–2.8), 5-year PCCRC rate of 3.1% (95% CI 2.5–3.8), and 10-year PCCRC rate of 4.1% (95% CI 3.3–4.8).

PCCRC characteristics

The characteristics of the PCCRC cases are described in Table 1. Seventy-one (66.4%) PCCRCs occurred in male patients, and the mean (±SD) age at the time of PCCRC diagnosis was 72.1 ± 11.1 years. The median delay between index colonoscopy and PCCRC diagnosis was 34 months (IQR 38 months). Most PCCRCs were in the right colon (46.7%). The distribution of PCCRC among the eight included hospitals is shown in Figure 2.

Root-cause analysis

Of the 107 PCCRC cases, 33 (30.8%) appeared >4 years after the index colonoscopy and were categorized as likely new cancers; 74 were diagnosed within 6–48 months of the index colonoscopy and classified according to their most plausible explanation as follows: 36 (48.6%) category A, 19 (25.7%) category B, 4 (5.4%) category C, and 15 (20.3%) category D (Figure 3).

Index colonoscopy-related predictive factors for PCCRC

For each of the 107 PCCRC cases with index colonoscopy, 4 controls without CRC matched by age, sex, date of index colonoscopy,

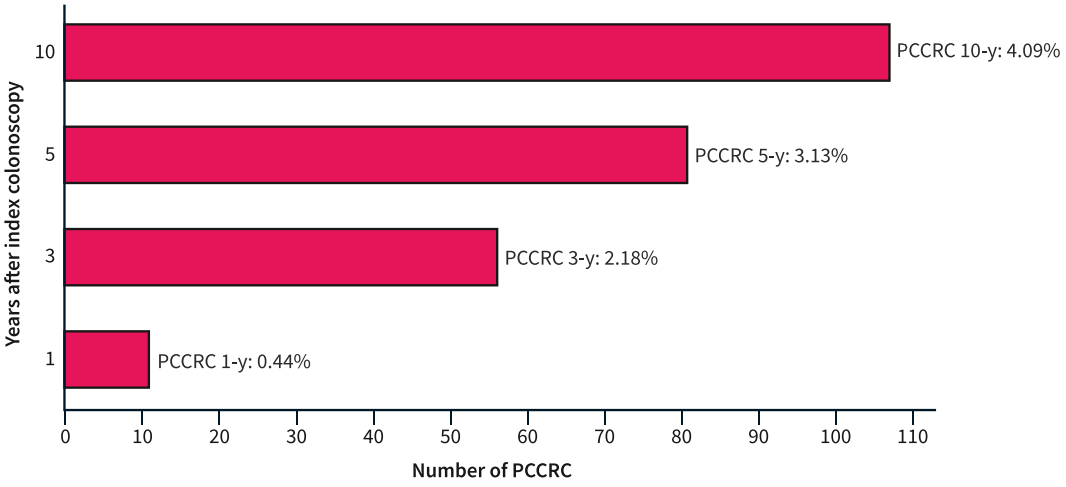

FIGURE 1 Time of diagnosis of PCCRC with respect to index colonoscopy and 1-, 3-, 5-, and 10-year rates. PCCRC, post-colonoscopy colorectal cancer.

TABLE 1 Characteristics of the PCCRC population.

		PCCRC (*N* = 107) *N* (%)
Age at PCCRC diagnosis (years)	Mean (SD)	72.1 (11.1)
Sex	Male	71 (66.4)
	Female	36 (33.6)
Indication of PCCRC colonoscopy	Direct screening	9 (8.4)
	+FIT	5 (4.7)
	Surveillance	33 (30.8)
	Symptoms	48 (44.9)
	Unknown	12 (11.2)
Size of PCCRC (mm)	Median (IQR)	30 (22)
Previous CRC in a different colonic segment	Yes	4 (3.7)
	No	103 (96.3)
Location of PCCRC	Right colon	50 (46.7)
	Transverse colon	11 (10.3)
	Left colon	18 (16.8)
	Rectum	25 (23.4)
	Unknown	3 (2.8)
Stage of PCCRC	I	28 (26.2)
	II	22 (20.6)
	III	29 (27.1)
	IV	10 (9.3)
	Unknown	18 (16.8)

Abbreviations: FIT, fecal immunochemical test; PCCRC, post-colonoscopy colorectal cancer.

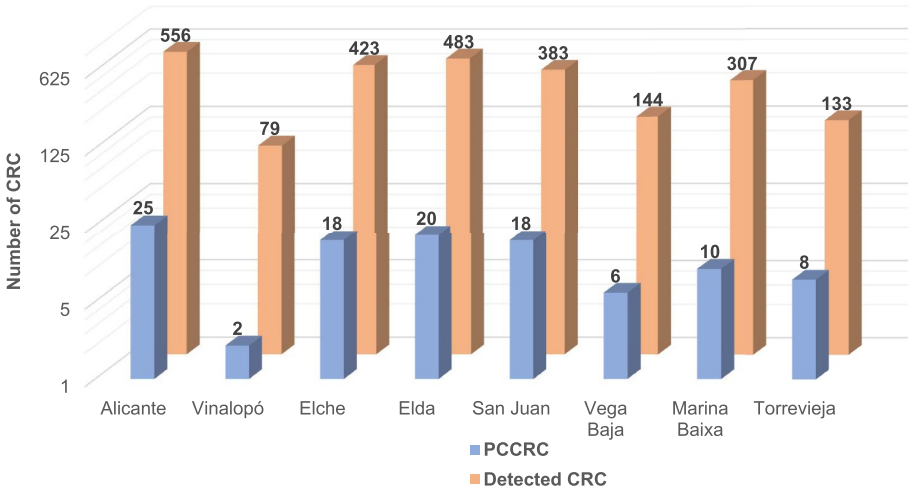

FIGURE 2 Distribution of PCCRC and detected CRC among participating centers. CRC, colorectal cancer; PCCRC, post-colonoscopy colorectal cancer.

endoscopist of index colonoscopy, indication of index colonoscopy, and center were selected. The characteristics of the cases, controls, and matched colonoscopy examinations are detailed in Table 2.

In the multivariate analysis, the characteristics of the index colonoscopy that were significantly associated with the subsequent development of PCCRC were inadequate bowel preparation (OR

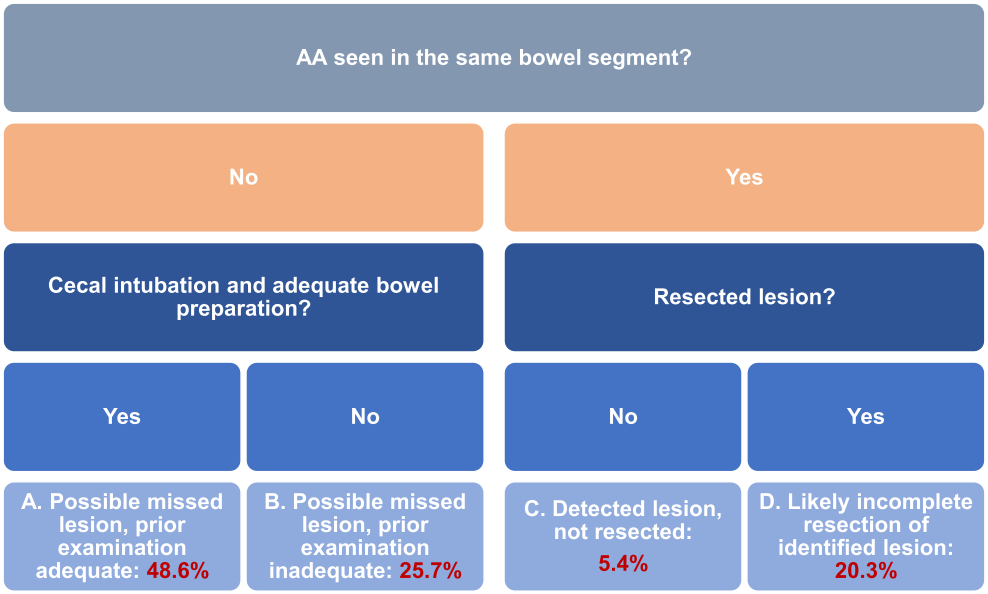

FIGURE 3 Root-cause classification of PCCRC according to the most plausible explanation following the WEO algorithm. PCCRC, post-colonoscopy colorectal cancer; WEO, World Endoscopy Organization.

TABLE 2 Index colonoscopy characteristics and univariate and multivariate analyses.

	PCCRC (*N* = 107) *N* (%)	Controls (*N* = 428) *N* (%)	OR (95% CI)	*p*	OR (95% CI)	*p*
Age (years), mean (SD)	69.1 (11.2)	68.6 (10.7)	1.16 (−1.80–2.76)	0.678		
Male sex	71 (66.4)	284 (66.4)	1.00 (0.64–1.57)	0.999		
Indication						
Direct screening	8 (7.5)	32 (7.5)	1.00 (0.04–3.64)	0.999		
+FIT	9 (8.4)	36 (8.4)				
Surveillance	31 (29.0)	124 (29)				
Symptoms	54 (50.5)	216 (50.5)				
Unknown	5 (4.7)	20 (4.7)				
Low-volume endoscopist	56 (52.3)	224 (52.3)	1.00 (0.50–2.65)	0.999		
No fecal intubation	13 (12.3)	23 (5.4)	2.46 (1.20–5.04)	**0.011**	1.93 (0.89–4.15)	0.121
Inadequate bowel preparation	28 (26.4)	44 (10.3)	3.13 (1.84–5.34)	**<0.001**	3.05 (1.73–5.36)	**0.001**
Presence of polyps	67 (62.6)	187 (43.7)	2.16 (1.40–3.34)	**<0.001**	1.46 (0.706–3.03)	0.685
Presence of adenomas	55 (51.4)	139 (32.5)	2.20 (1.43–3.38)	**<0.001**	1.75 (0.85–3.59)	0.674
Presence of AA	30 (28.0)	72 (16.8)	1.93 (1.18–3.15)	**0.008**	0.58 (0.23–1.45)	0.242
Presence of serrated polyps	14 (13.1)	48 (11.2)	1.19 (0.63–2.25)	0.589		
	PCCRC (*N* = 55)	**Controls (*N* = 139)**	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
≥3 adenomas	18 (32.7)	29 (21.0)	1.83 (0.91–3.67)	0.087		
Flat morphology	6 (10.9)	19 (13.7)	0.77 (0.29–2.05)	0.605		
Size ≥10 mm	24 (43.6)	56 (40.3)	1.14 (0.61–2.15)	0.669		
Size ≥20 mm	12 (21.8)	14 (10.1)	2.49 (1.07–5.80)	**0.030**	0.85 (0.24–3.01)	0.536
Proximal adenoma	28 (50.9)	71 (51.1)	0.99 (0.53–1.86)	0.983		
Villous component	15 (27.3)	21 (15.1)	2.11 (1.02–4.47)	**0.049**	1.47 (0.49–4.36)	0.376
HGD	7 (12.7)	9 (6.5)	2.11 (0.74–5.97)	0.154		
Piecemeal polypectomy	37 (67.3)	13 (9.4)	19.92 (8.93–44.42)	**<0.001**	19.89 (8.67–45.61)	**<0.001**

Note: Controls comprised a cohort of colonoscopies in patients without CRC matched 1:4 by sex, age, endoscopist, date, indication of index colonoscopy, and center. Significant values are bolded.

Abbreviations: CI, confidence interval; CRC, colorectal cancer; HGD, high-grade dysplasia; PCCRC, post-colonoscopy colorectal cancer.

3.05, 95% CI 1.73–5.36; $p = 0.001$) and piecemeal polypectomy (OR 19.89, 95% CI 8.67–45.61; $p < 0.001$) (Table 2).

Since some of the index colonoscopies included were performed more than 15 years ago and may not be representative of current quality standards, a second analysis was performed including only those PCCRCs diagnosed within 3 years from the index colonoscopy and their matched controls, and therefore included only index colonoscopies performed between 2012 and 2018 (Supplementary Table S1). In this analysis, inadequate bowel preparation and piecemeal polypectomy remain the only factors independently associated with the subsequent development of PCCRC.

DISCUSSION

A total of 107 PCCRC cases were described and categorized according to their most plausible explanation following the WEO algorithm. In addition, our PCCRC population was compared to a control cohort without CRC adjusted for important confounders to help identify the index colonoscopy-related factors associated with the development of PCCRC. Our PCCRC rates were slightly lower than those described in previous studies. Regarding the root-cause analysis, we found that possibly missed lesions are the main cause of PCCRC, especially with a prior examination that was considered adequate. Importantly, in our case-control study, we found inadequate bowel preparation and a history of piecemeal polypectomy to be independent risk factors for PCCRC.

The WEO consensus proposes using the 3-year PCCRC rate to benchmark services. Our 3-year PCCRC rate was 2.2%, which is similar to the rates reported in Canada (3.4%),[7] Utah, USA (3.5%),[11] and Córdoba, Spain (3.6%),[12] but less than the rates reported in England (4.7%),[13] Sweden (7%),[14] and Belgium (7.6%).[15] Differences in methodology used to calculate the PCCRC rate, with different time frames and inclusion or exclusion criteria, could explain these variations.[16] For example, in our study, we exclude high-risk populations, such as patients with IBD or hereditary nonpolyposis CRC, whereas these patients are often included in previous studies,[11–15] which could explain part of the differences. Furthermore, some studies were published before the WEO consensus and do not use a standardized and uniform method to calculate PCCRC.[4]

Similar to previous studies, most of the PCCRCs in our series (55.8%) were located in the proximal colon.[6] This right-side predominance could be explained by the higher rate of inadequate bowel preparation in proximal segments or by right-sided lesions being more frequently serrated or flat, which make them more difficult to detect and remove completely.[17] In line with previous studies,[13,15] we found a relatively high proportion of stage I cancer (26.2%). However, despite the predominance of this early stage, shorter survival times have been reported for PCCRC compared to detected CRC, especially when controlling for both lead time bias and immortal time bias.[14,15] The association of proximal tumor location, an earlier stage at diagnosis, and survival disadvantage compared with detected CRCs suggests differences in tumor biology, and further research is needed to clarify whether the mismatch repair or serrated pathways of tumorigenesis play a determining role in the pathogenesis of these lesions.[18–20]

In our population, more than 45% of PCCRCs appearing in the first 6–48 months after index colonoscopy were attributed to missed lesions in a prior adequate colonoscopy. Previous studies have already described missed lesions as the main explanation for PCCRC,[21,22] and two studies reported up to 66%–70% of PCCRC cases being attributable to missed lesions in a prior adequate examination.[22,23] In addition, some difficulties in classifying PCCRC according to the four categories proposed by the WEO were noted. First, to consider a PCCRC for categories C (detected lesion, not resected) or D (likely incomplete resection), we required the identification of an AA in the same bowel segment at index colonoscopy, which was challenging in some cases due to the index colonoscopy report being unclear about the location or the size of the lesion or the inability to recover the piece for pathology analysis. Second, there were cases in which PCCRCs appeared after index colonoscopy in which a NAA or serrated lesion was resected on the same segment, but as these lesions did not fulfill the WEO definition, these PCCRCs were categorized as A or B (possible missed lesion). Finally, some PCCRCs, especially those in the left bowel, were categorized as B (possible missed lesion, prior examination inadequate) because the index colonoscopy had poor bowel preparation or was incomplete, even though the bowel segment where the PCCRC appeared had been adequately examined.

Previous studies have suggested several potential risk factors for PCCRC, including patient factors, such as comorbidity, older age, female sex, diverticular disease,[24] and personal or family history of CRC[11]; colonoscopy factors such as preparation quality[25]; endoscopist factors, such as endoscopy volume, colonoscopy completion rate, ADR, or withdrawal time[25]; and tumor molecular characteristics, such as mismatch repair deficiency.[26] However, the vast majority of these studies compared PCCRC with detected cancers. In our results comparing PCCRC cases' index colonoscopy with a control cohort with colonoscopies without CRC adjusted for age, sex, endoscopist, indication, center, and date, inadequate bowel preparation and prior piecemeal polypectomy were the only factors independently associated with the subsequent development of PCCRC. Regarding inadequate bowel cleansing, some studies have shown that patients with suboptimal bowel preparation present with up to 27% missed AAs in early repeat colonoscopy.[27,28] On the other hand, large polyps with piecemeal excision are known to be associated with high rates of incomplete resection and adenoma recurrence.[29,30] However, another factor classically linked with PCCRC, incomplete colonoscopy,[26] was not significantly associated in our population. We think this could be explained by our current clinical practice: patients with incomplete procedures undergo second examinations or CT-colonoscopy in the first 6 months, turning these lesions into

diagnosed CRC. To the best of our knowledge, only two other studies[11,31] have compared PCCRC with a cohort of non-CRC individuals to assess index colonoscopy-related factors. However, its multivariate analysis was not adjusted by important cofounders (e.g., endoscopist or indication), its analysis did not include important potential predictive factors for PCCRC, such as serrated or flat lesions, or piecemeal resection, and in one of them[31] the nomenclature was not actualized according to WEO recommendations (CRC diagnosed up to 1 year after index colonoscopy considered as detected CRC).

Despite our low PCCRC rates, there is still room for improvement. Our results emphasize the need to adhere to post-polypectomy surveillance guidelines[32,33] and ensure optimal follow-up of patients after index colonoscopy, especially for large polyps with piecemeal excision for which early review of the polypectomy scar is advised due to the high rates of incomplete resection.[32] Furthermore, early repeat colonoscopy or non-colonoscopy imaging should be performed in the first 6 months after an incomplete index colonoscopy or with suboptimal bowel preparation.[27] Previous studies have proposed the use of FIT in high-risk populations in the intervals between surveillance colonoscopy to minimize the risk of PCCRC, with a reported detection rate of 2% of CRCs in FIT-positive patients despite having a colonoscopy in the previous 3 years.[34] Finally, several studies have reported an important association between PCCRC and endoscopist quality indicators[9,35]; therefore, these indicators should be routinely measured and reported in endoscopy units.

Our study has several strengths. This was a large population-based study performed in academic and non-academic medical centers, encompassing more than 100,000 colonoscopies with a large number of PCCRC cases. Our PCCRC rate calculation methods are actualized and adapted to the WEO recommendations. Also, as suggested in the WEO consensus, we provide PCCRC rates for various time cutoffs (1, 3, 5, and 10 years) to develop an evidence-base for different timeframes and how they evolve in time. In our endoscopy services, all colonoscopies are performed by a gastroenterologist, with high-quality index procedures and endoscopy reports with actualized nomenclature, and bowel cleansing reported using a validated scale. Moreover, we used non-cancer controls from the same underlying population and adjusted for age, sex, center, date, indication of index colonoscopy, and endoscopist to minimize selection bias and provide an adjustment of OR estimates for important potential confounders. Finally, most of the previous studies regarding PCCRC use administrative databases, whereas in this population-based study, we used chart review to verify diagnoses of PCCRC and index colonoscopy-related risk factors.

Our study also has some limitations. First, it is an observational retrospective study with an inherent risk of bias. Second, we were unable to account for important clinical factors (e.g., family history of CRC, obesity, diverticulosis), endoscopist-related factors (ADR, withdrawal time), or molecular characteristics of the PCCRCs. Finally, some PCCRCs may have been misclassified as detected if patients underwent a colonoscopy performed 6–120 months before the diagnosis at a different center from those included in our study.

In conclusion, following the WEO methodology, we estimated a 3-year PCCRC rate of 2.2% over a 4-year period, attributed mostly to missed lesions despite an adequate index colonoscopy. In addition, in our population of 107 PCCRC cases and 428 matched non-CRC patients, inadequate bowel preparation and piecemeal polypectomy were independently associated with PCCRC, indicating the high-risk populations where we must target our efforts to try to prevent these lesions. We think our findings may help identify opportunities for improved colonoscopy performance and help other services initiate monitoring and review of their PCCRC cases and rates.

AUTHOR CONTRIBUTIONS

Sandra Baile-Maxía and Rodrigo Jover conceptualized and designed the study and drafted the manuscript. All authors acquired the data from their respective centers. Sandra Baile-Maxía, Pedro Zapater, and Rodrigo Jover analyzed and interpreted the data and performed the statistical analysis. All authors contributed to the critical revision of the manuscript for important intellectual content and approved the final version.

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CONFLICT OF INTEREST STATEMENT

R.J. has received research grants from MSD and participated as an advisor to MSD, Norgine, Alpha-Sigma, and GISupply. The rest of the authors have nothing to disclose.

DATA AVAILABILITY STATEMENT

Data, analytical methods, and study materials will be made available to other researchers from the corresponding author, [R.J.], upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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