

Diagnostic miss rate for colorectal cancer: an audit

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Abstract

Background Colorectal cancer (CRC) is a common cancer worldwide. While screening improves survival, avoiding delayed diagnosis in symptomatic patients is crucial. Computed tomographic colonography (CTC) or colonoscopy is recommended as first-line investigation and most societies recommend counseling patients undergoing colonoscopy about a miss rate of 5%. This audit evaluates “miss rate” of colorectal investigations, which have led to diagnostic delay in symptomatic cases in a district general hospital in the United Kingdom.

Methods This is a retrospective review of 150 consecutive CRC cases presenting between August 2010 and July 2011. Evidence of bowel investigations done in the 3 years prior to diagnosis was obtained from computerized health records. Data regarding previous bowel investigations such as colonoscopy, CTC, double contrast barium enema (DCBE), and CT abdomen/pelvis were collected.

Results 6.7% cases were identified via screening pathway while 93% were identified through symptomatic pathway. 17% (26/150) of newly diagnosed CRC had been investigated in the preceding 3 years. Of these, 8% (12/150) had false negative results. The false negative rate for CRC diagnosis was 3.5% for colonoscopy (3/85), 6.7% for CTC (1/17), 9.4% for CT (5/53), and 26.7% for DCBE (4/15). Some patients had a missed diagnosis despite more than one diagnostic test. Time delay to diagnosis ranged from 21-456 days.

Conclusions 17% of patients diagnosed with CRC had been investigated in the previous 3 years. Higher miss rate of barium enema should preclude its use as a first-line modality to investigate CRC.

Keywords Investigation, colorectal cancer, miss rate

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Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide and fourth most common cause of cancer death; with a 5-year survival rate of approximately 50-60% [1]. Screening programs are offered in most western countries with a high incidence of CRC. While screening can improve survival, avoiding a delayed diagnosis in symptomatic patients is also

crucial. Results of special interest group in gastrointestinal and abdominal radiology (SIGGAR) trials recommend computed tomographic colonography (CTC) or colonoscopy as first-line investigation for patients with symptoms suggestive of CRC [2,3]. However these investigations do not have 100% sensitivity and specificity and can miss lesions. Most societies recommend counseling patients undergoing colonoscopy about a miss rate of 2.1-5.9% for significant polyps/cancers [4].

We planned an audit to evaluate the miss rate of colorectal investigations that has led to diagnostic delay in symptomatic cases. The aim of our study was to assess the miss rate of different investigations for CRC in daily practise and to analyze the delay in diagnosis of the symptomatic group due to missed cancers on investigation.

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This study was conducted at Princess of Wales Hospital, Bridgend, United Kingdom

Conflict of Interest: None

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Patients and methods

This study was performed at a district hospital in the UK. Patients with CRC who presented between August 2010 and July 2011 were identified from the hospital database. 150 consecutive cases, based on the date of surgery were selected for this retrospective analysis. Details of all bowel-specific

investigations such as colonoscopy, CTC, barium enema, and CT abdomen/pelvis, performed in the 3 years prior to cancer diagnosis were accessed from electronic results (Indigo 4 systems®), PACS® (picture archiving and communication system) and endoscopy database. Besides previous bowel investigations, data regarding route of referral, presenting symptoms, mode of diagnosis were also collected in a proforma from the electronic records.

Statistical analysis

We used SPSS® version 17 to perform the final analysis. Clinical and disease related variables were analyzed and described as frequency (percentage) and mean (standard deviation) or median and extreme values as appropriate.

Results

Median age of these patients was 71 (range 32-90) years with a male:female ratio of 1:1. 7% cases were identified via screening pathway while 93% were identified through symptomatic pathway (Table 1). Outpatient referral or a direct access endoscopy by a general practitioner was the most frequent modality of referral (68%).

The predominant presenting symptoms were rectal bleeding (29.3%), anemia (24.7%), weight loss (16.7%), pain (20%), and change in bowel habits (15.3%). Most cancers were identified on colonoscopy (Table 2). We found that 17% (26/150) of

Table 1 Referral routes

	Number (N=150)	Percentage
Outpatients/general practitioner referral	102	68
Inpatient referral/ward	12	8
Emergency	26	17.3
Bowel screening	10	6.7

Table 2 Mode of initial diagnosis of colorectal cancer

Investigation	Number (N=150)	Percentage
Endoscopy (sigmoidoscopy/ colonoscopy)	76	50.7
CT scan	30	20
On-table histology	17	11.3
CT colonography	12	8
Barium enema+Rigid sigmoidoscopy	15	10

*Rigid sigmoidoscopies denote endoscopies done in the clinic on an outpatient basis, prior to ordering barium enemas. Sigmoidoscopy denotes flexible endoscopies done electively in the endoscopy suite with a full bowel preparation CT, computed tomography

cancers diagnosed had been investigated in the preceding 3 years. 14 of these 26 patients had some abnormality found on investigations, for example sigmoid stricture, which merited either surgery/follow up or additional investigations. These were not considered missed cancers. However, 8% (12/150) patients had a normal investigation in the 3 years preceding diagnosis of CRC. The details of investigations done, stage of diagnosis and sites of the missed cancers are shown in Tables 3 and 4. Seven of these 12 patients had advanced disease, 2 with stage III disease and 5 with stage IV disease.

Time from symptoms to diagnosis ranged from 21-456 days. Three of 4 cancers missed on DCBE were left-sided. Overall two-thirds of the cancers missed by all modalities combined were left-sided. Most common reason for a miss was presence of diverticular disease especially with missed sigmoid, recto-sigmoid and rectal cancers.

Discussion

CRC is a common cause of cancer and cancer-related mortality worldwide with almost 60% of cases occurring in developed countries [1]. In our database, a large number of cancers were advanced stage Dukes C/D or TNM III/IV (69/150, 46%). The overall 5-year survival remains 50-60% in these groups, despite advances in surgery and adjuvant therapy.

Currently, national bowel screening program in the UK targets patients in the age group 60-74 years. This is based on Guaiac-based fecal occult blood testing (FOBT), which can have sensitivity from 6.2% (specificity 98.0%) to 83.3% (specificity 98.4%) [5]. While this decreases cancer-related mortality by 15%, interval cancer rates are approximately 25% [6]. The uptake rates for most FOBT-based screening programs vary widely and range between 40-60% in the UK and 15-70% worldwide in various programs. Results of a trial evaluating once only flexible sigmoidoscopy at 55 years have shown a reduction in CRC incidence by 23% and mortality by 31% [7]. This however is still to be implemented.

Less than 10% of our patients were detected by screening program while most were diagnosed via symptomatic pathway. While results of SIGGAR trials have shown superiority of colonoscopy/CTC over DCBE, DCBE continues to be used in the UK as it lacks long waiting list compared to colonoscopy and CTC [3,4].

While our study does not show exact distribution of investigations of bowel symptoms, it does reflect practise. 50.7% of cancers were diagnosed using colonoscopy (these also include 6.3% referred from screening through FOBT), 4% by DCBE, and 8% by CTC, which is a reflection of our current practise. Our miss rate of colonoscopy was 3.5%, better than other reported studies [4].

Flexible sigmoidoscopy also missed some left-sided lesions in our study. While clinical trials using flexible sigmoidoscopy have criteria for completion such as reaching the splenic flexure, in real-life scenario, polyp detection rate may be influenced by the patient's tolerance and experience of the operator. These factors may lead to incomplete investigation with procedure

Table 3 Cancers missed on investigations (some missed on more than one test)

	Location of tumor	Investigations done in preceding 3 years	Dukes stage at diagnosis	TNM stage at diagnosis	Time delay in days
1	Rectum	Barium enema	D	IV	336
2	Rectosigmoid	Barium enema, flexible sigmoidoscopy	D	IV	441
3	Rectosigmoid	Flexible sigmoidoscopy	B	II	237
4	Sigmoid colon	CT scan	B	II	160
5	Sigmoid colon	Flexible sigmoidoscopy and colonoscopy	B	II	57
6	Sigmoid colon	CT scan	C1	III-A	456
7	Sigmoid colon	Colonoscopy, CT scan, barium enema	B	II	21
8	Splenic flexure	CT scan	C1	III-A	61
9	Hepatic flexure	CT colonography	B	II	120
10	Hepatic flexure	Colonoscopy	D	IV	330
11	Cecum	CT scan	D	IV	163
12	Cecum	Barium enema	D	IV	385

CT, computed tomography

Table 4 Sites of missed cancers

Site of missed tumor	Number (n=12)
Rectum	1
Rectosigmoid	2
Sigmoid	4
Splenic flexure	1
Transverse colon	0
Hepatic flexure	2
Cecum	2

Numbers too small to analyze for meaningful statistical analysis

sometimes being terminated in distal sigmoid itself. In such incomplete investigations for rectal bleeding, completion of investigation should be achieved by additional imaging such as CTC/DCBE.

A population-based study by Toma *et al* had shown that almost a quarter (22.4%) of patients diagnosed with CRC had a normal barium enema investigation within 3 years of diagnosis [8], similar to our study. While this may reflect cancers arising from flat adenomas/polyps, some of the cancers or advanced polyps could also be missed. This rate of interval cancers (or missed cancer) may not be acceptable even for screening programs, but for symptomatic pathway it has serious implications such as underperformance/inappropriate investigation and delayed diagnosis resulting in a more advanced stage at presentation and hence a poorer outcome.

The aim of investigation in symptomatic pathway should not only be the detection of cancers but also the elimination of advanced polyps; hence colonoscopy seems to be the only viable option. In fact, Toma *et al* felt physicians who use barium enema to evaluate the colon must inform their patients that if a cancer is present, there is an approximately one in five chance that it will be missed [8].

Barium enema in our study seems to have a high miss rate (26.6%). Common problems recorded were sigmoid stricture due to co-existing diverticular disease and the difficulty in characterizing the nature of the stricture without tissue confirmation. While there is much evidence that diverticulosis on barium ultimately still requires direct visualization, there seems to be hesitation to do this, putting the onus on radiologists. Best practise reflected in the 2011 NICE (National Institute for health and Care Excellence, UK) guidelines clearly states the need to do both flexible sigmoidoscopy in conjunction with DCBE when used in patients with major comorbidities [9].

Anderson *et al* reviewed the radiographs and clinical records of 26 patients with CRC missed on DCBE (subsequently detected at colonoscopy) to analyze the cause of radiological error. They found about 50% of missed cancers were in sigmoid colon. Retrospective analysis of barium enemas revealed cancers present in 76% cases with 50% being very obvious. They suggested double reporting of barium enemas to minimize errors [10]. Tan *et al* found a lower miss rate of DCBE (4.1%) and suggested that tumors less than 3 cm in length and not circumferential may be missed, however they included only investigation done less than 6 months (3 years in our study) prior to diagnosis of CRC [11]. Likewise, McDonald *et al* found a miss rate of 6.7% (24 months) on barium enemas. In the SIGGAR trials, the miss rate of DCBE was 14% compared to 3.6-7% of CTC and 0% (no missed cancers) of colonoscopy [2,3]. However there was no significant difference in the miss rates of distal versus proximal cancers.

Our miss rate of diagnostic investigation is similar to Frenette *et al*, who found miss rate of colonoscopy, barium enema, and flexible sigmoidoscopy to be 9%, 20%, and 50%, respectively [12] (Tables 3 and 5). National training programs/accreditation for colonoscopy have contributed to improved detection rates on colonoscopy [13]. While for frail patients CT scans are often performed to look for gross lesions, it may

Table 5 Literature review of the miss rate of colonic investigations

Investigation	Cancers missed/ total cancers diagnosed by the investigation	Missed %	Missed rate in literature (reference)
Colonoscopy	3/85	3.5%	9% [12]
Sigmoidoscopy	3/8	37.5%	50% [12]
Barium	4/15	26.6%	20% [12] 22.4% [8]
CT colonography	1/17	6.7%	18.9% [16]
CT scan	5/53	9.4%	

Some cancers were missed on more than one investigational modality, while some were diagnosed after a repeat examination of similar nature; CT, computed tomography

have a miss rate higher than in our study (10%). Probably for these patients minimal preparation CT scan (MPCT) is a better alternative. MPCT involves taking prolonged oral iodinated contrast (gastrografin) prior to the examination. It does not require purgative bowel preparation, rectal insufflation, patient mobility or sedation thus making MPCT a more acceptable investigation for such patients. MPCT has a high sensitivity and specificity and is better tolerated by frail patients [14].

Besides miss rate of diagnostic modalities, failure to investigate symptoms also may cause delayed diagnosis, which was not evaluated in our study. Attributing a few episodes of rectal bleeding to benign causes such as hemorrhoids and hence not investigating further could also cause delay in diagnosis in CRC. Flexible sigmoidoscopy trial also showed that the numbers needed to be screened to prevent one CRC diagnosis or death were 191 (95%CI 145-277) and 489 (95%CI 343-852), respectively [7]. A single routine flexible sigmoidoscopy in symptomatic patients may be worthwhile.

The percentage of symptomatic patients investigated at hospital level/primary care may be much higher in countries with inadequate healthcare infrastructure. Miss rate of diagnostic investigations in symptomatic pathway is 8% in a country that has well-organized pathways (2-week referral for patients suspected to have bowel cancer/rectal bleeding clinic/direct referral to endoscopy services by general practitioners). Barium enemas and incomplete flexible sigmoidoscopies have a high miss rate and complete colonoscopy or CTC may avoid delay in diagnosis.

The median age of patients seen in developing countries like India is younger and there is a lower prevalence of diverticular disease as compared to the west. However, a significant number of the patients with CRC have advanced disease at presentation. In such resource-constrained settings with a lack of well-structured screening as well as symptomatic pathway, miss rate of diagnostic investigations may be higher and needs to be investigated. Lack of organized primary healthcare and referral pathways may lead to inadequate investigations and significant delays in diagnosis.

This is also seen to some extent in developed countries where there is a variation in diagnostic modalities offered, with some underprivileged sections having less access to endoscopy

Summary Box

What is already known:

- The overall 5-year survival remains 50-60% in patients with advanced colorectal cancer (CRC) despite advances in surgery and adjuvant therapy
- Investigations used in diagnosis and screening patients for CRC do not have 100% sensitivity and specificity and can miss lesions

What the new findings are:

- In this retrospective review of 150 consecutive patients with CRC, less than 10% of our patients were detected by screening program
- False negative or miss rate of colonic investigations was 8% which has serious implications for symptomatic patients and may lead to diagnosis at an advanced stage and poorer outcomes
- Barium enema is associated with a high miss rate and should not be recommended for evaluating symptomatic patients

especially patients in low income groups [15]. Due to resource limitations, education regarding appropriate investigations for symptomatic pathway may be a better alternative to screening programs.

In conclusion, 17% of patients diagnosed with CRC in our series were investigated in the last 3 years. False negative or miss rate of colonic investigations was 8%. Higher miss rate of barium enema may mean that it should be no longer be used as a first line modality to investigate bowel cancer. Failure of symptoms to settle may justify a second complementary investigation (better imaging/colonoscopy). Auditing miss rate of diagnostic investigation is essential to improve services and patient care.

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