Raised carcinoembryonic antigen level as an indicator of recurrent disease in the follow up of patients with colorectal cancer

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SUMMARY

Background. *Serum carcinoembryonic antigen level is raised in 80% of patients undergoing colonic resection for cancer. Subsequent elevation in the follow-up period may precede signs and symptoms as an indicator of recurrent disease. There is little evidence that 'classical' follow up of patients in the general surgical outpatient clinic improves either survival or quality of life. Regular carcinoembryonic antigen level estimation requested by the general practitioner, allied to day-case colonoscopic surveillance may be a more rational approach.*

Aim. *A study was undertaken to investigate the relationship between raised carcinoembryonic antigen level and the recurrence of colorectal cancer in patients following a curative primary resection.*

Method. *Retrospective analysis was carried out on the notes of 125 patients who had attended a dedicated hospital colorectal follow-up clinic between 1988 and 1992. Carcinoembryonic antigen level data were obtained by subsequent examination of the University of Edinburgh Department of Clinical Chemistry (immunoassay section) carcinoembryonic antigen database.*

Results. *A single carcinoembryonic antigen level result of more than 100 ul^{-1} (normal range less than 60 ul^{-1}) was found to be a highly sensitive (87%), specific (89%) and accurate (88%) indicator of recurrent disease. Raised carcinoembryonic antigen level preceded symptoms in 72% of patients with recurrence of colorectal cancer.*

Conclusion. *Sequential laboratory estimation of carcinoembryonic antigen level organized by the general practitioner may represent an accurate method of detecting recurrent colorectal disease. Hospital review could be limited to colonoscopic surveillance and restaging of patients referred with evidence of recurrent disease.*

Keywords: colorectal cancer; antigens; disease recurrence; follow up; tumour markers.

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Introduction

SINCE its identification 30 years ago[1] there has been debate as to the importance of serum carcinoembryonic antigen level estimation in the follow up of patients with colorectal cancer,[2-5] and in particular its relationship to the presence of curable recurrent disease.[6] Serum carcinoembryonic antigen level is raised in 80% of patients with colorectal cancer.[5] Regular colonoscopic surveillance has been shown to reduce the incidence of subsequent cancers by the detection and removal of polyps and should be included in follow-up protocols.[7]

A study was undertaken to examine the relationship between a rise in carcinoembryonic antigen level and the presence of recurrent colorectal cancer using retrospective analysis.

Method

Patients who underwent a resection, with curative intent, of colorectal cancer at the Western General Hospital, Edinburgh between January 1988 and January 1992 were identified from the Lothian surgical audit database. Patients were excluded where, on inspection of the patients' notes, it was found that primary surgery was palliative, follow up was incomplete or there were fewer than one preoperative and two postoperative carcinoembryonic antigen level estimations.

The computerized notes (both patient notes and Department of Clinical Chemistry (immunoassay section) notes) of patients who were not excluded were reviewed to obtain data on carcinoembryonic antigen levels and cases of recurrent colorectal cancer. At each visit to the hospital colorectal follow-up clinic a history is recorded and clinical examination (including rectal examination and rigid sigmoidoscopy), faecal occult blood test and estimation of carcinoembryonic antigen level are undertaken. The presence of recurrent disease is confirmed by clinical examination, colonoscopy, biopsy, chest radiography, ultrasonography, computerized axial tomography scanning and laparotomy.

A raised carcinoembryonic antigen level was considered to be a value above 100 ul^{-1} (normal range less than 60 ul^{-1}). Chi square analysis using a four-fold table with one degree of freedom (df) was used to test the relationship between raised carcinoembryonic antigen level and the presence of recurrent disease. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of a raised carcinoembryonic antigen level were calculated. A true positive investigation was a serum carcinoembryonic antigen level of greater than 100 ul^{-1} with evidence of recurrent disease. A carcinoembryonic antigen level of 100 ul^{-1} (using international standard International Reference Preparation 73/601, National Institute for Biological Standards and Control) corresponds in this assay to approximately 10 μgl^{-1} of carcinoembryonic antigen.

Results

A total of 265 patients were identified from the Lothian surgical audit database, 140 of whom were excluded by the study criteria. The study sample was made up of 125 patients of whom 65 were men. The mean age at diagnosis was 69 years (range 41–90 years). The mean duration of follow up was 28 months. Dukes

stage at presentation was recorded in 97 patients as A in 10, B in 27, C in 38, and D in 22 patients.

The carcinoembryonic antigen level was greater than 100 ul^{-1} on at least one occasion in 54 patients, 46 of whom developed recurrent disease. The carcinoembryonic antigen level did not rise to more than 100 ul^{-1} in 71 patients, seven of whom developed recurrent disease ($\chi^2 = 76.21$, 1 df, $P<0.001$). Six of these seven patients had no elevation of carcinoembryonic antigen level prior to their primary colonic resection. In 38 of the 53 patients with recurrence (71.7%) a raised carcinoembryonic antigen level preceded clinically apparent disease. In 16 patients restaging investigations were instigated on the basis of a single high carcinoembryonic antigen level result alone. The sensitivity, specificity, positive and negative predictive values and accuracy of raised carcinoembryonic level as an indicator of recurrent colorectal cancer are shown in Table 1.

Discussion

In this series of patients, elevation of serum carcinoembryonic antigen level to greater than 100 ul^{-1} was a reliable indicator of recurrence of colorectal cancer. It must, however, be recognized that this is a retrospective observational study. The patients in whom carcinoembryonic antigen data were collected were selected for follow up and do not represent a random sample of those who presented with colorectal cancer. There were fewer patients presenting at Dukes A stage and more presenting at Dukes C stage than would be expected from a larger series.[8] This bias, however, does not reach significance when compared with smaller control groups.[9] The results must be considered within this context.

There are identifiable aims for follow up of patients with colorectal cancer which include the detection and treatment of curable local and metastatic disease, the palliation of incurable local and metastatic disease and the detection and treatment of subsequent polyps and cancers. Unfortunately, 'classical' clinical review consisting of repeated outpatient consultations and examinations does not address these aims.[7] The detection and treatment of subsequent polyps and cancers may be achieved by regular colonoscopy,[10-12] the periodicity of which continues to be debated.

The identification of patients with potentially curable recurrent disease remains a problem. Bi-annual computerized axial tomography scanning would detect hepatic metastases[13] but at considerable cost for a limited benefit. Only a very small number of scanned patients would have resectable disease (3% of patients overall) and only 33% of these (1% overall) would obtain a survival benefit from hepatic resection.[14]

Patients with incurable disease form the largest group with recurrence during follow up.[11] The identification of tumour related symptoms in these patients is of primary importance to direct appropriate palliative therapy. A raised carcinoembryonic antigen level above 100 ul^{-1} will identify 87% of patients who have recurrent disease. The data from the present study would suggest that normal carcinoembryonic antigen level prior to primary colorectal resection is a contraindication to the use of carcinoembryonic antigen level as sole marker of recurrent disease in the follow-up period.

As an alternative to patients receiving regular review from hospital specialists, general practitioners could take blood samples every three months in order for serum carcinoembryonic antigen level to be estimated by a laboratory. Hospital review could be limited to procedures which are of proven benefit, such as colonoscopy. Patients would be referred to the surgical clinic only when they developed signs, symptoms or biochemical evidence of recurrent disease. Under these circumstances intensive restaging to identify the site of recurrence would be undertaken to direct appropriate treatment. Patients who have undergone palliative resection should not be subjected to regular classical outpatient review as it is unlikely to be of benefit; they should continue to receive symptomatic treatment.[15]

In conclusion, if patients are to be followed up after resection of colonic malignancy with the intention of detecting recurrent disease, repeated carcinoembryonic antigen level estimation organized by the general practitioner, allied to a programme of colonoscopic surveillance, represents a sensitive and accurate alternative.

Table 1. Performance of a single raised carcinoembryonic antigen level (>100 ul^{-1}) in indicating patients who have developed recurrent colorectal cancer during follow up.

	Performance (%)
Sensitivity	*86.8*
Specificity	*88.9*
Positive predictive value	*85.2*
Negative predictive value	*90.1*
Accuracy	*88.0*

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