Clinical Scoring of Positive Histopathology Findings for Inflammatory Bowel Disease at Four Hospitals in Jakarta

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ABSTRACT

Background: *Inflammatory bowel disease (IBD) in the form of Crohn's disease (CD) or ulcerative colitis (UC) is chronic IBD which still difficult to diagnose and clinically characterized by exacerbation and spontaneous remission. A precise diagnosis is needed and essential for appropriate treatment. Most of internists in Indonesia have to cope with a condition of poorly equipped endoscopic facilities - especially colonoscopy and subsequently refer their patients to endoscopic centers with colonoscopy facilities as well as sending biopsy specimens for histopathology examination. They also should be concerned that it would be expensive, time-consuming, and patients may suffer from considerable distress while waiting for the results of diagnostic confirmation. Therefore, we were interested in studying the clinical scoring for IBD to determine the diagnosis of possible IBD by assessing the combination of clinical reporting aspects, identification of probable IBD and histopathology examination.*

Method: *The study design was cross-sectional. We collected data pertinent to this study from medical records of patients with IBD clinical features at the endoscopic units of four hospitals in Jakarta between 1999 and 2009. Student t-test and logistic regression analysis were used for the statistic examination.*

Results: *Based on colonoscopy examination, there were 213 patients with positive IBD and 173 patients with negative results. Histopathology results were considered as the gold standard in diagnosis of IBD. The mean clinical score was 9 (nine) points. Subjects with positive histopathology findings were significantly had higher average score than those with negative histopathology findings. Using receiver operating characteristic (ROC) curves, we found cut-off score of 10 points with a sensitivity and specificity of 73% and 88% consecutively; while by applying logistic regression analysis, we found odds ratio (OR) of 20 (9.9-40.0).*

Conclusion: *The clinical scoring for IBD is a valuable diagnostic tool in determining definitive diagnostic of IBD based on histopathology findings.*

Keywords: *clinical scoring, histopathology findings, definitive IBD*

INTRODUCTION

The diagnosis of inflammatory bowel disease (IBD), either in the form of Crohn's disease (CD) or ulcerative colitis (UC), may be difficult when it is based on clinical evaluation, i.e. by history taking, physical examination, or even colonoscopy. Histopathology findings will remain as the gold standard in diagnosis of definitive IBD and hence, physicians may provide definitive and appropriate treatment.[1-6] However, diagnostic facilities - particularly histopathology examination, are not available for Indonesian patients in all regions of the country and satisfying results may not be provided since no confirm answer may be given. The following answer usually includes "IBD may be suspected" or "IBD may not be excluded" and it may still depend on clinical description enclosed by the sender.

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In addition, the colonoscopy reports for IBD lesions by the Central Education and Peripheral Endoscopy Service Units may not use the same language; therefore, the histopathology result often may comply our expectation.[5,7] Moreover, the colonoscopy facilities in Indonesia is very limited and only available in big cities; thus, it is difficult for internists who have their practice in rural area to establish the diagnosis of IBD.

Endeavors to improve IBD diagnosis based on colonoscopic findings have not been reported yet in Jakarta. Therefore, we would like to study the clinical scoring for IBD to determine the diagnosis of possible IBD by considering histopathology examination as the gold standard of diagnosis.[1,2,5,6,8,9] We also would like to identify the positivity of fecal occult blood test (FOBT) in patients with definitive IBD who previously had no history of bloody stool.[10,11,12]

Our study was expected to answer the research question about sensitivity and specificity of the clinical scoring for IBD to determine the diagnosis of possible IBD by considering histopathology examination as the gold standard.[13,14] In addition, it was also expected to establish a formulation of clinical scoring[14,15,16] which may become a gold standard substituting histopathology examination in making diagnosis of IBD, especially for our colleagues in peripheral rural area who had no colonoscopy facilities or histopathology laboratory. Moreover, we expect that the study would provide some advantages for The Indonesian Society for Digestive Endoscopy (ISDE) and Faculty of Medicine University of Indonesia, especially the Department of Internal Medicine, i.e. providing input and evaluation for IBD training curriculum to maintain our professionalism and to obtain some data about the diagnosis of possible, probable, and definitive IBD in Jakarta.[17]

METHOD

The study design was cross sectional.[14,15,16] Data were collected from medical records of patients at four hospitals in Jakarta (Cipto Mangunkusumo, Gatot Subroto, Usada Insani, and Sukanto hospital) and were based on chronological number and examination years. The inclusion criteria were patients with possible IBD who had IBD lesion confirmed by colonoscopy with specific features such as ulcerations, polyposis, hyperemia and edematous mucosa, skip area or mass with suggestive IBD and compare to gold standard.[1,5,6,17,18] The population of sample were patients who came to endoscopy units between 1999 and 2009 with complaints of chronic lower gastrointestinal disorder such as abdominal pain on left or right quadrant, especially intermittent abdominal pain on lower quadrant and it might have coincidence with diarrhea and bloody stool.

Possible IBD was defined when patients had signs and symptoms of IBD based on history and physical examination.[6,13] Probable IBD was defined when the patients had possible IBD with IBD lesion confirmed by colonoscopy; while definitive IBD was defined as probable IBD supported by histopathology finding.[5,17]

Patients who fulfilled the inclusion criteria subsequently underwent biopsy, colonoscopy and histopathology examination. Patients who may have possible and probable IBD, but did not have biopsy, colonoscopy or histopathology examination or who might have underwent those examinations but with no adequate results were excluded.

This study was performed upon permission by Faculty of Medicine University of Indonesia Division of Gastroenterology Department of Internal Medicine and Medical Record Division of Cipto Mangunkusumo hospital, and also other hospitals (Gatot Soebroto, Usada Insani, and Sukanto hospitals). Complete names, colonoscopy and histopathology results were concealed. All data remained confidential and we respected our subjects' privacy by keeping their record in appropriate manner, such as using initial name etc.

Data processing was done manually and then was computerized with excel and SPSS programs.

Table 1. The degree of clinical score [1,13]

Clinical variables	Degree of score		
	1	2	3
Diarrhea	liquid positive mucus positive	liquid positive mucus positive blood positive	blood more dominant
Abdominal pain	pain negative	pain on the left or right	pain on all of abdomen
Febrile (°C)	$t \leq 37$	t 37.1–37.2	t > 37
Tenesmus	negative		positive
Appetite	positive	decreased	negative
Body weight (kg)	decreased 0-2	decreased 3-9	decreased $\geq$ 10
Abdominal mass	+/-, /stool +	small, permanent/ constipation	large, permanent/ obstipation
Fecal occult blood test	negative		positive

t: temperature

Data analysis were performed by SPSS program to recognize sensitivity and specificity of the clinical scoring for IBD and subsequently, compared it with histopathology examination as the gold standard.[8,9,13-17]

RESULTS

A total number of 386 patients took part in this study. There were 213 patients with probable IBD and 173 patients with possible IBD. Positive histopathology results were found in 52 patients; consist of 30 males and 22 females. The patients in this study ranged in age from 12 to 83 years with 3 patients at 12-18 years, 23 patients at 19-39 years, 8 patients at 40-59 years, and 8 patients at $\geq$ 60 years of age. Positive results of FOBT were found in 20 (5%) patients, whereas

negative results were found in 366 (95%) patients.

Statistical analysis showed that the minimal and maximal clinical score was 7 and 15 consecutively, with the average of 8.76 and the mean value of 9 points. The clinical score of positive histopathology results were 11.04 as shown by t-test independent. It was significantly higher than other patients who had negative histopathology results, with median score of 8.41 and p > 0.001. Using receiver operating characteristic (ROC) curves, we found cut-off score of 10 points with a sensitivity and specificity of 73% and 88% consecutively; while by applying the cut-off on logistic regression analysis, we found odds ratio (OR) of 20 (9.9-40.0).

Table 2. Characteristic of patients with positive histopathology results

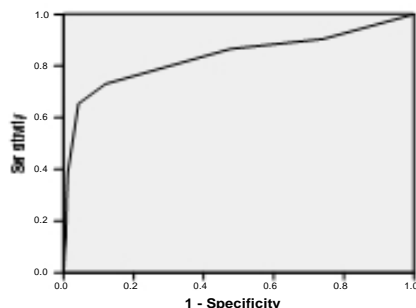| Characteristic	n (%)
Sex	
Male	30 (57.69)
Female	22 (42.31)
Age (years)	
12-18	3 (5.77)
19-39	23 (44.23)
40-59	18 (34.62)
≥ 60	8 (15.38)
City	
Jakarta	9 (18.14)
Others	5 (9.65)

Figure 1. ROC curve showed sensitivity and specificity clinical scoring of IBD

Table 3. p value of Pearson Chi-square test between the clinical symptoms with the diagnosis and anatomical pathology

Clinical symptoms	p
Diarrhea	0.376
Abdominal pain	0.001
Febrile	0.001
Tenesmus	0.001
Loss of appetite	0.001
Body weight	0.001
Abdominal mass	0.629
Fecal occult blood test	0.168

DISCUSSION

The mean value of clinical scoring in this study was 9 points, which is considered as important value. The independent t-test with consideration of histopathology examination as the gold standard for IBD diagnosis revealed that the number of patients with positive IBD was 11 times significantly higher than patients with negative IBD.

Our study showed that the clinical score included 8 clinical variables such as diarrhea, abdominal pain, febrile, tenesmus, loss of appetite, body weight, abdominal mass, and fecal occult blood test (FOBT); which were strong independent variables. When they are being utilized, such as clinical scoring would provide some advantages including its role as a valuable diagnostic tool in making diagnosis of IBD, especially for our colleagues in peripheral rural area who had no colonoscopy facilities or histopathology laboratory.

In ROC curve for the clinical scoring, we found that the score which was higher than the cut-off point of 10 had a sensitivity and specificity of 73% and 88% respectively. Hence, the 8 clinical variables with total score more than 10 points are strongly suggested as a diagnostic instrument to determine the diagnosis of definitive IBD with 88% specificity.[14,16]

In order to determine whether the clinical variables have role in establishing the diagnosis of possible IBD or not, we should give scores on all of the eight variables and calculate them as a total score. When the total score is more than 11 points by using t-test or ≥ 10 on ROC curve then the diagnosis of possible IBD should be considered. However, since we only used certain clinical variables in this study, the total scores did not represent the scoring system, so such clinical scoring system might be useless.

For example, look at table 2; the clinical variables include diarrhea, abdominal mass and FOBT. Although those 3 variables have non-significant (p > 0.05), but they have important role in calculating the total score; therefore, the variables may not be excluded from such calculation until the clinical score can be applied. The validity of such scoring system in this study may be fulfilled when all independent clinical variables have been calculated.[14,16]

Generally, as a diagnostic study, the aim of our study was to exclude other diseases that may have similar clinical manifestation. Therefore, we need to know the accuracy level of such diagnostic study that should have high specificity but the sensitivity should be not too low. As we utilized a cut-off score of 10 points in this study, we found sensitivity 73% and specificity of 88%; therefore, the specificity is higher than sensitivity. It demonstrates that the clinical scoring is a quite good diagnostic tool with a considerable accuracy level above the sensitivity of screening test.

The application of such clinical scoring for diagnosing possible IBD based on this study is easier, non-invasive, faster, and less expensive compared to determination of probable IBD by the gold standard. Such scoring system may be used by internists who live in area without any colonoscopy facilities or

histopathology laboratory. Hence, the advantage of the scoring system may include its role as a substituting diagnostic tool.[13,14,15]

Determination of colonoscopy score by examining patients with probable IBD could be performed by similar method. It may become an important method in some area without histopathology facilities and may substitute histopathology examination as the gold standard.[13,14,15]

These studies have not been tested specifically to histopathology examination as the gold standard for each subtype of IBD (CD or UC) since there was a little amount of data of probable IBD which specifically mentioned either CD or UC forms. Many endoscopy and histopathology reports only render that there are a features of IBD without mentioning whether CD or UC subtypes. Thus, such facts give us an impression that it is still difficult to establish the diagnosis of CD or UC in Jakarta. In addition, there is another IBD subtype – the indeterminate colitis (IC) - which may occur in 5% cases as mentioned by several literatures and it usually has more severe clinical manifestations[1,7,9,19,20] IC may not be classified as CD or UC subtypes.

There was a special consideration for this study. If we specifically studied the diagnosis of CD or UC subtypes compared to diagnosis of IBD, then we would have lack of sample quantity. However, if there is any visible and prospective study in the future without time limitation and with a more detailed study design, it would be easy to find the features and the characteristics of such IBD subtypes precisely.[1,2,5,8,9,17-24]

CONCLUSION

This study found that males was more likely to have positive histopathology results in IBD patients than females and it was more frequently found in adult age group. UC form was more frequently found than CD. The clinical score of ten or higher could be used to substitute the histopathology examination as gold standard for possible IBD patients, especially in some areas which minimal colonoscopy and histopathology facilities - by twenty times greater than clinical score less than ten points.

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