Primary-to-secondary care referral experience of suspected colorectal malignancy in young adults

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ABSTRACT

INTRODUCTION Colorectal cancer in patients younger than 50 years of age is increasing steadily in the UK with limited guidelines available indicating need for secondary care referral. The aims of this study were to report the cancer incidence in those aged under 50 years referred to secondary care with suspected colorectal malignancy and also to analyse the quality of those referrals.

METHODS A total of 197 primary care referrals made between 2008 and 2014 to a UK district general hospital for suspected colorectal malignancy were analysed. All confirmed cancers were further evaluated regarding presenting symptoms, tumour characteristics and clinical outcomes. Each referral was given a referral performance score (out of 9) dependant on relevant information documented.

RESULTS The overall malignancy rate was 9.1% (11 male and 7 female patients). The median age in this cohort was 41.5 years (interquartile range [IQR]: 37–49 years). Abdominal pain was the only presenting symptom to differ significantly when comparing malignant with non-malignant patients (44.4% vs 21.8% respectively, $p=0.042$). The median time period between referral date and colorectal specialist consultation was 11 days (IQR: 7–13 days) and the median referral performance score was 5 (range: 3–9).

CONCLUSIONS Malignancy is prevalent in patients under 50 years of age who are referred to secondary care for suspected colorectal cancer. Those referred with abdominal pain in the presence of other high risk lower gastrointestinal symptoms are at significant risk of having a malignancy. Major deficiencies are apparent in urgent primary care referrals, highlighting the need for further national guidance to aid early diagnosis of colorectal cancer in the young.

KEYWORDS

Colorectal neoplasm – Early onset – Referral

Accepted 28 June 2015

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Colorectal cancer in those under the age of 50 years is steadily on the increase, accounting for approximately 4–11% of all cases.^{1–3} The incidence of such malignancies in the UK has risen to more 73.7 per 100,000 population in 2012 compared with 69.4 per 100,000 in 2002.⁴ The primary diagnosis is frequently of later stage disease with previous studies postulating that this is due to aggressive tumour characteristics and diagnostic delay from late referrals to secondary care along with initial patient reluctance to seek medical attention.^{5,6}

In England, all suspected colorectal malignancies require urgent referral under the ‘two-week rule’ where all primary care patients referred by general practitioners (GPs) are seen by hospital specialists within 14 days to ensure early investigation and diagnosis.⁷ National guidelines for diagnosis of colorectal cancer were developed originally in 2005 to aid GPs in appropriately referring patients to surgical outpatient clinics for further investigation and were revised

subsequently in 2015.^{8,9} These were However, these guidelines only provide vague and limited guidance to diagnosing colorectal malignancy in patients under 50 years of age.

Thorough systematic risk assessment for malignancy with a full examination is essential in young patients presenting with suspicious lower gastrointestinal symptoms or strong risk factors. Deficiencies in GP consultations including failure of ‘high risk’ symptom recognition and neglected examination can lead to delays in diagnosis with subsequent disease presentation proving to be inoperable. Referral letters form the pathway of communication between GPs and colorectal surgeons, and must indicate clearly the rationale for malignancy suspicion with all relevant information included. Inadequacies in such referrals have the potential to influence further management by hospital specialists, in particular investigations requested,¹⁰ or they may even result in delay of appropriate investigation and treatment.

Previous studies have reported dissatisfaction by consultants in the quality of referral letters from GPs with lack of relevant information cited as the main reason.^{11–13} Implementation of standardised proforma templates has enabled referring clinicians to clearly indicate the reason for suspected cancer referrals by ticking boxes adjacent to guideline defined high risk symptoms while also allowing for free text to include additional relevant information. This has shown to improve the quality of the referral but it must be completed properly and include all relevant clinical information.¹⁴

The primary aim of our study was to report the incidence of colorectal cancer in patients younger than 50 years of age referred for suspected malignancy by GPs, with further analysis of tumour characteristics, operative details and postoperative clinical outcomes. Secondary aims were to analyse the quality of GP primary care referral proformas, especially in relation to relevant information included.

Methods

Retrospective data analysis was performed on all patients aged under 50 years referred by GPs for suspected colorectal malignancy between December 2008 and May 2014 at West Suffolk Hospital. A list of all patients seen in colorectal or rapid access surgical outpatient clinics was obtained from our medical records department. Exclusion criteria consisted of age above 50 years, routine referrals where malignancy was not suspected on surgical specialist review, follow-up appointments and patients referred from other departments in the hospital.

GP referral proformas and accompanying letters were analysed retrospectively for inclusion of relevant information as per National Institute for Health and Clinical Excellence (NICE) recommendations for diagnosis of colorectal malignancy (Table 1).⁸ Each referral was scored out of nine points with one point awarded for each individual item of relevant information included (referral performance score). Further information was obtained on patients in our cohort subsequently diagnosed with colorectal malignancy including patient demographics, preoperative imaging, operative details, tumour histology, postoperative clinical outcome and survival time. Survival time reflected the time period between confirmation of diagnosis and date of death or present date (September 2014). Electronic patient records and hardcopy case notes were used to source and analyse GP referral letters and to extract relevant data for cancer patients.

Statistical analysis

Statistical analysis was performed using SPSS® version 22.0 (IBM, New York, US) with a *p*-value of <0.05 representing statistical significance. The Mann–Whitney U test was used for continuous data and Fisher’s exact test for categorical data.

Results

A total of 197 patients (107 female, 90 male) under 50 years old with suspected colorectal malignancy were

Table 1 Relevant information required for primary care referral to colorectal specialists

Basic administrative details*

Patient name, date of birth and contact details
Referring general practitioner name and contact details

Clinical details

*Symptoms present/reason for referral** – rectal bleeding, change in bowel habit, weight loss, abdominal pain, abdominal mass, rectal mass, iron deficiency anaemia

*Duration of symptoms**

*Relevant past medical history**

*Relevant family history**

*Smoking history**

Examination findings

*Abdominal examination – masses**

*Rectal examination – masses, blood**

Further tests

Full blood count and iron studies – including haemoglobin and mean corpuscular volume*

*Individual points contributing to a referral performance score (out of 9). Evidence of documentation on proformas and accompanying letters of each piece of information scored one point.

referred to our hospital by GPs over the 5½-year study period. The median age was 45 years (interquartile range [IQR]: 41–48 years) with the youngest aged 25 years. There was 1 patient (0.5%) aged under 30 years, 28 patients (14.2%) aged 30–39 years and 168 patients (85.3%) aged 40–49 years.

Of the 197 patients referred, 18 (11 male, 7 female; 9.1%) were diagnosed subsequently with a colorectal malignancy. The median age in this cohort was 41.5 years (IQR: 37–49 years) with the youngest aged 32 years. There were 7 patients (38.9%) aged 30–39 years and 11 patients (61.1%) aged 40–49 years.

In our institution, a total of 37 patients under the age of 50 years were diagnosed with colorectal cancer from all routes of presentation (emergency presentations, routine and urgent referrals) during the study period. Our reported 18 cancer cases from GP referrals suspecting malignancy therefore represented 48.6% of all newly diagnosed early onset malignancies over the time period studied.

Presenting symptoms

The presenting symptoms resulting in referral from GPs to secondary care for the malignant and non-malignant patient groups are shown in Table 2. The most common symptoms overall at time of referral were change in bowel habit (159/197, 80.7%) and rectal bleeding (158/197, 80.2%). There were similar observations in the cancer cases: 12 patients (66.7%) experienced change in bowel habit and 13 (72.2%) had rectal bleeding. Abdominal pain was the only symptom to be significantly different (*p*=0.042) between the two cohorts, with increased prevalence in the cancer group. Of

Table 2 Presenting symptoms

Symptoms	Cancer patients (n=18)	Non-cancer patients (n=179)	p-value
Rectal bleeding	13 (72.2%)	145 (81.0%)	0.760
Duration* in months (IQR)	4.0 (3.0–6.0)	1.5 (1.5–3.0)	0.291
Change in bowel habit	12 (66.7%)	147 (82.1%)	0.123
Duration* in months (IQR)	4.0 (2.6–4.5)	1.5 (1.5–3.0)	0.831
Weight loss	1 (5.6%)	22 (12.3%)	0.701
Duration* in months (IQR)	3.0	2.0 (2.0–4.5)	0.842
Abdominal pain	8 (44.4%)	39 (21.8%)	0.042
Duration* in months (IQR)	2.5 (1.0–3.3)	2.5 (1.5–6.0)	0.620
Tenesmus	1 (5.6%)	13 (7.3%)	1.000
Duration* in months (IQR)	4.0	2.5 (1.5–6.0)	0.833
Abdominal mass	0 (0.0%)	20 (11.1%)	0.225
Rectal mass	2 (11.1%)	11 (6.1%)	0.632
Iron deficiency anaemia	7 (38.9%)	27 (15.1%)	0.205
*duration of symptoms up to time of referral			

those referred, 47 patients (23.9%) had experienced abdominal pain with other bowel symptoms. Eight (17.0%) of these had colorectal cancer.

There was no significant difference in the duration of any symptoms at time of referral between the malignant and non-malignant groups. No symptoms demonstrated more than a three-month median duration at time of referral. The time interval between onset of symptoms and date of GP referral was not significantly different between the two groups (malignant: 3.8 months, non-malignant: 2.0 months; $p=0.422$).

Tumour characteristics, operative management and clinical outcomes

Of the 18 cancer patients, 2 (11.1%) had a positive family history. One of these had confirmed hereditary non-polypoid colon cancer on postoperative genetic testing. Only one other patient (5.6%) had predisposing ulcerative colitis disease.

The majority of patients had tumours in the rectum (12/18, 66.7%), with further left-sided colon distribution in the sigmoid (2/18, 11.1%) and descending colon (2/18, 11.1%). Only two tumours (11.1%) occurred in the right colon. One of these patients had iron deficiency anaemia as the reason for referral.

All but one malignancy (94%) demonstrated adenocarcinoma characteristics, with the exception being a carcinoid tumour in a rectal polyp snared endoscopically. Of the 17 adenocarcinomas, 4 (23.5%) were classified as T1, 4 (23.5%) as T2, 5 (29.4%) as T3 and 4 (23.5%) as T4. Seven (38.9%) of the eighteen cancer patients had evidence of nodal disease. Synchronous metastasis was confirmed in four patients (22.2%), with all exhibiting hepatic spread and

two with pulmonary disease in addition. Of the 17 adenocarcinoma cases, 16 (94.1%) were moderately differentiated with 2 (11.8%) displaying areas of mucinous/signet ring differentiation and 1 (5.9%) showing poor differentiation.

For the 18 malignant cases, resectional surgery was performed in 12 (67.7%): 5 patients (41.7%) had a high anterior resection, 3 (25.0%) had a low anterior resection with total mesorectal excision, 2 (16.7%) had a right hemicolectomy, 1 (8.3%) had a left hemicolectomy and 1 (8.3%) had an abdominoperineal excision. Of the 12 patients undergoing surgery, 4 (33.3%) were classified as Dukes' A, 2 (16.7%) as Dukes' B, 3 (25.0%) as Dukes' C and 2 (16.7%) as Dukes' D. Two of these patients presented initially with synchronous solitary liver metastases and underwent hepatic resection following their original colorectal resection.

Of the remaining six patients with malignancies who did not undergo surgical resection, two had foci of malignancy in pedunculated polyps (managed endoscopically and requiring no further surgery), two had advanced metastatic disease not amenable to surgery (managed palliatively), one had radiologically staged T4 N2 M0 disease with poor response to chemoradiotherapy (subsequently had palliative surgery) and one had radiologically staged T4 N1 M0 disease (required a palliative defunctioning colostomy in the emergency setting for obstruction from progressive disease).

Only one patient (8.3%) developed pelvic recurrence following R0 oncological resection. Following surgery, no patients presented with metachronous metastases during the study period.

Two (11.1%) of the eighteen cancer patients died during the study period: one who was palliated for advanced metastatic disease died at 6.4 months following the initial diagnosis and one died from local recurrence 12.7 months.

The median survival time until death or until September 2014 for all 18 patients was 27 months (range: 6–68 months).

Quality of GP referrals to secondary care

All GP referrals in this study were made via a locally agreed referral proforma according to NICE recommendations for investigation of lower gastrointestinal cancer.⁸ Of all 197 patients referred, the median time from GP referral to date to outpatient review in a specialty clinic was 11 days (IQR: 7–15 days). All of these referrals contained essential information including patient name, date of birth, address, phone number, and name and contact details of the referring GP. A complete list of relevant information included on referrals can be seen in Table 3.

For the 197 referrals, the median referral performance score was 5 (range: 3–9), with only 5 referrals (2.5%) awarded the maximum 9 points for demonstrating documentation of all important data. Thirty-five referrals (17.8%) accounted for the lowest scores recorded with 3 points. The 18 patients diagnosed subsequently with cancer had a median referral performance score of 6 whereas non-malignant initial referrals scored a median of 4 ($p=0.027$).

Discussion

This study is the first in the literature to report incidence of colorectal cancer in patients referred to secondary care with suspected malignancy under the age of 50 years. In this population, 9.1% (18/197) had a lower gastrointestinal malignancy. When examining cancer incidence from suspected colorectal malignancy referrals for patients of all ages, previous UK studies have reported rates varying between 7% and 14%.^{15–17} In comparison, the incidence of colorectal cancer in those referred urgently with suspected malignancy aged over 50 years during our study period was 7.1% (352/4,929). These findings suggest urgent primary care referrals made for younger patients have a higher subsequent cancer yield (conversion rate) for colorectal cancer than those for patients over 50 years old.

This could possibly be accounted for by a significant increase in the number of two-week rule urgent referrals for suspected colorectal cancer from primary care physicians and also increased patient awareness, particularly in light of recent public campaigns.¹⁸ The majority of such referrals are for patients aged over 50 years, thereby potentially diluting conversion rates down in this age group, especially with previously reported significant proportions of inappropriate two-week rule referrals that do not adhere to NICE recommendations.¹⁹ We do recognise there are limitations to our study, including retrospective analysis of a single institution cohort over a limited time period. Nevertheless, these are interesting findings, which warrant examination of larger, multicentre populations to determine whether a significant difference really exists.

Our data also suggest that just under half (48.6%) of all malignancies in patients under the age of 50 years were diagnosed initially via the primary-to-secondary care outpatient referral route. This percentage appears low but matches findings from the literature. One UK review reported only 45% of malignancies in the young presenting through outpatient referral, with just over half of these through the two-week rule referral pathway.¹ The authors of this paper also concluded that if age were excluded as a patient factor, many early onset malignancies would have met the 2005 NICE criteria for referral under the two-week rule. However, they were initially referred as non-urgent by their GPs owing to their age and as a result, their diagnosis was delayed.

On retrospective analysis of colorectal malignancies in all ages, another study reported that 68% of cases were diagnosed via outpatient specialist referral.²⁰ This difference may reflect a higher proportion of young patients presenting as an emergency with late stage disease attributed to diagnostic delay from both patient and physician related factors.^{2,21,22}

Rectal bleeding and change in bowel habit were the most common symptoms reported on initial presentation in all patients referred and our results in the malignant cohort were no different. This correlates with results in previous studies with similar observations reported for the older population diagnosed with colorectal cancer.²³

Abdominal pain was the only symptom that demonstrated a difference in frequency between the malignant and non-malignant groups. Abdominal pain alone is a poor predictor of malignancy and has the same yield of colorectal cancer as for asymptomatic patients on colonoscopic investigation.²⁴ One study has reported higher rates of abdominal pain in those with colorectal malignancies of early onset than in the older malignant cohort; the authors attributed this to possible ageing nociceptive afferent nerves and decreased production of chemical nociceptive mediators.²⁵ Young patients presenting with abdominal pain and associated rectal bleeding and/or change in bowel habit should therefore alert the assessing physician to potential malignancy. There should be a low threshold for formal colonoscopic examination in such patients.

Current NICE guidance is limited for young patients presenting with lower gastrointestinal symptoms.⁹ In terms

Table 3 Data included on primary care referrals contributing to the referral performance score

Information	n
Basic administrative details	197 (100%)
Symptoms present	197 (100%)
Duration of symptoms	183 (89.7%)
Relevant past medical history	90 (44.1%)
Relevant family history	49 (24.0%)
Smoking history	22 (10.8%)
Abdominal examination	71 (34.8%)
Rectal examination	76 (37.3%)
Full blood count and iron studies	82 (40.2%)

of the under-50 age group, the only indication listed for urgent referral (within 2 weeks) for suspected colorectal cancer is presence of unexplained weight loss and abdominal pain for patients aged over 40 years. NICE recommends considering urgent referral for adults with an abdominal or rectal mass and also for those aged under 50 years with rectal bleeding accompanied by abdominal pain, change in bowel habit, weight loss or iron deficiency anaemia. From our data, we would particularly advocate abdominal pain as a strong influential factor when considering specialist referral.

GPs may be inclined to employ a 'watch and wait' policy in many young patients with lower gastrointestinal symptoms given the more prevalent differential pathology such as inflammatory bowel disease. Nevertheless, these patients will generally require a diagnostic colonoscopy at some stage so adoption of a lower threshold for referral under the two-week rule if malignancy presents as a possibility seems logical.

Predisposing factors such as hereditary non-polyposis colon cancer only account for a minority of colorectal malignancies in the young, with strict surveillance strategies implemented by most clinicians. Several reports conclude colorectal cancer of early onset is mostly sporadic,^{2,22,24} a finding we observed in our data with only four patients having predisposing conditions or strong family history.

Regarding other tumour characteristics, most cancers in our study were distal to the splenic flexure (88.9%) and moderately differentiated (94.1%). Of those operated on, half were staged as Dukes' C1 or higher. Similar observations are evident in previous studies analysing colorectal malignancy in patients aged under 50 years.^{2,5,22,23,25} In our malignant cohort, late disease and metastasis was not infrequent, highlighting the importance of early diagnosis. However, young age as an entity is not associated with poor prognosis as one study has shown overall survival following diagnosis is comparable stage for stage when comparing early onset with late onset disease.²⁶

In 2000 the Department of Health introduced guidelines for urgent referral of suspected lower gastrointestinal malignancies.²⁷ Subsequently, NICE created specific recommendations to aid GPs in referring high risk patients for urgent investigation for possible colorectal malignancies.^{8,9} National Health Service hospitals have incorporated referral proformas based on such national guidance as part of their local referral system for suspected malignancies, including our institution. As well as tick boxes for indications for referral, our proforma contains an important free text box to allow documentation from the GP of all relevant information regarding patients referred (Appendix 1 – available online). Our study quantified quality of referral using a simple, non-validated tool (referral performance score). An average score of 5/9 was observed for our sample population. Only 2.5% of the referral proformas had top scores of 9/9, implying significant deficiencies in referral quality.

Worryingly, only 24% of proformas in our study documented family history for suspected malignancies in those aged under 50 years. Physicians rarely take an adequate

family history as part of risk assessment of colorectal cancer, resulting in failure to recognise potential hereditary and predisposing conditions in the young.²⁸ Rectal examination was documented in just 37% of proformas, which was particularly significant given our high proportion of rectal carcinomas diagnosed. The 2005 NICE recommendations stated that all patients with unexplained bowel symptoms should undergo digital rectal examination unless refused by the patient.⁸ One previous study reported GPs detecting only 56% of all palpable rectal tumours.²⁹ Furthermore, 27% of patients with easily palpable tumours referred for treatment of presumed haemorrhoids without prior rectal examination were subject to delayed specialist review and treatment.

It remains difficult to comment on adequacy of GP risk assessment for colorectal malignancy. Simply because relevant information is not present on a referral proforma does not necessarily infer that GPs are failing to ascertain that particular information from a patient. Inadequacies may arise from GPs not properly documenting relevant signs, symptoms and risk factors from their consultations. Nevertheless, important information may not subsequently be communicated to the colorectal specialist, and this has the potential to impact and delay secondary care management of early onset colorectal malignancy.

Conclusions

This study found a 9.1% incidence of colorectal cancer in patients under the age of 50 years referred from primary care for suspicion of a lower gastrointestinal malignancy. We suggest that GPs should have a higher index of suspicion of malignancy in this group of patients, particularly in those with abdominal pain alongside persistent rectal bleeding and/or change in bowel habit. We believe this warrants referral to a colorectal surgeon under the two-week rule. Our study highlights major deficiencies in completion of referral proformas from GPs, which could affect further investigation and management. With the rate of colorectal cancer in patients aged under 50 years increasing, thorough risk assessment is essential in patients of all ages to facilitate early detection and subsequent curative treatment.

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