THE RELATIONSHIP BETWEEN CLINICAL AND COLONOSCOPIC FEATURES IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS

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Abstract:
Objective: The objective of this study was to advance a classification to mark disease activity based on clinical manifestations in patients with active ulcerative colitis. Another objective was to assess the association of this score with endoscopic disease rigorousness as measured by colonoscopy.
Methods: In a pilot study of 43 patients, nine clinical variables were examined by uni-variate analysis.The study was carried in Surgical Department of Allied Hospital Faislabad There were 6 causes which correlated with disease severity, patient's age, well-being, defecation frequency, stool, extra intestinal manifestations (Ext) and hemoglobin (Hb). Analysis concluded the generation of a new activity index to predict the severity of the disease. This index was performed on 88 patients and validated the definite diagnosis of ulcerative colitis based on previous histological examination.
Results: The activity index is derived as follows: (18×bloody stool) + (20×defecation frequency) + (5×Ext) + (15×Hb)- (well-being×17) + (age×2) + 158. Values less than 280 were considered mild, amid 280-310 were considered moderate, and higher than 310 indicated severe disease. This model proved to be correct in almost 71% of the patient's included in the study.
Conclusion: The index results of our study are found to be helpful in considering this technique as useful in evaluating the disease severity levels non-invasively.

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INTRODUCTION:

Ulcerative colitis (UC) disease activity is assessed using evaluation which is symptomatic in nature including physical examination, lab tests, and colonoscopic evaluation.[1] In the absence of a validated gold standard for disease activity, several different indices have been advocated.[2,3] It's been attempted to validate these measures of disease activity in clinical trials. However, all these indices include colonoscopy, [4-8] which adds to patient discomfort and cost. Hence, developing a marker of disease activity based solely on readily assessable clinical manifestations was undertaken.[9,10,11] However, the relationship of scores on such clinical activity indices with the degree of endoscopic activity remains controversial.

We tried to design a new activity index (AI) for UC based on simple clinical manifestations and laboratory findings, and examined its relationship with the endoscopic severity of the disease as assessed at colonoscopy.

METHODS:

In a pilot study, we examined the relationship between clinical and laboratory variables and colonoscopic findings in 43 consecutive patients (mean age 34.2 [16.5] years, range: 17 to 68) with UC, using simple regression analysis. Only patients who were included in the study had definite histological diagnosis of UC with active disease as defined by the St. Mark's index.[5] The selected variables had been used in previous studies in UC,[5,8] and included age, general well-being (0-3), abdominal pain or tenderness (0-1), defecation frequency (0-3), bloody stool (0-2), extraintestinal (Ext) manifestations (eye inflammation, arthralgia, oral ulceration, related skin lesions) (0-2), weight (0-1), Hb (0-3) and ESR (0-1) (Table 1). The significant criteria (Table 2) were compared with disease se- verity and extent as determined by endoscopy.

Next, we performed multiple stepwise regression analysis, with disease severity and extent as the dependent variables and clinical and laboratory parameters as independent variables. We tried to devise two equations (for disease extent and severity) as below: Index = $(K1 \times Ext) + (K2 \times Hb) + \ldots$ Using Tukey's test we estimated the cut-off values for classification of disease severity and extent.

Subsequent comparison of the designated index was made on a series of 88 patients (mean age 39 [15.4] years, range: 15 to 75; 48 female) with the extent and severity of colitis based on colonoscopy. That is how calculation of the accuracy index in predicting colonoscopic severity and extent of disease was completed in the study.

The assessment of colonoscopy was done using a modification of Baron's criteria.[12] Grades 0 and 1 were classified as mild, 2 and 3 as moderate, and 4 as severe disease. The extent of colitis determined by colonoscopy was classified as *distal colitis* (inflammation not extending proximal to the sigmoid-descending junction) *total colitis* (inflammation extending proximal to hepatic flexure), and *left-sided colitis* (extent of involvement in between these categories).[9] Written informed consent was obtained from all patients. The study was approved by the Committee on Ethics of our university.

Statistical analysis

The analyses were done using Spearman's correlation coefficient and one-way analysis of variance (ANOVA) and Tukey's test. $\square^2$ test was used for analysis of incidence considered significant. SPSS for Windows (release 12.0.0) was used for statistical analysis. That showed significant relationship with severity and extent of disease: age, well-being, Hb, defecation frequency, extra intestinal manifestations (Ext), ESR and bloody stool (Table 2). Using these factors in a multiple regression analysis, we obtained the following equations for predicting the severity and extent of the disease:

Extent Index = $(age \times 1)$ + $(well\text{-}being \times 23)$ + $(Hb \times 5)$ + $(defecation\ frequency \times 16)$ - $(Ext \times 6)$ + $(ESR \times 54)$ + 93. Activity Index = $(age \times 2)$ + $(well\text{-}being \times 17)$ + $(Hb \times 15)$ + $(defecation\ frequency \times 20)$ + $(Ext \times 5)$ + $(bloody\ stool \times 18)$ + 158.

Table 1: Definition of clinical and laboratory variables used in calculating indices

Parameter	Score	Severity
Well-being		
Normal	0	Mild
Impaired but able to continue activities	1	Mild
Activity reduced	2	Moderate
Unable to work	3	Severe
Abdominal pain or tenderness		
None	0	Mild
Present	1	Moderate
Defecation frequency (stools/day)		
No diarrhea	0	Mild
<4	1	Mild
5-7	2	Moderate
>8	3	Severe
Bloody stool		
None	0	Mild
Trace	1	Moderate
More than trace	2	Severe
Extraintestinal manifestations		
Absent	0	
1	1	Mild
>1	2	Moderate
Weight loss		
None or <5%	0	Mild/moderate
5% or more	1	Severe
Hemoglobin (g/dL)*		
Normal	0	
10 g/dL to normal range	1	Mild
<10 g/dL	2	Moderate
Transfusion required	3	Severe
ESR <30	0	Mild/moderate
>30	1	Severe
A g e Years	-	-

Normal value: males >13 g/dL,   females >12 g/dL

Table 2: Result of univariate analysis of clinical and labora-tory variables

Clinical manifestation	p value
Well-being	<0.001
Abdominal pain or tenderness	0.427
Defecation frequency	<0.001
Bloody stool	0.048
Extraintestinal manifestations	0.017
Weight loss	0.40
Hemoglobin	0.009
ESR	<0.001
A g e	0.001

Validation of indices

In the validation population of 88 patients, 23 (26.1%) had total colitis, 59 (67%) had left-sided disease, 6 (6.8%) had distal disease. Six patients (6.8%) had grade 1, 15 (17%) had grade 2, 44 (50%) grade 3, and 23 (26.1%) grade 4 activity.

For the suggested activity prediction power index was $R^2 = 0.714$ and for the extent index was $R^2 = 0.289$. The significant relationship between mean activity index and endoscopic severity was significant ($p < 0.05$); values less than 280, between 280 and 310, and greater than 310 corresponded to mild, moderate, and severe disease, respectively. The actual ex- tent of disease and extent index did not show significant correlation ($p = 0.562$) except in patients with distal colitis ($p < 0.0001$). Individuals who had extent index less than 250 had distal colitis.

DISCUSSION:

The first qualitative grading of UC activity was introduced by Truelove and Witts[4] using five criteria of temperature, pulse rate, hemoglobin, erythrocyte sedimentation rate, and bowel frequency. The category of disease activity was mild, moderate and severe. Considerable changes may occur in disease activity without a change in category.[13] To include a wider range of symptoms, examination for abdominal tenderness, Powell-Tuck *et al*[9] developed their index for clinical trials of corticosteroid

treatment and the sigmoidoscopic scoring system was developed by Baron and colleagues.[12] Drossman *et al* shows the importance that a self-assessment of the patient's own health should be included [14] in developing a health status scale for UC based on an extensive questionnaire.

The activity index was able to predict the severity of UC in 71% of patients of the equations that we gathered. However, symptoms, physical signs, hematological and biochemical criteria also the mucosal macroscopic evaluation should be included in the assessment of activity indices which incorporate all of these criteria, but these are cumbersome to use in practice and are not available. [8, 14, 15, 16]

CONCLUSION:

An initial assessment in outpatients, our activity index could be useful to adjust treatment, and in reduction of requirement for colonoscopy. Walmsley *et al*[17] shows that some clinical indices could be used to evaluate the severity of the disease by patients and physicians without the need for colonoscopic or laboratory assessment.

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