Colorectal cancer detection: time to abandon barium enema?

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Objectives To assess the sensitivity of double contrast barium enema (DCBE) for diagnosing colorectal cancer (CRC).
Design Retrospective evaluation of DCBE performed in the 2 years prior to diagnosis of CRC.
Setting Teaching hospital in Cambridge, UK.
Patients 1310 consecutive cases of CRC identified from cancer registry data.
Interventions DCBE and colonoscopy.
Main outcome measures Sensitivity of DCBE for diagnosing CRC.
Results 215 patients had undergone a DCBE within the 2 years prior to diagnosis with CRC. After excluding those reported as inadequate, 37 of these were reported as normal, giving a sensitivity of 83% (81–85%).
Conclusions The performance of DCBE is inadequate for the exclusion of CRC. Expansion of colonoscopy and CT colonography capacity is urgently required nationally so that DCBE can finally be abandoned as a firstline test in patients at risk of CRC.

Introduction

Over 35 000 cases of colorectal cancer (CRC) are diagnosed annually in the UK leading to over 15 000 deaths.[1] Most CRC is thought to develop from adenomas with the accumulation of mutations, as originally described by Fearon and Vogelstein.[2] If detected and removed at the adenoma stage, cancer can be prevented. Once cancer has developed, prognosis is intimately related to stage of diagnosis, with a 5 year survival of 93.2% for patients with early cancers, which falls to 6.6% for those with disseminated disease. Unfortunately, only 13% of symptomatic cases are diagnosed early in the UK at present.[3] As a result, a national bowel cancer screening programme was introduced in 2006 using biennial faecal occult blood testing followed by colonoscopy for those testing positive. This has been shown to reduce the risk of bowel cancer related mortality by 15%.[4]

There are a number of potential modalities for diagnosing CRC. Traditionally, double contrast barium enema (DCBE) has been widely used for this purpose, either alone or in combination with flexible sigmoidoscopy. In the current study, we have investigated all 1310 consecutive patients diagnosed with CRC in Cambridge, UK, over a 7 year interval from 2000 to 2006 and undertaken a detailed interrogation of clinical, radiological and endoscopic records for each patient to estimate the sensitivity of DCBE and colonoscopy for the detection of CRC. We have also attempted to quantify the current level of DCBE activity compared with colonoscopy activity for patients with symptoms in England and Wales.

Methods

Addenbrooke's Hospital serves a population of 450 000 around Cambridge, UK. The Eastern Cancer Registration and Information Centre (ECRIC) registers all malignant neoplasms and selected benign tumours at the time of diagnosis for our surrounding region—a total population of 5.5 million. All consecutive Addenbrooke's Hospital patients with a new diagnosis of CRC, as recorded on the Eastern Cancer Registry from January 2000 until December 2006, were included in the study.

A retrospective analysis of all cases was undertaken by using the hospital electronic patient databases which date back to 1996. Information pertaining to the patient demographics, mode of initial diagnosis, and site and stage of CRC was extracted by searching the above systems, including records of any DCBE or colonoscopy undertaken in the 3 years prior to diagnosis (stratified by whether this was the index diagnostic modality or was reported as normal). CRC with incomplete or missing information on the mode of diagnosis were excluded.

All CRC were confirmed histologically. Any investigation which first raised the suspicion of CRC, later confirmed on histology, was recorded as the initial mode of diagnosis. The site of CRC was defined as left-sided if the CRC was located distal to the splenic flexure and right-sided if located proximal to the splenic flexure. Cancers were defined as having been missed if a DCBE or colonoscopy had been performed within the 2 years prior to the date of diagnosis without identifying the lesion.[5] The DCBE was defined as inadequate if the report mentioned incomplete examination due to technical or patient reasons. Colonoscopy was defined as inadequate if the endoscopist failed to reach the site of CRC. No colonoscopy was defined as inadequate based on poor bowel preparation.

Where possible, barium radiographs of patients with missed cancers were retrieved and independently reviewed by two experienced gastrointestinal radiologists, each of whom was aware that all investigations had failed to detect a cancer. For each patient, the segment with a possible abnormality was noted or the examination was called normal.

To establish the relative activity for DCBE and colonoscopy in England and Wales, provider based diagnostic returns were interrogated on the Department of Health website (http://www.performance.doh.gov.uk/diagnostics/200809provider.html). The total number of DCBE and colonoscopies, excluding planned (surveillance) cases, between January and March 2009 were calculated. Results were presented as total number of DCBE as a percentage of total number of 'colonic investigations' (DCBE combined with colonoscopies).

Statistics

Statistical analysis was performed using SPSS V.9.0. Data were compared using the independent samples t test, the Mann–Whitney U test or the Pearson χ^2 test. Two tailed significance was set at the 5% level.

Ethics

As a service evaluation, ethics approval was not required for this study under the National Health Service Research Governance Framework (confirmed by Cambridge Local Research Ethics Committee).

Results

A total of 1310 cases of CRC were recorded during the time period. The locations of these tumours can be seen in table 1. The commonest methods of diagnosis were colonoscopy (291, 22%), rigid sigmoidoscopy (290, 22%), CT (286, 22%), barium enema (165, 13%) and flexible sigmoidoscopy (106, 8%). The remaining 156 (12%) CRC were diagnosed by a variety of other methods. Twelve cases were excluded due to incomplete information, 696 (54%) cases were male, mean age was 72 years and 439 (34%) CRC were right-sided. A total of 215 (17%) cases had undergone DCBE within 2 years prior to diagnosis and 304 (23%) had undergone colonoscopy.

Missed by DCBE

Fifty of 215 (23%) patients with CRC had undergone a DCBE reported as normal in the 2 years prior to diagnosis of CRC. After excluding those examinations reported as inadequate, this was reduced to 37 of 215 (17%), giving an overall sensitivity of 83% (95% CI 81% to 85%) for the detection of CRC. The most common sites for missed cancers were ascending colon/caecum (44%) and sigmoid colon (32%).

The mean delay from time of initial false negative DCBE to diagnosis of CRC in those cases missed on index study was 8.2 (SD 6.9) months. There was no statistically significant difference in terms of age, sex,

Table 1 Site of colorectal cancer in overall study population and in those missed by double contrast barium enema and colonoscopy

Site	Study population (n=1298) (n (%))	Missed by DCBE (n=37) (n (%))	Missed by colonoscopy (n=13) (n (%))
Caecum	196 (15)	11 (30)	4 (31)
Ascending colon	133 (10)	5 (14)	0
Hepatic flexure	22 (2)	2 (5)	2 (15)
Transverse colon	88 (7)	1 (3)	1 (8)
Splenic flexure	21 (2)	0	0
Descending colon	51 (4)	0	0
Sigmoid colon	311 (24)	11 (30)	2 (15)
Rectum	463 (35)	6 (16)	3 (23)
Unspecified	13 (1)	1 (3)	1 (8)

DCBE, double contrast barium enema.

Table 2 Comparison between characteristics of colorectal cancer diagnosed or missed on double contrast barium enema

	Diagnosed on DCBE (n=165)	Missed on DCBE (n=37)
Age (years) (mean (SD))	69.2 (9.5)	70.4 (10.6)
Male (n (%))	88 (53)	18 (49)
Female (n (%))	77 (47)	19 (51)
Right-sided CRC (n (%))	67 (41)	19 (51)
Left-sided CRC (n (%))	98 (59)	17 (46)
Stage 1 (n (%))	25 (15)	9 (24)
Stage 2 (n (%))	60 (36)	14 (38)
Stage 3 (n (%))	59 (36)	5 (14)
Stage 4 (n (%))	21 (13)	9 (24)

All differences between groups p>0.05.
CRC, colorectal cancer; DCBE, double contrast barium enema.

location or stage between patients diagnosed or missed on DCBE (table 2).

If the definition of missed CRC was varied to 1 or 3 years, the number of missed cancers was 26 and 45, respectively, after excluding inadequate examinations. Thus 58% of the missed cancers were diagnosed in the first year and 82% in the first two.

Missed by colonoscopy

Twenty-four of 304 (8%) patients with CRC had undergone a colonoscopy reported as normal in the 2 years prior to diagnosis of CRC. After excluding inadequate examinations, 13 of 304 (4%) remained, giving an overall sensitivity of 96% (95–97%) for the diagnosis of CRC. The mean delay to diagnosis from time of initial false negative colonoscopy was 10.4 (SD 6.4) months. The numbers of cases missed was too small to provide any meaningful comparison between the characteristics of CRC diagnosed and missed by colonoscopy.

Comparison between DCBE and colonoscopy

DCBE was significantly more likely to miss cases of CRC than colonoscopy ($p<0.001$). There were no statistically significant differences between the cases missed by DCBE and colonoscopy in terms of age, sex, location or stage, although the numbers of cases missed by colonoscopy was again too small for meaningful comparison (table 3).

Barium enema review

It was possible to obtain 26 sets of barium films for patients with missed cancers. Both radiologists identified a possible abnormality in the correct segment of colon in only seven (26.9%) cases (of which six were in the sigmoid colon) despite knowing that a cancer had been missed in each examination.

Table 3 Comparison between characteristics of colorectal cancer missed by double contrast barium enema and colonoscopy

	Missed on DCBE (n=37)	Missed on colonoscopy (n=13)
Age (years) (mean (SD))	70.3 (10.6)	72.7 (7.3)
Male (n (%))	18 (49)	5 (36)
Females (n (%))	19 (51)	9 (64)
Right-sided (n (%))	19 (53)	8 (62)
Left-sided (n (%))	17 (47)	5 (38)
Stage 1 (n (%))	9 (24)	5 (38)
Stage 2 (n (%))	14 (38)	2 (15)
Stage 3 (n (%))	5 (14)	2 (15)
Stage 4 (n (%))	9 (24)	4 (31)
Delay in diagnosis (months) (mean (SD))	8.2 (6.9)	10.2 (6.4)

All differences between groups p>0.05.
DCBE, double contrast barium enema.

Barium enema activity in England

Between January and March 2009, a total of 28 023 barium enemas and 60 813 colonoscopies were performed in England. Out of the total of 88 836 procedures, 31.5% were barium enemas.

Discussion

We have evaluated the performance of DCBE for detecting CRC in a large cohort of 1310 patients over a 7 year period and identified a sensitivity of 83% in this population. The poor sensitivity of DCBE (63–90%) has been recognised for some time.[5–11] Increasingly, DCBE is being superseded by colonoscopy which has a higher sensitivity (97%)[5] and allows tissue sampling and polypectomy to be performed. CT colonography also appears to outperform DCBE[12] and is becoming more widely used. There has been a steady increase in the number of lower gastrointestinal endoscopies performed in England and Wales in the past decade but potential demand still exceeds supply. Given the lack of lower gastrointestinal endoscopy capacity and strict waiting time targets, many hospitals use DCBE as a demand management technique—a situation that risks being exacerbated by screening activities in the absence of significant expansion in endoscopy capacity.

This study has a number of strengths and weaknesses. The fact that the sensitivity is within the range of previous reports from hospital settings which have used different methods to evaluate DCBE supports the validity of our study, its findings and the fact that it does not merely reflect poor quality barium enema at our institution. The use of population based cancer registry data to identify cases has ensured a comprehensive, large, consecutive sample of patients with CRC, reflecting real world practice rather than clinical trial conditions, allowing greater generalisability for National Health Service clinicians. While this strategy has been used previously,[6] we have been able to review case notes of all patients. The previous informatics based study assumed that a diagnosis of CRC within 6 months of DCBE reflected correct diagnosis with the index DCBE. In our study, significant numbers of missed cancers were picked up by a second diagnostic test within that 6 month interval. By changing the cut-off from 6 to 3 months, sensitivity fell to 69.1% in the study of Toma *et al* although admittedly with a longer 3 year definition of missed CRC.

One potential criticism of our study and a number of previous studies is the assumption that those cases diagnosed within 2 years of a normal DCBE or colonoscopy represent a missed cancer rather than the development of an interval CRC. The finding of only eight additional cases with an increase in definition from 2 to 3 years suggests that the majority of these are indeed missed cases. If not, one would expect a constant number of new cases in each of the 3 years.

Another criticism is that we have only identified DCBE performed at our institution. It is possible that patients may have undergone DCBE at another hospital in the 2 years prior to diagnosis. Patients may also have migrated from our region prior to CRC diagnosis and would, therefore, not be identified by ECRIC. Neither of these potential weaknesses would have increased the sensitivity of DCBE.

While it had previously been noted that older age and female sex were independent risk factors for missed CRC,[6] this was not the case in our study. We did confirm, however, that as many right-sided cancers were missed as left-sided. This debunks the myth that the combination of DCBE with flexible sigmoidoscopy is a valid strategy.

There is good evidence that experts perform better with DCBE than non-experts,[13] and one could argue that DCBE would perform better if concentrated in the hands of experts. However, the segment in which CRC had been missed could only be reliably identified by expert gastrointestinal radiologists in the minority of cases on review in this study despite knowing that a diagnosis of CRC had been made soon afterwards in each case. Our study thus convincingly indicates that most of the limitations of DCBE relate to technical aspects rather than problems of interpretation.

Given that it has been recognised for many years that DCBE performs poorly as a test for the identification or exclusion of CRC, it is surprising that so many are carried out. Extrapolating the January to March 2009 data to a whole year, it is reasonable to assume that more than 100 000 DCBEs are still performed each year in England. Over the study period, 8603 DCBE were carried out in our institution. Assuming an equivalent miss rate for CRC across England to that observed in our study, this would translate into between 245 and 477 missed cancers each year depending on whether or not DCBE was combined with flexible sigmoidoscopy. The numbers of DCBE are falling steadily (15 376 in January 2007, 13 322 in January 2008 and 10 165 in January 2009) but more needs to be done to expedite this process.

Bowel cancer screening in the UK currently relies on faecal occult blood testing, with colonoscopy reserved for those testing positive. In the future, even more endoscopy intensive modalities will be utilised with the recent announcement of one-off flexible sigmoidoscopy screening. This has been demonstrated to produce a reduction in mortality from CRC of 43% but required 489 screening procedures to prevent one CRC related death.[14] Given the expected higher diagnostic yield in symptomatic individuals, it is clear that optimal diagnostic tests should be used here given that the prior probability of CRC is much higher than in the general population.

This study provides further robust evidence that the performance of DCBE in the real life situation of UK medical practice is inadequate for the exclusion of CRC. Particularly in the current era of bowel cancer screening, gastroenterology and colorectal services should not be so heavily dependent on this test to manage their workloads. In Cambridge, DCBE has now been entirely replaced by colonoscopy for the investigation of lower gastrointestinal symptoms. Further expansion of colonoscopy and CT colonography capacity is urgently required nationally so that DCBE can finally be abandoned as a firstline colonic test in patients at risk of CRC.

Competing interests None.

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