

COLORECTAL CANCER SCREENING

Screening guidelines for colorectal cancer and polyps in patients with acromegaly

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Acromegaly is characterised by excessive levels of circulating growth hormone and its tissue mediator, IGF-1. Before effective treatment and lowering of growth hormone and IGF-1 the majority of patients with the disease died by the aged of 60 years.^{1,2} This was largely attributable to diabetes mellitus and cardiovascular and cerebrovascular diseases. More recently, it has become apparent that patients with acromegaly have an increased prevalence of colorectal adenomas and cancer.³⁻²⁰ It is probable that with more effective and aggressive treatment of both the underlying acromegaly and its metabolic and vascular complications, patients are now surviving long enough to develop malignant complications of the disease. That this increased risk might be related to serum growth hormone and/or IGF-1 levels is supported by recent epidemiological studies in the non-acromegalic population that have demonstrated an association between serum IGF-1 and the risk of colorectal cancer.^{21,22}

EXECUTIVE SUMMARY

1 Patients with acromegaly should be offered regular colonoscopic screening, starting at the age of 40 years. (**Recommendation Grade: B**)

2 The frequency of repeat colonoscopy should depend on the findings at the original screening and the activity of the underlying acromegaly. (**Recommendation Grade: B**)

3 Patients with an adenoma at first screening or increased serum IGF-1 level above the maximum of the age corrected normal range should be offered screening at three year intervals.

4 Patients with either a negative first colonoscopy or a hyperplastic polyp should be offered screening at five year intervals.

5 Total colonoscopy is required rather than sigmoidoscopy, although the colonoscopy is associated with technical difficulties (**Recommendation Grade: B**).

PREVALENCE AND INCIDENCE

Acromegaly is a rare disease with an annual incidence of approximately 4–6 per million. There are approximately 2500 patients with acromegaly in the UK. Because of the complexity of the disease and its treatment, tertiary referral centres manage the majority of these patients with the number of patients in each centre varying between 20 and approximately 350. The recognition that these patients have an increased prevalence of colorectal neoplasia originally came from retrospective epidemiological surveys.^{3,11,12} These suspicions have been repeatedly confirmed during the past 15 years by a number of prospective colonoscopic surveys,^{7,9,10,14,15,19,20,23,24} the largest of which was from St Bartholomew's Hospital, London.²⁵ Since the report from St Bartholomew's, colonoscopic screening has continued to be offered to all patients with acromegaly at St Bartholomew's Hospital. To date, it has been performed on 222 patients of whom 10 (4.5%) had an adenocarcinoma and 45 (24%) a tubular adenoma. Two further patients had an adenocarcinoma diagnosed either at the same time as their acromegaly or in the preceding six

months. Although almost all cross sectional studies are hampered by a lack of a matched control population, comparison with prevalence figures for colorectal cancer in non-acromegalic subjects aged over 55 years, suggests an increased risk of up to 13-fold to 14-fold for colorectal cancer in acromegaly. A recent large retrospective cohort study has shown a 2.5-fold increase in mortality from colon cancer in acromegaly²⁶ and a small prospective study demonstrated colon cancer in 3 of 12 patients.²³

INTERVENTION

The youngest patient with an adenoma in the Bart's series was 39 years, and the mean age of the 10 patients with carcinoma was 67 years. To determine which acromegalic patients are at particular risk of colorectal neoplasia and to obtain preliminary data on appropriate screening levels, repeat colonoscopy is being performed on the original cohort of patients at St Bartholomew's Hospital. Currently, 66 patients have had a second colonoscopy; of those who had an adenoma at the original screening, 25% developed a new adenoma in a mean of 24 months compared with none of the patients with a normal original screening examination ($p < 0.07$). Furthermore, at the repeat colonoscopy, the serum IGF-1 level of patients with a new adenoma was significantly higher than those with either a hyperplastic polyp or normal colon ($p < 0.005$), suggesting that IGF-1 and disease activity is implicated in the development of neoplasia in this group of patients.²⁷ Further evidence in support of the role of IGF-1 is the correlation between degree of activity of the acromegaly and mortality from colorectal cancer²⁶ as well as the correlation with increased colonic crypt epithelial proliferation.²⁸

At present, controlled trials investigating the optimal frequency of colonoscopic screening in acromegaly have not been performed. However, based on these preliminary data, it is suggested that colonoscopic screening should be offered to all patients with acromegaly aged 40 years or over. Thereafter, repeat screening intervals depend on the findings at this colonoscopy and the serum IGF-1 level. In the presence of an adenoma or a serum IGF-1 that is above the maximum of the age corrected normal range, the authors' policy is to offer repeat screening after three years, while in those with normal colon or hyperplastic polyp a five year screening is performed.

In the largest series 25% of adenomas and 50% of carcinomas occurred in the ascending or transverse colon.²⁵ Total colonoscopy is therefore recommended.

Practical issues affect the success of total colonoscopy in acromegalic patients. These patients have increased length of colon, as well as increased circumference.²⁹ In addition, these patients have colonic transit time that is more than twice that of normal subjects and thus standard bowel preparation is usually inadequate.³⁰ In the authors' experience, twice the "standard" preparation of PEG-electrolyte solution gives good results. Two litres are given at six, four, and two hours before colonoscopy with a liquid only diet for 24 hours beforehand. Despite this, inadequate bowel clearance still occasionally

occurs. In view of the technical difficulties of the examinations, an experienced colonoscopist should perform the tests.

COSTS AND BENEFITS

The small number of acromegalic patients in the UK means that assessment of the cost:benefit ratio is difficult. There are approximately 2500 acromegalic patients in the UK, of whom about 2000 are aged 40 years or over. According to the data, about 25% of these (500) will have an adenoma and thus would be offered screening every three years, while the remainder would be offered screening at five yearly intervals.

RECOMMENDATIONS FOR AUDIT

The suggested guidelines are based on current knowledge and will be revised as further data become available. The small number of patients affected means that collaboration between centres will be required to increase the number of patients under study.

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