Relationship between disease activity indices and colonoscopic findings in patients with colonic inflammatory bowel disease

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SUMMARY   The Crohn's disease activity index, a similar index devised for patients with ulcerative colitis, and other commonly used laboratory indicators of disease activity have been studied in 50 patients with colonic inflammatory bowel disease undergoing routine colonoscopic assessment and compared with the histological extent and activity of disease. There was only poor correlation between the colonoscopic or histological findings and the indices of disease activity studied, showing that these are not reliable measures of disease activity or extent at the tissue level.

Because inflammatory bowel disease is a relapsing disorder in which the clinical presentation depends on a number of different factors, not least the personality of the patient, it is very difficult to assess disease activity accurately. Although this is of no great relevance in everyday management, as this depends more on general wellbeing, it is important in the design of any study aiming to show therapeutic benefit. Thus, a number of clinical indices have been developed to try to standardise disease assessment. These include measurement of haemoglobin, white blood cell count, platelet count, ESR, serum albumin concentrations and other acute phase reactants including C-reactive protein and Orosomucoid.[1-4] From these and from clinical observations, a Crohn's disease activity index (CDAI) has been devised[5] and simplified,[6] and similar systems devised for use in patients with ulcerative colitis.[7 8] Because increasing reliance has been placed on these measurements in trials involving patients with inflammatory bowel disease, we have attempted to discover how well they relate to the extent or severity of disease in patients with colonic inflammatory bowel disease undergoing colonoscopy.

Methods

PATIENTS
Twenty eight patients with ulcerative colitis and 22

with Crohn's colitis undergoing routine colonoscopic assessment were studied. Patients with evidence of small bowel disease on radiological studies were excluded. Before colonoscopy, blood was taken for full blood count, ESR, platelet count, albumin and C-reactive protein concentrations using established techniques. A full Crohn's disease activity index[5] and a recently described simplified index[6] was scored for patients with Crohn's colitis.

We devised a scoring system for ulcerative colitis, based on that of previous studies.[7 8] This involved giving patients a score of one if each of the following was present: general malaise, abdominal pain, rectal bleeding, anorexia, abdominal tenderness, complications and pyrexia. This was added to the number of bowel movements a day (averaged over one week). At colonoscopy the colon was divided into six notional sections defined as the caecal area, the hepatic flexure area, splenic flexure area, descending colon, sigmoid colon, and rectum. Each of these sections was assessed for the presence or absence of macroscopic disease by one of three experienced colonoscopists on a scale of 0–3. On this scale, 0 was normal, 1 was defined as mild inflammation with loss of vascular pattern plus or minus granularity or localised apthus ulcers, 2 as severe inflammation with contact bleeding and 3 as more severe disease with friability, ulcers or spontaneous bleeding. At least one biopsy was taken from the area of maximum inflammation within the notional section, and the histological extent of disease assessed by one histopathologist with a special interest in gastrointestinal diseases who was unaware of the

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colonoscopic appearances or the clinical activity index. Each biopsy was graded on a scale of 0–4. Zero was graded as being normal, 1 as showing mild oedema and inflammation in the lamina propria, 2 as crypt abscess formation and inflammation in the lamina propria, 3 as more severe inflammation with destructive crypt abscesses plus or minus granulomata and 4 as more severe inflammation with active ulceration. A total microscopic and macroscopic score for each patient was then achieved by adding the individual scores of the six biopsies together (maximum 24 and 18 respectively). Eighteen patients were also assessed using a [111]Indium labelled leucocyte imaging technique as described elsewhere.[9]

The study was approved by the district ethical committee and all patients gave written consent for the study. Linear regression analysis was used to assess the results. Probability values of <5% were considered to be significant.

Results

In patients with Crohn's colitis there was excellent correlation between the simple activity index and the Crohn's disease activity index (R=0·88, p<0·01). Comparison of the microscopic score and the macroscopic score with the clinical activity index in patients with Crohn's colitis is shown in Figure 1 and that for ulcerative colitis in Figure 2. Significant but not close correlation between macroscopic score and the simple index for patients with Crohn's disease was found (R=0·68, p<0·05). There was no significant correlation between microscopic score and index score for Crohn's colitis or either macroscopic or microscopic score and index score in ulcerative colitis. In both Crohn's colitis and ulcerative colitis the macroscopic appearances underestimated the histological extent of the disease. In the
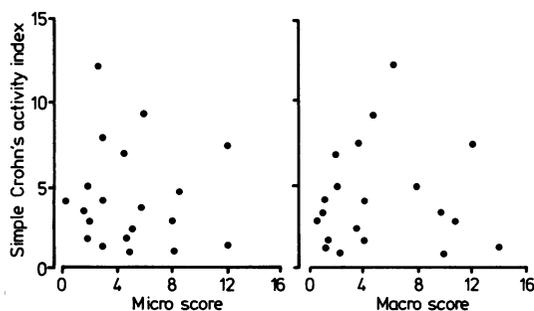
patients with Crohn's colitis there was also good correlation between the microscopic and the macroscopic scores, (R=0·76, p<0·001), but with no correlation of microscopic score with C-reactive protein (R=0·34), ESR (R=0·25), white blood count (R=0·23), platelet count (R=0·37) or albumin concentration (R=0·028). In patients with ulcerative colitis there was good correlation between micro- and macroscopic score (R=0·61, p<0·001), but no significant correlation of microscopic score with C-reactive protein (R=0·01), ESR (R=0·13), white blood count (R=0·131), platelet count (R=13) or albumin concentration (R=0·028).

In both ulcerative colitis and Crohn's colitis there was no significant correlation of the above variables with macroscopic score and no correlation between the maximum severity at any one site macroscopically or microscopically and the clinical or laboratory indices. The results of the [111]Indium labelled leucocyte imaging are shown in the Table.

Discussion

The concept of the macroscopic and microscopic scores that we have used can be criticised because of the difficulties in interpretation of the sometimes
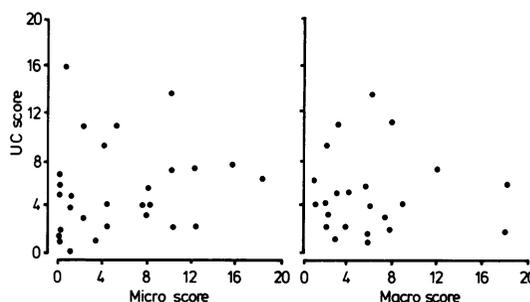
Fig. 2   *Ulcerative colitis clinical score correlated against histology score (micro) and endoscopic macroscopy score (macro).*

Fig. 1   *Simple Crohn's disease activity[6] correlated against histology score (micro) and endoscopic macroscopy score (macro).*

Table   *Result of [111]Indium leucocyte imaging in 18 patients. All 'active' patients were hospitalised, others were outpatients*

Disease activity	Patients (no)	Image result	
		Positive	Negative
Quiescent	6	0	6
Moderately active	6	2	4
Active	6	5	1

patchy changes within the notional colonic sites and even within the biopsies. To keep these to a minimum, both assessments were made by a single colonoscopist (GH) and pathologist (C du B) and both were achieved without knowledge of the clinical index scores or laboratory results. This avoids as far as possible the known observer variation in the assessment of sigmoidoscopic findings.[10] [11] The clinical score for ulcerative colitis has not been fully evaluated in the same way as that for Crohn's disease, but we felt that it was a reasonable means of assessing clinical status.

Our failure to show any close relationship between the histological or macroscopic appearances of the colon and the various clinical or laboratory indices of disease activity studied is disappointing. Many of the patients being investigated were on medication, which may have modified clinical expression, and it is possible that if patients on no treatment had been studied the relationship may have been closer. The importance of these findings is that they show that clinical and laboratory indices may not represent changes at tissue level. The difference between our own and previous studies[1–3] is that we have studied macroscopic and histological appearances of the whole colon, whereas previous ones were based on sigmoidoscopic biopsies and radiological findings. Our conclusions are compatible with those of a recent study in patients with small bowel Crohn's disease which showed that these indices were not good indicators of the severity or extent of disease.[12]

All gastroenterologists will be familiar with patients with inflammatory bowel disease with evidence of extensive disease who remain remarkably well and patients with very severe symptoms but very limited disease. This observation, together with our findings, strongly suggests that neglected factors such as stress, coexistent infection, personality and motility disorders, may play important roles in disease presentation.

The management of inflammatory bowel disease depends mainly on the clinical assessment of the patient's wellbeing, and is only aided by varying degree by the indices of activity studied. While these may be helpful indicators of disease activity, our study shows that they are of limited value as a means of assessing disease extent or severity at tissue level. We believe that this suggests that the emphasis placed on them in therapeutic trials is misplaced. As colonoscopy in these patients is often easy to do, it is possible that, in addition to these clinical indices currently used, a histological or macroscopic assessment along the lines suggested in this study could be used when assessing therapeutic benefit. In this way it would be possible to know the true effects of the agents on the disease at tissue level as well as on symptomatology.

Our results with [111]Indium labelled leucocyte imaging are preliminary and not as encouraging as some previous studies.[13–15] Although a good indicator of disease in those with clinically very severe disease, they were often normal in patients with clinically inactive disease, even when these had extensive histological involvement. Indeed, four of the six patients with inactive disease but negative scans had histological evidence of total colitis and three had microscopic scores of 12 or more. The difference between this study and those previously is probably explained both by methodological differences and by the observation that our patients were mainly outpatients with less severe disease than many included in previous reports. These preliminary results and those reported elsewhere showing good correlation with the imaging and clinical disease activity index[15] lead us to suggest that [111]Indium leucocyte imaging, while being another good indicator of clinical disease activity, is also unlikely to be a sensitive representation of disease at tissue level.

We conclude that the clinical and laboratory indices studied are a relatively inaccurate means of assessing disease severity at tissue level. They provide useful information regarding future disease course in patients who, although clinically well, have markedly abnormal results, but may well be near normal in patients with quite extensive and severe disease. Repeated macroscopic and microscopic assessment should be considered in the design of future studies in patients with colonic inflammatory bowel disease.

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