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Official Journal of the Irish Medical Organisation

Ir Med J; September 2026; Vol 119; No. 8; P155
28th September, 2026
Original Paper

Evaluating the oncological value of extended colorectal cancer surveillance

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Abstract

Aims

To record the incidence of polyps, new primary tumours or other pathologies and thus evaluate the value of colorectal cancer (CRC) surveillance beyond standard 5-years period. The American Society of Colon and Rectal Surgeons (ASCRS) recommend surveillance for 5-years following colorectal cancer (CRC) resection. The oncological value of extended surveillance remains controversial.

Methods

A retrospective cohort study was performed. Patients who underwent curative surgery for CRC between 2004-2023 with endoscopic and commuted tomography (CT) surveillance were identified from a prospectively maintained database. A comprehensive review of electronic medical, endoscopic, and radiological records was performed. Descriptive statistics were preformed using SPSS v26.0.

Results

Overall, 217 patients were included, with overall incidence of polyps, new primary tumours and distant metastases discovered during surveillance were 33 (17.6%), 14 (7.4%), and 47 (26.7%) respectively. Of these, 2 patients (14.3%) diagnosed with new primary tumours were diagnosed after 5-years surveillance, as were 4 (9.2%) of those who developed distant metastases. Furthermore, 11 (33.3%) of polyps were detected after 5-years surveillance.

Discussion

The study suggests the possibility that current ASCRS guidelines may result in a proportion of pathology occurrence to be missed in surveillance. Ultimately, the provision of well-designed, prospective randomised clinical trials will be necessary to ratify and support any potentially practice changing results.

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Introduction

In 2022, colorectal cancer (CRC) was the second most common newly diagnosed cancer among men and third most common among women in Ireland[1], with 2,800 new cases reported[2]. It is the second most common cause of cancer-related premature death, with an annual average of 1,012 deaths[1]. Despite predominantly providing high quality healthcare in well-established healthcare models, patients in western Europe persistently succumb to among the highest CRC mortality rates globally[3]. Thus, it is imperative that novel approaches to improve oncological outcomes in this population are explored.

In 2019, data demonstrated that 69.3% of medical oncologists in the Republic of Ireland provide cancer surveillance for 5 years post-resection, results concordant with the recommendations of National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and European Society of Medical Oncology (ESMO). Notwithstanding these consensus statements and recommendations, there is data to indicate that approximately 9% of recurrence and metastases occur after completion of 5-year surveillance[4]. Accordingly, the aim of the current study was to record the incidence of polyps, new primary tumours or other pathologies and thus evaluate the value of CRC surveillance beyond standard 5-year period.

Methods

A retrospective cohort from a single Irish surgeon's database was assessed. Local hospital ethical approval was obtained from the hospital research ethics committee. Patients included in this study had previously undergone curative surgery for CRC between 2004 and 2023. Data pertaining to patient demographics, comorbidities, clinicopathological data, surgical and oncological outcomes were all recorded. Patient follow-up was ratified using electronic and paper medical files.

Early pathology development was defined as any polyps, distant metastases or metachronous tumours detected during standard surveillance (i.e., within 5-years of curative CRC surgery). Late pathology development was defined as pathology development after 5-years of follow-up. Synchronous CRC was defined as second primary CRC found on surveillance within six months of initial curative surgery. Metachronous CRCs were defined as any new second primary CRC found on surveillance after six months of initial curative surgery, not including initial CRC recurrence.

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Fisher Exact and Chi Square tests were used as appropriate to identify possible associations between categorical variables. All values were considered significant where P=<0.05. Statistical analyses were performed using IBM SPSS Statistics predictive analytics software version 29.0.

Results

Patient Data

Of the initial 217 patients, 29 (13.4%) did not opt for any method of surveillance. Therefore, 188 patients were included in statistical tests in this research. Of these 188 patients, 76 (42.7%) were female and 102 (57.3%) were male. The mean patient age was 66-years (range 28-91-years). The caecum was the location for the highest number of primary tumours with 36 (19.1%), followed by the rectum (34 [18.1%]), sigmoid (30 [16%]), recto-sigmoid junction (25 [13.3%]) and finally by the left (23 [12.2%]) and right colon (16 [8.5%]). Other locations including hepatic flexure, splenic flexure, pan-colon, perineal, and transverse colon accumulatively accounted for the locations of 24 (12.7%) primary tumours. On investigation of TNM staging; Stage III had the largest proportion of patients with 69 (37.9%), followed by Stage II, I and IV with 61 (33.5%), 28 (15.4%), and 21 (11.5%) respectively. Patients that did not fit criteria for Stage I, having carcinoma in situ, accounted for 1.6% (3) of participants. The remaining proportion of patients (6) were unable to be assessed using TNM staging, and therefore represented missing values in this analysis. The most prominent surgical resection was right hemicolectomies (60, 31.9%), followed by left hemicolectomies (45, 23.9%), low anterior resections (44, 23.4%) and subtotal colectomies (23, 12.2%). The remainder (16, 8.5%) included abdominal perineal resection, anterior resection, and Hartman & sigmoid resection. The mean length of follow-up was 60 months, with a range of <1 to 216 months.

While 188 patients fit the surveillance criteria, differences in methods of follow-up resulted in differing numbers within tests of polyp (188) and distant metastases (179) categories. This difference represents a cohort of patients that did not opt for CT surveillance and therefore could not be analysed for new diagnoses of distant metastases. These patients did receive colonoscopies, and therefore could be assessed for new primary cancers and polyps.

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***Table 1**: Association between patient factors and early and late pick-up of post-operative polyps*

	Early Development (<5-years): N (%), N=21	**Late Development (>5-years): N(%), N=11**	**Significance**
Gender			NS
Male	10 (48)	6 (55)	
Female	11 (52)	5 (45)	
History of polyps			NS
Yes	3 (14)	1 (9)	
No	18 (86)	10 (91)	
Stage			NS
0	1 (5)	0	
1	5 (25)	1 (9)	
2	7 (35)	6 (55)	
3	7 (35)	4 (36)	
4	0	0	
Risk factors			NS
HTN			
Yes	8 (38)	7 (64)	
No	13 (62)	4 (36)	
HC			
Yes	9 (43)	2 (18)	
No	12 (57)	9 (82)	
DD			
Yes	6 (29)	2 (18)	
No	15 (71)	9 (82)	

NS = Not significant

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Overall, 17.6% (33/188) of patients developed polyps during surveillance after curative surgery. The mean time to polyp development was 44.2 months. Of the 188 patients included in this study, 11.7% (22) of patients had a history of polyps prior to their cancer diagnosis. There was no association found between history of polyps and polyps found on post-operative surveillance (P>0.05). Of these patients, 33.3% (11/33) were found to have polyps on surveillance after 5-years. Differences in individual patient factors are included in the table 1.

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***Table 2**: Association between patient factors and early and late pick-up of post-operative metachronous CRCs.*

	Early Development <5-years: N (%) N=13	**Late Development >5-years: N(%) N=2**	**Significance**
Gender			NS
Male	6 (46)	2 (100)	
Female	7 (54)	0 (0)	
Stage			NS
0	0	0	
1	1 (8)	0	
2	5 (38)	1 (50)	
3	7 (54)	1 (50)	
4	0	0	
Characteristics			NS
HTN			
Yes	8 (62)	1 (50)	
No	5 (38)	1 (50)	
HC			
Yes	2 (15)	1 (50)	
No	11 (85)	1 (50)	
DD			
Yes	2 (15)	1 (50)	
No	11 (85)	1 (50)	

NS = Not significant

Overall, 7.4% (14) of patients had new primary CRC out of a sample of 188 patients, with 2.1% (4) of these developed a synchronous cancer during the first six months of surveillance. Among all second de novo tumours, the mean time to development was 26.6 months (range: 9 – 92 months). Of these new primary CRCs, 14.3% (2/14) developed after the 5year standard

surveillance. This proportion represents that 1.1% (2/188) of patients overall developed a new primary cancer beyond 5-years.

Incidence of Distant Metastases

***Table 3**: Association between patient factors and early and late pick-up of post-operative metachronous metastases*

	Early Development (<5-years): N (%) N=39	**Late Development (>5-years): N(%), N=4**	**Significance**
Gender			NS
Male	24 (62)	2 (50)	
Female	15 (38)	2 (50)	
Stage			NS
0	0	0	
1	2 (6)	0	
2	10 (26)	2 (50)	
3	21 (55)	2 (50)	
4	5 (13)	0	
Characteristics			NS
HTN			
Yes	18 (46)	2 (50)	
No	21 (54)	2 (50)	
HC			
Yes	9 (23)	0	
No	30 (77)	4 (100)	
DD			
Yes	8 (21)	0	
No	31 (79)	4 (100)	

NS = Not significant

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Of the 179 patients, 26.7% (47) developed distant metastases during follow-up. Of these, 59% (28) developed liver metastases, while 53% (25) developed lung metastases. The mean time from curative surgery to the development of distant metastases was 23.8 months (range: 1 – 92 months). Importantly, 9.2% (4) of patients developed distant metastases after the 5-year surveillance follow-up period. Overall, this proportion represents that 2.2% (4) of all participants developed distant metastases beyond 5-years.

Discussion

Overall, this study was performed to decipher the benefit of extended CRC surveillance through the investigation of the prevalence of post-operative polyps, metachronous CRC and distant metastases in a single surgeon's database. By documenting incidence rates in 188 patients after curative resection for CRC, this study found similar results to other international studies with 17.6%, 7.4% and 26.7% for polyp, new primary CRC and distant metastases respectively. Of these pathology occurrence proportions incidence of polyps, metachronous tumours and distant metastases after the standard 5-year follow-up was 33.3%, 14.3% and 9.2% respectively. While this is a lesser proportion when compared with incidence of pathology development within the standard surveillance recommended by NCCN and ESMO, it represents a number of patients succumbing to later diagnoses, albeit few. Cost and expense of surveillance must be balanced against the benefit of further follow-up, and it is important to note that just 1.1% of patients were diagnosed with new primaries following extended surveillance. On average, lifetime cost of CRC management per patient is €39,000 in Ireland in 2008, which includes the significant cost of surveillance. Extended surveillance would vastly increase health care expenses towards CRC management overall[5]. While the current study questions current ASCRS surveillance guidelines recommending just 5-year surveillance, it may not be fruitful in less well-resourced healthcare economies to interpret these results to suggest all patients require extended surveillance. In essence, the provision of well-designed, prospective randomised clinical trials will be necessary to support any potentially practice changing results.

While the current study demonstrated a 7.4% incidence of new primary cancer diagnosis in patients who are undergoing surveillance for CRC, just 1.1% occurred following 5-year surveillance. Similar analyses demonstrated a 2% rate of new primary cancer diagnosis[6], similar to another that demonstrated incidence rates at 3- and 10-years as 2% and 3.1% respectively[7]. Congruent with our findings, another study noted an incidence rate of 9% in their previous analysis, however, they differed in that they included patients aged 40 years and younger, indicating that hereditary may explain this increased incidence of early-age CRCs and subsequent new primary tumours[8]. While this study does not account for patients with

hereditary CRC or Familial Adenomatous Polyposis (FAP), it includes just two patients with previous diagnoses of Lynch Syndrome. The current study demonstrates a synchronous cancer detection rate of 2.1%, similar to other reports at 2.6% incidence[9]. Our and previous research demonstrate a proportion of patients who may be subject to synchronous and new primary cancer diagnoses in which present in desultory timeframes.

In this study, the mean time to new primary tumour development was 26.6-months and 14.3% of these new primary cancers developed after the typical five-year surveillance. These are important findings, which contrast the findings of previous authors: in an observational study, a mean of 81 months after first CRC to identification of new primary CRC was demonstrated[10], while another detailed an incidence of new primary cancers to be consistent when comparing the rate in (a) less than two years, (b) 2-5-years and (c) greater than five years surveillance respectively[11]. Several studies describe similar findings and which propagates proposals the possibility that new primary cancers being sporadic in aetiology as to their time to presentation and might not favour proximity to time from initial curative surgery[7, 10, 11]. Notwithstanding these reports, our analyses suggests that approximately 1 in 7 new cancers diagnosed occurred in the period after regular 5-year surveillance, suggesting further surveillance may be necessary in certain cases.

In this study, just 1.1% of overall patients treated developed new cancers following 5-year surveillance, strongly suggesting that no further surveillance is warranted after the contemporary surveillance period. This data contrasts the results of previous studies. Two separate studies reported results that show a greater incidence of rectal new primary cancer were occurring beyond five years compared to colonic cancers, 10.7% vs 2.1%[12, 13]. Other risk factors for development of new primary CRC were found in research such as occurrence of synchronous cancers, proximal CRC location, and MMR deficient CRCs, perhaps indicating that these potential risk factors may indicate patients who may benefit from further surveillance beyond the standard threshold[11, 14, 15, 16].

This current study demonstrated an incidence rate 26.7% for distant metastases during follow-up. At 40 months post-surgery, a Dutch study illustrated that patients with right sided, left sided, and rectal cancer had 14%, 12% and 16% incidence rates of distant metastases respectively[17]. While the time from curative surgery to development of metastases was significantly shorter in this study (23.8months), the incidence of metastases was considerably higher, indicating a worrying trend. Many studies highlighted the classic tendency toward hepatic metastases, the current study delineated a 59% and 53% rate of hepatic and pulmonary metastases respectively, in line with a previously published study from China (as many as 50% of patients developed hepatic metastasis)[13]. When investigating the prevalence of distant metastases after the typical 5-year follow-up, this study had an incidence rate of

9.2% and is similar to the 13.3% and 11% outlined by two prior separate studies, respectively[18, 19].

This study identified post-operative polyps on surveillance in 17.6% of patients which lies lower than previously described values of 25% and 17-30%[20, 21]. The mean time to development of these lesions was 44.2 months, congruent with a likely development period between 6 months and 4 years found previously[22]. This previous study also demonstrated that 34.1% of polyps were diagnosed on surveillance after 5-years, results not ratified in the current study. Given the propensity to develop to adenocarcinoma, adenomatous polyps remain relevant findings on follow-up after 5-years.

While analyses in the current study failed to demonstrate predictors of polyp development, association with polyp development with smoking and diverticular disease was found in previous studies[23, 24]. Strong associations have been previously described between polyps and increased adiposity, low fibre diets, and excessive saturated fats intake[25, 26].

This study is subject to certain limitations. Firstly, this is a single centre study of retrospective design rendering it subject to selection, ascertainment, and confounding biases. Moreover, this study was conducted in healthcare institution responsible for the provision of cancer care to a population in the west of Ireland; this suggest that these patients may possess unique cultural and hereditary characteristics. Ultimately, this study will be limited by the small sample size making its transferability to larger populations challenging. Nevertheless, the authors do believe that novel insights have been ascertained from the data accrued in the current study.

In conclusion, the current study presents evidence that extended CRC surveillance may be warranted in certain patient populations. It suggests a small proportion of patients' risk missed pathology occurrence using the standard 5-year follow-up. Ultimately, the provision of well-designed, prospective randomised clinical trials will be necessary to ratify any potentially practice changing results or challenge current ASCRS surveillance guidelines.

Declarations of Conflicts of Interest:
None declared.

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