Nakov et al., Intern Med 2017, 7:4
DOI: 10.4172/2165-8048.1000248

Internal Medicine: Open Access

Research Article OMICS International

Correlation between Ulcerative Colitis Endoscopic Index of Severity, Lichtiger Index and Fecal Calprotectin in Ulcerative Colitis Patients

Nakov RV[1]*, Nakov VN[1], Gerova VA[1], Penchev PI[1], Tankova L[1] and Kundurzhiev TG[2]

[1]*Clinical Center of Gastroenterology, University Hospital Queen Joanna, Medical University of Sofia 1527, Bulgaria*
[2]*Department of Social Medicine and Health Management, Section of Biostatistics, Medical University of Sofia, Bulgaria*

Abstract

Aim: The aim of the current study was to assess the correlation between the Ulcerative Colitis Endoscopic Index of Severity (UCEIS), Lichtiger Index and the fecal calprotectin (FC) levels in ulcerative colitis (UC) patients.

Methods: This prospective study included 58 patients with UC, referred for colonoscopy to our Center. The diagnosis of UC was based on the clinical, endoscopic, and histological criteria. FC was analyzed in stool samples by means of point-of-care desk-top Quantum Blue Reader® method.

Results: The UCEIS significantly correlated with levels of FC (r=0.869, p<0.001) and the Lichtiger Clinical Activity Index (r=0.862, p<0.001). Moreover, the Lichtiger Index demonstrated significant correlation with FC levels (r=0.869, p<0.001).

Conclusion: The strong correlation between clinical and endoscopic disease activity shows that FC is a useful biomarker for noninvasive activity monitoring in UC patients.

Keywords: UCEIS; Lichtiger index; Fecal calprotectin; Ulcerative colitis

Introduction

Ulcerative colitis (UC) is a heterogeneous, inflammatory disease which is characterized by diffuse inflammation of the large intestine mucosa and a relapsing disease course. Assessment of disease activity is vital in view of clinical management [1]. In order to determine it, physicians count on combination of clinical features, endoscopic findings and levels of laboratory biomarkers [2].

At present, the most accurate way to evaluate the severity of UC and extent of intestinal inflammation is endoscopy with biopsy [3]. This technique allows assessment of extent and severity of disease but it is also invasive, time-consuming, and expensive. Furthermore this procedure is painful, and requires an uncomfortable preparation and a trained endoscopist [4]. These limiting factors are often a burden to UC patients, and often prevent the frequent evaluation of UC activity by endoscopy [5]. On the other hand, patient symptoms cannot reliably reflect the extent of disease and response to therapy, and their correlation with endoscopic activity is often limited [6]. For this reason, in order to assess the disease activity, a combination of clinical examination, levels of laboratory biomarkers, endoscopic and microscopic findings is used in routine clinical practice [7].

Among all laboratory biomarkers fecal calprotectin (FC) has demonstrated the best sensitivity for assessing intestinal disease activity [8]. It is frequently used for follow-up of inflammatory bowel disease (IBD) activity and its elevated concentrations can predict relapse in IBD patients in clinical remission [9,10].

Many disease activity indices or clinical criteria for UC have been proposed through the years, but none have been adequately validated. The Lichtiger Index, also known as the modified Truelove and Witts Severity Index, also has not been validated, although it has been used in several adult clinical trials [11,12]. Up to this moment there are not enough data about the correlation of the Lichtiger Index with the endoscopic severity and levels of FC.

There are several different scoring systems for the endoscopic evaluation of UC severity, such as Mayo endoscopic score, modified baron score, etc. However, none of these instruments have been validated for a reliable assessment [13]. Recently, the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) has been reported by Travis et al. [14]. This score was developed as an index that catches 90% of the variance in the overall assessment of endoscopic severity and is the first validated endoscopic index of severity in UC [15]. Basically, the UCEIS is calculated as the simple sum of three descriptors: vascular pattern (score 0-2), bleeding (score 0-3), and erosions and ulcers (score 0-3) (Table 1) [16].

Up to our best knowledge, there have been no prospective studies that have assessed how endoscopic activity, evaluated using UCEIS, correlates with clinical activity, assessed using the Lichtiger Index, and with FC concentrations in UC. Therefore, the purpose of this study was to answer the following question: what is the correlation between UCEIS, Lichtiger Index and FC levels in UC patients.

Methods

Patients

This prospective study enrolled 58 patients -32 male and 26 female at an average age of 39.4 ± 9 (18-63) years with UC, referred for colonoscopy to our Clinical Center of Gastroenterology between May 2014 and April 2016. The diagnosis of UC was made on the basis of appropriate clinical, endoscopic, and histologic criteria [7]. Inclusion

***Corresponding author:** Radislav Nakov, Clinic of Gastroenterology "Tsaritsa Yoanna" University Hospital, 1000 Sofia, Bulgaria, Tel: 359889807559; E-mail: radislav.nakov@gmail.com

Received June 17, 2017; **Accepted** July 25, 2017; **Published** July 28, 2017

Citation: Nakov RV, Nakov VN, Gerova VA, Penchev PI, Tankova L, et al. (2017) Correlation between Ulcerative Colitis Endoscopic Index of Severity, Lichtiger Index and Fecal Calprotectin in Ulcerative Colitis Patients. Intern Med 7: 248. doi: 10.4172/2165-8048.1000248

Descriptor (scoremost severe lesions)	Likert scale anchor points	Definition
Vascular pattern	Normal (0)	Normal vascular pattern with arborisation of capillaries clearly defined, or with blurring or patchy loss of capillary margins
Bleeding	None (0)	No visible blood
	Mucosal (1)	Some spots or streaks of coagulated blood on the surface of the mucosa ahead of the scope, which can be washed away
	Luminal mild (2)	Some free liquid blood in the lumen
	Luminal moderate or severe (3)	Frank blood in the lumen ahead of endoscope or visible oozing from mucosa after washing intra-luminal blood, or visible oozing from a haemorrhagic mucosa
Erosions& ulcers	None (0)	Normal mucosa, no visible erosions or ulcers
	Erosions (1)	Tiny (≤ 5mm) defects in the mucosa, of a white or yellow colour with a flat edge
	Superficial ulcer (2)	Larger (>5mm) defects in the mucosa, which are discrete fibrin-covered ulcers when compared to erosions, but remain superficial
	Deep ulcer (3)	Deeper excavated defects in the mucosa, with a slightly raised edge

Table 1: Ulcerative colitis endoscopic index of severity (UCEIS).

	Scores					
Variable	0	1	2	3	4	5
Diarrhea (number of daily stools	0-2	3-4	5-6	7-9	≥ 10	
Nocturnal diarrhea	No	Yes				
Visible blood in stool (% of movements)	0	<50	≥ 50	100		
Fecal incontinence	No	Yes				
Abdominal pain or cramping	None	Mild	Moderate	Severe		
General well-being	Perfect	Very good	Good	Average	Poor	Terrible
Abdominal tenderness	No	Mild and localized	Mild to moderate and diffuse	Severe or rebound		
Need for anti-diarrheal drugs	No	Yes				

Table 2: Lichtiger Clinical Index for ulcerative colitis.

criteria included: (1) age 18-85 years, (2) complete colonoscopy with intubation of the cecum, (3) biopsies, (4) completion of a written informed consent, and (5) fecal specimens collected within 1–2 days before colonoscopy. In the 24 h period before the procedure, the patients had bowel cleaning for endoscopy. All the patients had undergone a full medical assessment including a detailed medical history and physical examination. Exclusion criteria for this study were: (1) incomplete colonoscopy, (2) inadequate fecal sample, (3) colorectal cancer or colon polyps, (5) Crohn's disease, (6) indeterminate colitis, (7) history of colorectal surgery, (8) urinary incontinence (due to the risk of contamination of fecal samples), (9) pregnancy, (10) history of active non-steroidal anti-inflammatory drugs (NSAID) intake (2 tablets/week), (11) having infectious colitis, (12) primary immunodeficiency, and (13) underlying chronic disease at the time of the study.

All the patients included in this study responded to all the inclusion and exclusion criteria. Indications for colonoscopy were clinically active disease (flare), having unexplained symptoms, evaluation of disease activity after treatment and dysplasia surveillance for longstanding disease. The Lichtiger Index for each patient was calculated by a doctor not performing the colonoscopy. Endoscopies were carried out by two experienced gastroenterologists who graded the findings according to the UCEIS.

Lichtiger index

The Lichtiger Index is defined by eight variables (Table 1): Diarrhea (number of daily bowel openings), nocturnal stools, visible blood in stool (percentage of movements), fecal incontinence, abdominal pain/cramping, general well-being, abdominal tenderness, and need for antidiarrheals. Scores range from 0 to 21 points. Clinical remission was determined as a Lichtiger Index of 3 points or less [12,17]. Similar to a study of Schoepfer et al. [18] we defined the different degrees of clinical activity of UC as follows: remission: 0-3 points; mild activity: 4-8 points; moderate activity: 9-14 points; and high activity of the disease: >15 points (Table 1).

Ulcerative Colitis Endoscopic Index of Severity (UCEIS)

The UCEIS score is a scoring tool based on a visual analogue scale (VAS) that supplies a model accounting for UC endoscopic severity (Table 2).

We evaluated the patients by total colonoscopy, whereas in the original determination of the UCEIS score Travis and colleagues [14] used sigmoidoscopy. We identified the worst affected part of the colon visualized by colonoscopy and the final score was calculated by adding the scores from each component ranging from 0 (normal) to 8 (the worst.) We stratified the UCEIS scores into four groups: remission (UCEIS 0-1); mild (UCEIS 2-4); moderate (UCEIS 5-6); and severe (UCEIS 7-8). It was assumed that UCEIS 1 in the remission group was a descriptor limited to vascular patterns. Colonoscopy findings were compared to Lichtiger Index and FC level in each patient (Table 2).

Fecal calprotectin

Calprotectin was examined in stool samples using point-of-care desk-top Quantum Blue Reader® (POC Reader) method. It is a lateral flow technology based on ELISA techniques. The test was performed according to the manufacturer's instructions (Quantum Blue® Calprotectin, Buhlmann Laboratories AG, Switzerland) [19].

The POC device uses internal standards within a range of 30-300 µg/g and a sensitivity of <10 µg/g, thus, guarantying consistency in results. When we received results >300 µg/g, we performed additional 1:10 dilution with extraction buffer according to the manufacturer's instructions, allowing us to receive FC levels up to 3000 µg/g. FC values above the upper limit of the measurement ranges were registered as 3000 µg/g and FC values below the lower limit were accordingly registered as 30 µg/g.

Statistical analyses

The statistical analysis was performed using SPSS for Windows, Version 16.0. (SPSS Inc., Chicago, USA). The following statistical methods were used for data analysis: Descriptive statistics for tabular and graphical presentation of results, Kolmogorov-Smirnov test and Spearman's correlation coefficient. The obtained results were assessed as statistically reliable in threshold level of significance $p<0.05$.

Ethical consideration

The study protocol was approved by the Ethics Committee of University Hospital Queen Joanna, Sofia. Written informed consent was obtained from all patients.

Results

The demographic and clinical characteristics of UC patients are shown in Table 3**.** Twenty-eight patients (48,28%) were with active UC, of which 8 newly-diagnosed and 20 with flare of the disease, and 30 (51,72%) patients were in clinical remission.

The UCEIS correlated significantly with FC concentrations (Spearman's rank correlation coefficient r=0.869) and the Lichtiger Clinical Activity Index (r=0.862). For both items, $p<0.001$ was found. Figure 1 shows the correlation between the UCEIS and FC levels and Figure 2 demonstrates the relationship between the UCEIS and the Lichtiger Index (Figures 1 and 2).

Furthermore the Lichtiger Index demonstrated significant correlation with FC concentrations (Spearman's rank correlation coefficient r=0,836, $p<0.001$). The relationship between these parameters is shown in Figure 3.

Discussion

The present study provides additional evidence to the evaluation that FC is a reliable and valuable biomarker for noninvasive monitoring of disease activity in UC patients.

During the last decade the correlation of FC levels and clinical, endoscopic and histological activity in IBD has been provoking great interest in gastroenterologist. Up to now most studies described a weak correlation of FC levels and clinical indices [20]. In contrary, it has been found that FC correlates well with endoscopic and histological activity in IBD [18]. It is interesting that FC is more accurately correlated to histopathological findings than macroscopic findings on colonoscopy [21]. The correlation to histopathology is also more accurate than clinical and para-clinical symptoms of the disease. Moreover, FC was able to discriminate endoscopic remission from mild, moderate and severe endoscopically active disease [18].

Although weak correlation between FC and clinical indices was demonstrated in most studies, in our study the Lichtiger Index demonstrated a very good correlation with FC levels and endoscopic activity. In the current study we focused on the Lichtiger Clinical Activity Index because it is based just on clinical characteristics, does not require laboratory data, and is very simple to use and can be very rapidly calculated. According to our best knowledge this is one of the first studies to assess the correlation between the Lichtiger Index and the UCEIS. In a recent study of Arai et al. [22] the UCEIS demonstrated good correlation with the pMayo score (r=0.637), it was also correlated with the Lichtiger index but the data were not shown in the article.

Characteristics	Absolute number	Percentage (%)
Number of patients	58	-
Sex		
Male	32	55
Female	26	45
Age, mean ± SD, range (years)	39,4 ± 9 (18-63)	-
Duration of the disease, mean ± SD (years)	4.2 ± 3.5	-
Smoking habit		
Smokers	17	29,3
Never smoked	37	63,8
Ex-smokers	4	6,9
Disease location		
Proctitis – E1	9	15,5
Left-sided colitis – E2	27	46,6
Extensive colitis – E3	22	37,9
Medication at endoscopy		
None	3	5
Topical 5-ASA	10	17
Systemic 5-ASA	33	52
Azathioprine	15	26
TNF-alpha inhibitor	10	17

Table 3: Characteristics of Ulcerative Colitis Patients Enrolled in the Study.

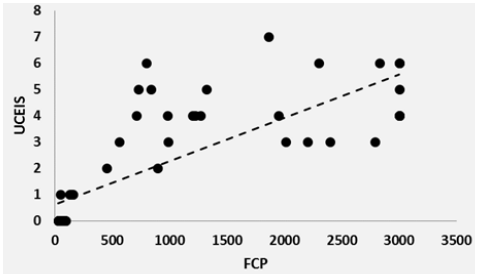

Figure 1: Relationship between ulcerative colitis endoscopic index of severity (UCEIS) and fecal calprotectin concentration (FCP).

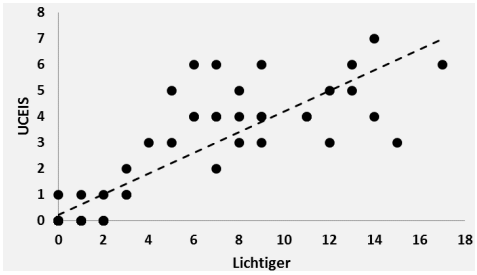

Figure 2: Correlation between ulcerative colitis endoscopic index of severity (UCEIS) and the Lichtiger Clinical Activity Index.

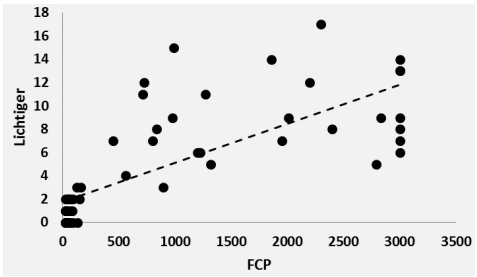

Figure 3: Correlation of the Lichtiger Clinical Activity Index and the fecal calprotectin (FCP) level.

Schoepfer et al. [18] showed significant correlation of the Lichtiger Clinical Index with the modified Baron Score (r=0.682). Moreover, the study established that the Lichtiger Clinical Activity Index could differentiate between all the subclasses of endoscopic severity, except between a modified Baron Score of 0 and 1 [18].

Surprisingly, in this study we observed one of the strongest correlations between clinical (Lichtiger Index) and endoscopic score (UCEIS) in UC patients r=0.862. Moreover, the Lichtiger Index demonstrated significant correlation with FC levels (r=0,836). A possible explanation for this could be lack of functional symptoms in our UC patients in remission.

The UCEIS score is an accepted instrument to assess disease activity in patients with UC and is closely correlated with former endoscopic and clinical activities [14]. The original and modified Baron scores and the Mayo score have been broadly used in the clinical practice and are easy to implement. However, recent studies [14,15,23] have demonstrated that the rate of agreement is only 27% for endoscopic remission [Baron score 0] and 37% for moderate activity [Baron 2]. Inter-observer disagreement has been reported for the severity of inflammation in UC [14]. Therefore, the development of new methods/techniques for the assessment of severity is warranted. More recently, the UCEIS and the ulcerative colitis colonoscopic index of severity (UCCIS) were established to address the issue of low inter-observer agreement for endoscopic scores [14,15,23].

Travis et al. [24] recently reported that clinical information has minimal impact on the endoscopic scoring of disease activity as determined by the UCEIS. In the present investigation we evaluated the UCEIS score in a clinical practice setting and therefore with initial clinical knowledge of the patients' UC. This should mean that clinical knowledge did not influence our UCEIS assessment outcomes.

Close correlation between UCEIS and FC levels was indicated by study of Taghvaei et al. [25] (r=0.607, p=0.001). FC concentrationss in patients with an overall UCEIS >1 were significantly higher than in patients with normal colonoscopy findings. However, that study did not directly show the differences in FC levels between the patients with a UCEIS of 0 or 1. Another recent investigation also indicated that FC levels were correlated with MES and UCEIS [26].

We found a very strong correlation between the UCEIS score and the FC levels (0.869, p<0.001) FC can be used as an alternative to the UCEIS score and can be accepted as a direct biomarker of intestinal inflammation. It is cheaper and non-invasive compared to colonoscopy.

In this study calprotectin was examined in stool samples by point-of-care Quantum Blue Reader® method. According to us this test is really useful, because it is simple, can be done in doctor's office and is really fast (results can be obtained in less than 30 min including protein extraction). Another big advantage of the test are the simplicity of sample preparation, the user-friendly analysis and the lack of need of special equipment. Moreover, the point-of-care test can serve as a reliable alternative to ELISA [27,28]. It has been shown that the Quantum Blue Reader® method is the tool of choice for rapid and reliable determination of fecal calprotectin concentrations [28].

There are some limitations to this study. Firstly, we subdivided the UCEIS score into four groups. However, because of the small sample size, we could not evaluate if FC levels and the Lichtiger Clinical Activity Index could differentiate between all the groups of endoscopic severity. Secondly, we did not compare FC level with pathologic status of the patients, because this was not the aim of this study. Thirdly, two experienced endoscopist provided the endoscopic score, however we did not evaluate intra-observer variability. Finally, further larger studies are needed to better assess the correlation between these three parameters-FC, UCEIS and the Lichtiger Index in UC patients.

In conclusion, up to our best knowledge this is one of the first studies with a major focus on evaluating how UCEIS, correlates with clinical activity, assessed using the Lichtiger Index, and with FC concentrations in UC patients. Based on our thorough evaluation, we can confidently say that FC levels demonstrated very strong correlated with endoscopic severity according to the UCEIS and with clinical severity according to the Lichtiger Index. The results of the current study provide further evidence that FC is a useful and reliable biomarker for noninvasive activity monitoring in UC patients.

References

1. Langhorst J, Elsenbruch S, Mueller T, Rueffer A, Spahn G, et al. (2005) Comparison of 4 neutrophil-derived proteins in feces as indicators of disease activity in ulcerative colitis. Inflamm Bowel Dis 11: 1085-1091.
2. Sandborn WJ, Feagan BG, Stoinov S, Honiball PJ, Rutgeerts P, et al. (2007) Certolizumab pegol for the treatment of crohn's disease. N Engl J Med 357: 228-238.
3. Fefferman DS, Farrell RJ (2005) Endoscopy in inflammatory bowel disease: Indications, surveillance, and use in clinical practice. Clin Gastroenterol Hepatol 3: 11-24.
4. Konikoff MR, Denson LA (2006) Role of fecal calprotectin as a biomarker of intestinal inflammation in inflammatory bowel disease. Inflamm Bowel Dis 12: 524-534.
5. Carpenter HA, Talley NJ (2000) The importance of clinicopathological correlation in the diagnosis of inflammatory conditions of the colon: Histological patterns with clinical implications. Am J Gastroenterol 95: 878–896.
6. Schoepfer AM, Beglinger C, Straumann A, Trummler M, Renzulli P, et al. (2009) Ulcerative colitis: Correlation of the rachmilewitz endoscopic activity index with fecal calprotectin, clinical activity, c-reactive protein, and blood leukocytes. Inflamm Bowel Dis 15: 1851-1858.
7. Nikolaus S, Schreiber S (2007) Diagnostics of inflammatory bowel disease. Gastroenterology 133: 1670-1689.
8. Vermeire S, Van Assche G, Rutgeerts P (2006) Laboratory markers in IBD: Useful, magic, or unnecessary toys? Gut 55: 426-431.
9. Lewis JD (2011) The utility of biomarkers in the diagnosis and therapy of inflammatory bowel disease. Gastroenterolgy 140: 1817-1826.e2.
10. Tibble JA, Sightorsson G, Bridger SS, Fagerhol MK, Bjarnason I (2000) Surrogate markers of intestinal inflammation are predictive of relapse in patients with inflammatory bowel disease. Gastroenterology 119: 15-22.
11. Lichtiger S, Present DH (1990) Preliminary report: Cyclosporin in treatment of severe active ulcerative colitis. Lancet 336: 16-19.
12. Lichtiger S, Present DH, Kornbluth A, Gelernt I, Bauer J, et al. (1994) Cyclosporine in severe ulcerative colitis refractory to steroid therapy. *N* Engl J Med 330: 1841-845.
13. Dhaens G, Sandborn WJ, Feagan BG, Geboes K, Hanauer SB, et al. (2007) A review of activity indices and efficacy end points for clinical trials of medical therapy in adults with ulcerative colitis. Gastroenterology 132: 763-786.
14. Travis SP, Schnell D, Krzeski P, Abreu MT, Altman DG, et al. (2012) Developing an instrument to assess the endoscopic severity of ulcerative colitis: The Ulcerative Colitis Endoscopic Index of Severity (UCEIS). Gut 61: 535-542.
15. Dignass A, Eliakim R, Magro F, Maaser C, Chowers Y, et al. (2012) Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 1: Definitions and diagnosis. J Crohns Colitis 6: 965-990.
16. Travis SP, Schnell D, Krzeski P, Abreu MT, Altman DG, et al. (2013) Reliability and initial validation of the ulcerative colitis endoscopic index of severity. Gastroenterology 145: 987-995
17. Baumgart DC, Targan SR, Dignass AU, Mayer L, Van AG, et al. (2010) Prospective randomized open-label multicenter phase I-II dose escalation trial of visilizumab (HuM291) in severe steroid refractory ulcerative colitis. Inflamm Bowel Dis 16: 620-629.

18. Schoepfer A, Beglinger C, Straumann A, Safroneeva E, Romero Y, et al. (2013) Fecal calprotectin more accurately reflects endoscopic activity of ulcerative colitis than the lichtiger index, c-reactive protein, platelets, hemoglobin, and blood leukocytes. Inflamm Bowel Dis 19: 332-341.

19. Quantum blue® calprotectin normal range quantitative lateral flow assay LF-CAL20 package insert (2010-11-10).

20. Schoepfer A, Beglinger C, Straumann A, Trummler M, Vavricka S, et al. (2010) Fecal calprotectin correlates more closely with the Simple Endoscopic Score for Crohn's disease (SES-CD) than CRP, blood leukocytes, and the CDAI. Am J Gastroenterol 105: 162-169.

21. Canani RB, Terrin G, Rapacciuolo L, Miele E, Siani MC, et al. (2008) Faecal calprotectin as reliable non-invasive marker to assess the severity of mucosal inflammation in children with inflammatory bowel disease. Dig Liver Dis 40: 547–553.

22. Arai M, Naganuma M, Sugimoto S, Kiyohara H, Ono K, et al (2016) The ulcerative colitis endoscopic index of severity is useful to predict medium- to long-term prognosis in ulcerative colitis patients with clinical remission. J Crohns Colitis 10: 1303-1309.

23. Samuel S, Bruining DH, Loftus EV, Thia KT, Schroeder KW, et al. (2013) Validation of the ulcerative colitis colonoscopic index of severity and its correlation with disease activity measures. Clin Gastroenterol Hepatol 11: 49-54.

24. Travis SP, Schnell D, Feagan BG, Abreu MT, Altman DG, et al. (2015) The impact of clinical information on the assessment of endoscopic activity: Characteristics of the Ulcerative Colitis Endoscopic Index Of Severity (UCEIS). J Crohns Colitis 9: 607-616.

25. Taghvaei T, Maleki I, Nagshvar F, Fakheri H, Hosseini V, et al. (2015) Fecal calprotectin and ulcerative colitis endoscopic activity index as indicators of mucosal healing in ulcerative colitis. Intern Emerg Med 10: 321-328.

26. Theede K, Holck S, Ibsen P, Ladelund S, Nordgaard-Lassen I, et al. (2015) Level of fecal calprotectin correlates with endoscopic and histologic inflammation and identifies patients with mucosal healing in ulcerative colitis. Clin Gastroenterol Hepatol 13: 1929-1936.

27. Coorevits L, Baert FJ, Vanpoucke HJ (2013) Fecal calprotectin: Comparative study of the quantum blue rapid test and an established ELISA method. Clin Chem Lab Med 51: 825-831.

28. Sydora MJ, Sydora BC, Fedorak RN (2012) Validation of a point-of-care desk top device to quantitate fecal calprotectin and distinguish inflammatory bowel disease from irritable bowel syndrome. J Crohns Colitis 6: 207-214.

Citation: Nakov RV, Nakov VN, Gerova VA, Penchev PI, Tankova L, et al. (2017) Correlation between Ulcerative Colitis Endoscopic Index of Severity, Lichtiger Index and Fecal Calprotectin in Ulcerative Colitis Patients. Intern Med 7: 248. doi: 10.4172/2165-8048.1000248