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Ulcerative Colitis Activity Index: a Useful Prognostic Factor for Predicting Ulcerative Colitis Outcome

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We evaluated the usefulness of various parameters in predicting the prognosis of ulcerative colitis. The records of 73 patients with ulcerative colitis were examined retrospectively. Patients were divided into two groups according to whether they had received only 5-aminosalicylic acid (5-ASA; *n* = 26) or glucocorticoids and/or azathioprine with or without 5-ASA (*n* = 47). The disease extent, endoscopic activity and ulcerative colitis activity index (UCAI) before therapy were recorded, together with the disease outcome. No statistically significant differences in outcome were observed in relation to therapy group, disease extent or endoscopic activity. UCAI had a significant effect on outcome, however: patients with lower UCAI values were more likely to remain in remission and less likely to require urgent surgery or experience a fatal outcome than those with higher UCAI values. This difference was apparent in both treatment groups. Thus a high pre-treatment UCAI may indicate a worse outcome.

KEY WORDS: Ulcerative colitis activity index; Predictive factor; Ulcerative colitis; Outcome

Introduction

Ulcerative colitis (UC) is a chronic inflammatory disease that has three main clinical manifestations.[1] Most patients suffer a chronic intermittent course, with remissions between the exacerbations, whereas in other patients the disease is chronically active but tolerable with multiple flare-ups. More rarely, in approximately 5 – 10% of patients, UC has a fulminant course. These patients may suffer rapid weight loss due to poor nutritional status and the condition can be fatal. Such patients usually require urgent colectomy.

When UC is first diagnosed it is usually impossible to predict the clinical disease course. Many factors influence the outcome of UC, including the extent of the disease, endoscopic activity, clinical activity, the age of the patient, the treatment modalities used and patient compliance. Other factors that have a significant impact on the prognosis of this multifactorial disease include smoking, non-steroidal anti-inflammatory drugs, appendectomy and irritable bowel syndrome.[2]

In this retrospective study we aimed to evaluate the influence of a number of clinical, laboratory and endoscopic

parameters of activity and therapeutic regimens on the outcome of UC.

Patients and methods

PATIENTS

The medical records of patients with UC admitted to the Department of Gastroenterology (Medical Faculty, Uludag University) during the previous 10 years were examined retrospectively. Patients diagnosed during the past year were excluded from the study due to an insufficient follow-up period. Potential study participants were contacted by telephone to gain consent for inclusion in the study and obtain details of their current clinical status. The Uludag University Medical Faculty Ethics Committee approved the study.

The patients were divided into two groups according to the treatment they had received. Patients treated only with 5-aminosalicylic acid (5-ASA) preparations (orally or with enemas) were classified as group 1, while those who had received immunosuppressive drugs (corticosteroids and/or azathioprine), either alone or in combination with 5-ASA preparations, were classified as group 2. The length of therapy administration was not taken into account.

The age, gender and disease duration were recorded for each patient.

ASSESSMENT OF EXTENT OF DISEASE

The extent of the disease was assessed on the basis of anatomical involvement, and was classified as either left-sided colitis, defined as involvement of colonic segments up to the splenic flexure (limited disease), or pancolitis, defined as involvement as far as the caecum (extensive disease). The extent of disease was taken to be the greatest extent recorded by colonoscopy at any stage in the course of the illness.

ASSESSMENT OF ENDOSCOPIC ACTIVITY

Endoscopic activity was classified according to the appearance of the disease lesions and mucosa: grade 1 (mild), oedematous, erythematous, smooth and glistening mucosa with masking of the normal pattern; grade 2 (moderate), oedematous, erythematous mucosa with a fine granular surface, with sporadic areas of spontaneous mucosal haemorrhage and friability to gentle endoscopic pressure; and grade 3 (severe), as oedematous, erythematous, granular and friable mucosa with spontaneous haemorrhage and mucopus in the lumen, and occasional mucosal ulceration.[3] This grading occurred before treatment commenced.

CLINICAL ACTIVITY INDEX

Several UC clinical activity indexes (UCAIs) have been defined in the literature.[4] They usually incorporate frequency of bowel habits and rectal bleeding as well as haemoglobin, albumin and erythrocyte sedimentation rate (ESR) values. The present study used the UCAI as defined by Seo *et al.*,[5] which was calculated using parameters recorded during the patient's first attack of UC as follows:

UCAI = [60 × no. of bloody stools per day] + [13 × no. of bowel movements per day] + [0.5 × ESR (mm/h)] – [4 × haemoglobin (g/dl)] – [15 × serum albumin (g/dl)] + 200.

ASSESSMENT OF CLINICAL COURSE

The clinical course of UC in each patient was classified into one of the following three subgroups: remission, chronic or fulminant. In this study, remission was defined as a symptom-free period of at least a year.

A chronic intermittent UC disease course is marked by long periods of quiescence interspersed with acute attacks lasting weeks to months, while a chronic continuous course presents with persistent symptoms

and no periods of remission, or a requirement for continuous treatment with steroids to maintain remission. In this study, these two chronic patterns were both classified as chronic.

A fulminant course was defined as having frequent loose stools (greater than 10 per day) with severe cramps, fever up to 39.5 °C and bleeding often necessitating a blood transfusion.

STATISTICAL ANALYSIS

Non-parametric data with two or more grouping variables were compared using the Mann–Whitney test and the Kruskal–Wallis test, respectively. Numerical categorical variables were analysed using the Pearson χ^2 test, and survival analyses were performed using the Kaplan–Meier test. A *P*-value < 0.05 was considered to be statistically significant. Data entry and statistical analyses were performed using SPSS for Windows (Version 11.5, SPSS Inc., Chicago, IL, USA).

Results

A total of 73 patients (38 males and 35 females) were included in the study. The mean (± SEM) age was 45.2 ± 1.8 years (range 19 – 86 years) and the mean (± SEM) disease duration was 76.5 ± 6.0 months. Table 1 summarizes the patient characteristics in both treatment groups.

TABLE 1:
Characteristics of patients with ulcerative colitis included in this study of factors affecting clinical outcome

	Therapy group		
Parameter	**5-ASA**	**Corticosteroids and/or azathioprine with and without 5-ASA**	***P*-value**
No. of patients	26	47	
Age (y)[a]	50.7 ± 3.1	40.5 ± 2.48	0.015[b]
Gender			NS[c]
Male	12	26	
Female	14	21	
Disease duration (months)[a]	78.5 ± 9.5	70.8 ± 8.6	NS[b]
Extent of disease (%)			0.0001[c]
Left-sided colitis	82	31	
Pancolitis	18	69	
Endoscopic disease activity (%)			NS[c]
Mild	22	10	
Moderate	31	32	
Severe	47	58	
UCAI[a]	526.2 ± 67.0	741.8 ± 87.3	NS[b]

5-ASA, 5-aminosalicylic acid; UCAI, ulcerative colitis activity index, as used by Seo *et al*;[5] NS, not significant. [a]Mean ± SEM. [b]Mann–Whitney U-test. [c]χ^2 test.

The effect of therapy, extent of disease, endoscopic activity and UCAI on disease outcome are shown in Fig. 1. In group 1, 56% of patients were in complete remission, while 44% of patients demonstrated a chronic course (Fig. 1A). There were no fulminant cases or deaths in this group. Remission and chronic course rates in group 2 were 30% and 52%, respectively, while a fulminant course was observed in eight cases (18%), three of whom had died. There was no statistically significant difference in outcome between the therapy groups at the end of the period studied.

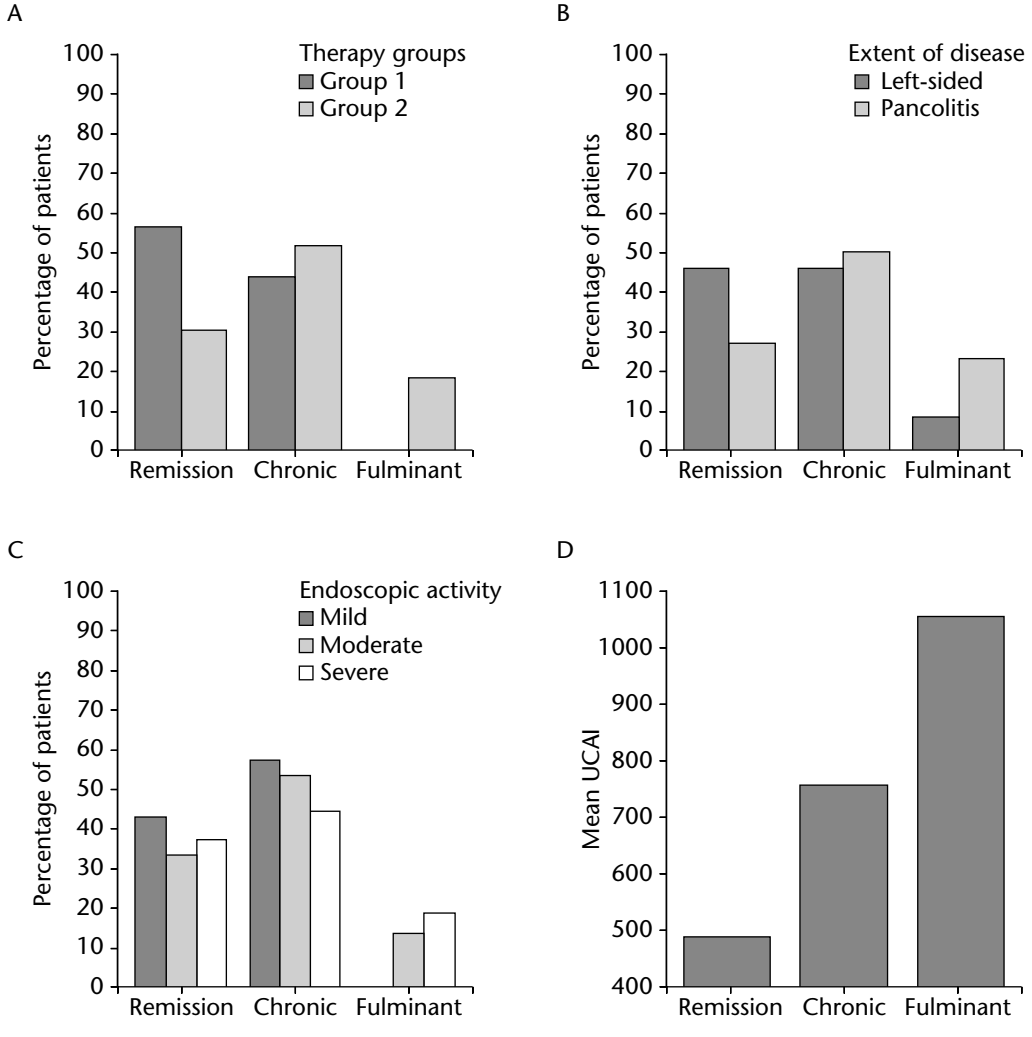

FIGURE 1: Effect of therapy (A), extent of disease (B), endoscopic activity (C) and ulcerative colitis activity index (UCAI; D) on the disease course in 73 patients with ulcerative colitis. Group 1 received 5-aminosalicylic acid (5-ASA) therapy and group 2 received corticosteroids and/or azathioprine with and without 5-ASA

Remission and chronic course rates were equal (46%) in patients with left-sided colitis, while a fulminant course was encountered in the remaining 8% (Fig. 1B). Among the patients with pancolitis, 50% experienced a chronic course. The remission rate was lower (27%) and the fulminant course rate much higher (23%) than in patients with left-sided colitis. These differences were not statistically significant.

Remission and chronic course rates were very similar in all patients, irrespective of endoscopic activity (Fig. 1C). The differences in outcome related to endoscopic activity were not statistically significant.

The mean pre-treatment UCAI was 487, 755 and 1054 in patients in remission and with a chronic or fulminant course, respectively (Fig. 1D). Analysis using the Kruskal–Wallis test demonstrated a significant difference between these three courses ($P = 0.003$). Comparison of each pair of outcomes showed that the mean pre-treatment UCAI of patients in remission was significantly lower than that of the other two groups ($P = 0.017$ for remission compared with chronic and $P = 0.001$ for remission compared with fulminant, Mann–Whitney test). There was no significant difference between the pre-treatment UCAI for the chronic and fulminant course patients.

Kaplan–Meier analyses were performed to determine the survival of UC patients (Fig. 2). The end-point used for survival was a fulminant course requiring total colectomy or causing death. There were no significant differences in survival according to therapy groups (Fig. 2A), extent of disease (Fig. 2B) or endoscopic activity (Fig. 2C).

A number of Kaplan–Meier analyses were performed to assess the effect of UCAI on survival. The median UCAI value of our subjects (i.e. 561) was used to separate them into two sub-groups. Using this distribution, a significant difference was observed between the outcomes of patients with a low UCAI and those with a high UCAI ($P = 0.0226$; Fig. 2D). Patients with lower UCAI values at the beginning of their disease were more likely to remain in remission and were less likely to require urgent surgery or experience a fatal outcome than those with higher UCAI values. Thus a high pre-treatment UCAI may indicate a worse outcome.

When patients were divided into three equal subgroups of low, moderate and high pre-treatment UCAI values, similar results were obtained (Fig. 2E; $P = 0.0283$). In addition, when the survival of patients with a low or high UCAI within each therapy group was compared, a significant difference was again found (Fig. 2F; $P = 0.0251$): there was a higher survival rate in patients with a low UCAI than in those with a high UCAI in both groups.

Discussion

Until recently, many authors have considered the extent of colonic involvement to be the main predictive factor for UC outcome. It has been demonstrated that in approximately one third to a half of patients, disease confined to the rectum (proctitis) eventually spreads to involve the entire colon, however.[6] One third of patients with left-sided colitis will also progress to pancolitis within 7 years.[7] It is, therefore, now generally accepted that the extent of colonic involvement in UC is not constant and may change over time, so predicting the outcome based on the current anatomical location is unreliable.

Other possible parameters with the potential to influence UC outcome are clinical and endoscopic activity; several clinical and endoscopic activity indexes are available in the literature. Gomes *et al.*[8] reported that these two parameters do not correlate well, whereas two other reports have shown a correlation between a clinical

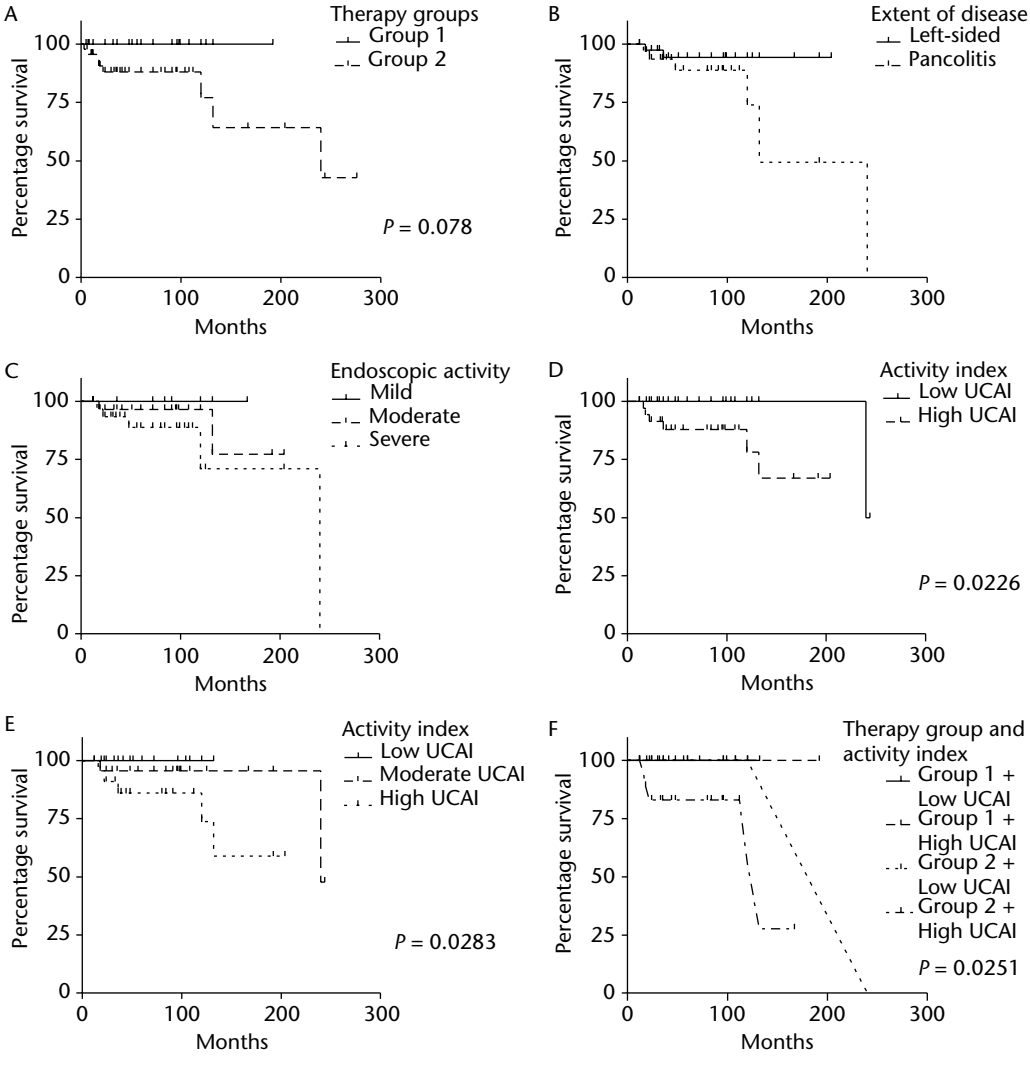

FIGURE 2: Kaplan–Meier plots of survival in patients with ulcerative colitis according to various parameters, using the end-point of a fulminant course requiring total colectomy or causing death. Group 1 (26 patients) was treated with 5-aminosalicylic acid (5-ASA) only; Group 2 (47 patients) was treated with corticosteroids and/or azathioprine with or without 5-ASA. UCAI, ulcerative colitis activity index

activity index and endoscopic activity.[9,10] This issue is yet to be clarified and there is insufficient knowledge about the relationship between endoscopic activity and the prognosis of UC. No correlation between endoscopic activity and the course of UC was observed in our study.

Sinclair *et al.*[11] reported that neither the severity of the first attack nor the extent of colonic involvement at the time of diagnosis has any effect on the frequency of recurrence; the severity and extent of the disease at initial presentation may affect the likelihood and timing of subsequent

colectomy, however. For those with severe disease at initial presentation, the rate of colectomy was about 50% within 2 years; in contrast, fewer than 10% of patients who initially presented with mild disease or proctitis alone had undergone colectomy after 10 years.[11] In another epidemiological study, it was similarly demonstrated that the need for surgery for UC was influenced by the extent of colonic involvement at initial diagnosis and the severity of initial symptoms.[12] These results emphasize the importance of first attack severity (clinical activity) for prognosis.

Glucocorticoid treatment can significantly reduce mortality in patients with severe UC.[13] 5-ASA preparations are generally used in limited disease with mild to moderate clinical activity and are especially useful for maintaining remission, whereas steroids tend to be used in more severe and extensive UC patterns. The choice of therapy largely depends on clinical preference, however. In our study, no difference was observed in the disease course of patients in different therapy groups. This may have been due to a tendency to prescribe immunosuppressive therapy to patients with severe clinical activity and/or pancolitis. There was a significant difference in the disease course patterns of patients with a low or high UCAI in both therapy groups, suggesting that the UCAI may be an important predictive factor of survival, even when different therapeutic regimens are used.

Patients with UC have a higher risk of colorectal cancer than the general population.[14] It has been suggested that this risk is related to the extent and duration of disease but not its activity. We did not observe any cases of colonic malignancy in the present study, and it is therefore not possible to comment on the possible relationship between UCAI and colorectal cancer.

Our study suggests that the UCAI at the onset of UC is predictive of its course: when the UCAI is high, a severe course is likely, while a low UCAI suggests that the course will be uneventful. Different therapeutic regimens do not seem to modify the long-term survival rate. Furthermore, the anatomical location and extent of UC and endoscopic activity varied widely during the study period and did not significantly influence survival. These findings suggest that surgical options to eliminate colonic complications should be considered earlier in patients with UC who have a high UCAI.

Conflicts of interest

No conflicts of interest were declared in relation to this article.

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