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A Review of Three-Year Post-Colonoscopy Colorectal Cancer (PCCRC) Rates in the Published Literature

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Abstract

Background: Although colonoscopy remains the cornerstone of CRC screening, a small proportion of patients who have a negative endoscopic evaluation will subsequently be diagnosed with CRC – so termed a Post-Colonoscopy Colorectal Cancer (PCCRC). PCCRC rate has been proposed as a critical indicator of colonoscopic quality.

Aims: This study aims to determine an accurate 3-year PCCRC rate in a westernised population with a colorectal cancer screening programme and to analyse secondary quality assessment indicators.

Methods: A systematic review of the literature was performed to evaluate the rate of post-colonoscopy colorectal cancers. Two electronic databases were searched using a considered search strategy and a number of variables were extracted in order to determine a 3-year PCCRC rate.

Results: The search identified 2022 studies for screening. 39 studies were retrieved and reviewed in full and six studies were selected for inclusion. The median PCCRC rate among included studies was 7.69% (IQR 6.42% - 8.2%). PCCRC is associated with older age, female sex and a high Charlson comorbidity index. PCCRCs were more likely to be located in the proximal colon and have a lower TNM pathological stage. Secondary quality assessment indicators were inconsistently reported amongst studies.

Conclusion: PCCRC rate is a marker of colonoscopic quality and reducing it increases the efficacy of endoscopy services. The methods used to calculate and report PCCRC rate vary between jurisdictions and care must be taken when interpreting these statistics in order to ensure an accurate patient consent process.

Introduction

Colorectal cancer is the second leading cause of cancer-related mortality, and survival rates are markedly improved with diagnosis at an early stage [1]. It is widely accepted that the majority of colorectal cancers develop along the adenoma-carcinoma sequence, thus providing a rationale for population-based screening to identify pre-malignant lesions and enable timely intervention. Colonoscopy is a widely recommended and cost-effective screening modality for colorectal cancer and its use as part of screening programmes is known to reduce cancer-related morbidity and mortality [2,3]. Despite this, a small proportion of patients who have a negative endoscopic examination will subsequently be diagnosed with CRC – so termed a Post-Colonoscopy Colorectal Cancer (PCCRC). PCCRCs occur for a variety of reasons, including poor patient compliance or inadequate bowel preparation, but a significant number of PCCRCs occur as a result of a pre-existing lesion being incompletely excised or missed by the endoscopist [4,5]. Minimizing the occurrence of PCCRCs improves the quality of a screening service and measurement of PCCRC rate allows endoscopic units to identify and rectify performance issues. Therefore, PCCRC rate has been proposed as a surrogate marker of endoscopic quality assurance [6,7].

PCCRC rates in the literature vary considerably from 1.2% to 10.6% [8,9]. Whilst this may be partially due to variations in service quality between endoscopic units, it also reflects different methods of defining and calculating PCCRC. A variety of interval time cut-off points are reported, with studies using a range of 3-year, 5-year and 10-year screening intervals. The World Endoscopy Organisation's consensus statement defines PCCRC rate as the number of PCCRCs divided by the total number of PCCRCs plus

the number of detected cancers, expressed as a percentage [10]. PCCRCs are more likely to occur in older comorbid females, arise in the proximal colon and have favorable histopathologic features [11]. The aim of this review was to determine the 3-year PCCRC rate of published studies and to analyse the reported secondary quality assessment indicators.

Methods

A systematic literature search of the PubMed and Scopus electronic databases was performed using Medical Search Headings (MeSH terms) "Colorectal cancer" AND "Colonoscopy" AND ("Interval cancer" OR "Post-colonoscopy cancer"). The search was limited to original articles published in the English language in the past 10 years. In order to determine an accurate PCCRC rate of a westernised population with a colorectal cancer screening programme, only studies from Europe and North America were included. Data extracted from selected studies included: year of publication, location, study design, number of patients and their baseline demographics, method of identification, definition of PCCRC, rate of PCCRC, stage, grade and location of CRCs, caecal intubation rate, withdrawal time and quality of bowel preparation. Statistical analyses were performed only on the extracted data from selected studies. Basic descriptive statistics were used to summarise the patient, study and outcome data. The rate of PCCRC was expressed as a percentage of the total number of detected cancers plus PCCRCs.

For this review, PCCRCs were defined as interval CRCs diagnosed between 6 and 36 months following a colonoscopy (i.e. false negative colonoscopy), and 'detected CRCs' were defined as those diagnosed within 6 months of colonoscopy (i.e. true positive colonoscopy). Only studies that reported a 3-year PCCRC were included. Proximal, or right-sided colon refers to the caecum, ascending and transverse colon up to the splenic flexure, while distal, or left-sided colon relates to the splenic flexure, descending colon, sigmoid and rectum. A specialist endoscopist refers to a clinician who has completed specialist training in either gastroenterology or general surgery and is practicing at attending/consultant level.

Results

2022 studies were identified for screening using the aforementioned search strategy, with six studies [8,12-16] ultimately meeting the inclusion criteria for this review (Figure 1). The study characteristics are outlined in Table 1. Patient details are shown in Table 2. The majority of the studies (n=4) originated from Canada and the USA, with two European studies [8,14] also included. The six studies included a total of 191,971 CRCs with a colonoscopy in the preceding 36 months, of which 14,492 were PCCRCs (Table 1), giving a 3-year PCCRC rate of 7.6% (median 7.69%; interquartile range 6.42%-8.2%). The individuals in the PCCRC cohort tended to be older than those in the detected CRC group (mean age 72.7 years vs. 71.5 years) and were more likely to be female (49% vs. 45%) with a higher incidence of comorbidities (Charlson Comorbidity Index [5] score ≥2 19.2% vs. 13.7%). The majority of studies used population-based registries to collect data and as a result did not have access to the indications for colonoscopy in the study cohorts. One study [15] conducted a retrospective chart review of PCCRC cases and reported that 62.5% of their PCCRC cohort were in a screening programme, with the remainder being symptomatic.

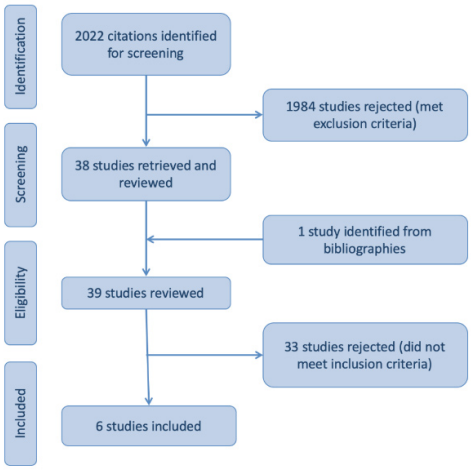

Figure 1: PRISMA diagram showing selection of studies for inclusion.

Reference	Year	Location	Study Design	Definition PCCRC	Detected CRCS	No of PCCRCs	PCCRC RATE (%)
Baxter	2011	Canada	Retrospective cohort	3 years	12,804	1,260	8.96
Cooper	2011	USA	Population-based cohort	3 years	53,647	4,192	7.25
Forsberg	2017	Sweden	Population-based cohort	3 years	15,033	1,286	7.88
Gotfried	2015	USA	Retrospective cohort	3 years	1,102	45	3.92
Morris	2014	UK	Population-based cohort	3 years	90,398	7,321	7.49
Singh	2010	Canada	Population-based cohort	3 years	4,495	388	7.95
TOTAL					**177,479**	**14,492**	**7.60%**

CRC = colorectal cancer; PCCRC = post-colonoscopy colorectal cancer; PCCRC = (number of PCCRCs) / (number of PCCRCs + number of detected CRCs)

Table 1: Study characteristics.

Reference	No of patients (% men)		Median age (years)		CCI high (≥2)		Proximal location (%)		Early Stage (ie TNM I + II) (%)	
	PCCRC	Detected	PCCRC	Detected	PCCRC	Detected	PCCRC	Detected	PCCRC	Detected
Baxter	1,260 (52.7)	12,804 (56.7)	71	68	130 (10.3)	634 (5)	676 (53.7)	4,796 (37.4)	NR	NR
Cooper	4,192 (43.4)	23,585 (44)	3,085 >74 (74)	38,221 >74 (71)	908 (21.5)	7,870 (10.7)	2,851 (68)	25,870 (48.2)	2,444 (58.3)	29,172 (54.38)
Forsberg	1,286 (48.7)	15,033 (53.2)	749 >70 (58)	8,563 >70 (57)	NR	NR	606 (47.1)	5,877 (39.1)	NR	NR
Gotfried	24 (37.5)	1,123 (NR)	69	NR	NR	NR	13 (54.2)	NR	13 (54.17)	NR
Morris	7,321 (53.3)	90,398 (57)	73	72	1,540 (21)	13,923 (15.4)	3,077 (42)	34,040 (37.7)	2,630/ 5,121 cases (73.4)	38,339/ 71,934 cases (53.3%)
Singh	388 (50.5)	4,495 (57.5)	NR	NR	55	938 (20.9)	225 (58)	1,758 (39.1)	70/137 cases (51.1)	727/ 1,396 cases (52.1)
TOTAL	**14,492 (50%)**	**147,438 (55%)**	**72.7**	**71.5**	**19.50%**	**13.70%**	**51.40%**	**39.60%**	**66%**	**53.50%**

CCI = Charlson Comorbidity Index; PCCRC = Post-Colonoscopy Colorectal Cancer; NR = Not Recorded; TNM = Tumour, Node, Metastasis staging system

Table 2: Patient details.

PCCRCs were more likely to be an earlier pathological stage, with 66% reported as TNM stage I or II, compared with 53.5% of the detected CRCs. In addition, PCCRCs were more likely to be proximally located (51.4% vs. 39.6%). Secondary quality assessment indicators were generally poorly reported across the included studies (Table 3). None of the studies recorded withdrawal time or rectal retroflexion rate of the PCCRC cohort.

Reference	Caecal intubation rate (%)	Adequate bowel preparation (%)	rectal retro-flexion (%)	withdrawal time	colonoscopies per annum	pccrc rate (%)
Baxter	87.6	NR	NR	NR	129	8.96
Cooper	NR	NR	NR	NR	≤85 – 50.1% >85 – 49.9%	7.25
Forsberg	NR	NR	NR	NR	NR	7.88
Gotfried	NR	Poor – 11.1%* Good/Excellent – 72.2%*	NR	NR	NR	3.92

Morris	NR	NR	NR	NR	NR	7.49
Singh	NR	NR	NR	NR	<259 – 47.8% ≥260 – 52.2%	7.95
NR = Not Recorded; PCCRC = Post-Colonoscopy Colorectal Cancer Rate. *Data refers to PCCRC cohort only.						

Table 3: Secondary Quality indicators reported by included studies.

Discussion

This review showed a PCCRC rate of 7.6% over a 3-year time period, which is in keeping with previous published reports [8,17]. However, it can be difficult to ascertain an accurate PCCRC rate as the definition of PCCRC varies between institutions, as do the methods used to calculate PCCRC. For this review, interval time period was defined as 6-36 months following index colonoscopy. Some studies define PCCRCs as those occurring within 6-36 months of colonoscopy but preclude any endoscopic diagnoses being labelled PCCRC, thus focusing on other diagnostic methods e.g. radiological [18], while others necessitate an endoscopic diagnosis [13,16].

Quality assessment measures recommended by the British Society of Gastroenterology and the Association of Coloproctology of Great Britain and Ireland are outlined in Table 4. These guidelines advise that endoscopic units have a target PCCRC rate of <5% at 3 years [6]. Only one of the six studies in this review met this target, and the overall rate of 7.6% is significantly higher than recommended. At present a lack of standardization hampers accurate assessment of PCCRC rates, emphasizing the need for a collaborative approach in order to improve cancer prevention strategies [19]. Secondary quality indicators were not consistently reported across included studies. Got fried and colleagues [15] note that a significant proportion of their reported PCCRCs were in fact due to administrative errors, with 43% of those with inadequate bowel preparation at index colonoscopy failing to attend for a repeat examination.

QUALITY ASSESSMENT INDICATOR	MINIMUM STANDARD	ACHIEVABLE STANDARD
CAECAL INTUBATION RATE	>90%	>95%
ADENOMA DETECTION RATE	>15%	>20%
ADEQUATE BOWEL PREPARATION	>90%	>95%
RECTAL RETROFLEXION	>90%	100%
COLONOSCOPY WITHDRAWAL TIME	6 minutes for negative procedures	10 minutes for negative procedures
COLONOSCOPIES PER ANNUM	Achieving competency: >200	
	Maintaining competency: >100	
PCCRC RATE	<5% at 3 years	
[6] PCCRC = Post-Colonoscopy Colorectal Cancer.		

Table 4: Quality assessment indicators as outlined by Rees, et al.

In line with previous published reports [17], this review highlights the association between PCCRC and proximal tumour location. The reasons underlying this are likely multifactorial. Incomplete caecal intubation would result in inadequate surveillance of the right colon, resulting in lesions there more likely to be missed. In addition, right-sided colonic tumours are more likely to be associated with Microsatellite Instability (MSI) and indeed a number of studies have demonstrated a higher rate of MSI in post-colonoscopy CRCs [20,21]. MSI is associated with a propensity for accelerated tumorigenesis, meaning that in some cases these lesions may have simply not been present at the time of the index colonoscopy.

This review did not demonstrate a significant reduction in the PCCRC rate over time (Figure 2), however the six included studies only span a 7-year timeline and cover a range of jurisdictions. A decline in PCCRC rate has been noted in the UK, with the 3-year PCCRC rate falling from 10.2% in 2001 to 7.3% in 2007 [8], perhaps indicating that awareness of PCCRC rate as a quality indicator has led to an improvement in endoscopic service provision. Where possible, the endoscopic units should attempt to elicit the cause for a higher than average PCCRC rate in order to make service improvements. For example, if the rate is high

because of missed lesions and inadequate colonoscopy, units can take measures to improve endoscopic training and technique.

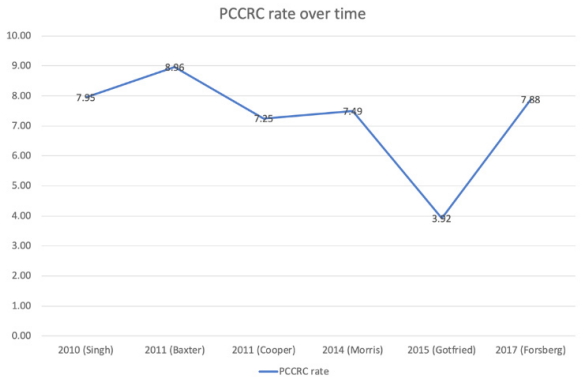

Figure 2: PCCRC rate of included studies over time.

It is worth noting that the term 'Post-colonoscopy cancer rate' is a misnomer of sorts and can be misleading as it refers, not to the rate of CRC diagnosis following colonoscopy, but rather to the percentage of endoscopically-diagnosed cancers that had a negative colonoscopy in the preceding three years. It is calculated as follows:

$$\frac{no.of\ PCCRCs\ (false\ negative\ colonoscopies)}{no.of\ PCCRCs\ (false\ negatives) + detected\ CRCs\ (true\ positives)} \times \frac{100}{1}$$

This terminology can be confusing to patients and care must be taken to ensure accurate interpretation and use of these statistics during the consent process. Morris, et al. note that a more patient-centric denominator might be the total number of colonoscopies, including true negatives, over a three-year period [8]. Using results outlined above and assuming a colonoscopy cancer detection rate of 1%, the risk of PCCRC would be in the order of 0.076% for all colonoscopies performed in a unit. Adherence to the recommended methods [10] of calculating and reporting PCCRC rate among endoscopy units will enable comparability between services and ultimately maximise the benefit of screening programmes.

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