Original research

Clinical follow-up does not improve survival after resection of stage I–III colorectal cancer: A cohort study

R.P. Jones [a, b, *], D. McWhirter [a, b], V.L. Fretwell [b], A. McAvoy [b], J.G. Hardman [b]

[a] School of Cancer Studies, Institute of Translational Medicine, University of Liverpool, Liverpool, UK
[b] Department of Colorectal Surgery, Mid Cheshire Hospitals Foundation Trust, Crewe, UK

HIGHLIGHTS

- We investigated follow up after surgery for colorectal cancer.
- The benefit of clinical review in addition to CT scanning is unclear.
- We compared CT scans, CEA and clinical review for detecting recurrent cancer.
- One third of recurrences were treatable by repeat surgery.
- Clinical review did not detect any additional recurrences.

ARTICLE INFO

ABSTRACT

Introduction: The benefit of clinical follow-up alongside CT & CEA in detecting recurrent colorectal cancer (CRC) remains unclear. Despite this, clinical review remains part of most surveillance protocols. This study assessed the efficacy of clinical follow-up in addition to CT/CEA in detecting disease recurrence.
Methods: Patients undergoing surgery for CRC at a single centre between 2009 and 2011 were identified. Follow-up included clinical review, CT and CEA for 5 years. The primary endpoint of the study was method of detection of recurrence. Secondary endpoints included detection of surgically treatable recurrence, compliance with follow-up, disease free survival and overall survival.
Results: 118 patients with stage I–III CRC were included. Only 68.9% of scheduled follow-up events were performed (76.6% clinical reviews, 76.2% CT scans and 60.4% CEA tests). At median follow-up of 36 months, 26 patients had developed recurrence (median DFS 45.8 months). 17 patients (14.7%) had died (median OS 49.3 months). Sensitivity and specificity of follow up modality in detecting recurrence were; CT (92.3%, 100%), CEA (57.7%, 100%), clinical review (23.0%, 27.2%). Addition of clinical review did not identify any disease recurrence that was not detected by scheduled CT. Eight patients (30.7%) had surgically treatable recurrence — all were identified by scheduled CT.
Conclusion: The addition of CEA testing and clinical review to scheduled CT scanning offered no benefit in the detection of recurrent disease. Clinical review could be removed from follow-up protocols without any reduction in the detection of recurrent cancer.

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1. Introduction

Colorectal cancer is the fourth commonest cancer in the UK, with 40,000 new cases diagnosed every year. Approximately two thirds will be treated with surgical resection with curative intent.

However, approximately 30% of these patients will develop recurrent disease within 2 years of this initial resection [1]. Recurrence has traditionally been associated with a dismal prognosis, but there is growing evidence that recurrent locoregional [2] and metastatic [3] disease can be resected with good long term outcomes; around 40% of patients with colorectal liver metastases undergoing surgical resection are alive 5 years after surgery [4]. The likelihood of survival after recurrence is increased if disease is detected and treated before it becomes symptomatic — usually a hallmark of

* Corresponding author. Department of General Surgery, Leighton Hospital, Crewe CW1 4QJ, UK.
E-mail address: robjones@liv.ac.uk (R.P. Jones).

advanced recurrence [5]. Even for irresectable disease, early detection and commencement of systemic chemotherapy is associated with improved long-term outcomes [6]. Despite the perceived benefits of detecting disease recurrence, there remains significant confusion about the optimal modality and timing of follow-up.

CEA (carcinoembryonic antigen) and CT (computed tomography) scanning have been identified as the only modalities likely to detect surgically treatable recurrence [7,8]. The recently reported FACS (Follow up After Colorectal cancer Surgery) randomised study suggested that CEA and CT were equally effective in detecting surgically treatable recurrence, and performed significantly better than clinical follow up alone [9]. However, the benefit of clinical follow-up in addition to CT and/or CEA after resection remains unclear. Despite this uncertainty, regular outpatient clinical review remains a part of most surveillance protocols across the US and Europe [10–12].

This study therefore aimed to assess the efficacy of clinical follow up in addition to routine CT and CEA assessment in detecting recurrence in patients who had undergone curative resection of primary colorectal cancer.

2. Methods

All patients undergoing surgery for colorectal cancer at a single specialist colorectal unit between January 2009 and January 2011 were identified from a prospectively maintained database. A retrospective review of electronic and paper casenotes was performed, and patients with pathologically confirmed colorectal adenocarcinoma with an R0 resection were identified for further analysis. All patients were discussed at a specialist colorectal multidisciplinary team (MDT) either before (elective) or immediately after (emergency) surgery. Patients who presented with metastatic disease confirmed by imaging at MDT were excluded.

2.1. Surveillance protocol

Institutional follow-up (based on existing UK National Institute for Health & Clinical Excellence guidance) included regular clinical review, contrast CT chest/abdomen/pelvis and CEA measurements. The same surveillance protocol was used irrespective of cancer stage. A raised CEA or symptoms on clinical review triggered an automatic CT scan. Routine follow-up finished 5 years after resection. The timing of surveillance assessments are outlined in Fig. 1.

2.2. Study endpoints

The primary endpoint of the study was method of detection of recurrence. Recurrence was defined as radiological appearances suggestive of recurrence, clinical symptoms triggering an off-protocol CT scan that confirmed recurrence or CEA > 7 (the same

Table 1
Patient demographics. ASA = American Society of Anaesthesiology Classification.

	No of patients (%)
Age (median, range yrs)	69.4 (24.1–90.2)
Male	73 (61.9%)
Female	45 (38.1%)
Colonic primary	66 (55.9%)
ASA ≤2	111 (94.1%)

cut off defined by the FACS study) [13]. Secondary endpoints included detection of surgically treatable recurrence, compliance with follow up protocol, disease free survival and overall survival.

2.3. Statistical analysis

Quantitative and qualitative variables were expressed as medians (with range) and frequencies. Comparisons between groups were analysed with the chi-square test or Fisher exact test for proportions and the Mann–Whitney U test for continuous variables. Overall and disease free survival were calculated from the date of surgery to the date of last follow-up, recurrence or death using the Kaplan Meier method. For patients undergoing resection of recurrence, survival was also calculated from the date of secondary resection. Comparisons were made using log-rank test. To identify factors associated with survival in the entire cohort, variables were assessed using univariate analysis. All variables associated with $P < 0.05$ in the univariate proportional hazards model were entered into a cox proportional hazards multivariate model using a forward step wise procedure. $P < 0.05$ was considered significant. All statistical analyses were performed using IBM SPSS Statistics (v.21).

3. Results

3.1. Patients

Between January 2009 and January 2011, 132 patients underwent surgery for histologically confirmed colorectal adenocarcinoma, of whom 14 were known to have synchronous metastatic disease. One hundred and eighteen patients with AJCC stage I–III colorectal cancer were therefore eligible for analysis. Patient demographics are detailed in Table 1. The majority of patients had colonic lesions (55.9%). For patients with rectal cancer, 11/52 (21.1%) had short course chemoradiotherapy and 8/52 (15.3%) had long course chemoradiotherapy.

Histopathological examination confirmed 26 (22.0%) with stage I, 47 (39.8%) stage II and 45 (38.1%) stage III disease. 73 patients (61.9%) received 5-FU based adjuvant chemotherapy based on high-risk histopathological features.

Months	Year 1				Year 2				Year 3				Year 4				Year 5			
	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
Clinical	■	■	■	■		■		■				■				■				■
CT C/A/P		■		■		■		■				■				■				■
CEA	■	■	■	■		■		■				■				■				■

Fig. 1. Institutional follow up protocol after curative resection of colorectal cancer. Clinical = clinical review in outpatient department, CT C/A/P = CT chest/abdomen/pelvis, CEA = carcinoembryonic antigen.