Original article

Deprivation, comorbidity and survival in a cohort of patients with colorectal cancer

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We studied a regionally based cohort of 483 consecutive patients with colorectal cancer referred for chemotherapy and/or radiotherapy. These patients were assessed and managed according to consistent policies. We investigated the effects of socio-economic deprivation and comorbidity upon survival. Significant comorbidity was present in 48% of the patients. Overall survival and cause-specific survival were summarized using Kaplan-Meier curves. Equality of survivor functions was assessed using the logrank procedure and Cox's proportional hazards analysis. In univariate analysis, the following variables significantly affected survival: comorbidity, performance status, age and clinical stage. We could find no correlation between deprivation and comorbidity. The presence of comorbidity significantly affected cause-specific survival (3-year cause-specific survival without comorbidity 54.2%; with comorbidity 44.6%). In adjusted analysis, deprivation had an independently adverse effect on overall survival, hazard ratio 1.04 (95% confidence interval 1.00–1.08), but this was only of borderline statistical significance, $P = 0.049$. This study demonstrates that the interrelationships between comorbidity, deprivation and outcome in this group of patients are complex: even when care is readily available, patient assessments are uniform, and clinical decision making is consistent.

Keywords: colorectal neoplasm, socio-economic deprivation, comorbidity.

That a class that lives under the conditions already sketched and is so ill-provided with the most necessary means of subsistence, cannot be healthy and can reach no advanced age, is self evident. (Engels 1892)

INTRODUCTION

Poor people are, in general, not as healthy as affluent people, nor do they live as long. These general relationships between general ill-health, premature death, and socio-economic deprivation have been well-documented for over 150 years (Engels 1892; Kogevinas & Porta 1997; Gordon *et al.* 1999). Comorbidity is a useful term, introduced by Feinstein (Feinstein 1967), which describes those elements of ill-health that arise from conditions distinct from that illness, such as cancer, with which we might primarily be concerned.

Socio-economic deprivation (McLaren & Bain 1998; Coleman *et al.* 2001) and comorbidity (De Marco *et al.* 2000) both decrease the probability of survival in patients with colorectal cancer. The extent to which comorbidity and deprivation might act independently to lower survival is, however, unknown. Investigation of this problem is difficult because of the confounding effects of the possible variables involved. For example, if poor people have limited access to health care, then this alone, and independently of whether or not there is an increased prevalence of comorbidity amongst the poor, will adversely affect outcome. Conversely, if access to health care were unaffected by socio-economic status then any observed rela-

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tionship between deprivation and outcome might well be mediated by comorbidity. Similar issues arise in relation to referral for adjuvant or palliative treatment, and to any subsequent therapeutic decisions. In order to investigate any interrelationship between comorbidity and deprivation it is helpful to have a cohort of patients in whom decisions concerning assessment and clinical management have been uniform and consistent over time. We have performed a retrospective review of just such a cohort in an attempt to evaluate the relative contributions of deprivation and comorbidity to mortality in patients with colorectal cancer.

PATIENTS AND METHODS

A cohort of 483 consecutive patients with colorectal cancer was prospectively accrued between 1 July 1997 and 31 December 1999. These patients were referred to the Tayside Cancer Centre for non-surgical management of histologically proven colorectal cancer: either with newly diagnosed tumours or with recurrent disease after initial surgical management. The Tayside Cancer Centre serves a defined population of approximately 450 000. This population is relatively stable and is ethnically homogeneous: only two of the 483 patients were non-white, both were of Asian origin. Comparison with cancer registry data shows that 74% of all incident cases of colorectal cancer were referred for opinion. During the period of this study a single consultant clinical oncologist (A.J.M.) provided all non-surgical oncology services for patients with colorectal cancer. Management policies were consistent throughout this period (Table 1).

All patients were assessed prospectively and the full clinical history and examination were entered into electronic patient records. This provided a database which was then used retrospectively to obtain the data for analysis. Permission for the study was obtained from the regional ethics committee and from the Caldicott guardian.

Comorbidity was assessed using the Charlson index (Charlson *et al*. 1987), expressed as both total score and final score (Table 2), and the original 13-item Cumulative Illness Rating Score (CIRS) (Linn *et al*. 1968). Socioeconomic deprivation was assessed using indices, Carstairs (Carstairs & Morris 1991; McLoone 2000) (Table 3) and the Scottish Area Deprivation Index (Gibb K *et al.* 1998), linked to the patient's postcode. Patients were classified, again according to postcode, as urban dwellers, resident in the cities of Dundee or Perth, and rural dwellers, resident elsewhere in Tayside. By these criteria 249 patients had urban residence and 234 had rural residence.

Table 1. Management policies for colorectal cancer during the study period

Chemotherapy

Adjuvant chemotherapy with 5FU/Folinic acid

Dukes B Colon and Rectum: not routinely used, but discussed with selected patients (adverse histological features, patient's wish for further therapy, etc.).

Dukes C Colon and Rectum: routinely discussed with all fit patients, recommendations adapted according to age of patient.

Palliative chemotherapy

Discussed with all fit patients with metastatic disease. Active monitoring mentioned as a reasonable policy. First line treatment: 5FU/Folinic acid; Irinotecan or Capecitabine as second-line therapy.

Surgical resection or *in situ* ablation of liver metastases

Considered in patients with technically suitable disease and who were in reasonable general condition.

Radiotherapy for patients with rectal cancer

Short-course pre-operative radiotherapy

Used as part of the CR07 trial. Used electively in selected patients with locally advanced, but operable, tumours.

Long-course pre-operative chemoradiotherapy

Used in patients with localized, but inoperable, disease.

Post-operative long-course chemoradiotherapy

Used in patients with positive circumferential margins after surgical resection.

5FU, 5-fluorouracil; CR07, Medical Research Council (MRC) randomized trial of pre-operative radiotherapy vs. selective post-operative chemoradiotherapy for operable rectal cancer.

Table 2. Charlson index of comorbidity

Assigned weights for diseases	Conditions
1.	Myocardial infarct
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Ulcer disease
	Mild liver disease
	Diabetes
2.	Hemiplegia
	Moderate or severe renal disease
	Diabetes with end organ damage
	Any tumour
	Leukaemia
	Lymphoma
3.	Moderate or severe liver disease
6.	Metastatic solid tumour
	AIDS

Total score is simply the sum of the assigned weights for each comorbid condition

Final score is derived from total score as:

Total	**Final score**
0	0
1–2	1
3–4	2
>5	3

Pathological classification of the tumour used Dukes stage, the UICC TNM system [Union Internationale Contre le Cancer (UICC) Tumour, Nodes Metastases (TNM)] and, for rectal tumours, the Quirke system (Quirke & Dixon 1988) for assessing circumferential margin involvement. Full staging information was not available for all patients as some patients with metastatic disease, or with unresectable primary tumours, had biopsy without formal surgical resection of the primary tumour. The staging used in the analysis was that assigned at original diagnosis, rather than the stage at the time of oncology referral.

Patients were followed up regularly in the oncology clinic. Follow-up information was obtained from the electronic patient record. For patients unable or unwilling to attend for clinical follow-up there is an established system of postal follow-up for cancer patients in Tayside. When patients are discharged from clinics we regularly write to their general practitioners requesting follow-up information. This information is used to update the patient records. Date and cause of death, for patients who have died, is therefore obtained directly without recourse to cancer registry data or information from death certificates. For cause-specific survival, an event was defined as death directly because of colorectal cancer. All patients dying from other causes were considered censored at the date of death. For overall survival, an event was defined as death from any cause. The follow-up data were analysed in June 2002, giving a minimum follow-up period of 2.5 years. Survival time was calculated from the date of pathological diagnosis. There have been 289 deaths in the 483 patients.

Statistical analyses were performed using Stata (StataCorp 2001). The Kaplan-Meier method was used for survival analysis and statistical significance was estimated using the logrank procedure. The Cox proportional hazards model was used to assess the impact of key variables, corrected for the effects of other relevant variables, upon outcome. Group comparisons used the Mann–Whitney (two-group comparisons) or the Kruskal–Wallis tests (more than two groups with ordinal scores). Correlation coefficients were calculated by Spearman's method.

Table 3. Criteria used to construct Carstairs index of deprivation

Overcrowding: the proportion of all persons living in private households with a density of more than one person per room.
Male unemployment: the proportion of economically active males seeking or waiting to start work.
Low social class: the proportion of all persons in private households with an economically active head with head of household in social class 4 or 5.
No car: the proportion of all persons in private households which do not own a car.
The score allocated, on the basis of the above criteria, is then normalized to the mean for Scotland – so that the mean score for Scotland is effectively set at zero. A positive score means that a locality is more deprived than the national mean, a negative score indicates relative affluence. For convenience, the Carstairs scores are often divided into categories, either by quintiles or septiles.

RESULTS

Table 4 summarizes the main details of the 483 patients in the study.

Table 4. Details of patients included in the study

Age (years)		
Mean	68.7	
Median	70	
Range	22–95	
	n	%
Gender		
Female	214	44
Male	269	56
WHO performance status		
0	157	33
1	242	50
2	63	13
3	14	3
4	7	1
Dukes stage		
A	18	4
B	109	25
C	192	43
D	124	27
Deprivation quintiles		
1 (least deprived)	161	33
2	137	28
3	62	13
4	54	11
5 (most deprived)	69	14
T stage		
1	12	3
2	42	10
3	201	49
4	159	38
N stage		
0	148	38
1	153	39
2	89	23
M stage		
0	359	74
1	124	26
Comorbidity		
Present	252	48
Absent	231	52
Charlson		
0	277	57
1	189	39
2	17	4
Cumulative illness rating score		
0	68	14
1–3	214	44
4–5	89	18
>5	112	23

WHO, World Health Organization.

The mean Carstairs score in the 483 patients in this study was –1.19 [95% confidence interval (CI) –1.47 to –0.91]. This compares with a score of –1.04 (95% CI –1.39 to –0.68) in 256 consecutive patients registered with the regional cancer registry after 1 January 2000. There is no significant difference in Carstairs scores between the two groups ($P = 0.22$, Mann–Whitney).

The reasons for referral to oncology were as follows: 291/483 (60%) were recently diagnosed patients referred for radical treatment; 124/483 (26%) were recently diagnosed patients referred for palliative treatment; 68/483 (14%) were referred for management of recurrent disease following previous surgery.

The cause-specific survival in newly diagnosed patients was 52% at 3 years (Fig. 1). Overall survival was strongly influenced by the reason for referral of patients (Fig. 2) $P < 0.00001$ (logrank). Patients with metastatic disease had the worst survival 11% at 3 years; new patients referred with localized disease had the best survival 62% at 3 years. Survival in patients whose disease had recurred was estimated from date of original diagnosis, rather than date of recurrence, and was 50% at 3 years.

Overall survival in recently diagnosed patients was strongly influenced by clinical stage, $P < 0.00001$ for both M0 vs. M1 and for Dukes' stage (Fig. 3). Carstairs deprivation category, divided into categories according to Scottish quintile data (from 1, least deprived, to 5, most deprived), had no significant effect on overall survival ($P = 0.66$). Cause-specific survival was influenced by the presence of comorbidity, $P = 0.02$ (Fig. 4). The cause-specific survival at 3 years was 54.2% in patients without comorbidity and 44.6% in those with comorbidity. There was no demon-

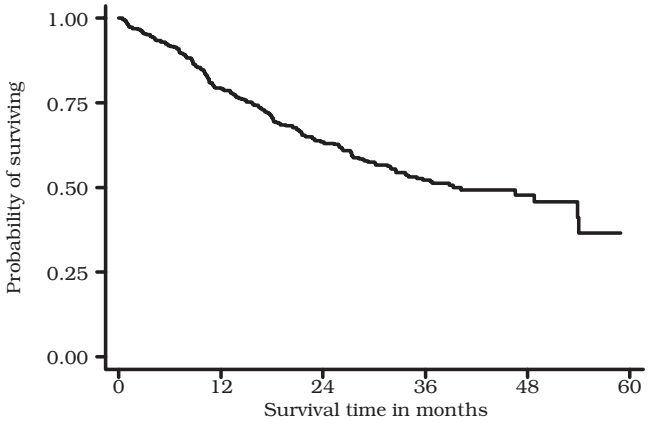

Figure 1. Cause-specific survival: all newly diagnosed patients ($n = 415$).

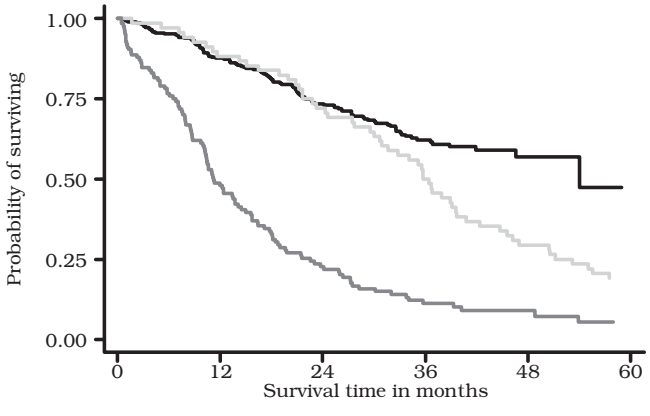

Figure 2. Overall survival by reason for referral: newly diagnosed patients with localized disease (black line); newly diagnosed patients with metastatic disease (dark grey line); patients with recurrent disease (pale grey line): $P < 0.0001$ (logrank).

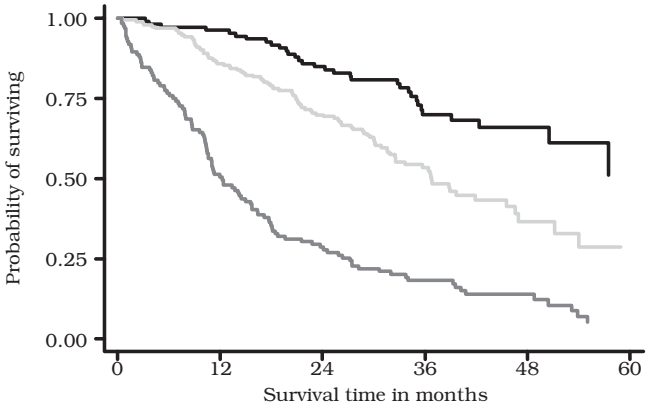

Figure 3. Overall survival in newly diagnosed patients according to Dukes' stage: black = Dukes' B; light grey = Dukes' C; dark grey = Dukes' D (M1): $P < 0.00001$ (logrank).

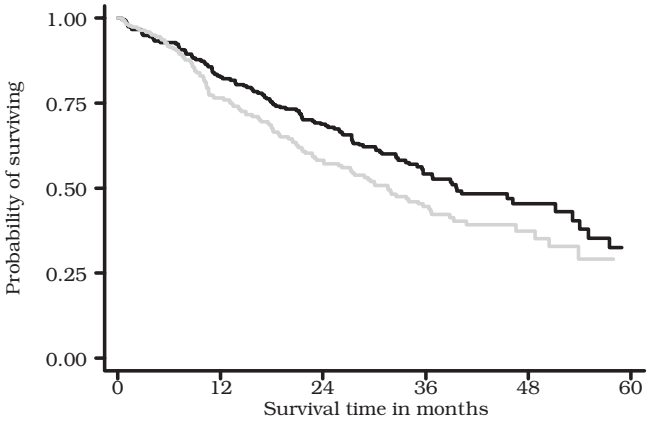

Figure 4. Cause-specific survival according to presence (grey line) or absence (black line) of comorbidity: $P < 0.02$ (logrank).

strable effect of rural, as opposed to urban, residence on survival. The 3-year overall survival in urban dwellers was 45% and in rural dwellers 48%, $P = 0.65$.

The correlations between key variables, calculated using the Spearman rank correlation coefficient, are shown in Table 5. There is no demonstrable correlation between comorbidity (as measured by CIRS, Charlson total score, Charlson index) and deprivation (as assessed by the Carstairs score or any of its derivatives) or the area deprivation index. There are good correlations between performance status and age; performance status and comorbidity; age and comorbidity.

In univariate analysis (Table 6) the total Charlson score emerges as the index of comorbidity that most clearly influences survival. Increased deprivation, as assessed by Carstairs score, is associated with decreased overall survival in patients with no evidence of metastatic disease. The analysis also clearly demonstrates the dominant effect of metastatic disease upon outcome: the hazard ratio, using deaths from all causes as outcome, is 3.22 (95% CI 2.53–4.09; $P < 0.0001$) when patients with metastases at presentation are compared to those with localized disease. Age influenced overall survival, but not cause-specific survival. Neither site of primary tumour nor gender influenced survival. Performance status, which reflects both the effects of cancer and any concomitant medical conditions, was strongly associated with outcome. If the baseline hazard in patients with World Health Organization (WHO) grade 0 is taken as 1.0 then, with all-cause mortality as outcome, the hazard ratios (HR) for the other grades are as follows: Grade 1 HR 1.67 (95% CI 1.47–1.91); Grade 2 HR 2.80 (2.15–3.65); Grade 3 HR 4.68 (3.15–6.96); Grade 4 HR 7.84 (4.62–13.30).

On the basis of the results summarized in Table 6, the following variables were selected for entry into the full Cox model: presence of metastases; total Charlson score; Carstairs deprivation score; WHO performance status; age. In the analysis of patients without metastatic disease Dukes stage was entered into the model. Given the territorial overlap between WHO performance status and comorbidity, the model was estimated both with and without WHO grade as a variable. The results are shown in Table 7. Comorbidity has a significantly adverse impact upon survival when correction is made for age, presence of metastatic disease (or Dukes stage in M0 patients) and deprivation. When correction is also made for WHO performance status then the independent effect of comorbidity disappears, except for a decrease in overall survival in patients without metastatic disease.

When correction is made for metastases, comorbidity, age and WHO performance status then deprivation, as measured by the Carstairs score, decreases overall survival: for each one point increase in Carstairs score, survival is 4% (95% CI 0.15–8%) less. This effect is of borderline statistical significance: $P = 0.049$.

The potential relationship between deprivation and stage at presentation was assessed by looking at mean Carstairs scores, with 95% confidence intervals, in patients grouped according to stage (Fig. 5). Deprived patients (higher Carstairs scores) appear to have more advanced Dukes stage; this trend is not statistically significant ($P = 0.27$ by Kruskal–Wallis test). There is a genuine difference in T stage according to deprivation ($P = 0.02$ by Mann–Whitney test) when Carstairs scores in patients with T1 or T2 tumours are compared with those in patients with T3 or T4 tumours. There was no differ-

Table 5. Correlation matrix for variables studied

	WHO	Age	CIRS	Charlson index	Charlson total	Carstairs quintiles	Carstairs total	Area DI
WHO	1.0							
Age	**0.30** $P < 0.00001$	1.0						
CIRS	**0.33** $P < 0.00001$	**0.30** $P < 0.00001$	1.0					
Charlson index	**0.27** $P < 0.00001$	**0.26** $P < 0.00001$	**0.55** $P < 0.00001$	1.0				
Charlson total	**0.36** $P < 0.00001$	**0.24** $P < 0.00001$	**0.54** $P < 0.00001$	**n/a**	1.0			
Carstairs quintiles	**–0.02** $P = 0.70$	**0.01** $P = 0.89$	**0.09** P = 0.047	**–0.01** $P = 0.83$	**–0.02** $P = 0.71$	1.0		
Carstairs total	**0.08** $P = 0.10$	**0.05** $P = 0.33$	**0.08** $P = 0.09$	**0.06** $P = 0.22$	**0.04** $P = 0.37$	**n/a**	1.0	
Area DI	**–0.04** $P = 0.46$	**0.03** $P = 0.52$	**0.08** $P = 0.07$	**0.07** $P = 0.10$	**0.05** $P = 0.32$	**0.76** $P < 0.00001$	**0.51** $P < 0.00001$	1.0

WHO, World Health Organization performance status; Carstairs quintiles, Carstairs deprivation index by Scottish quintiles; Area DI, area deprivation index; CIRS, cumulative illness rating scale; Charlson total, Charlson total score; n/a, not applicable.

Table 6. Univariate analysis of potential prognostic factors

	All patients		M0 patients	
	OS HR 95% CI *P*-value	**CSS HR** 95% CI *P*-value	**OS HR** 95% CI *P*-value	**CSS HR** 95% CI *P*-value
Comorbidity				
Charlson index	**1.44** 1.17–1.79 *P* = 0.001	**1.33** 1.06–1.68 *P* = 0.01	**1.59** 1.21–2.10 *P* = 0.001	**1.43** 1.05–1.95 *P* = 0.024
Charlson total	**1.34** 1.19–1.52 *P* < 0.0001	**1.29** 1.13–1.48 *P* < 0.0001	**1.45** 1.24–1.69 *P* < 0.0001	**1.39** 1.16–1.65 *P* < 0.0001
CIRS	**1.09** 1.04–1.14 *P* < 0.0001	**1.06** 1.01–1.11 *P* = 0.02	**1.11** 1.05–1.17 *P* < 0.0001	**1.07** 1.01–1.14 *P* < 0.03
Present/absent	**1.40** 1.11–1.77 *P* = 0.005	**1.30** 1.02–1.67 *P* = 0.04	**1.56** 1.16–2.11 *P* = 0.003	**1.39** 1.00–1.94 *P* = 0.05
Deprivation				
Carstairs score	**1.03** 0.98–1.08 *P* = 0.27	**1.03** 0.97–1.09 *P* = 0.32	**1.09** 1.02–1.12 *P* = 0.008	**1.09** 1.02–1.16 *P* = 0.01
Area DI	**1.02** 0.99–1.06 *P* = 0.20	**1.02** 0.98–1.06 *P* = 0.329	**1.03** 0.99–1.08 *P* = 0.16	**1.03** 0.98–1.08 *P* = 0.282
Others				
Rectum vs. colon	**1.07** 0.84–1.36 *P* = 0.61	**1.05** 0.81–1.36 *P* = 0.715	**0.94** 0.69–1.28 *P* = 0.69	**0.90** 0.64–1.27 *P* = 0.556
Gender	**1.02** 0.81–1.23 *P* = 0.87	**0.97** 0.75–1.25 *P* = 0.81	**1.12** 0.84–1.62 *P* = 0.42	**1.10** 0.79–1.53 *P* = 0.572
WHO PS	**1.67** 1.47–1.91 *P* < 0.0001	**1.64** 1.42–1.90 *P* < 0.0001	**1.71** 1.45–2.02 *P* < 0.0001	**1.67** 1.39–2.01 *P* < 0.0001
M0 vs. M1	**3.23** 2.54–4.11 *P* < 0.0001	**3.75** 2.90–4.84 *P* < 0.0001	**n/a**	**n/a**
Dukes stage	**2.30** 1.94–2.74 *P* < 0.0001	**2.55** 2.12–3.07 *P* < 0.0001	**1.92** 1.39–2.64 *P* < 0.0001	**2.09** 1.46–3.00 *P* < 0.0001
Age	**1.02** 1.01–1.03 *P* = 0.002	**1.01** 1.00–1.20 *P* = 0.179	**1.03** 1.02–1.05 *P* < 0.0001	**1.02** 1.00–1.03 *P* = 0.07

OS, overall survival; CSS, cause-specific survival; M0 patients, patients without metastatic disease at presentation; HR, hazard ratio; 95% CI, 95% confidence interval for the hazard ratio; CIRS, cumulative illness rating scale; Area DI, area deprivation index; WHO PS, World Health Organization performance status; n/a, not applicable.

ence in overall survival when patients with T1 or T2 tumours were compared with those presenting with T3 or T4 tumours (P = 0.19 by logrank). This may result from the relatively small proportion of patients with T1 or T2 tumours: 54/414 (13%) of the patients with full T stage data.

DISCUSSION

There are several problems with the interpretation of the results of this study. There were relatively few patients with severe socio-economic deprivation: Tayside is, compared with much of Glasgow, relatively prosperous. Only 20% of the population of Tayside is in Carstairs deprivation category 6, fewer than 1% are in category 7. In Greater Glasgow 30% of the population are in category 7 and 21% in category 6 (McLaren & Bain 1998). Given the greater numbers, both absolute and relative, of severely deprived people in Glasgow it is unlikely that conclusions drawn from Tayside will apply to Glasgow, or vice versa. The sample size is far smaller than would be usual in a population-based study using record linkage. The advan-

Table 7. Results of adjusted analyses using Cox's proportional hazards model

	Hazard ratio	95% CI	*P*-value
OS all			
M0 vs. M1	3.09	2.41–3.95	0.0001
Charlson (total)	1.12	0.98–1.27	0.099
WHO PS	1.51	1.29–1.77	0.0001
Age	1.02	1.00–1.03	0.03
Carstairs score	1.04	1.00–1.08	0.049
M0 vs. M1	3.34	2.62–4.27	0.0001
Charlson (total)	1.25	1.10–1.42	0.001
Age	1.02	1.01–1.04	0.001
Carstairs score	1.03	0.99–1.07	0.136
CSS all			
M0 vs. M1	3.47	2.68–4.51	0.0001
Charlson (total)	1.10	0.95–1.27	0.211
WHO PS	1.53	1.29–1.81	0.0001
Age	1.00	0.99–1.02	0.5
Carstairs score	1.03	0.99–1.08	0.112
M0 vs. M1	3.78	2.92–4.90	0.0001
Charlson (total)	1.23	1.07–1.41	0.004
Age	1.01	1.00–1.03	0.095
Carstairs score	1.02	0.98–1.07	0.253
OS M0			
Charlson (total)	1.22	1.01–1.48	0.039
Dukes stage	1.95	1.41–2.68	0.0001
Carstairs score	1.04	0.99–1.09	0.16
Age	1.01	0.99–1.03	0.295
WHO PS	1.63	1.30–2.05	0.0001
Charlson (total)	1.36	1.13–1.65	0.001
Dukes stage	1.95	1.42–2.68	0.0001
Carstairs score	1.03	0.98–1.09	0.222
Age	1.02	1.00–1.04	0.031
CSS M0			
Charlson (total)	1.17	0.94–1.45	0.164
Dukes stage	2.10	1.47–3.02	0.0001
Carstairs score	1.02	0.97–1.08	0.45
Age	1.00	0.98–1.02	0.916
WHO PS	1.63	1.27–2.08	0.0001
Charlson (total)	1.29	1.04–1.60	0.023
Dukes stage	2.10	1.47–3.00	0.0001
Carstairs score	1.02	0.96–1.08	0.549
Age	1.01	0.99–1.03	0.373

OS, overall survival; CSS, cause-specific survival; 95% CI, 95% confidence interval for the hazard ratio; CIRS, cumulative illness rating scale; WHO PS, World Health Organization performance status.

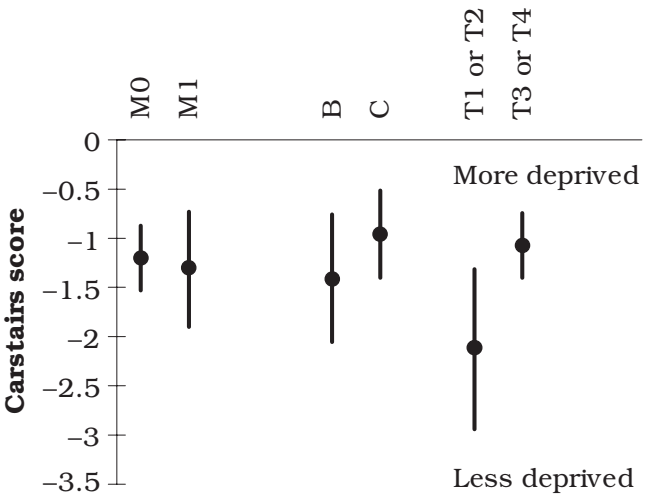

Figure 5. Carstairs score (mean and 95% confidence intervals) plotted against M stage, Dukes stage and T stage. The difference between T1/T2 and T3/T4 is statistically significant ($P = 0.02$, Mann–Whitney test).

tages of uniformity and homogeneity have been purchased at the expense of statistical power. A major countervailing advantage is the elimination of interphysician variability as a confounding factor. The assessment of patients, clinical decision making and implementation of management policy were, inasmuch as any individual is self-consistent, uniform.

In terms of outcome, the patients in this study appear to be reasonably representative of Scottish patients in general. The overall survival in newly diagnosed patients was 52% at 3 years; this is close to the figure of 50% for Scotland as a whole (ISD 2002). The deprivation scores in the study patients were not significantly different from those in a contemporary, but non-overlapping, regional cohort of patients from Tayside.

In this study the prevalence of comorbidity, defined as total Charlson score of greater than zero, was 48%. This compares with 58% and 52% from two separate studies using data from the Eindhoven cancer registry (Schrijvers *et al*. 1995; Coebergh *et al*. 1998; Coebergh *et al*. 1999). If the Charlson index, rather than total score, is used as the discriminator, then 43% of patients had values greater than zero; this compares with 49% of patients in a large Veteran's Affairs study from the USA (Dominitz *et al*. 1998).

Only one previous study has specifically addressed the relationship between socio-economic status and comorbidity in patients with colorectal cancer. This was a population-based study from the South-East Netherlands (Schrijvers *et al*. 1997). The assessment of comorbidity was performed retrospectively by clerical staff and there were uncertainties concerning the completeness of reporting. Although the Charlson system had been applied, the analysis was presented using a simple enumerative approach, with no attempt made to assess the severity of any concomitant illness. The clinical assessment of comorbidity in the current study, by contrast, was performed prospectively, by the two clinicians involved in the care of the patients. The recorded comorbidity was coded retrospectively and the severity of concomitant illness was graded using two different systems: Charlson and

CIRS. The Dutch study was unable to show any increase in comorbidity with lower socio-economic status in patients with colorectal cancer. With a baseline of 1.0 for comorbidity in the least deprived, the hazard ratio for the presence of comorbidity was 1.16 (95% CI 0.66–2.03) in the most deprived group. The present study provides stronger evidence for the lack of any simple relationship between socio-economic deprivation and comorbidity in patients with colorectal cancer. Each was assessed by two different methods and no significant correlations were found between any measure of comorbidity and any measure of deprivation. The highest correlation coefficient was 0.043, for area deprivation index and total Charlson score (Table 5).

Data from the USA suggest that the relationship between comorbidity and socio-economic status might be complex. A large study, using Surveillance, Epidemiology and End Results (SEER) data from Detroit, shows that the prevalence of cardiovascular disease in patients with cancer is significantly lower in unskilled workers than in managers/professionals but that the rates of respiratory disease and cerebrovascular disease are lower in the better off (Ogle *et al*. 2000). Looking in detail at the relationship between patterns of comorbidity and deprivation requires a sample size far greater than that available in the present study.

A previous study from this region, looking at all new patients with colorectal cancer, showed a relationship between Dukes stage and deprivation (Ionescu *et al*. 1998). The gradient was mainly between the Dukes A tumours and the rest. Our study, of patients referred for non-surgical management, fails to confirm this finding, probably because of the very few patients with Dukes A disease. A much larger Scottish study failed to show any relationship between deprivation and Dukes stage at presentation in patients with colorectal cancer (Brewster *et al*. 2001). Our study does show, we believe for the first time, an association between deprivation and more advanced T stage. We could not demonstrate any effect of T stage on survival, possibly because there were relatively few patients with T1 or T2 tumours included in the study.

The present study shows that, even when corrected for the presence of comorbidity and other relevant variables, socio-economic deprivation has a demonstrable adverse effect upon overall survival. We can conclude that any effect of deprivation upon survival in this group of patients is not mediated exclusively by comorbidity. There is good evidence that deprivation may be associated with more advanced pathological stage at presentation, even when access to care is not constrained by ability to pay. This might mediate some of the adverse effect of deprivation on survival in patients with colorectal cancer, but is unlikely to be the only important factor. Other possible explanations need actively to be sought. These include effects of smoking and alcohol abuse upon treatment-related morbidity and mortality; problems with transport to and from the cancer centre; delays in reporting potentially significant symptoms; effects of diet and general nutritional state upon ability to complete planned or recommended treatment.

This study shows, quite clearly, that comorbidity is an important influence upon both overall and cause-specific survival in patients with colorectal cancer. There are a variety of mechanisms which might mediate this effect. Comorbidity could influence decision making concerning adjuvant chemotherapy. Regimes using 5-fluorouracil (5FU) can cause coronary vasospasm as well as direct myocardial damage (Kuropkat *et al*. 1999) and there might be an understandable reluctance to use 5FU-based regimens in patients with a history of cardiac disease. Comorbidity might also compromise the effectiveness of chemotherapy: the accumulation of problems arising from concomitant illness, and from the chemotherapy itself, might influence decisions to curtail or attenuate treatment. Such compromises are, through reduction in dose intensity, likely to diminish the effectiveness of any treatment that is given. Comorbidity may be directly life-shortening: patients dying from their concomitant illness, rather than cancer. This effect can be assessed, in the current study, by comparing the effects of comorbidity on cause-specific, as opposed to overall, survival. The corrected hazard ratios for the total Charlson score, as a measure of comorbidity, are similar for both overall survival and cause-specific survival (Table 7). This would suggest that death from concomitant disease is not the main mediator of the effect of comorbidity upon outcome in this group of patients.

Comorbidity was significantly associated with age but was still an independent predictor of survival when correction was made for age in the Cox proportional hazards analysis (Table 7). Age was, unsurprisingly, an independent prognostic factor for overall survival, but not for cause-specific survival. These findings suggest that the adverse impact of comorbidity on survival is not simply explained by increased comorbidity in older patients.

Although this study has raised some interesting questions, it provides few answers. There is a need for studies which combine the fine-grained analysis of a relatively homogeneous group of patients with the statistical power of larger population-based studies. We are currently using a record-linkage approach in Tayside in an attempt to combine some of the virtues of the current study with the advantages of a larger sample in which referral bias will

not apply. Another approach would be to look at decision making as well as outcome. It is possible that the adverse effects of comorbidity, and perhaps deprivation, are not mediated by direct mechanisms but are the result of the influence of these factors upon oncologists' decision making.

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