

Predicting colorectal cancer risk in patients with rectal bleeding

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ABSTRACT

Background

Rectal bleeding is an important symptom of colorectal cancer but has low predictive value in primary care.

Aim

To determine which characteristics of rectal bleeding, along with other factors, are predictive of colorectal cancer.

Design of study

Observation study of patients with rectal bleeding referred to an open-access diagnostic clinic.

Setting

Primary care, southern England.

Method

Symptom data were collected, using a self-completed questionnaire. Logistic regression techniques were used to determine predictors of colorectal cancer.

Results

There were 604 patients in the study and 22 (3.6%, 95% confidence interval [CI] = 2.0% to 5.2%) were diagnosed with colorectal cancer. Significant predictors of colorectal cancer were found to be age (<50 years: odds ratio [OR] = 1; 50–69 years: OR = 5.1, 95% CI = 1.4 to 18.6; ≥70 years: OR = 8.2, 95% CI = 2.1 to 31.8) and blood mixed with the stool (Likelihood ratio [LR] 1.5; adjusted OR = 3.8; 95% CI = 1.4 to 10.5).

Presence of haemorrhoids associated with bright red bleeding not mixed with stool reduced the likelihood of cancer (OR = 0.4, 95% CI = 0.1 to 1.2) but did not eliminate it — a cancer was present in 2% of patients with these symptoms.

Conclusion

Patient-reported type of rectal bleeding as an isolated symptom has insufficient diagnostic value to be useful in general practice. By studying referred patients, we may even have overestimated its value. At best, it could be useful as a component of a composite symptom score to guide referral decisions.

Keywords

colorectal neoplasms; early diagnosis; general practice; sigmoidoscopy; signs; symptoms.

INTRODUCTION

Colorectal cancer is a major public health problem, particularly in western countries, with over 30 000 new cases diagnosed each year in the UK and an average 5-year survival of 40%.^{1,2} Mortality is highest in those diagnosed with later stage disease.³ Most cases present with symptoms that prompt patients to consult their GPs. In order to improve survival through earlier diagnosis, symptoms indicative of a high risk of cancer must be better understood and recognised by both patients and GPs.

GPs face significant challenges in discriminating between symptoms that may indicate colorectal cancer or other conditions, which also require urgent specialist investigation, and those that do not. Lower gastrointestinal symptoms are common in the general population and in general practice,^{4–9} but are mainly non-specific: for example, although 19% of patients of general practice will report rectal bleeding in the previous year,⁹ it is estimated that 97% of patients consulting with this symptom will not have cancer.¹⁰

In order to support the decision-making process in primary care, referral guidelines for colorectal cancer based on the best current evidence have been published,^{11–14} and critiqued:^{15–17} these identify rectal

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Submitted: 1 September 2005; Editor's response: 12 December 2005; final acceptance: 12 April 2006.

©British Journal of General Practice 2006; 56: 763–767.

How this fits in

Rectal bleeding is a common symptom of colorectal cancer, but it has a low positive predictive value in primary care populations. Previous statistical modelling has shown that along with increasing age and a change in bowel habit, 'blood mixed with stool' is a significant predictor of malignant colorectal disease. This study supports the evidence that age and 'blood mixed with stool' are significant predictors of colorectal cancer, although the latter would only be of diagnostic value in a consultation if included in an overall risk assessment score. Nevertheless, our study has reinforced an important clinical message; the presence of haemorrhoids with bright red bleeding does not reduce the risk of colorectal cancer significantly, and GPs should be guided by other features of the clinical presentation in assessing risk for this disease.

bleeding and a change in bowel habit as the most important symptoms, but the characteristics of the rectal bleeding are not included in any of these guidelines. Some studies in primary care have suggested that blood mixed with stool has a strong association with a diagnosis of colorectal cancer,^{18,19} although this was not demonstrated in a more recent study.²⁰ Consideration of the type of rectal bleeding may have the potential to improve referral sensitivity and specificity.

An open-access haematuria clinic has previously been used as a proxy for patients attending their GP to determine factors predictive of malignancy.²¹ This current study used a similar approach with the aim of determining which characteristics of rectal bleeding, along with other factors, were related to a diagnosis of colorectal cancer in primary care patients with self-reported rectal bleeding who had been referred by their GP to a rapid-access, community-based flexible sigmoidoscopy service for patients with rectal bleeding.

METHOD

Patients in the intervention arm of the Southampton Community Sigmoidoscopy Study were included in this study.

The Southampton Community Sigmoidoscopy Study was a trial of a community-based, rapid access, flexible sigmoidoscopy service organised by nurse endoscopists. The service was available from September 1996 until June 1999 and provided rapid access (within 2 weeks of referral) to a flexible sigmoidoscopy investigation, at a time before the introduction of the '2-week standard' in 2000.²² GPs in the intervention arm of the trial were invited to refer all patients with rectal bleeding.

At the flexible sigmoidoscopy clinic patients completed a two-page questionnaire which included questions on recent bowel symptoms: increase in frequency of bowel motions or loose motions, bleeding from the back passage (bright red blood, dark blood, separate from the motions, mixed with the motions), abdominal pain and weight loss; family

history of bowel cancer; history of haemorrhoids, irritable bowel syndrome, ulcerative colitis, diverticular disease, and bowel cancer; and current aspirin or warfarin therapy. For analysis, answers to some questions were combined to make one variable: 'more frequent bowel motions' and 'loose motions' were combined to make 'increased/looser motions'; 'dark blood' was combined with not having 'bright blood'; and 'blood mixed with stool' was combined with bleeding not being 'separate from stool'.

Deprivation categories were allocated to participants by mapping their postcodes with national deprivation categories (septiles) derived from the Carstairs scores generated by MIMAS at Manchester University using 1991 census data.²³

Final diagnosis of colorectal cancer, our main outcome, was obtained from hospital records for patients referred to secondary care and from the South and West Cancer Intelligence Unit for all patients. The minimum time from flexible sigmoidoscopy to examination of cancer registry records was 4 years.

Patients who stated on the questionnaire that they did not have rectal bleeding were excluded. Cases with either self- or GP-reported ulcerative colitis or current warfarin treatment were also excluded from the analysis because of the likely association of rectal bleeding with anticoagulants and ulcerative colitis, as were cases with missing data for the kind of bleeding, because these variables were key items of interest in the analysis.

Symptom data and other patient data were analysed univariately to find associations with a diagnosis of colorectal cancer using the χ^2 test. If the probability of there being no association was <0.1 the variable was included in a binary logistic regression model along with any variables previously associated with colorectal cancer.

Data were managed and analysed using SPSS releases 10 and 11.0.0. Ninety-five per cent confidence intervals (CIs) were calculated for odds ratios (ORs) for variables with zero odds using Epi-Info. Statistical significance was defined as P -values <0.05 .

RESULTS

Six hundred and four patients referred by GPs to the open-access flexible sigmoidoscopy service were included in the study. Two hundred and seventy-three (45%) cases were male and the median age was 52 years (range = 18–97 years). The proportion of patients in deprivation categories 1 (least deprived) to 7 (most deprived) were 12.7, 20.4, 26.6, 23.5, 9.1, 4.3 and 3.3% respectively (Table 1).

A further 197 cases were excluded either because they were considered ineligible on account of coexisting pathology ($n = 36$; ulcerative colitis = 15, warfarin therapy = 21), or inappropriate referral — they

did not have rectal bleeding ($n = 99$), or because they had incomplete data ($n = 62$).

Univariate analysis

Twenty-two (3.6%, 95% CI = 2.0% to 5.2%) cases were diagnosed with cancer. Older age groups were more likely to be diagnosed with colorectal cancer (Table 1). Thirteen (4.8%) men and nine (2.7%) women were diagnosed with cancer but this difference was not statistically significant (age adjusted OR = 2.3, 95% CI = 0.94 to 5.63).

The prevalence, the likelihood ratio (LR) of being diagnosed with colorectal cancer, and the age adjusted OR of being diagnosed with cancer for various symptoms and conditions can be seen in Table 2. The presence of dark blood, blood mixed with stool or both of these were the only symptoms associated with a greater likelihood of colorectal cancer. Irritable bowel syndrome was associated with a lower risk of colorectal cancer. The presence of haemorrhoids with bright red bleeding not mixed with stool reduced the likelihood of cancer (LR = 0.5); nevertheless colorectal cancer was present in three (2%) of the 159 patients with these symptoms. There was no relationship between a diagnosis of cancer and deprivation category, having a family or personal history of colorectal cancer, or aspirin therapy.

Table 1. Number of cancers by age and sex.

	Total <i>n</i> (%)	Cancers <i>n</i> (%)
Total	604 (100)	22 (3.6)
Age in years		
<50	270 (44.7)	3 (1.1)
50–69	227 (37.6)	11 (4.8)
≥70	107 (17.7)	8 (7.5)
Linear trend		$P = 0.003$
Sex		
Male	273 (45.2)	13 (4.8)
Female	331 (54.8)	9 (2.7)
Probability ^a		$P = 0.27$
Deprivation category ^b		
1 (least deprived)	74 (12.7)	3 (4.1)
2	119 (20.4)	4 (3.4)
3	155 (26.6)	4 (2.6)
4	137 (23.5)	8 (5.8)
5	53 (9.1)	0 (0.0)
6	25 (4.3)	0 (0.0)
7 (most deprived)	19 (3.3)	1 (5.3)
Linear trend		$P = 0.72$

^a χ^2 , 1 degree of freedom. ^bNumbers do not add up to total because of missing data

Multivariate analysis

Age group, sex, the presence of dark blood, the

Table 2. Diagnostic value of bleeding characteristics and other factors in patients investigated for rectal bleeding in a general practice open-access sigmoidoscopy clinic.

Factors	Patients with factor			Patients without factor			LR ^a	Age-adjusted OR ^b (95% CI)
	Total (<i>n</i>)	Cancer (<i>n</i>)	%	Total (<i>n</i>)	Cancer (<i>n</i>)	%		
Type of blood								
Dark	121	9	7.4	483	13	2.7	2.1	3.2 (1.3 to 7.8)
Mixed with stool	314	17	5.4	290	5	1.7	1.5	3.8 (1.4 to 10.6)
Both dark and mixed with stool	88	9	10.2	516	13	2.5	3.0	4.9 (2.0 to 12.2)
Neither dark nor mixed with stool	257	5	1.9	347	17	4.9	0.5	0.3 (0.1 to 0.9)
Haemorrhoids								
Haemorrhoids	320	10	3.1	239	11	4.6	0.8	0.6 (0.3 to 1.5)
Haemorrhoids and bright red blood not mixed with stool	159	3	1.9	400	18	4.5	0.5	0.4 (0.1 to 1.2)
Haemorrhoids and no other symptoms except bright non-mixed bleeding	90	3	3.3	469	18	3.8	0.9	0.8 (0.2 to 2.9)
Other factors								
Increased frequency/loose motions	269	13	4.8	319	9	2.8	1.3	1.0 (0.7 to 1.4)
Abdominal pain	232	4	1.7	358	16	4.5	0.5	0.4 (0.1 to 1.4)
Weight loss	62	3	4.8	531	19	3.6	1.3	1.3 (0.4 to 4.7)
History of irritable bowel syndrome	96	0	0	481	21	4.4		0.0 (0.0 to 0.95) ^c
History of diverticular disease	34	0	0	536	21	3.9		0.0 (0.0 to 3.07) ^c

^aLR: the probability having the factor in people with colorectal cancer/the probability of having the factor in people without colorectal cancer. ^bOR for presence of factor versus absence of factor adjusted for age. ^cNon adjusted OR using Epi-Info. LR = likelihood ratio. OR = odds ratio.

presence of blood mixed in stool, having increased or looser stools and patient reported irritable bowel syndrome were entered into a forward (LR) stepwise binary logistic regression model. The factors that remained significant predictors were age group (<50 years: OR = 1; 50–69 years: OR = 5.09, 95% CI = 1.39 to 18.6; ≥70 years: OR = 8.19, 95% CI = 2.11 to 31.82), and the presence of blood mixed in the stool (OR = 3.78; 95% CI = 1.36 to 10.47). The OR for someone with a recent alteration in bowel habit to more frequent or looser stools was 1.9 (95% CI = 0.8 to 4.7). The regression model fitted the data well in the younger age groups (<59 and 50–69 years) although fit was slightly less good for age ≥70 years where the lack of linearity could not be mirrored in a linear model.

DISCUSSION

Summary of main findings

In a population with rectal bleeding, referred from general practice to an open-access flexible sigmoidoscopy clinic, the most significant predictor of a diagnosis of cancer was age group. The only other significant predictor was patient-reported rectal bleeding mixed with stool. Although univariate analysis indicated dark blood per rectum and a combination of dark and mixed blood had higher positive predictive values for a diagnosis of colorectal cancer (7.4% and 10.2% respectively) than blood mixed with stool (5.4%), when adjusted for other factors, inclusion of dark blood did not add significantly to the model. Overall the LRs associated with individual symptoms (range = 0.5–3.0) were too small to be of individual diagnostic value, particularly given the low prior probability of cancer in primary care.

In this study, haemorrhoids, even in the presence of bright red bleeding as an isolated symptom, did not significantly reduce the risk of colorectal cancer. Although this contradicts findings in one recent study,²⁰ Smith *et al* report a high proportion of patients diagnosed with colorectal cancer having peri-anal symptoms.²⁴ Our results emphasise that both patients and GPs should be cautious of ruling out the possibility of colorectal cancer without further investigation when haemorrhoids are present. So perhaps the most important immediate clinical message to emerge from our data is that patients presenting with bright red bleeding and haemorrhoids may still have cancer.

Strengths and limitations of the study

The existence of an open-access service provided a unique opportunity to examine the predictivity of rectal bleeding characteristics, in combination with other symptoms and patient demographics for colorectal cancer in a primary care population. GPs are selective in the patients with blood loss per rectum who they

refer to specialist services,^{25,26} and although GPs were encouraged to refer all patients presenting with rectal bleeding some degree of GP or patient selection bias is still likely to have occurred, probably causing an over-estimate of the predictive values in this study. The need to exclude 9% of eligible cases from the analysis because of lack of data could also bias our results. However, our study population has a similar distribution of age and sex to other primary care-based studies of rectal bleeding.^{18,19} There were fewer very affluent and very deprived people than would be expected in a random population sample.

A diagnosis of colorectal cancer has been used as the final outcome. In a larger study, analysis by cancer site and stage at diagnosis would give more refined information. It would be useful to know if the type of bleeding could help distinguish between cancers in different sites (that is: rectum, proximal or distal colon). It is also important to identify the risk factors that identify early stage cancers. It is possible that bleeding is predominantly a symptom of late stage cancer, although the work by Smith *et al* does not support this.²⁴

Our study relied upon a self-completion questionnaire and the participants' capacity to distinguish between various kinds of rectal bleeding. Little is known about the extent to which people can accurately report this, but Summerton's work is reassuring — there was moderate to substantial agreement over time between two questionnaire surveys of gastrointestinal symptoms, and the question on blood in the motions/toilet pan or on the toilet paper demonstrated almost perfect agreement.²⁷ The closeness of correspondence between responses to questionnaires and verbal reports to clinicians is also uncertain, however we know that reported symptoms tend to have better predicted value than those elicited by GPs.²⁸

Finally, the study depended upon the accuracy and timeliness of the records at the South and West Cancer Intelligence Unit. We are as confident as possible that all cancers present at the time of the flexible sigmoidoscopy have been detected as records were checked within a reasonable time frame.

Comparison with existing literature

The significance of the type of rectal bleeding as a predictor of colorectal cancer has been described in other primary care-based work,^{18,19} and in a study based in secondary care.^{24,29} Our work concurs with the study by Fijten *et al*¹⁸ where blood mixed with or on stool was the only type of rectal blood loss to have a statistically significant independent value when discriminating for colorectal cancer. There may be benefit in considering more refined definitions of rectal bleeding in referral guidelines based on overall

assessment of risk and evaluating the impact of this in reducing delay in cancer diagnosis.³⁰

A change in bowel habit is a common symptom of colorectal cancer,³¹ but sensitivity and specificity are low.^{19,32} Several studies in patients presenting to their GP with rectal bleeding have shown a change in bowel habit to be significantly associated with a diagnosis of colorectal cancer.^{19,20,32,33} The lack of significance in our study could reflect lack of statistical power or be a consequence of the specific study design. In particular, the definition of a change in bowel habit is likely to be different in the context of a GP reporting a clinical history and a patient-completed questionnaire.

Implications for future research and clinical practice

The nature of rectal bleeding has limited diagnostic value as an individual symptom in predicting the presence or absence of cancer. Although cancer was six times more likely in individuals with dark red bleeding mixed with the stool than with bright red bleeding, the maximum LR of 3 is unhelpful in a primary care context when the prior probability of cancer is low. Moreover, even the presence of bright red bleeding and haemorrhoids did not rule out cancer. However the type of bleeding could be important in refining future cancer referral guidance, particularly if this can be based on actual colorectal cancer risk assessment scores derived from primary care populations.

Funding body

This work was commissioned by the Policy Research Programme of the Department of Health (reference 1217521). The views expressed in the publication are those of the authors and not necessarily those of the Department of Health

Ethics committee

Ethical approval was obtained from the South and West Hampshire Clinical Research (Ethics) Committee (reference 153/95) and Basingstoke Ethics Committee (protocol 350)

Competing interests

The authors have stated that there are none

Acknowledgements

The authors would like to acknowledge Mrs Phyllis Daniels at Southampton University for the original data entry and liaison with the research staff, and thank all the patients and GPs who participated in the original research.

REFERENCES

- National Statistics. Cancer registration statistics, England 2002 — first release. <http://www.statistics.gov.uk/cci/nugget.asp?id=915> (accessed 15 Aug 2006).
- Scottish Health Statistics. Scottish cancer registry data. http://www.isd.scotland.org/isd/files/cancer_colorectal_inc_m.xls (accessed 15 Aug 2006).
- Mulcahy HE, O'Donoghue DP. Duration of colorectal cancer symptoms and survival: the effect of confounding clinical and pathological variables. *Eur J Cancer* 1997; **33**(9): 1461–1467.
- Chaplin A, Curlless R, Thomson R, Barton R. Prevalence of lower gastrointestinal symptoms and associated consultation behaviour in a British elderly population determined by face-to-face interview. *Br J Gen Pract* 2000; **50**: 798–802.
- Fijten GH, Muris JW, Starmans R, *et al*. The incidence and outcome of rectal bleeding in general practice. *Fam Pract* 1993; **10**(3): 283–287.
- Wauters H, Van Casteren V, Buntinx F. Rectal bleeding and colorectal cancer in general practice: diagnostic study. *BMJ* 2000; **321**(7267): 998–999.
- Thompson WG, Heaton KW, Smyth GT, Smyth C. Irritable bowel syndrome in general practice: prevalence, characteristics, and referral. *Gut* 2000; **46**(1): 78–82.
- Dent OF, Goulston KJ, Zubrzycki J, Chapuis PH. Bowel symptoms in an apparently well population. *Dis Colon Rectum* 1986; **29**: 243–247.
- Crosland A, Jones R. Rectal bleeding: prevalence and consultation behaviour. *BMJ* 1995; **311**: 486–488.
- Thompson MR, Heath I, Ellis BG, *et al*. Identifying and managing patients at low risk of bowel cancer in general practice. *BMJ* 2003; **327**: 263–265.
- Department of Health. *Referral guidelines for suspected cancer*. London: Department of Health, 2000.
- Scottish Executive. *Scottish referral guidelines for suspected cancer*. Edinburgh: Scottish Executive, 2002.
- Scottish Intercollegiate Guidelines Network. Management of Colorectal Cancer. <http://www.sign.ac.uk/guidelines/fulltext/67/index.html> (accessed 15 Aug 2006).
- National Institute for Health and Clinical Excellence. *Referral guidelines for suspected cancer*. London: National Institute for Health and Clinical Excellence, 2005.
- Hamilton W, Sharp D. Diagnosis of colorectal cancer in primary care: the evidence base for guidelines. *Fam Pract* 2004; **21**: 99–106.
- Jiwa M, Hamilton W. Referral of suspected colorectal cancer: have guidelines made a difference? *Br J Gen Pract* 2004; **54**: 608–610.
- Flashman K, O'Leary DP, Senapati A, Thompson MR. The Department of Health's 'two week standard' for bowel cancer: is it working? *Gut* 2004; **53**(3): 387–391.
- Fijten GH, Starmans R, Muris JWM, *et al*. Predictive value of signs and symptoms for colorectal cancer in patients with rectal bleeding in general practice. *Fam Pract* 1995; **12**(3): 279–286.
- Metcalf JV, Smith J, Jones R, Record C. Incidence and causes of rectal bleeding in general practice as detected by colonoscopy. *Br J Gen Pract* 1996; **46**: 161–164.
- Ellis BG, Thompson MR. Factors identifying higher risk rectal bleeding in general practice. *Br J Gen Pract* 2005; **55**(521): 949–955.
- Summerton N, Mann S, Rigby AS, *et al*. Patients with new onset haematuria: assessing the discriminant value of clinical information in relation to urological malignancies. *Br J Gen Pract* 2002; **52**(477): 284–289.
- NHS Executive. *The new NHS — modern, dependable*. (CM3807). London: Department of Health, 1997.
- Carstairs V, Morris R. *Deprivation and health in Scotland*. Aberdeen: Aberdeen University Press, 1991.
- Smith D, Ballal M, Hodder R, *et al*. Symptomatic presentation of early colorectal cancer. *Ann R Coll Surg Engl* 2006; **88**(2): 185–190.
- Fijten GH, Blijham GH, Knottnerus JA. Occurrence and clinical significance of overt blood loss per rectum in the general population and in medical practice. *Br J Gen Pract* 1994; **44**(384): 320–325.
- Heintze C, Matysiak-Klose D, Krohn T, *et al*. Diagnostic work-up of rectal bleeding in general practice. *Br J Gen Pract* 2005; **55**(510): 14–19.
- Summerton N, Mann S, Sutton J, *et al*. Developing clinically relevant and reproducible symptom-defined populations for cancer diagnostic research in general practice using a community survey. *Fam Pract* 2003; **20**(3): 340–346.
- Dobbs FF, Fleming DM. A simple scoring system for evaluating symptoms, history and urine dipstick testing in the diagnosis of urinary tract infection. *J R Coll Gen Pract* 1987; **37**(296): 100–104.
- Selvachandran SN, Hodder RJ, Ballal MS, Cade D. Prediction of colorectal cancer by a patient consultation questionnaire and scoring system: a prospective study. *Lancet* 2002; **360**: 278–283.
- Macdonald S, Macleod U, Mitchell E, *et al*. *Factors influencing patient and primary care delay in the diagnosis of cancer: a database of existing research and its implications for future practice*. Final report to Department of Health. Glasgow: University of Glasgow, 2004
- Kyle SM, Isbister WH, Yeong ML. Presentation, duration of symptoms and staging of colorectal carcinoma. *Aust N Z J Surg* 1991; **61**: 137–140.
- Muris JW, Starmans R, Fijten GH, *et al*. Non-acute abdominal complaints in general practice: diagnostic value of signs and symptoms. *Br J Gen Pract* 1995; **45**: 313–316.
- Norrelund N, Norrelund H. Colorectal cancer and polyps in patients aged 40 years and over who consult a GP with rectal bleeding. *Fam Pract* 1996; **13**: 160–165.