Original Article

Cancer of the proximal colon after a "normal" colonoscopy

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Summary **In common with other diagnostic tests, colonoscopy has a false negative rate which is infrequently assessed. The available literature suggests that lesion miss rate is higher for proximal colonic tumors. A total of 367 patients were diagnosed with cancer of the colon and rectum over a period of 2 years. Ninety-two of these patients had tumors proximal to the splenic flexure. Their 5-year pre-diagnosis colonoscopic exposure was analyzed. The primary end-point of this study was to confirm the false negative colonoscopy rate in patients subsequently diagnosed with cancer of the proximal colon. The secondary end-point was to assess the effects of diagnostic delay on tumor stage and presentation. In the group of patients with proximal colon cancer (n = 92) we identified 10 patients (11%) who, as a result of incomplete (2 cases) or falsely negative (8 cases) colonoscopies, suffered a median diagnostic delay of 17 months (range 3-60). At diagnosis, 4 of these patients had Dukes' D caecal cancer, 4 had Dukes' C caecal cancer and 2 had Dukes' B transverse colon cancer; 3 presented with perforated tumours and 1 with intestinal obstruction. In this small subgroup of patients therefore 40% presented with emergency complications compared to 8% in the rest of the group with proximal cancers ($p < 0.01$). Missed cancers are more likely to present with complications. This study highlights the importance of recognition of an incomplete examination and the adverse impact of missed diagnosis on subsequent presentation.**

Keywords: Colonoscopy, colon cancer, adenomatous polyps, quality assurance

1. Introduction

White light colonoscopy is considered to be the gold standard investigation for colorectal neoplasia. Diagnosis is made by direct visualization and tissue sampling for histological analysis. The accuracy of conventional colonoscopy may be enhanced by various adjuncts such as dye spray, fluorescent and narrow band techniques. Moreover, endoscopy lends itself well to snare polypectomy which has been proved in a landmark study to reduce the incidence of invasive cancer (*1*). Moreover, mucosal resection and dissection and laser endotherapy, may be employed to ablate suitable neoplastic lesions. The number of colonoscopies being performed is steadily rising particularly with the advent of colorectal cancer screening.

Colonoscopy carries a definite complication rate and on occasions these complications may be serious and life-threatening. Thus, patients who have an inadequate examination are denied its benefits, while being exposed to its risks. In theory, colonoscopy practice is difficult to assess objectively. An infrequently used but accurate technique is tandem colonoscopy (also known as back-to back colonoscopy), whereby, two successive colonoscopies are performed on the same patient on the same day (*2*,*3*). Pooled adenoma miss rates from studies employing this technique, are in the region of 22% for all polyps; broken down into 2.1% for adenomas equal to or larger than 10 mm and 26% for those 1 to 5 mm in size (*4*). Retrospective studies suggest that the miss rates for colonic neoplasia are higher for more proximal lesions with missed cancer rates of 4 to 5.9% in the right colon (*5*,*6*).

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2. Materials and Methods

An analysis of our prospective colo-rectal cancer audit database was performed. Three hundred and sixty-seven subjects were diagnosed with cancer of the colon and rectum in the period from January 2004 to December 2006, and therefore, before the introduction of colorectal cancer screening. The endoscopy (Endoscribe® and Unisoft®), operation and pathology records of these patients were then analyzed. The study was subsequently focused on 92 patients with cancers situated proximal to the splenic flexure and, therefore, inaccessible to conventional flexible sigmoidoscopy.

We determined the colonoscopic exposure of these patients in the five years preceding cancer diagnosis. In our study we employed the adenoma-carcinoma progression, originally postulated by Fearon and Vogelstein, as the model for colonic carcinogenesis (*7*). A recent analysis has calculated the median duration of this transition (*i.e.* from large adenoma to carcinoma) at 5.27 years, hence our choice of the five-year period (*8*).

The primary end-point of our study was to determine the false-negative colonoscopy rate in patients subsequently diagnosed with proximal colon cancer. Our secondary end-point was to confirm the effect of diagnostic delay on tumor stage and presentation at diagnosis.

3. Results

Figure 1 illustrates the distribution of all proximal colon cancers in the study group and the sites of missed cancers. Ten out of the 92 patients (11%) with proximal colon cancer had a previous colonoscopy 3 months to 5 years prior to cancer diagnosis (median diagnostic delay of 17 months). Table 1 depicts the details of these ten patients. In the first two patients colonoscopy was perceived to be incomplete by the operator because the caecal landmarks were not reliably identified; in one patient the bowel preparation was inadequate and in the other colonoscope advancement was impossible due to unmanageable looping and patient discomfort. The other eight patients had undergone a complete colonoscopy which was reported normal and we, therefore, termed these true false-negative colonoscopies. The actual false-negative rate for patients with proximal colon cancer in our study was, therefore, 8.7%.

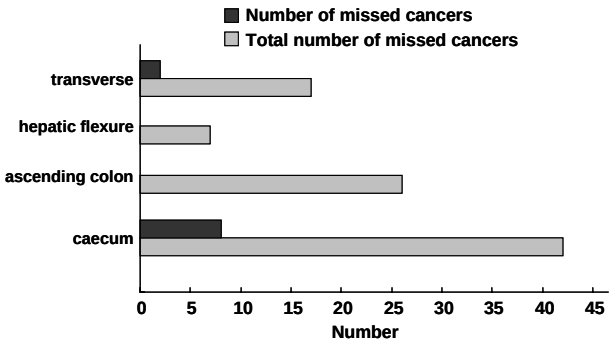

Figure 1. Distribution of cancers, including missed lesions, within the proximal colon.

Table 1 shows that 4 out of these 10 patients (*i.e.* 40% of patients with missed lesions) presented as an emergency (obstruction or perforation). This is in marked contrast to 7 emergency presentations in the remaining 82 patients (8.5%) who had no prior colonoscopy ($p < 0.01$).

When the two groups were compared for age, gender, Duke stage, extra-mural tumor vascular invasion and plasma C-reactive protein concentration, we did not register any useful statistically significant associations.

4. Discussion

Colonoscopy is an expanding practice and in the setting of colo-rectal cancer screening, it is leading to a re-design of service provision. Rising numbers of referrals have to be matched by qualified endoscopists supported by trained nursing staff and colorectal specialists, working within modern institutions. In the United Kingdom, the Joint Advisory Group has clear guidelines pertaining to training and accreditation in colonoscopy. The Group encourages attendance to training courses and this is supported by at least one study which suggests that such courses lead to sustained improvement in colonoscopy skills (*9*). Clear identification of caecal landmarks should be achieved in at least 90% of procedures. Given a satisfactory level of training and experience, failure to achieve such a percentage is multi-factorial, ranging from inadequate bowel preparation, endoscope looping, recognition of a

Table 1. Patients with missed proximal colon cancers

Site	Reason for delay	Delay (months)	Duke stage	Presentation
Caecum	Poor prep	24	D	Peforationm
Caecum	Technical	16	C	Elective
Caecum	False-ve	60	D	Elective
Caecum	False-ve	16	D	Obstruction
Caecum	False-ve	18	D	Elective
Caecum	False-ve	27	C	Elective
Caecum	False-ve	13	C	Elective
Caecum	False-ve	3	C	Peforationm
Transverse	False-ve	27	B	Obstruction
Transverse	False-ve	14	B	Elective

complication and the distressed patient. In addition, our unit has recently demonstrated that completion rate is lower in patients being investigated on in-patient basis and this cannot be entirely explained by poor bowel preparation alone (*10*). Magnetic imaging in the form of the Scope-guide® (Olympus Optical Company) has been shown to improve caecal intubation rates in both trainee and established endoscopists (*11*). It is clearly important that the colonic mucosa is inspected during careful withdrawal of the instrument (*12*).

The methodology of our study is simple, its main limitation being our assumption that the cancers which we have classified as "missed" were arising in line with the well known adenoma – carcinoma sequence. This assumption necessarily excludes the other theory of colonic carcinogenesis, namely non-polypoid or *de novo* colon carcinogenesis (*13*). *De novo* cancers tend to be small, flat or depressed, progress rapidly and have a tendency to be located proximally in the colon (*14,15*). They may account for as many as 40% of all colo-rectal malignancies and, therefore, merit due consideration. It has to be said, however, that all the missed tumors in our study had exophytic and/or polypoid features which are in general not in keeping with *de novo* cancers.

We derive two main conclusions from our study. Firstly, a significant number of patients with colon cancer will have had a reportedly normal colonoscopy prior to having a confirmed diagnosis. Secondly, as a group, these patients are more likely to present with sequalae on an emergent basis. We, therefore, recommend regular audit and appraisal of colonoscopy practice.

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