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Research Article

Can we predict colorectal cancer?

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Abstract

Background: Colorectal cancer is a common and lethal cancer worldwide, In the UK, it is the second most common cause of cancer death. 5% of UK population is at risk of colorectal carcinoma during lifetime. 30% of patients with colorectal cancer present with a metastatic disease. Detecting colorectal cancer is challenging patients may present with slight symptoms or asymptomatic. By the time patients becomes symptomatic, the cancer may be more advanced. Therefore, screening for colorectal cancer is recommended for people at average risk.

Method: All patients diagnosed with colorectal cancer at the Luton and Dunstable University Hospital UK from January 2015 through December 2019 were retrospectively identified from the referral database created by colorectal specialist nurses in the colorectal service. Data were retrieved by detailed review of the hospital case notes, ICE/Evolve (Computer database for investigations and correspondence) including endoscopy; radiographic imaging; operative course and cancer follow up.

Results: In the study period 976 patients were diagnosed with colorectal cancer, Male 52.6% (513) Female 47.4% (463). The mean age of 74.14 years (range, 25 to 101). Sixty six 6.76% patients were excluded from the study, therefore the percentages of studied participant were Male 53 % (482) and Female 47 % (428) ratio 1: 1.12. Incidence of colorectal cancer among young adult was low 1.75% (16) up to 39 years of age) and 94.61% are diagnosed in people over the age of 50 years, 60.43% are diagnosed in people aged 70 or over.

Conclusion: Increasing awareness of the symptoms and signs of colorectal cancer be helpful and beneficial. Establish integrated care pathways, centralization of complex procedures and comparison of international cancer outcomes.

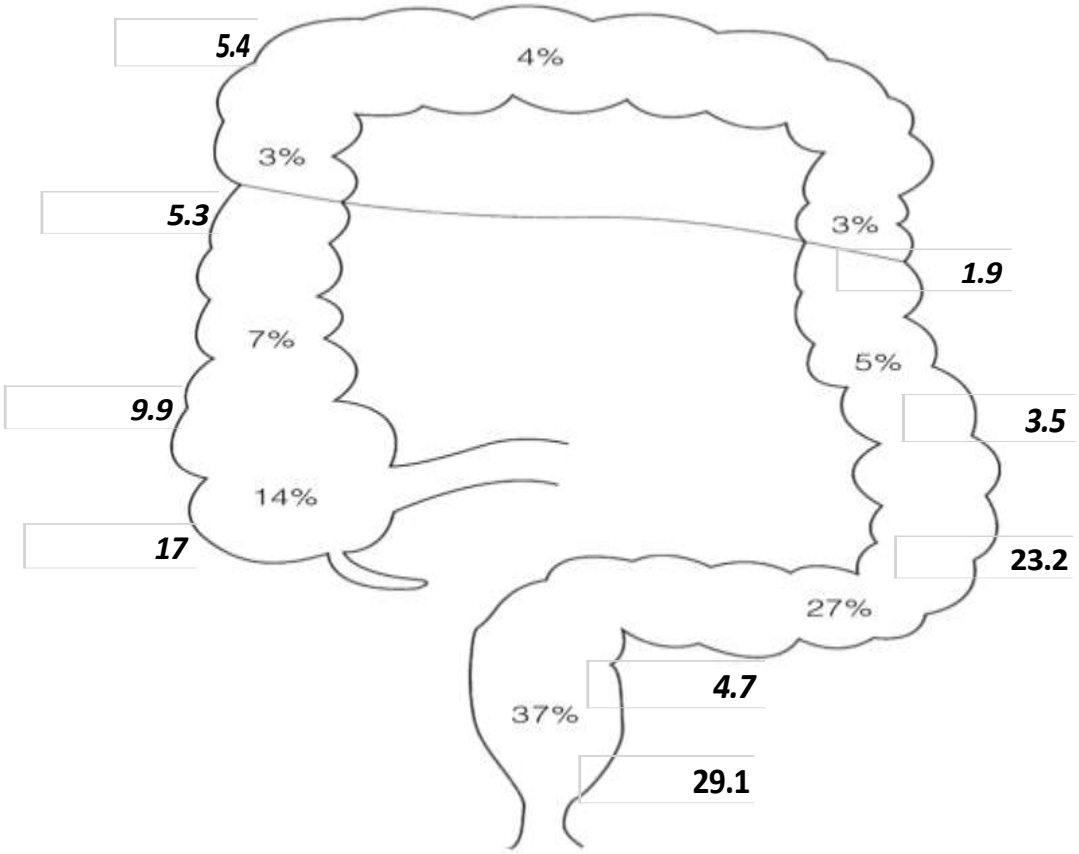
Key words: colorectal cancer; familial adenomatous polyposis

Introduction

Colorectal cancer is a major health problem. In the UK, it is the second most common cause of cancer death. 5% of UK population is at risk of colorectal carcinoma during lifetime. Within the colon, about 50% of cancers arise in the left side and 25% in the right; in 4–5% of cases there are synchronous lesions (Figure 1). Most colorectal cancers arise from adenomatous colon polyps that progress from small (<8 mm) to large (≥8 mm) polyps, then to dysplasia and carcinoma. Adenomatous polyps occur in about 30 percent of men and up to 20 percent of women. Progression from adenoma to carcinoma is believed to take an average of at least 10 years. It is now widely accepted that the majority of colonic cancers arise from pre-existing adenomatous polyps. (Figure 2). Detecting colorectal cancer is challenging patients may present with slight symptoms or asymptomatic. By the time patients becomes symptomatic, the cancer may be more advanced. Therefore, screening for colorectal cancer is recommended for people at average risk.

A diagnosis of colorectal cancer results either from an evaluation of a patient symptoms, or as a result of screening. When colorectal cancer or its precursor lesion is diagnosed early, its 5-year relative survival rate is very high, however advanced colorectal cancer reduces the quality of life of patients. Therefore, novel methods that would allow the early diagnosis of colorectal cancer are chosen. In England almost a 30% of bowel cancer cases are diagnosed through the 'two-week wait' referral route[1]. More than 44%) of these cases diagnosed early (stage I or II [2]. Around 24% of bowel cancer are diagnosed after presenting as an emergency in England [1]. Around 20% of patients presenting with Colo Rectal Cancer have metastatic disease at time of diagnosis [3]. Around 66% presented as an emergency are via Accident and Emergency (ED), with the other cases coming via an urgent GP referral, inpatient referral or outpatient referral [4].

Natural History:



*dark bold our cohort
* light colour literature

Figure 1.

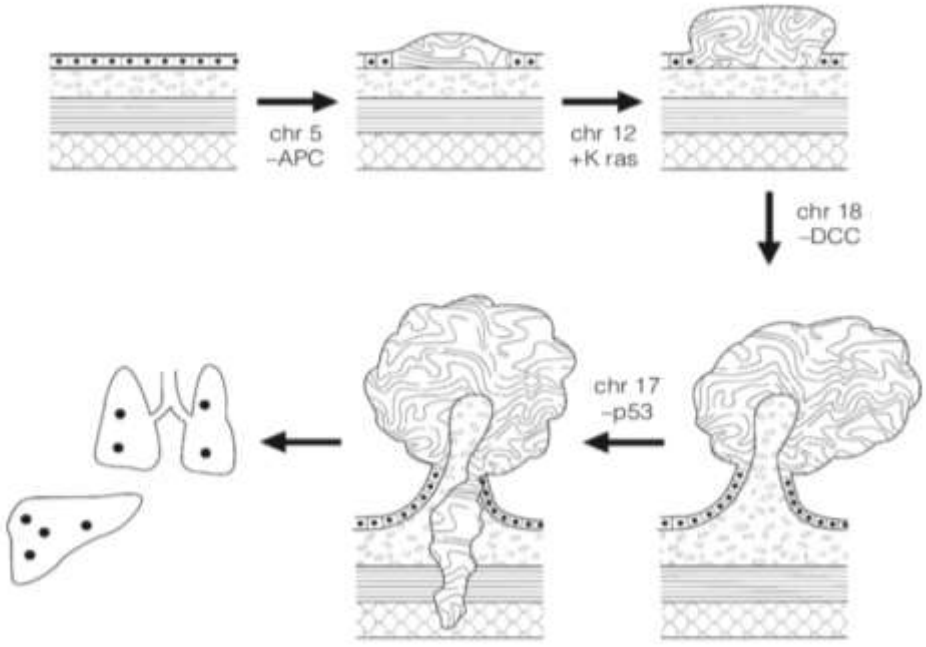
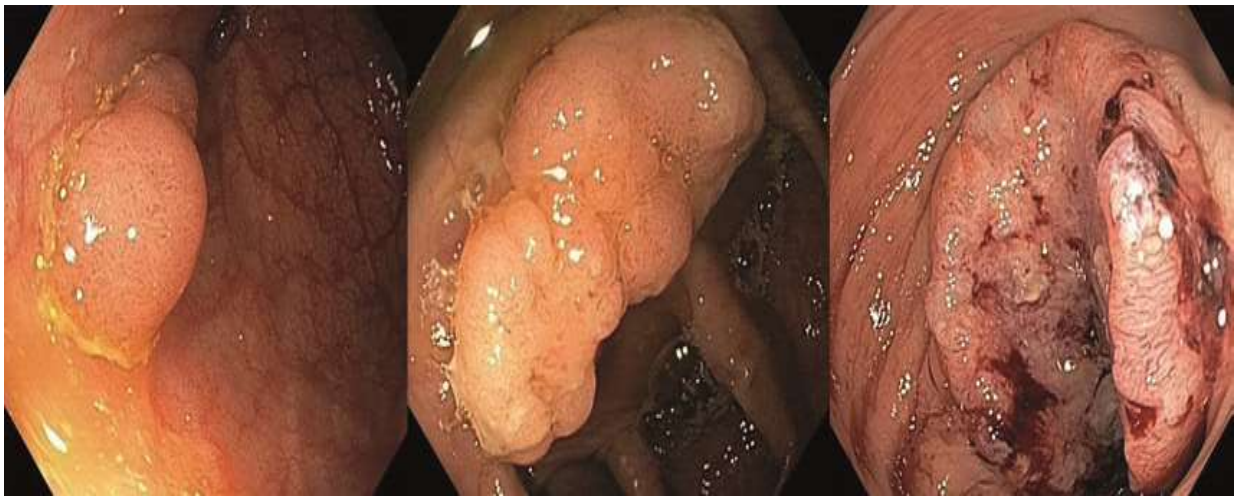


Figure 2a. A possible sequence of genetic changes in the development of colorectal polyps and invasive cancer.



Small sessile adenoma large adenoma carcinoma

Figure 2b.

<table>
<tr><td colspan="2">976 Study</td><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="2">66 Exclude</td><td>29 Anal Canal</td><td>19 Appendix</td><td>10 Small Bowel</td><td>8 CRC? Primary</td></tr>
<tr><td colspan="2">910 Studied patients</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Right colon 342</td><td>Left colon 568</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Male 482</td><td>Female 428</td><td></td><td></td><td></td><td></td></tr>
</table>

Figure 3. Cohort

Aim

Overview of diagnosis and management of the colorectal cancer patients.

Methods

All patients managed with colorectal cancer at the Luton and Dunstable University Hospital UK from January 2015 through December 2019 were retrospectively identified from the referral database created by the colorectal specialist nurses in the colorectal service. Data were retrieved by detailed review of the hospital case notes, ICE/Evolve (Computer database for investigations and correspondence) including endoscopy; radiographic imaging; operative course and cancer follow up. The following parameters were recorded: age, gender, and source of referral, presentation, stage of the disease, MDT discussion, intervention, and outcome. Tumour locations were classified as the right colon (i.e. caecum, ascending colon, hepatic flexure, transverse colon, and left colon (i.e. splenic flexure, descending colon, sigmoid, Recto sigmoid, and rectum

Inclusion: All patients diagnosed with colorectal cancer.

Exclusion: Colo Rectal Cancer of unknown primary site. Anal cancer, Appendix, Small bowel carcinoma

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 26). Mean values were compared using the Student *t* test (Table 1). Univariate analysis of categorical variables was performed by the chi-square test (Table 2). Pearson's chi squared test was used for comparing two proportions (Table 3). An OR with corresponding 95% confidence interval >1 implied a positive association where as an OR with corresponding 95% confidence interval <1 implied a negative association (Table 4). Two-sided p values < 0.05 were considered significant. The results are mainly illustrated by descriptive statistics. Fisher's exact and Student's t tests were used to compare the frequencies of both categorical and continuous variables (Table 5)

One-sample Statistics				
	N	Mean	Std. Deviation	Std. Error Mean
Age	910	6.6978	1.33494	0.04425
Gender	910	1.5297	0.49939	0.01655
Cancer	910	1.6242	0.4846	0.01606
Colon	910	6.6681	3.08083	0.10213

Table 1

Test Statistics				
	Age	Gender	Cancer	Colon
Chi-square	869.844a	3.204b	620.376a	
Df	8	1	1	8
Asymp. Sig.	0	0.073	0	0
a 0 cells (0.0%) have expected frequencies less than 5. The minimum expextecd cell frequency is 101.1				
b 0 cells (0.0%) have expected frequencies less than 5. The minimum expextecd cell frequency is 455.0				

Table 2

		Correlation			
		Age	**Gender**	**Cancer**	**Colon**
Age	Pearson Correlation	1	-0.01	-0.135**	-0.180**
	Sig. (2-tailed)		0.753	0	0
	N	910	910	910	910
Gender	Pearson Correlation	-0.01	1	1.32**	0.132**
	Sig. (2-tailed)	0.753		0	0
	N	910	910	910	910
Cancer	Pearson Correlation	0.135**	0.132**	1	0.931**
	Sig. (2-tailed)	0	0		0
	N	910	910	910	910
Colon	Pearson Correlation	-0.180**	-0.132**	-0.931**	1
	Sig. (2-tailed)	0	0	0	
	N	910	910	910	910
** Correlated is significant at the 0.01 level (2-Tailed)					

Table 3

Risk Estimate	**Value**	**95% Confidence Interval**	
		Lower	**Upper**
Odds Ratio for Gender (Female / Male)	1.733	1.322	2.272
For cohort cancer = Right colon	1.408	1.189	1.667
For cohort cancer = Left colon	0.812	0.732	0.901
N of Valid Cases	910		

Table 4

		Chi-square Tests				
	Value	Df	Asym pto	Exact Sig	Exact Sig. (1-10)	Point Probability
Person chi-square	15.975a	1	0	0	0	
Continuity correction	15.432	1	0			
Likelihood Ratio				0	0	
Linear by Linear Assst	15.958v	1	0	0	0	0
N of Valid cases	910					
a 0 cells (0.0%) have expected count less than 5. The minimum expected count is 160.85						
B Computed only for a 2x2 table						
C The standardized statistics is 3.995						

Table 5a

Age	**Age *colon**

Colon	Mean	N	Std. Deviation
Caecum	7.0645	155	1.34202
Ascending Colon	6.9556	90	1.13089
Hepatic Flexura	6.7083	48	1.21967
Transverse Colon	6.6735	49	1.37519
Splenic Flexura	7.0588	17	1.29762
Descending Colon	6.7813	32	1.67975
Sigmoid Colon	6.7393	211	1.25862
Recto Sigma	6.907	43	1.30592
Rectum	6.2981	265	1.34199
Total	6.6978	910	1.33494

Table 5b. Student t test

Results

In the study period 976 patients were diagnosed with colorectal cancer, Male 52.6% (513) Female 47.4% (463). The mean age of 74.14 years (range, 25 to 101). Sixty six 6.76% patients were excluded from the study 29 Anal canal cancer (2.97%), Appendix 19 (1.94%) small bowel cancer 10 (1.02%) and eight patients 8 (0.87 %), as no primary site of colorectal cancer was identified (Fig: 3), therefore the percentages of studied participant were Male 53 % (482) and Female 47 % (428) ratio 1: 1.12. (Table 6) In the Right colon subset of patients there was a total of 342 patients 190 female and 152 male, In 568 patients with Left Colon cancer there were 330 Male and 238 Female. (Table 7)Incidence of colorectal cancer among young adult was low 1.75% (16) up to 39 years of age) and 94.61% are diagnosed in people over the age of 50 years, 60.43% are diagnosed in people aged 70 or over. (Table 8) Incidence of colorectal cancer were more marked for cancers of the left side of colon than right colon. 64.13% (583) of colorectal cancer cases were diagnosed through "GP" (two -week and urgent call) referral route. 10.89% (99) were diagnosed as a colorectal cancer after presenting as an emergency and 24.97% (227) were referred as in patients and other sources after diagnosis of bowel cancer. **(Table 9).**

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Female	428	47	47	47
Male	482	53	53	100
Total	910	100	100	

Table 6

cancer	Frequency	***Percent***	Valid Percent	Cumulative Percent
Right colon	342	*37.6*	37.6	37.6
Left colon	568	*62.4*	62.4	100
Total	910	*100*	100	

Table 7

	Cancer		
Age	Right Colon	Left Colon	Total
20 -29 years	0	1	1
30 -39 years	3	12	15
40 -49 years	15	18	33
50 - 59 years	28	98	126
60 - 69 years	59	126	185
70 -79 years	117	164	281
80 -89 years	94	124	218
90 -99	24	21	45
100 -110	2	4	6
Total	**342**	**568**	**910**

Table 8

Referral	**Gender**		**Total**
	Female	Male	
GP	267	31	583
Emergency	47	52	99
Other	114	113	227
Total	428	481	909

Table 9

Discussion

Colorectal cancer is a common and lethal cancer worldwide, 30% of patients with Colorectal cancer present with a metastatic disease [5, 6] more than nine out of ten new cases (94%) are diagnosed in people over the age of 50, and nearly six out of ten cases (59%) are diagnosed in people aged 70 or over. bowel cancer can affect anyone of any age. Colorectal cancer is specific and considers the history of clinical symptoms and signs of bowel disease, family history together with investigation results. In our study we found 5.38% (49) up to 49 years of age , 34.17% (311) between 50 - 69 years of age and 60.43% (550) age 70 -101 years this is in contrast to study of Haggar et al [7] and other published studies.[8] More than 2,500 new cases are diagnosed each year in people under the age of 50. 1 in 15 men and 1 in 18 women will be diagnosed with bowel cancer during their lifetime. Incidence and mortality rates vary markedly around the world. Environmental and genetic factors can increase the likelihood of developing colorectal cancer [9]. Unfortunately we still know very little about the causes of colorectal cancer. However, studies have shown that 5% of bowel cancers are because of two inherited conditions that can increase the risk of developing colorectal cancer. They are Familial Adenomatous Polyposis (FAP) and Hereditary Non-Polyposis Colon Cancer (HNPCC). Incidence of bowel cancer is greater in countries, which eat a diet high in fat and low in fibre (roughage). It has been suggested that an excessive alcohol intake, particularly of beer, may be linked to bowel cancer. A history of inflammatory bowel disease affecting the large bowel may also increase the risk of developing colorectal cancer. A diagnosis of colorectal cancer results either from an assessment of a patient symptoms or as a result of screening. The disease can be associated with a range of symptoms, including change in bowel habits, bleeding per rectum, tenesmus. Other symptoms include tiredness, anaemia-related symptoms, such as pale appearance and shortness of breath, and weight loss. "*Be Clear on Cancer*" [10] campaign in the United Kingdom, in 2011, was launched to raise awareness of colorectal cancer symptoms and signs at a local and nationwide level. It was particularly successful in fighting the embarrassment associated with alarming symptoms [11]. In our study, we found increase incidence of colorectal cancer were more marked for cancers of the left side of colon than right colon this is similar to United State studies (Austin et al and Siegel et al) [12, 13]. we found colorectal cancer among young adult was low (1.75% (16) age up to 39 years) , this is in contrast to other published studies [14, 15] red-flag symptoms in a younger patients such as persistent changes in bowel habits, bleeding per rectum or abdominal pain should not be lightly dismissed as being unlikely to stem from a serious cause. In our cohort we diagnosed 64.13% (583) colorectal cancer through two -week wait "GP" referral route this is in contrast to study of Logan RF et al. In England almost a 30% of bowel cancer cases are diagnosed through the 'two-week wait' referral route, [1] More than 44%) of these cases diagnosed early (stage I or II [3] Around 24% of bowel cancer are diagnosed after presenting as an emergency in England, [1] Whereas in our study 10.89% (99) were diagnosed as a colorectal cancer after presenting as an emergency. Around 20% of patients presenting with Colorectal Cancer have metastatic disease at time of diagnosis.[2] A further 20%–25% will develop metastatic disease during follow-up after initial curative intent treatment of their primary tumour. In our study 0.88% (8) patients presented as a metastatic colorectal cancer of unknown primary site this is in contrast to other published studies. Around (68%) with known stage are diagnosed late (stages III or IV). [3] Around 66% presented as an emergency are via Accident and Emergency (A&E), with the other cases coming via an urgent GP referral, inpatient referral or outpatient referral [4]. In our study 24.97% (227) were referred as inpatients after diagnosis of bowel cancer. A 10% of bowel cancer cases in England are diagnosed by screening. Bowel cancer screening reduces risk of dying from bowel cancer by at least 25%, survival rates are greatly improved if an individual is diagnosed early [16]. The cancer detection rate in UK rapid investigation clinics is 6 – 11%; however, these clinics identify only around a third of colorectal cancers [17]. Surgery is the mainstay curative treatment for patients with non-metastasized colorectal cancer. However, outcome is strongly related to the quality of surgery [18, 19] the quality of preoperative staging and treatment selection. There have been major developments in surgical resection of both primary and metastatic diseases, with advanced techniques permitting radical resection [20]. Special attention should be given to the circumferential surgical resection margins [21] however; fundamental questions remain unanswered such as whether primary tumor resection in the presence of synchronous inoperable metastatic disease affects the natural history of the disease. The proportion of colorectal cancer patients having surgery is strongly influenced by stage at diagnosis, other factors are also important, such as the patient's fitness to tolerate the treatment, the patient's age, and their own treatment preference. The resected tumour specimen can be used to judge the quality of surgery; if the margin around the specimen is free of cancer cells in both colon and rectal cancer, the surgery is considered high quality [22, 23]. The removal and assessment of the lymph nodes is another guide for determining whether the mesocolic or mesorectal resection is adequate [24]. Colorectal surgery is aimed at minimizing trauma and preserving organ function. One of the strengths of our study is that the sample size is not small. The limitations of this study were retrospective and single-institution design, some missing notes/data although detailed charts were available for most patients, large number of patients were excluded due to presentation of cancer at other segments of the bowel and Colorectal cancer of unknown primary. Most patients with colorectal cancers are diagnosed after the onset of cancer-related symptoms [25] and it is imperative that frontline providers recognize early diagnostic clues to colorectal cancer, Studies have shown that rectal bleeding as an initial presentation of colon cancer and are associated with an early stage of the disease and better survival [26, 27]. This study estimate the risk of colorectal cancer across different ages, gender, source of referral, and tumours located in different areas of the colon and rectum.

Conclusion

It is imperative to recognize early diagnostic clues to colorectal cancer, increasing awareness of the symptoms and signs be beneficial and helpful. Establish integrated care pathways, centralization of complex procedures and comparison of international cancer outcomes.

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