Survival of patients with colorectal cancer complicating ulcerative colitis

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SUMMARY The crude five year survival of patients with colorectal cancer complicating ulcerative colitis in a large series of patients under long term review has, for the first time, been compared with the survival of patients with colorectal cancer in the general population (West Midlands region) from which the colitic patients were drawn. Thirty five cases of colorectal cancer were diagnosed in 676 patients with ulcerative colitis between 1944 and 1976. An actuarial five year survival curve was computed for the colitic and non-colitic patients with colorectal cancer. In ulcerative colitis patients with cancer the five year survival was 33-5% (range 16-9–50-1%) compared with 32-6% (28-2–37-0%) in the non-colitic cancer patients drawn from the relevant general population. Overall the prognosis is much better than earlier reports suggest. It is perhaps disappointing that in a closely monitored group the outcome is only as good as that in the general population. Surveillance programmes should improve the outcome in those patients with ulcerative colitis who accept the need for regular review.

Patients with extensive ulcerative colitis for 10 years or more carry an increased risk of developing colorectal cancer. Early reports suggested that these patients had a poor prognosis. None of the 20 cases of colorectal cancer complicating ulcerative colitis reported by Bargen from the Mayo Clinic survived five years, 12 of them dying in the early postoperative period. Two further studies from the same centre reported a five year survival of 3%. In 1959 Slaney and Brooke calculated a five year survival of 18-6% from an analysis of all cases of colorectal cancer reported in the literature. This was a selected analysis as only 112 of the 468 cancers reported included sufficient data for estimating the five year survival.

Recent reports using the method of matched controls suggest that the five year survival from colorectal cancer complicating ulcerative colitis is of the order of 40% and not significantly different from the outcome of colorectal cancer arising de novo in the general population. In these analyses ulcerative colitis patients developing colorectal cancer were matched for age, sex, site of disease, and Dukes’ staging with non-colitic cancer controls (Table 1).

An even better survival was reported by Ritchie for colorectal cancer in both colitic and non-colitic groups. The control population used were patients with colorectal cancer but no evidence of colitis presenting at St Mark’s Hospital over the same period as the ulcerative colitis patients with colorectal cancer (Table 1).

Hulten and his colleagues showed a poor survival in both colitic and non-colitic cancers in an analysis confined to patients developing cancer before 40 years of age. The poor outlook with 12% five year survival in colitic cancers and 25% in controls of non-colitic cancers is surprising. In a large selected series of 951 such young patients developing colorectal cancer below 40 years of age the crude five year survival was 32%, which is similar to the survival reported from colorectal cancer in the general population.

In this study we have examined the actuarial five year survival for patients with colorectal cancer complicating ulcerative colitis in a large series under long term review and for the first time compared this with the outcome in patients with colorectal cancer (matched for age) in the general population from which the colitic patients were drawn.
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Table 1  Crude five year survival in patients with colorectal cancer complicating ulcerative colitis (UC). Summary of reported studies

<table>
<thead>
<tr>
<th>Study</th>
<th>UC patients with colorectal cancer (no)</th>
<th>Mean interval symptoms of UC to diagnosis of cancer (years)</th>
<th>Crude five year survival %</th>
<th>Patients with distant metastases on referral N %</th>
<th>Incidental with multiple cancer N %</th>
<th>Cancers discovered at operation N %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hughes et al. 1978</td>
<td>29</td>
<td>19-6</td>
<td>55-1</td>
<td>NK</td>
<td>4 14</td>
<td>NK</td>
</tr>
<tr>
<td>Lavery et al. 1982</td>
<td>79</td>
<td>17</td>
<td>41-0</td>
<td>28 35</td>
<td>3 4</td>
<td>19 24</td>
</tr>
<tr>
<td>van Heerden and Beart' 1980</td>
<td>70</td>
<td>17-1</td>
<td>41-7</td>
<td>17 24</td>
<td>16 23</td>
<td>14 20</td>
</tr>
<tr>
<td>Ritchie et al. 1981</td>
<td>67</td>
<td>10</td>
<td>65-1</td>
<td>19 29</td>
<td>15 26</td>
<td>NK</td>
</tr>
<tr>
<td>Present series</td>
<td>35</td>
<td>19-7</td>
<td>33-5</td>
<td>8 28*</td>
<td>4 11-4</td>
<td>10 29</td>
</tr>
</tbody>
</table>

* Data not available in six of 35 cancers. NK = not known.

Methods

Patients
Thirty five cases of colorectal cancer were diagnosed among 676 patients with ulcerative colitis under the care of Dr W T Cooke and Professor Bryan Brooke at the Queen Elizabeth and General Hospitals, Birmingham, between the years 1944-1976 and constitute the series under review. All patients who developed colorectal cancer had previous barium enema evidence of extensive colitis and no examples of colorectal cancer complicating left sided colitis or proctitis were seen. Twelve patients were referred with established cancer. Ten cases were ‘non-symptomatic’ in that they were only diagnosed by histological examination of resected specimens in patients undergoing panproctocolectomy for symptomatic colitis. Thirteen cancers were diagnosed in patients after they had been under review for at least one year. The clinical details have been summarised elsewhere. The distribution of the colorectal cancers is shown in Figure 1.

Statistical Method
An actuarial five year survival curve was computed for the 35 patients with colorectal cancer. The median age at diagnosis was 45-49 years. For comparison, therefore, men and women aged 45-49 years registered at the Birmingham and West Midland Cancer Registry between 1962-1967 were selected and analysed in the same way.

Results
The mean age at diagnosis of cancer in patients with ulcerative colitis was 47-5 years (range 33-70 years). The actuarial five year survival was 33-5% (95% confidence limits 16-9-50-1%).

The comparable figure for the general population at five years was 32-6% (95% confidence limits 28-2-37-0%) (Table 2).

The percentage survival with time of patients with colorectal cancer complicating ulcerative colitis compared with the general population is shown in Figure 2.

The five year survival rate between cases and controls was not significantly different (33-5% and 32-6% respectively).

Dukes' Classification
There was sufficient histological evidence to establish the Dukes' classification in 22 of the 35 cancers. Three cancers were multicentric in origin and were

Fig. 1  Macroscopic site of colorectal cancer (n=35) identified among 676 patients with ulcerative colitis from the Birmingham series 1944-1976.
excluded from the Dukes’ classification. Of the remaining 19 cancers four were Dukes’ A, five Dukes’ B, three Dukes’ C, and seven had distant metastases. The proportion of Dukes’ A lesions was higher in the colorectal cancers detected unexpectedly and their survival much better than that observed in the interval cancers detected during the period of follow up.

The degree of histological differentiation was assessed in 27 colorectal cancer. Four were well differentiated (15%), nine moderately well differentiated (33%), and 14 poorly differentiated (52%).

Discussion

Matched control studies have shown that there is no significant difference in survival between patients with colorectal cancer complicating ulcerative colitis who are diagnosed and treated at the same Dukes’ stage as non-colitic patients developing colorectal cancer. The crude five year survival in reported studies varied between 33–65%.\(^5\)\(^-\)\(^12\) The outcome in the present series is similar.

Poor differentiation in the colorectal cancers complicating ulcerative colitis does not seem significantly to affect the outcome. There was a high proportion of poorly differentiated cancers in both this and other series of patients with ulcerative colitis.\(^10\)\(^-\)\(^12\) Despite the high proportion of less well differentiated cancers patients with Dukes’ A lesion complicating ulcerative colitis survived equally well to non-colitic matched controls.\(^9\)\(^-\)\(^11\)

It is difficult to assess the effect on survival of the increased incidence of multiple cancers in the ulcerative colitic group as most authors exclude such patients from their analysis of survival. The incidence of multiple cancers in patients with ulcerative colitis varies from 4–26% in reported series (Table 1). The proportion of patients with multiple cancers in this series was 11-4% whereas the incidence of multiple cancers for non-colitic cancers was 2-3-5%.\(^12\)\(^-\)\(^14\) Presumably the survival of patients with multiple synchronous cancers will be determined by the Dukes’ staging of the most advanced lesion at the time of diagnosis.

The survival among patients with colorectal cancer complicating colitis and those with non-colitic cancers from the general population will depend on the proportions of Dukes’ A, B, C, and distant metastases present at the time of diagnosis in each group. The observation that the survival curves in the two groups are similar (Fig. 2) in our series suggests that the proportion of Dukes’ A, B, C, and distant metastases at diagnosis was the same in the ulcerative colitis patients as in the general population. Certainly in other series the proportion of patients presenting with distant metastases at diagnosis in colitic and non-colitic colorectal cancer is around 30% for the colitic group and 25% for the general population\(^12\)\(^-\)\(^14\) (Table 1).
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This study and earlier reports in the literature suggest that colorectal cancer complicating ulcerative colitis are not yet being diagnosed any earlier than in the population at large. This is surprising as patients with ulcerative colitis are usually under regular review and many cancers are diagnosed incidentally on histological examination of resected specimens at panproctocolectomy for symptomatic colitis (Table 1). In our analysis all but one of the patients found to have colorectal cancer incidentally at panproctocolectomy for symptomatic colitis survived for more than 12 years. Colorectal cancers diagnosed incidentally at surgery, however, are not always early lesions. Lavery\textsuperscript{11} reported 19 such cancers of which six were carcinoma \textit{in situ}, five Dukes’ A, six Dukes’ B, and two Dukes’ C lesions.

Certain factors militate against early diagnosis of cancer in ulcerative colitis, however. For example, patients with extensive colitis may become asymptomatic and are lost to follow up, only to return many years later with symptomatic cancer. Some patients have only mild colitic symptoms and are only seen in hospital for the first time with colorectal cancer. Finally, the symptoms of colorectal cancer – for example, rectal bleeding – may not occasion alarm in colitic patients whereas such symptoms would alert the individual experiencing them for the first time to seek medical advice.

There is a small subgroup of patients with extensive disease of longstanding in any series of ulcerative colitis patients who are particularly at risk of developing colorectal cancer and must be considered either for careful monitoring or elective panproctocolectomy especially if their colitis started when they were young.\textsuperscript{4, 15} One recent report estimates the cumulative risk at more than 30\% at 25 years and more than 40\% in patients with early onset colitis.\textsuperscript{3}

Lennard-Jones and his colleagues have shown that colorectal cancer can be diagnosed at an early stage with a good prognosis by careful monitoring of the patients with extensive colitis by colonoscopy and multiple biopsies to detect dysplasia.\textsuperscript{16} Recent advances in colonoscopic biopsy of specific high-risk areas may make even earlier diagnosis of cancer feasible.\textsuperscript{17}

The risk figures though widely quoted, however, have wide confidence limits. For example, the cumulative cancer risk of 34\% at 25 years is based on only 73 patient years at risk and two colorectal cancers.\textsuperscript{3}

In order to decide whether to continue conservative management or advise elective panproctocolectomy it is important to establish the colorectal cancer risk experienced in a large cohort of patients with ulcerative colitis under long term review with defined criteria of entry. We are currently undertaking such a multicentre study.

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