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Can Inflammatory Indexes Predict the Severity of Mucosal Inflammation in Ulcerative Colitis?

İnflamatuar İndeksler Ülseratif Kolitte Mukozal İnflamasyonun Şiddetini Tahmin Edebilir mi?

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ABSTRACT

Aim: Inflammatory indexes can relate to disease activity in ulcerative colitis (UC). This study aimed to evaluate whether the inflammatory indexes of neutrophil-lymphocyte ratio (NLR), C-reactive protein (CRP)-albumin ratio (CAR), CRP-lymphocyte ratio (CLR), and systemic immune-inflammation index (SIII) might predict the severity of mucosal inflammation in UC.
Material and Methods: This retrospective case-control study included 184 UC patients and 101 healthy controls. The Mayo clinical score and Mayo endoscopic score were used for the clinical and endoscopic features of UC. Truelove and Richards's method for the severity of mucosal inflammation determined the histological activity index (HAI).
Results: The inflammatory index values, were higher in UC patients compared to the control group ($p=0.007$ for NLR, and $p<0.001$ for the others). The patients having endoscopic, clinic, and histologically active disease had higher inflammatory index values than those in remission ($p<0.001$ for all). UC patients with extensive disease had higher inflammatory index values than the patients who had limited disease ($p<0.001$ for all). The HAI values were positively correlated to all inflammatory indexes, and the correlation was the strongest between the HAI and CLR (rho=0.737, $p<0.001$). Regarding HAI, the diagnostic accuracy of all inflammatory indexes for detecting the clinically active disease was statistically significant, and there was no significant difference between them in terms of diagnostic accuracy.
Conclusion: The inflammatory indexes of NLR, CAR, CLR, and SII might predict the severity of histological inflammation in UC.
Keywords: Ulcerative colitis; inflammatory indexes; mucosal inflammation.

ÖZ

Amaç: İnflamatuar indekslerin ülseratif kolitte (ÜK) hastalık aktivitesi ile ilişkili oldukları bilinmektedir. Bu çalışma nötrofil-lenfosit oranı (NLR), C-reaktif protein (CRP)-albümin oranı (CAR), CRP-lenfosit oranı (CLR) ve sistemik immün-inflamasyon indeksini (SIII) içeren inflamatuar indekslerin ÜK'de mukozal inflamasyonun şiddetini tahmin edip edemeyeceğinin değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntemler: Bu retrospektif vaka kontrol çalışmasına 184 ÜK hastası ve 101 sağlıklı kontrol dahil edilmiştir. ÜK'nin klinik ve endoskopik özellikleri için Mayo klinik skoru ve Mayo endoskopik skoru kullanılmıştır. Mukozal inflamasyon şiddeti, Truelove ve Richards yöntemine göre histolojik aktivite indeksi (HAI) ile belirlenmiştir.
Bulgular: ÜK hastalarında, inflamatuar indeks değerleri kontrol grubuna göre daha yüksek bulunmuştur (NLR için $p=0,007$ ve diğerleri için $p<0,001$). Endoskopik, klinik ve histolojik olarak aktif hastalığı olan vakaların inflamatuar indeks değerleri remisyonda olan vakalardan daha yüksek idi (tümü için $p<0,001$). Yaygın hastalığı olan ÜK hastalarının sınırlı hastalığı olan hastalardan daha yüksek inflamatuar indeks değerleri vardı (tümü için $p<0,001$). HAI değerleri tüm inflamatuar indekslerle pozitif korelasyon göstermekteydi ve en güçlü korelasyon HAI ile CLR arasında idi (rho=0,737; $p<0,001$). HAI ile ilişkili olarak, klinik olarak aktif hastalığın tespiti için tüm inflamatuvar indekslerin tanısal doğruluğu istatistiksel olarak anlamlıydı ve tanısal doğruluk açısından aralarında anlamlı bir fark yoktu.
Sonuç: NLR, CAR, CLR ve SIII'i içeren inflamatuar indeskler, ÜK'de histolojik inflamasyonun şiddetini tahmin edebilir.
Anahtar kelimeler: Ülseratif kolit; inflamatuar indeksler; mukozal inflamasyon.

INTRODUCTION

Inflammatory bowel diseases (IBDs) have relapsing and remitting courses. Exact pathogenic mechanisms in IBDs remain elusive, and the pathogenesis is multifactorial. The prevalence of IBDs is increasing, especially in developed countries. Inflammation is confined to the colonic mucosa in ulcerative colitis (UC). Bloody diarrhea is a common symptom of UC, which causes a psychosocial burden (1).

For the choice of therapeutic modalities, assessment of the disease activity is mandatory in UC. In the follow-up period, patients usually undergo colonoscopy, which can cause discomfort. Clinical, endoscopic, and laboratory features do not always correlate in UC patients. Easily applicable and inexpensive markers estimating the clinical, endoscopic, biochemical, and histological features of the disease are needed in daily clinical practice (2).

The neutrophil-lymphocyte ratio (NLR), the C-reactive protein (CRP)-albumin ratio (CAR), the CRP-lymphocyte ratio (CLR), and the systemic immune-inflammation index (SIII) are overlooked parameters in inflammatory conditions, including IBDs (3-12). Inflammatory indexes are cheap and easily interpreted tests by practitioners and have been attractive to clinicians in chronic inflammatory diseases so far. Many studies evaluated the effectiveness of inflammatory indexes in IBDs. It is worth noting that while not all studies have found a correlation, the majority have identified positive associations between disease activity and inflammatory indexes in UC (4,7-13).

Inflammation in the gut wall is related to worse clinical outcomes and relapse in IBDs, and therefore, mucosal healing was declared as an ideal therapeutic target (2,14,15). The severity of mucosal inflammation represents a target distinct from endoscopic mucosal healing (15). Mucosal inflammation in UC can be evaluated quantitatively, and there are different histological scoring systems in UC (15-19).

Although inflammatory indexes have been reported to correlate with different disease activity parameters, there is currently no data regarding the relationship between inflammatory indexes and the severity of histopathological activity in UC. With this regard, this study aimed to delineate whether inflammatory indexes might predict the inflammatory activity in the colonic mucosa of patients with UC, along with the clinical and laboratory characteristics of the disease.

MATERIAL AND METHODS

Subjects

This is a single-center retrospective, cross-sectional study. Patients with UC admitted to the gastroenterology department of our institute and underwent colonoscopy between January 2012 and July 2023 were retrospectively evaluated in the study. This group included both newly and previously diagnosed patients. A second cohort of healthy subjects served as controls. The local ethics committee approved the study (05.12.2023, 2021/147).

Subjects with clinical conditions that can alter inflammatory indexes, such as sepsis, any malignancies, any hematological diseases, severe organ failure, including cirrhosis, acute or chronic infections, autoimmune and other chronic inflammatory diseases, and patients with gut resection, were excluded from the study. In addition, patients with active disease due to infectious causes (amebiasis and cytomegalovirus colitis) were also excluded from the study. The healthy control group included participants who underwent a colonoscopy for indications other than IBD and whose colonoscopy results were normal. Medical records of all patients were reviewed, and 184 eligible patient files and 101 healthy controls were evaluated.

Assessment of the Clinical and Endoscopic Activities

The Mayo clinical score (MCS) was applied for the clinical activity of patients with UC, and it was scored between 0-12. Scores of ≤2 were classified as clinical remission, whereas scores of >2 indicated an activation. The disease extent of the patients with UC was defined in agreement with the Montreal classification (20). Proctitis and left-sided colitis were recorded as limited diseases, whereas extensive colitis and pancolitis were recorded as extensive diseases. Mayo endoscopic score (MES) index was used for the endoscopic activity of UC and was classified as remission (0), mild (1), moderate (2), and severe (3) colitis. Scores of (0) and (1) were recorded as inactive diseases, whereas (2) and (3) were recorded as active diseases.

Determination of the Inflammatory Indexes

Laboratory data were noted from the subject files prior to colonoscopy, one week before the procedure. Inflammatory indexes, including the NLR, SIII, CAR, and CLR, were calculated as defined in the literature (8). The CAR and CLR values were obtained by the division of the CRP levels (mg/L) by the albumin (gr/dl) and lymphocyte values ($10^3/mm^3$). The NLR was calculated as the neutrophil counts ($10^3/mm^3$) divided by the lymphocyte counts ($10^3/mm^3$). For SIII, neutrophil counts ($10^3/mm^3$) were multiplied by the platelet counts ($10^3/mm^3$) and divided by the lymphocyte counts ($10^3/mm^3$).

Histopathologic Evaluation in Ulcerative Colitis

The same pathologist who was blind to the participants evaluated the formalin-fixed, paraffin-embedded, and hematoxylin and eosin (H&E)-stained colonic biopsies of the UC patients and performed grading through a scale similar to that developed by Truelove and Richards (16). According to the severity of inflammatory mucosal inflammation, each component of the scale was scored. Active inflammation (0-3), chronic inflammation (0-2), and crypt distortion (0-3) were the components of the scale. The histologic activity index (HAI) was defined as the sum of the scores of these components. The highest mucosal inflammation score was 8, and scores of <5 were recorded as histological remission, whereas ≥5 was recorded as activation (16).

Statistical Analysis

Statistical analyses were performed using the MedicReS E-PICOS Version 21.3. Descriptive statistics were presented by frequencies and percentages for categorical variables, and the median was presented with its interquartile ranges for continuous ones. Kolmogorov-Smirnov and Shapiro-Wilk tests were used for testing normality. Any continuous variables did not fit the criteria for normality, so comparisons were performed using the Mann-Whitney U test. Associations were checked by using Spearman's rank correlation due to at least one of the variables being ordinal. A chi-squared test was used for comparison of categorical variables. Fisher's exact test and Yates's correction for continuity were used according to the range of expected

values. Diagnostic accuracy was evaluated using receiver operating characteristics (ROC) curve analysis, and cut-off levels were estimated by Youden's index. The confidence level for statistical significance was defined as 95 percent.

RESULTS

In total, 184 (140 males and 44 females) UC patients and 101 (78 males and 23 females) healthy controls eligible for the study were evaluated. The groups were similar with respect to age and gender. Demographic, clinical, and laboratory characteristics of the subjects are presented in Table 1. Erythrocyte sedimentation rate (ESR), CRP, leucocyte, neutrophil, and platelet values were higher, whereas albumin value was lower in UC patients, as expected. Although the median lymphocyte value was numerically lower in the patients with UC compared to the control group, the difference was not statistically significant (p=0.299). Most patients with UC had limited and active disease in the colonoscopy, and the number of patients in activation was higher than those in remission, according to MCS. The median HAI was 5 in the patient group. The number of patients under treatment was also higher than the number of patients without any treatment. CLR, CAR, NLR, and SIII values were higher in the UC patients compared to healthy controls (p=0.007 for NLR, and p<0.001 for the others).

With respect to disease activity parameters, UC patients having endoscopic, clinic, and histologically active disease had higher CLR, CAR, NLR, and SIII values than those in remission (p<0.001 for all). There was no statistically significant difference between the patients who were under treatment and those without any treatment. In colonoscopy, UC patients with extensive disease had higher inflammatory index values than the patients who had limited disease (p<0.001 for all, Table 2).

HAI was positively correlated to inflammatory indexes, and the correlation was the strongest between HAI and CLR (rho=0.737, p<0.001, Table 3).

Table 1. Demographic, clinical, and histopathologic characteristics of the study groups

	Ulcerative Colitis Patients (n=184)	**Healthy Controls (n=101)**	**p**
Gender, n (%)			
Female	44 (23.9)	23 (22.8)	0.828
Male	140 (76.1)	78 (77.2)	
Age (years)	32 (24.2-46.7) [18-83]	35 (25.5-46) [19-65]	0.596
CRP (mg/L)	10.3 (3-23.4) [0.15-138]	2.8 (1.2-4.2) [0.20-22.39]	**<0.001**
ESR (mm/h)	19 (9-44.7) [1-120]	8 (3-15) [1-42]	**<0.001**
Leucocyte ($x10^3/\mu L$)	7.7 (6.4-9.6) [3.5-8.7]	7.1 (5.9-8.7) [3.2-15.7]	**0.024**
Neutrophil ($x10^3/\mu L$)	5 (3.6-6.7) [1.64-14.75]	4.5 (3.4-5.6) [1.6-481]	**0.036**
Lymphocyte ($x10^3/\mu L$)	1.9 (1.6-2.5) [0.63-5.03]	2.1 (1.6-2.6) [0.76-168]	0.299
Platelet ($x10^3/\mu L$)	305 (245.2-377.7) [108-1039]	251 (220.5-279) [130-389]	**<0.001**
Albumin (gr/dl)	4.3 (3.9-4.6) [2.1-5.4]	4.5 (4.3-4.7) [3.40-5.30]	**<0.001**
Disease duration (years)	3 (1-7) [0-35]	-	-
Location of UC, n (%)			
Remission	12 (6.5)		
Limited disease	128 (69.6)	-	-
Extensive colitis	44 (23.9)		
MES of UC, n (%)			
Remission (MES 0-1)	89 (48.4)	-	-
Activation (MES 2-3)	95 (51.6)		
MCS of UC, n (%)			
Remission (MCS ≤2)	53 (20.8)	-	-
Activation (MCS >2)	131 (79.2)		
HAI of UC	5 (2-7) [0-8]	-	-
HAI of UC, n (%)			
Remission (HAI <5)	76 (41.3)	-	-
Activation (HAI ≥5)	108 (58.7)		
Treatment, n (%)			
No treatment	39 (28.8)	-	-
Under treatment	145 (71.2)		
CLR	5.1 (1.5-13.3) [0.08-115]	1.2 (0.6-1.9) [0.01-9.78]	**<0.001**
CAR	2.4 (0.6-5.9) [0.03-54.20]	0.58 (0.2-0.9) [0.04-4.57]	**<0.001**
NLR	2.3 (1.7-3.6) [0.86-9.32]	2.1 (1.5-2.8) [0.03-188.63]	**0.007**
SIII	761.5 (474.2-1206.3) [178.29-4994.16]	518.5 (362-706.8) [7.28 -69980.78]	**<0.001**

CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, UC: ulcerative colitis, MES: Mayo endoscopic score, MCS: Mayo clinical score, HAI: histologic activity index, CLR: C-reactive protein-lymphocyte ratio, CAR: C-reactive protein-albumin ratio, NLR: neutrophil-lymphocyte ratio, SII: systemic immune-inflammation index, descriptive statistics for numerical variables were presented as median (interquartile range, 25^{th}-75^{th} percentile) [minimum-maximum]

Table 2. Inflammatory indexes of the patients according to the clinical activity, location, and treatment status

	Location of Ulcerative Colitis			p
	Remission (n=12)	**Limited (n=128)**	**Extensive (n=44)**	
CLR	2.2 (1.3-2.5) [0.1-5.4]	2.3 (1.8-3.5) [0.08-77.2]	3 (1.8-14.4) [0.3-115]	**<0.001**
CAR	0.4 (0.2-0.9) [0.06-4.4]	2 (0.5-4) [0.03-34.2]	7.1 (2.9-19) [0.1-54.2]	**<0.001**
NLR	2.2 (1.3-2.5) [0.9-5.7]	2.3 (1.8-3.5) [0.8-9.3]	3 (1.8-4.4) [1.09-7.79]	**<0.001**
SII	535 (305-742) [257-1529]	699 (461-988) [178.3-4994]	1231 (684-1807) [347-4645]	**<0.001**

	MES of Ulcerative Colitis		p
	Remission, MES 0-1 (n=89)	**Activation, MES 2-3 (n=95)**	
CLR	1.75 (0.8-5.46) [0.08-43.82]	10 (4.3-19.6) [0.33-115]	**<0.001**
CAR	0.9 (0.4-2.8) [0.09-25.23]	4.2 (2.2-9.8) [0.22-54.2]	**<0.001**
NLR	2.08 (1.5-3) [0.8-6.2]	2.7 (2-3.8) [0.9-9.32]	**<0.001**
SII	606 (404-888.5) [178.9-1971]	932 (622-1445) [178.3-4994]	**<0.001**

	MCS of Ulcerative Colitis		p
	Remission, MCS ≤2 (n=53)	**Activation, MCS >2 (n=131)**	
CLR	1.3 (0.5-2.9) [0.1-16.8]	7.8 (3.6-16) [0.08-115]	**<0.001**
CAR	0.6 (0.3-1.2) [0.05-15.7]	3.5 (1.7-7.9) [0.03-54.2]	**<0.001**
NLR	2 (1.4-2.6) [0.8-5.9]	2.6 (1.9-3.7) [0.9-9.3]	**<0.001**
SII	539 (375-815) [178.9-2030]	876 (566-1314) [178.3-4994]	**<0.001**

	HAI of Ulcerative Colitis		p
	Remission, HAI <5 (n=76)	**Activation, HAI ≥5 (n=108)**	
CLR	1.4 (0.7-3) [0.1-12.4]	10.3 (5-19) [0.08-115]	**<0.001**
CAR	0.6 (0.3-1.3) [0.05-4.4]	5 (2.5-10.3) [0.03-54.2]	**<0.001**
NLR	1.9 (1.4-2.5) [0.8-5.7]	2.9 (2.1-3.9) [1.1-9.3]	**<0.001**
SII	533 (364-769) [178-1627]	1014 (672-1443) [307-4994]	**<0.001**

	Treatment		p
	No Treatment (n=39)	**Under Treatment (n=145)**	
CLR	4.8 (1.4-10) [0.08-50.4]	5 (1.6-13.5) [0.1-115]	0.573
CAR	2.2 (0.5-4.5) [0.03-47.7]	2.7 (0.6-6) [0.05-54.2]	0.796
NLR	2.3 (1.7-4.4) [1.04-9.3]	2.4 (1.8-3.6) [0.8-7.8]	0.907
SII	763.05 (476.46-1384.16) [232.83-4994.16]	760 (473.8769-1095.93) [178.29-4645.9]	0.314

MES: Mayo endoscopic score, MCS: Mayo clinical score, HAI: histologic activity index, CLR: C-reactive protein-lymphocyte ratio, CAR: C-reactive protein-albumin ratio, NLR: neutrophil-lymphocyte ratio, SII: systemic immune-inflammation index, descriptive statistics for numerical variables were presented as median (interquartile range, 25th-75th percentile) [minimum-maximum]

Table 3. Correlations between the histological activity index and the inflammatory indexes

	CLR		CAR		NLR		SII	
	rho	**p**	**rho**	**p**	**rho**	**p**	**rho**	**p**
HAI	0.737	0.001	0.725	0.001	0.444	<0.001	0.501	0.001

HAI: histologic activity index, CLR: C-reactive protein-lymphocyte ratio, CAR: C-reactive protein-albumin ratio, NLR: neutrophil-lymphocyte ratio, SII: systemic immune-inflammation index

The ROC curve analysis revealed that significant predictive values of CLR, CAR, NLR, and SIII for the clinically active disease according to HAI (Figure 1). Regarding prediction for the clinically active disease according to HAI, none of these parameters was superior to the other (Table 4).

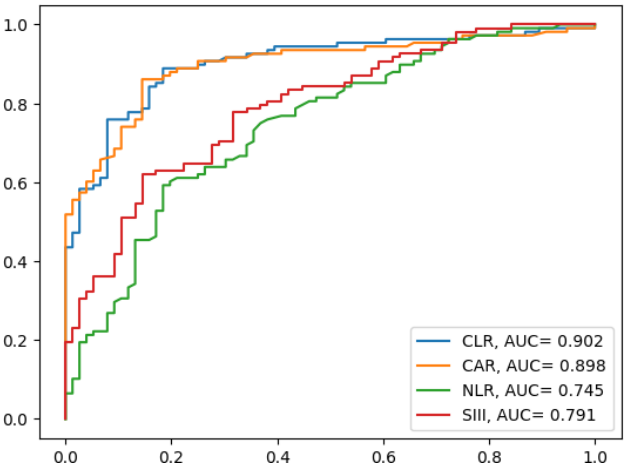

Figure 1. Receiver operating characteristics (ROC) curve of the inflammatory indexes in predicting clinically active ulcerative colitis

DISCUSSION

We reported higher CRP, CAR, CLR, and SIII values in the UC group compared to healthy controls, and the results were consistent with the previous reports. According to endoscopic, clinical, and histological parameters, our results revealed higher inflammatory index values in active UC patients than in remission. Extensive location of the disease also resulted in higher values of inflammatory indexes compared to limited location.

In a previous report, the clinical activity of UC was assessed according to Truelove and Witt's criteria (TWC).

Table 4. Predictive values of the inflammatory indexes for clinically active disease according to histologic activity index

	AUC	95% CI	p	Cut-off	Sensitivity	Specificity	PPV	NPV	LR+	LR-
CLR	0.902	0.858 - 0.945	**<0.001**	>3.389	0.888	0.816	0.872	0.838	4.820	0.137
CAR	0.898	0.853 - 0.943	**<0.001**	>2.011	0.860	0.855	0.893	0.813	5.942	0.164
NLR	0.745	0.675 - 0.815	**<0.001**	>2.561	0.608	0.803	0.813	0.592	3.078	0.489
SIII	0.791	0.727 - 0.855	**<0.001**	>866.983	0.617	0.855	0.857	0.613	4.263	0.448

CLR: C-reactive protein-lymphocyte ratio, CAR: C-reactive protein-albumin ratio, NLR: neutrophil-lymphocyte ratio, SIII: systemic immune-inflammation index, AUC: area under the curve, CI: confidence interval, PPV: positive predictive value, NPV: negative predictive value, LR: likelihood ratio

CAR and interleukin-6 (IL-6) values were higher in active UC patients (10). In a Japanese study, UC patients (n=273) with long disease duration (>7 years) were evaluated, and CAR was positively associated with moderate to severe endoscopic activity (MES 2 and 3) but not with mucosal healing (MES 0). In the mentioned study, clinical remission was determined according to the stool frequency (<3 stool per day), and there was no association between CAR and clinical remission (11). In the current study, we also used the MES method. Patients with endoscopic activation (MES 2 and 3) had higher CAR, CLR, NLR, and SIII values than those in remission (MES 0 and 1). We reported higher values of the inflammatory indexes in patients who were in clinical activation (MCS >2). Inconsistent results in these studies may partly be due to the methodological differences. Steroids, immunosuppressive, and other agents can alter the serum neutrophil, and lymphocyte counts, and resolution of the inflammation may also inhibit CRP secretion (4). Not only the correlation with the disease activity parameters but also inflammatory indexes were declared to be in association with response to treatment in UC (8,9).

In the liver, CRP is produced via the secretion of IL-6, tumor necrosis factor-alpha, and rapidly and it normalizes with the termination of the inflammation. IL-6 is known to be the most potent pro-inflammatory cytokine for CRP secretion (4). Although CRP is widely used in daily practice, it can be affected by gender, age, smoking, and body weight. Additionally, due to some genetic polymorphisms, CRP may not show an adequate acute phase response (21). Environmental and demographic factors (age, sex, smoking, obesity) and diabetes account for only 22 percent to 30 percent of the inter-individual variability in CRP. Family studies revealed that CRP levels have a heritable trait (22). Hypoalbuminemia at disease diagnosis of UC is also associated with poorer clinical outcomes (23).

Neutrophilic infiltration leads to mucosal damage and increased epithelial permeability (24). Neutrophil counts were higher in UC patients compared to the control group in the current study. Feng et al. (10) retrospectively evaluated UC patients (n=306). They reported higher NLR and platelet lymphocyte ratio values in clinically active patients than those in remission, according to TWC. It was noteworthy that there were strong correlations between NLR and fecal calprotectin, pointing to the diagnostic accuracy of NLR. In another study, after adjusting statistically significant traditional inflammatory markers, including CRP, ESR, and WBC counts, the NLR was not reported as a useful predictor of clinical activity in UC patients, according to TWC (25).

Lin et al. (8) found higher SIII values correlating to disease activity, and they pointed to the better diagnostic accuracy of SIII among the other indexes in UC patients (n=187). Similarly, a recent report declared higher SIII values compared to healthy controls and positive correlations between MCS and SIII values in 185 UC patients (13). Reactive thrombocytosis, neutrophilia, and lymphopenia are well-known laboratory results in IBDs, and they can be attributed to the ongoing inflammation leading to higher SIII values in UC (8). Our results about SIII values were similar to the previous reports.

Although not statistically significant, lymphocyte counts were lower in UC patients compared to healthy controls in our results. Lower lymphocyte counts in the circulation can be due to the recruitment of the lymphocytes into the inflammation site (8,26). CLR was reported to be in association with the disease activity in UC previously, as in our study. Unlike the other inflammatory indexes, CAR and CLR values were also found to be predictive for the treatment response, and these indexes might be important prognostic markers if they can be proven in further prospective research (8,9).

The body mentioned above highlights the diagnostic and prognostic utilities of the inflammatory indexes (7,8,27). The most important findings in our study were the associations between the inflammatory indexes and the severity of mucosal inflammation, and quantifying the different phenotypes of UC provided an objective approach. The severity of mucosal inflammation (HAI) in UC patients positively correlated to endoscopic and clinical activity indexes. These results point out the higher mucosal inflammatory activity in the different activity phases of UC and its possible relation to worse clinical outcomes. Besides the other positive correlations between HAI and inflammatory indexes, the strongest correlation between HAI and CLR may be due to lower lymphocyte counts and relatively higher CRP values, as mentioned above (8,26).

Persistent inflammation in the colonic mucosa of UC patients is related to poorer long-term clinical outcomes. Ongoing colonic inflammation is also a good predictor of the disease recurrence and the unresponsiveness to treatment (14,15,28). Ardizzone et al. (14) prospectively evaluated the newly diagnosed moderate-to-severely active UC patients (n=157) who had received steroids initially. After five years of follow-up, they reported that UC patients who had mucosal inflammation despite the steroid treatment had a high rate of colectomy and the need for immunosuppressive agents. This study points out the importance of the resolution of mucosal inflammation for better clinical outcomes (14).

Mucosal inflammation in UC can progress to dysplasia and cancer. It is a potential risk for colorectal cancer. The risk of malignity depends on the duration, extent, and inflammatory activity in UC. It was estimated that the risk

of colorectal cancer is increasing within the range of 0.5 percent to 1.0 percent per year after 8 to 10 years of disease in UC (1). The higher inflammatory index values in patients with extensive location may be a clue for the progression to malignity if further studies can prove it. The median disease duration was calculated as three years in this study, and the duration did not correlate to indexes. The anti-inflammatory effect of the medications may be a possible reason for this result.

Today, the best treatment goal of UC patients focuses on mucosal healing besides the control of symptoms (29). The colonoscopic biopsy is an invasive procedure, and even in clinically quiescent disease showing no endoscopic activity, the colonic mucosa can have the features of microscopic inflammation in 16-100 percent of the cases (15). Discrepancies are also common between the histologic and endoscopic results (17). If the diagnostic accuracies of the inflammatory indexes for predicting mucosal inflammation in UC can be proven prospectively, inflammatory indexes can be taken into consideration as non-invasive and inexpensive tests.

There are many histological activity scoring methods in UC. The Truelove and Richards method is the first developed one (16). Riley, Geboes, Rutter, and Rubin's methods are extensively used methods in clinical trials. The prognostic efficiencies of these scores were also evaluated during or after treatment in UC, and they quantified the severity of mucosal inflammation along with acute and chronic inflammatory activity (15-19). Although these scores are routinely used, they are partially or not validated, and inter-observer variabilities are also possible. The diagnostic accuracy of the serum inflammatory indexes and the histopathological scoring systems in UC can be evaluated prospectively.

In UC patients, CAR, CLR, NLR, and SIII values can predict the severity of mucosal inflammation (HAI) along with the other phenotypic features of the disease. Regarding clinical activity, ROC curves of inflammatory indexes for HAI in predicting the clinically active UC were not different. However, larger sample-sized cohorts might reveal significant results for inflammatory indexes to predict the clinical activity of UC.

We first examined the accuracy of serum inflammatory indexes for predicting the severity of mucosal inflammation according to Truelove and Richards's method. This study has several limitations. It was a single-centered retrospective research. Additional clinical features, including extra-intestinal manifestations, family history, types of medications, and smoking habits, were not evaluated in the current study. In the histopathological examination, only one pathologist evaluated the colonic mucosal biopsies, but the evaluation with more than one independent pathologist could expose the inter-observer variabilities.

CONCLUSION

Inflammatory indexes, as cheap and easily applicable tests, can predict the severity of mucosal inflammation in UC. Inflammatory indexes can be examined for the prediction of mucosal inflammation severity with different inflammatory scoring methods prospectively, and the different traits of UC can be evaluated. This study should be considered a preliminary and the first step for future research.

Ethics Committee Approval: The study was approved by the Ethics Committee of Şehit Prof. Dr. İlhan Varank Training and Research Hospital (05.12.2023, 2021/147).

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