

RESEARCH  
ARTICLE

 **Irfan Kucuk<sup>1</sup>**  
 **Suleyman Bas<sup>2</sup>**

<sup>1</sup> University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Department of Gastroenterology, İstanbul, Türkiye

<sup>2</sup> University of Health Sciences, Sancaktepe Sehit Prof. Dr. İlhan Varank Training and Research Hospital, Department of Internal Medicine, İstanbul, Türkiye

**Corresponding Author:**  
 Irfan Kucuk  
 mail: drirfn@gmail.com

Received: 21.10.2024  
 Acceptance: 23.02.2025  
 DOI: 10.18521/ktd.1570077

**Konuralp Medical Journal**  
 e-ISSN1309-3878  
 konuralptipdergi@duzce.edu.tr  
 konuralptipdergisi@gmail.com  
 www.konuralptipdergi.duzce.edu.tr



## Serum Procalcitonin Values Relate to Disease Activity in Patients with Inflammatory Bowel Diseases

### ABSTRACT

**Objective:** In inflammatory bowel disease (IBD) patients, the correlation between disease activity and serum procalcitonin (SPCT) values remains elusive. By using a number of clinical and laboratory phenotypes of disease activity in conjunction with the degree of mucosal inflammation in patients with ulcerative colitis (UC), we sought to determine whether the blood SPCT levels of IBD patients could be useful as a biomarker.

**Method:** This retrospective case-control study was conducted with 132 UC patients, 83 Crohn's disease (CD) patients, and 72 healthy controls (HCs). In UC, endoscopic and clinical activity were identified using the Mayo Clinical Scoring System (MCS), and the histological activity index (HAI) was calculated using the Truelove and Richards technique. The Crohn's disease activity index (CDAI) of CD patients was calculated. The Montreal classification was preferred for determining disease localization in IBD patients.

**Results:** The median SPCT levels were higher in the UC and CD patients compared to the HC (0.07 vs 0.26 vs 0.03 ng/ml, respectively,  $p<0.001$ ). The MCS of UC and the CDAI of CD patients having active disease showed higher median SPCT levels than the patients in remission ( $p<0.001$ ,  $p=0.033$ , respectively). The CD patients with a fistula and/or an abscess had higher SPCT concentrations than CD patients without a fistula and/or abscess ( $p<0.001$ ). In the UC group, SPCT levels were positively correlated to the MCS and HAI values ( $p<0.001$  for both values).

**Conclusions:** For the disease activity of IBDs, SPCT values may be a cost-effective and practical biomarker.

**Keywords:** Disease Activity, Inflammatory Bowel Disease, Procalcitonin.

## İnflamatuvar Bağırsak Hastalarında Serum Prokalsitonin Değerleri Hastalık Aktivitesi ile İlişkilidir

### ÖZET

**Amaç:** İnflamatuvar barsak hastalıkları (İBH) olan vakalarda hastalık aktivitesi ile serum prokalsitonin (SPCT) değerleri arasındaki korelasyonlar ile ilgili veriler çelişkili olup tam olarak belirlenememiştir. Çalışmamızda ülseratif kolitli (ÜK) hastalarda mukozal inflamasyonun derecesine ilave olarak, İBH hastalık aktivitesinin değişik klinik ve laboratuvar fenotipleri ile SPCT düzeyleri değerlendirilmiş ve SPCT'nin yararlı bir biyobelirteç olup olamayacağı araştırılmıştır.

**Yöntem:** Bu retrospektif vaka-kontrol çalışmasına 132 ÜK hastası, 83 Crohn hastalığı (CH) vakası ve 72 sağlıklı kontrol (SK) dahil edilmiştir. ÜK klinik aktivitesi için Mayo klinik skorlama sistemi (MKS), histolojik aktivite indeksi (HAI) için Truelove ve Richards yöntemleri kullanıldı. CH'da klinik aktivite için Crohn hastalığı aktivite indeksi (CHAI) kullanıldı. İBH'nın endoskopik lokalizasyonu Montreal sınıflandırmasına göre yapılmıştır.

**Bulgular:** Median SPCT düzeyleri ÜK ve CH hastalarında SK'e göre daha yüksekti (0.07 vs 0.26 vs 0.03 ng/ml, sırasıyla,  $p<0.001$ ). ÜK'de MKS ve CH'da CHAI'e göre aktif hastalığı olanlarda remisyonunda olanlara göre median SPCT değerleri daha yüksekti ( $p<0.001$ ,  $p=0.033$ , sırasıyla). Fistülü ve/veya apsesi olan CH vakalarında olmayanlara göre daha yüksek median SPCT seviyeleri tespit edildi ( $p<0.001$ ). ÜK hastalarında SPCT düzeyleri ile MKS ve HAI değerleri arasında pozitif korelasyon saptandı ( $p<0.001$  her ikisi için).

**Sonuç:** Hastalık aktivitesinin belirlenmesinde İBH'da SPCT değerleri uygun maliyetli ve pratik bir biyobelirteç olarak kullanılabilir.

**Anahtar Kelimeler:** Hastalık Aktivitesi, İnflamatuvar Bağırsak Hastalığı, Prokalsitonin

## INTRODUCTION

Inflammatory bowel disorders (IBDs) have been becoming more widespread worldwide. Two main subtypes of IBDs, ulcerative colitis (UC) and Crohn's disease (CD) have relapsing and remitting courses. Assessment of the disease activity plays a pivotal role, especially for the choice of treatment modality in the follow-up sessions of IBD patients (1-3). Until now, several clinical and endoscopic modalities were developed for the assessment of the disease severity and biomarkers that correlate to the clinical, endoscopic, and laboratory features of IBDs are gaining interest (4-8). The resolution of mural inflammation is the ideal therapeutic goal in IBDs and a useful biomarker should display the inflammatory activity in the gut wall (9,10).

The thyroid gland's parafollicular C-cells secrete procalcitonin (PCT), a 116 amino acid precursor of calcitonin that plays a role in calcium control. Normally, serum procalcitonin (SPCT) is detected in low ranges or is undetectable (11). Gram-negative bacteremia has a strong potential to stimulate the secretion of pro-inflammatory cytokines and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), which further induces calcitonin-related polypeptide gene 1 expression. Thus, extra-thyroidal synthesis of PCT occurs in severe bacterial infections, including sepsis, in which supranormal circulating SPCT can be encountered (12,13).

In previous reports, as an easily obtained and economic biomarker, SPCT has gained interest for clinical use in IBDs (14-18). However, studies about SPCT have revealed conflicting results (12,19-22). As a practical marker, the diagnostic and prognostic utility of SPCT in IBDs needs to be further elucidated. In this regard, we aimed to evaluate whether SPCT can be linked to the various clinical and laboratory traits of IBDs along with the severity of mucosal inflammation in patients with UC.

## MATERIAL AND METHODS

**Data Collection:** This research was a single-center retrospective, cross-sectional study. Patients with IBDs who were admitted to the gastroenterology department at the institute and who underwent a colonoscopy procedure between October January 2012 and July 2023 were retrospectively evaluated. In this group, both newly and previously diagnosed patients were included. A second cohort of healthy subjects served as the control group. The local ethics committee approved the study (2023/203).

Subjects with clinical conditions that can alter their SPCT values, such as infections whether acute or chronic, sepsis, inflammatory and autoimmune diseases, severe organ failure, any malignancy, and any physical trauma, as well as patients who underwent a bowel resection and/or had a history of surgery within the previous six months, were excluded from the study. The patients

who underwent colonoscopy for non-IBD indications and whose colonoscopy results were normal constituted the healthy control group.

The medical records of all patient and healthy control files were reviewed and the records of 215 eligible patients with IBDs and 72 healthy controls were evaluated. SPCT, C-reactive protein (CRP), erythrocyte sedimentation (ESR), and total blood count values were noted from the subject files prior to undergoing colonoscopy.

**Evaluation of Patients' Clinical and Endoscopic Activities:** For the clinical activity of patients with UC, the scores ranged from 0 to 12 using the Mayo Clinical Score (MCS). A score of  $\leq 2$  was categorized as clinical remission, while a score of  $>2$  referred to an activation (5). Proctitis, left-sided colitis, and widespread or pancolitis were the three categories used to classify the illness severity of UC patients. While pancolitis and extensive colitis were identified as extensive diseases, proctitis and left-sided colitis were identified to be limited disorders. The endoscopic activity of ulcerative colitis was classified using the Mayo Endoscopic Sub-scoring (MES) index; values ranging from 0 to 3 denote remission and mild, moderate, and severe colitis, respectively (5). A score of 0 and 1 was recorded as an endoscopic inactive disease, while a score of 2 and 3 was recorded as an endoscopic active disease.

For the clinical activity of CD patients, the Crohn's disease activity index (CDAI) was identified, and a score below 150 was defined as clinical remission while a score of  $\geq 150$  referred to activation (6). Ileal, colonic, and ileocolonic diseases were identified as locations of CD.

**An Analysis of Ulcerative Colitis using Histopathology:** A skilled pathologist who was blinded examined the formalin-fixed, paraffin-embedded, and H&E-stained colonic biopsies and graded them using a scale created by Truelove and Richards (23). The scale consisted of three components: active inflammation (0-3), chronic inflammation (0-2), and crypt distortion (0-3). The histologic activity index (HAI) was calculated by summing the scores of these components. The histological remission was defined as scores less than 5, whereas activation was defined as values more than 5 (16).

**Statistical Analysis:** The statistical analysis was performed in SPSS 23.0 (SPSS Inc., Chicago, IL). The normality tests were conducted using the Kolmogorov Smirnov tests and when both tests resulted in  $p$  values of  $> 0.05$ , the distribution was assumed to be normal. Median (interquartile range) was used for the data with non-normal distribution and frequencies with percentages were presented for the categorical data. The Mann-Whitney U and Kruskal-Wallis tests were used to compare non-parametric continuous variables. Additionally, equity with categorical variables was tested using

the chi-square test. Diagnostic accuracy was studied by the receiver operating characteristics (ROC) curved analysis. A  $p$ -value of  $<0.05$  was accepted as statistically significant.

## RESULTS

Totally, age and sex matched for the 132 UC patients (86 males and 46 females), for the 83 CD patients (54 males and 29 females), and for the 72 healthy controls (HCs) (47 males and 25 females)

that were included in the study. Table 1 shows the demographic, clinical, and laboratory characteristics of the subjects. The disease duration was similar between the patient groups. The ESR, CRP, and platelet values of IBD patients were higher compared to those of the HCs ( $p<0.001$ ). In comparison to the HCs, the leucocyte and neutrophil counts were higher in the CD patients ( $p=0.003$  and  $p<0.001$ , respectively).

**Table 1.** The sample's demographic, clinical, and laboratory characteristics.

	UC Patients (n=132)	CH Patients (n=83)	Control Group (n=72)	<i>p</i>
Gender, n (%)				
Female	46 (34.8)	29 (34.9)	25 (34.7)	0.989 <sup>a</sup>
Male	86 (65.2)	54 (65.1)	47 (65.3)	
Age (years), median (IQR)	35 (25-50)	36 (25-46)	38 (29.25-48.75)	0.706 <sup>b</sup>
Disease duration (years), median (IQR)	2.25 (0.50-6)	3 (0.50-5)		0.785 <sup>c</sup>
CRP (mg/L), median (IQR)	16.90 (3.64-76.65)	15.91 (4.58-42.65)	2.36 (0.94-4.09)	<b>&lt;0.001</b> <sup>b,1,*</sup>
ESR (mm/h), median (IQR)	36.50 (14-66.75)	30 (14-50)	9.50 (3-17)	<b>&lt;0.001</b> <sup>b,1,*</sup>
Leukocytes ( $\times 10^3/\mu\text{L}$ ), median (IQR)	7.71 (6.46-9.53)	8.59 (6.93-10.80)	7.27 (6.07-8.85)	<b>0.012</b> <sup>b,2,*</sup>
Neutrophils ( $\times 10^3/\mu\text{L}$ ), median (IQR)	5.04 (3.79-6.45)	5.99 (4.57-8.36)	4.58 (3.68-5.63)	<b>&lt;0.001</b> <sup>b,3,*</sup>
Platelets ( $\times 10^3/\mu\text{L}$ ), median (IQR)	319.50 (262.50-403)	313 (274-409)	244.50 (211-270.75)	<b>&lt;0.001</b> <sup>b,1,*</sup>
Procalcitonin (ng/ml)	0.07 (0.03-1.05)	0.26 (0.04-1.04)	0.03 (0.03-0.05)	<b>&lt;0.001</b> <sup>b,1,*</sup>
UC Localization, n (%)				
Limited disease	82 (62.1)			
Extensive disease	50 (37.9)			
CH Localization, n (%)				
Ileal		49 (59)		
Colonic		12 (14.5)		
Ileocolonic		22 (26.5)		
Mayo Endoscopic Score of UC, n (%)				
Inactive disease	2 (1.5)			
Mild disease	51 (38.6)			
Moderate disease	47 (35.6)			
Severe disease	32 (24.2)			
IBDs in first degree relatives, n (%)	18 (13.6)	15 (18.1)		0.380 <sup>a</sup>
Mayo Clinical Score of UC, median (IQR)	6 (3-9)			
Remission (score $\leq 2$ ), n (%)	28 (21.2)			
Activation (score $>2$ ), n (%)	104 (78.8)			
Crohn's Disease Activity Index, median (IQR)		182 (108-272)		
Remission (score $< 150$ ), n (%)		35 (42.2)		
Activation (score $\geq 150$ ), n (%)		48 (57.8)		
Histological Activity Index in UC, median (IQR)	6 (5-7)			
Fistula and/or abscess		18 (21.7)		
Extra-intestinal manifestations n (%)	13 (9.8)	26 (31.3)		<b>&lt;0.001</b> <sup>a,*</sup>

**Abbreviations:** CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; IQR: Interquartile range; UC: Ulcerative colitis; CD: Crohn's disease; IBDs: Inflammatory bowel diseases.

**Footnotes:** **1:** Significant difference in the comparison of UC vs controls, CD vs controls ( $p<0.001$ ,  $p<0.001$ ); **2:** Significant difference in the comparison of CD vs HCs ( $p=0.003$ ); **3:** Significant difference in the comparison of CD vs HCs ( $p<0.001$ ). a: Chi-Square Test, b: Kruskal-Wallis Test, c: Mann-Whitney U Test. \*: Statistically significant ( $p<0.05$ ).

Most of the UC patients had limited disease detected in the colonoscopy procedure, whereas terminal ileum was the most common location in the CD patients. With respect to the clinical activity scores, most of the patients with IBDs had an active disease. The ratio of the patients who were under treatment and the patients with IBDs in first degree relatives were similar between the UC and CD groups. Extra-intestinal manifestations were more prevalent in the CD patients than in the UC patients ( $p<0.001$ ) (Table 1).

The median SPCT levels of the UC and CD patients were higher than those of the HCs (0.07 [0.03-1.05] vs. 0.26 [0.04-1.04] vs 0.03 [0.03-0.05]

ng/ml, respectively,  $p<0.001$ ). CD patients had the highest median SPCT values (Table 1). Regarding the treatment status and presence of IBDs in first-degree relatives, the median SPCT values were not statistically significantly different in both the UC and CD groups (Table 2). According to the MCS values of the UC patients and the CDAI values of the CD patients, the patients with active disease had higher median SPCT levels than the patients in remission ( $p<0.001$  and  $p=0.033$ , respectively). In the CD group, the patients with a fistula and/or abscess had higher SPCT levels than the patients without a fistula and/or abscess ( $p<0.001$ ) (Table 2).

**Table 2.** Serum procalcitonin values according to the disease phenotypes in the patients with IBDs.

		Procalcitonin				
Ulcerative Colitis		n	%	Median	IQR	<i>p</i>
Mayo clinical scoring	Remission (score ≤ 2)	28	21.2	0.03	0.02-0.04	<0.001 <sup>a,*</sup>
	Activation (score >2)	104	78.8	0.89	0.04-1.07	
Localization of UC	Limited disease	82	62.1	0.04	0.02-0.06	<0.001 <sup>a,*</sup>
	Extensive disease	50	37.9	1.07	1.03-1.76	
IBDs in first degree relatives	Positive	18	13.6	0.50	0.03-2.05	0.383 <sup>a</sup>
	Negative	114	86.4	0.07	0.03-1.04	
Extra-intestinal manifestations	Positive	13	9.8	0.04	0.03-1.05	0.789 <sup>a</sup>
	Negative	119	91.2	0.07	0.03-1.05	
Crohn's disease						
Treatment status	No Treatment	34	41	0.22	0.05-1.03	0.550 <sup>a</sup>
	Under Treatment	49	59	0.82	0.03-1.07	
CDAI Score	Remission (score< 150)	35	42.2	0.06	0.03-1.02	0.033 <sup>a,*</sup>
	Activation (score ≥150)	48	57.8	0.84	0.09-1.06	
Localization of CH	Ileal	49	59	0.08	0.03-1.02	0.010 <sup>b,1,2,*</sup>
	Colonic	12	14.5	1.05	0.38-1.82	
	Ileocolonic	22	26.5	0.94	0.18-1.04	
IBDs in first degree relatives	Positive	15	18.1	0.93	0.14-1.07	0.187 <sup>a</sup>
	Negative	68	81.9	0.25	0.03-1.04	
Extra-intestinal manifestations	Positive	26	31.3	1.02	0.45-1.42	0.001 <sup>a,*</sup>
	Negative	57	68.7	0.14	0.03-1.02	
Fistula and/or abscess	Positive	18	21.7	1.07	0.91-2.02	<0.001 <sup>a,*</sup>
	Negative	65	78.3	0.14	0.03-1.02	

**Abbreviations:** CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; IQR: Interquartile range; UC: Ulcerative colitis; CD: Crohn's disease; CDAI: Crohn's Disease Activity Index

**Footnotes:** 1: Significant difference between ileal localization and colonic localization in patients with CD ( $p=0.014$ ); 2: Significant difference between ileal localization and ileocolonic localization in patients with CD ( $p=0.026$ ).

a: Mann-Whitney U Test, b: Kruskal-Wallis Test. \*: Statistically significant ( $p<0.05$ ).

No statistically significant correlation was determined between the disease duration and the SPCT levels in patients with IBDs. In the UC group, the SPCT levels were positively correlated to the MCS, HAI, CRP, ESR, leukocytes,

neutrophil, and platelet values ( $p<0.001$  for all). In the patients with CD, there were positive correlations between the SPCT values and the CRP, ESR, and platelet counts ( $p<0.001$ ,  $p=0.004$ ,  $p=0.039$ , respectively) (Table 3).

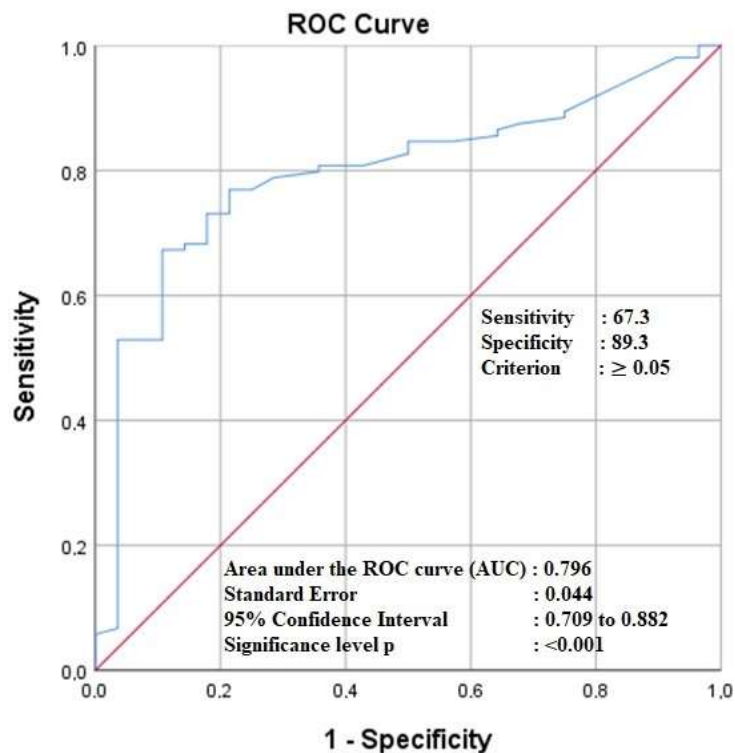
**Table 3.** Correlation analysis of the serum procalcitonin values with clinical and laboratory parameters in the patients with IBDs

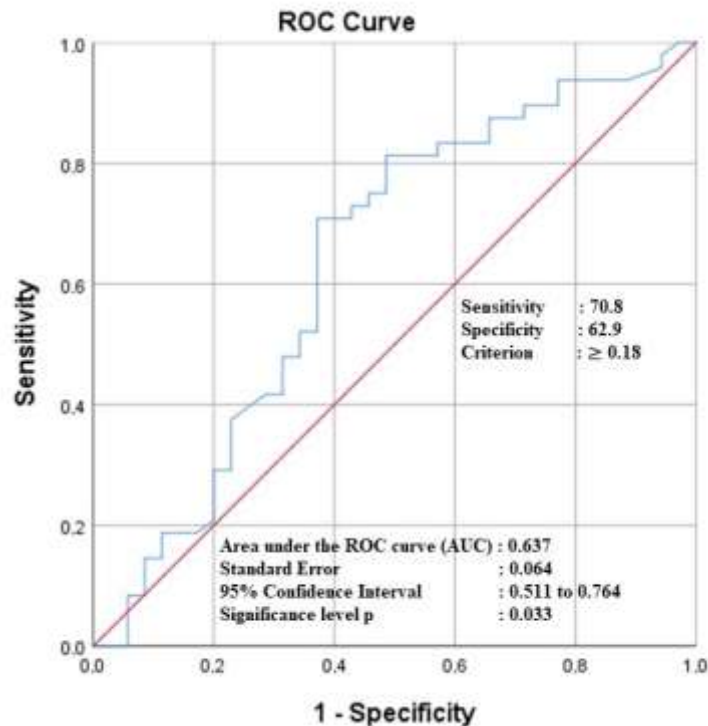
	Procalcitonin	
	rho	p
<b>Ulcerative Colitis</b>		
Disease duration	-0.058	0.506
Mayo Clinical Score	0.624	<b>&lt;0.001 *</b>
Histological Activity Index	0.757	<b>&lt;0.001 *</b>
C-Reactive Protein	0.861	<b>&lt;0.001 *</b>
Erythrocyte sedimentation rate	0.524	<b>&lt;0.001 *</b>
Leukocytes	0.313	<b>&lt;0.001 *</b>
Neutrophils	0.323	<b>&lt;0.001 *</b>
Platelets	0.442	<b>&lt;0.001 *</b>
<b>Crohn's disease</b>		
Disease duration	0.141	0.204
Crohn's Disease Activity Index	0.194	0.078
C-Reactive Protein	0.676	<b>&lt;0.001 *</b>
Erythrocyte sedimentation rate	0.313	<b>0.004 *</b>
Leukocytes	0.016	0.883
Neutrophils	0.009	0.935
Platelets	0.227	<b>0.039 *</b>

**Footnotes:** 1: Significant difference in the comparison of UC vs HCs, CD vs HCs ( $p<0.001$ ,  $p<0.001$ ); 2: Significant difference in the comparison of CD vs HCs ( $p=0.003$ ); 3: Significant difference in the comparison of CD vs HCs ( $p<0.001$ ). rho: Sperman Correlation Coefficient. \*: Statistically significant ( $p<0.05$ )

The area under the curve (AUC) for the SPCT concentrations showed a diagnostic accuracy of 0.796 (95% CI: 0.709-0.882,  $p<0.001$ ) for the clinical activity of UC (MCS), according to the receiver operating characteristic curve (ROC) analysis. For the cut-off value of  $\geq 0.05$  ng/ml, sensitivity was 67.3% and specificity was 89.3% (Figure 1).

The AUC for the SPCT concentrations had a diagnostic accuracy of 0.637 (95% CI: 0.511-0.764,  $p=0.033$ ) for the clinical activity of CH (CDAI), according to the ROC analysis. For the cut-off value of  $\geq 0.18$  ng/ml, the sensitivity and specificity were 70.8% and 62.9%, respectively (Figure 2).

**Figure 1.** The predicted serum procalcitonin values for the Mayo Clinical Scoring in ulcerative colitis were analyzed using ROC curves.



**Figure 2.** ROC curve analysis of the serum procalcitonin predicted concentrations for Crohn's disease CDAI scoring.

#### DISCUSSION

In daily clinical practice, CRP, as a traditional marker of inflammation, is widely used to assess the disease activity of IBDs patients. However, CRP has some drawbacks for the monitoring of disease activity (24). Serum CRP values depend on age, gender, weight, and smoking status, and sometimes, despite the overt inflammation, CRP may be normal or slightly elevated in 15-20% patients because of genetic polymorphisms and inter-individual variability (24). In addition, CRP may not exhibit mucosal healing (MH) in IBDs patients with lower inflammatory activity (25). SPCT levels have a tendency of early elevation and they can also rapidly normalize compared to serum CRP concentrations in bacterial infections (11). Thus, as a marker of inflammation, PCT may be more specific than CRP in infectious conditions (12,16).

Monitoring of fecal calprotectin (FCP) is a good choice in the follow up sessions of IBDs (8). However, the threshold values of FCP have not been accurately determined and it needs to be validated (8). In addition, FCP is an expensive test and obtaining the samples may cause discomfort for FCP. As a limitation, the FCP values of the IBD patients could not be noted for the comparison of FCP and SPCT levels.

Herrlinger et al. first evaluated the SPCT values in adult IBDs patients (26). In that study, regarding the discriminative efficacy of SPCT between self-limited infectious enterocolitis and IBDs, a PCT level greater than 0.4 ng/ml was noted as diagnostic for self-limited infectious

enterocolitis. The SPCT concentrations were within the normal ranges in all the patients with IBDs. However, according to Truelove and Witt's severity index (TWI) and the CDAI in the patients with UC and CD respectively, approximately 40% of the patients presenting with a clinically active disease tended to have higher SPCT values than the patients with an inactive disease (26). Additionally, Oruç et al. found that patients with CD had greater SPCT values than HCs, but there was no significant difference between the SPCT values of the UC patients and the SPCT values of the HCs (14).

In a previous report, the SPCT values were higher among the UC patients (n=18) compared to the HCs (n=11), and according to the TWI and Mayo endoscopic sub-scoring, severe UC patients had higher SPCT values compared to mild and moderate patients and the HCs, but no significant difference existed between the SPCT values of mild and moderate UC patients and the SPCT values of the HCs (15). Nishio et al. noted that SPCT values correlated to the CDAI values in patients with CD, whilst no correlation existed between the MCS and SPCT values in the UC patients (20). In another report, no correlation was found between the disease location, MCS values, partial MCS values, pelvic involvement, and the SPCT concentrations (21). In the study of Chung et al., there was no correlation between the clinical activity parameters and the SPCT levels (22).

In light of the current literature, SPCT values have a tendency to increase in IBDs patients with an active disease with respect to clinical and laboratory parameters. Although the

methodological differences in the clinical trials may partly be responsible for the variable results, the diagnostic and prognostic value is still controversial. However, most probably, SPCT can be a valuable marker for the infectious complications in IBDs (12,17).

SPCT values lower than 0.05 ng/ml are normal, whereas patients with limited but not systemic infection could present with SPCT values of 0.05-0.5 ng/ml (11). In our results, the median SPCT values of the UC and CD patients were within the ranges of limited bacterial infection that can be ascribed to localized intestine bacterial inflammation, which also have a pathogenic role in IBDs (1,11,12,28). In our data, the median SPCT values were the highest in the CD patients, but there was no significant difference between the SPCT values of the UC and CD patients. In the CD patients presenting with fever episodes, elevated SPCT values were also declared to be a marker that can discriminate an intra-abdominal abscess from disease flares (17). The highest SPCT concentrations in the CD patients might be due to the formation of an intra-abdominal abscess or fistula, which is directly related to bacterial infections, and 21.7 % of the CD patients in our cohort had a fistula and/or an abscess.

With respect to SPCT concentrations, we firstly evaluated extra-intestinal manifestations in the patients with IBDs. Extra-intestinal manifestations can relate to the severity of inflammation in the intestine and the treatment of IBDs can alleviate these symptoms (1,27). In our study, the ratio of patients with extra-intestinal manifestations was higher among the CD patients compared to the UC group and it can be another explanation for the elevated SPCT values in the CD group. Our results revealed higher median SPCT levels according to the respective MCS and CDAI scoring in patients with UC and CD. Despite the different scoring systems, which were settled in different clinical trials, the SPCT values displayed the clinically active disease (14-16).

Inflammation in the gut wall relates to disease recurrence and poorer clinical outcomes, including malignancy in IBDs (10). MH is defined as both endoscopic and histopathological remission (25). Current treatment modalities aim for complete MH; however, they cannot achieve complete MH (9). We found positive correlations between the SPCT values and the histological activity scores in the UC patients along with the other biochemical tests for inflammation. SPCT might a good marker

for MH and disease activity in UC. A limitation is that we were unable to ascertain the CD patients' histology activity. The CDAI scores were also positively correlated to the SPCT values in CD patients. In both diseases, the patients who had a clinically active disease had higher SPCT concentrations compared to the patients in the remission phase.

According to our results, patients with extensive location of UC and patients with colonic CD had higher median SPCT values. The disruption of mucosal integrity and intestinal permeability lead to high numbers of bacteria that cause uncontrolled inflammation within mucus layer (28). Colonic involvement represents the increased bacterial content leading to induced inflammatory activity that results in elevated SPCT values. The role of intestinal microbiota in the pathogenesis of CD and UC is a well-known entity and both diseases usually present in parts of the intestine with a high bacterial content (1). In addition, the use of antibiotics has a modest benefit over placebos for the induction of remission in patients with CD (28).

Although conflicting results exist in the literature, our results were consistent with some previous reports and highlight the clinical utility of SPCT in IBDs (12,26). We also reported a diagnostic accuracy for the clinical activity of IBD patients. Different results of the SPCT values for the disease phenotypes in IBDs may also be due to variations in demographic, clinical, and laboratory characteristics of populations among the studies.

The most important limitation of the current study is the retrospective examination of a single center. We were not able to evaluate the clinical and laboratory conditions that mimic IBDs. As noted earlier, determination of the FCP values could be more valuable in the study population. The prospective evaluation of the disease traits of patients with IBDs can provide more information for the diagnostic and prognostic utility of SPCT in these patients. Moreover, the evaluation of the histopathological severity of inflammation in CD patients may be more informative.

## CONCLUSION

Easily obtained and cost-effective tests have been attractive for clinicians of inflammatory diseases. Monitoring of SPCT values in the follow up sessions of IBD patients might be a practical and easy method for the determination of disease activity in these patients. SPCT concentrations might be a valuable biomarker for the severity of mucosal inflammation in UC patients.

## REFERENCES

1. Osterman MT, Lichtenstein GR. Ulcerative Colitis. In: Feldman M, Friedman SL, Brandt JL editors (Eds). Sleisenger and Fordtran's Gastrointestinal and Liver Disease. Philadelphia (USA): Elsevier Saunders; 2016. p. 2023-61.
2. Kırac Y, Yalçın B, Ustaoglu M. The Relationship between Smoking Status, Carbon Monoxide Levels and Quality of Life, Disease Characteristics in Inflammatory Bowel Diseases. Konuralp Medical Journal. 2023;15(1):69-77.

3. Con D, Andrew B, Nicolaides S, van Langenberg DR, Vasudevan A. Biomarker dynamics during infliximab salvage for acute severe ulcerative colitis: C-reactive protein (CRP)-lymphocyte ratio and CRP-albumin ratio are useful in predicting colectomy. *Intest Res.* 2022;20(1):101-13.
4. Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. *Br Med J.* 1955;2(4947):1041-8.
5. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. *N Engl J Med.* 1987;317(26):1625-9.
6. Best WR, Becktel JM, Singleton JW, Kern F Jr. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. *Gastroenterology.* 1976;70(3):439-44.
7. Rachmilewitz D. Coated mesalazine (5-aminosalicylic acid) versus sulphasalazine in the treatment of active ulcerative colitis: a randomised trial. *BMJ.* 1989;298(6666):82-6.
8. Chen F, Hu Y, Fan YH, Lv B. Clinical Value of Fecal Calprotectin in Predicting Mucosal Healing in Patients With Ulcerative Colitis. *Front Med (Lausanne).* 2021;8:679264.
9. Ardizzone S, Cassinotti A, Duca P, Mazzali C, Penati C, Manes G, et al. Mucosal healing predicts late outcomes after the first course of corticosteroids for newly diagnosed ulcerative colitis. *Clin Gastroenterol Hepatol.* 2011;9(6):483-9.
10. Bryant RV, Winer S, Travis SP, Riddell RH. Systematic review: histological remission in inflammatory bowel disease. Is 'complete' remission the new treatment paradigm? An IOIBD initiative. *J Crohns Colitis.* 2014;8(12):1582-97.
11. Samsudin I, Vasikaran SD. Clinical Utility and Measurement of Procalcitonin. *Clin Biochem Rev.* 2017;38(2):59-68.
12. Lippi G, Sanchis-Gomar F. Procalcitonin in inflammatory bowel disease: Drawbacks and opportunities. *World J Gastroenterol.* 2017;23(47):8283-90.
13. Demir İ, Yılmaz İ. The Effect of Polypharmacy on Procalcitonin Levels in The Intensive Care Admission of Geriatric Patients with Sepsis. *Konuralp Medical Journal.* 2020;12(2):216-22.
14. Oruç N, Özütemiz O, Osmanoğlu N, İlter T. Diagnostic value of serum procalcitonin in determining the activity of inflammatory bowel disease. *Turk J Gastroenterol.* 2009;20(1):9-12.
15. Koido S, Ohkusa T, Takakura K, Odahara S, Tsukinaga S, Yukawa T, et al. Clinical significance of serum procalcitonin in patients with ulcerative colitis. *World J Gastroenterol.* 2013;19(45):8335-41.
16. Oussalah A, Laurent V, Bruot O, Guéant JL, Régent D, Bigard MA, et al. Additional benefit of procalcitonin to C-reactive protein to assess disease activity and severity in Crohn's disease. *Aliment Pharmacol Ther.* 2010;32(9):1135-44.
17. Ge X, Hu D, Cao Y, Liu Z, Ding C, Tian H, et al. Procalcitonin in Crohn's disease with fever episodes, a variable to differentiate intra-abdominal abscess from disease flares. *Int J Surg.* 2016;36(Pt A):34-9.
18. Wu HM, Wei J, Li J, Wang K, Ye L, Qi Y, et al. Serum Procalcitonin as a Potential Early Predictor of Short-Term Outcomes in Acute Severe Ulcerative Colitis. *Dig Dis Sci.* 2019;64(11):3263-73.
19. Chen JM, Liu T, Gao S, Tong XD, Deng FH, Nie B. Efficacy of noninvasive evaluations in monitoring inflammatory bowel disease activity: A prospective study in China. *World J Gastroenterol.* 2017;23(46):8235-47.
20. Nishio E, Saruta M, Arihiro S, Matsuoka M, Mitsunaga M, Ide D, et al. The clinical benefit of procalcitonin to assess disease activity and severity in inflammatory bowel disease. *Gastroenterology.* 2016;150(4, Supplement 1):995.
21. Hosomi S, Yamagami H, Itani S, Yukawa T, Otani K, Nagami Y, et al. Sepsis Markers Soluble IL-2 Receptor and Soluble CD14 Subtype as Potential Biomarkers for Complete Mucosal Healing in Patients With Inflammatory Bowel Disease. *J Crohns Colitis.* 2018;12(1):87-95.
22. Chung SH, Lee HW, Kim SW, Park SJ, Hong SP, Kim TI, et al. Usefulness of Measuring Serum Procalcitonin Levels in Patients with Inflammatory Bowel Disease. *Gut Liver.* 2016;10(4):574-80.
23. Truelove SC, Richards WCD. Biopsy studies in ulcerative colitis. *Br Med J.* 1956;1(4979):1315-8.
24. Brull DJ, Serrano N, Zito F, Jones L, Montgomery HE, Rumley A, et al. Human CRP gene polymorphism influences CRP levels: implications for the prediction and pathogenesis of coronary heart disease. *Arterioscler Thromb Vasc Biol.* 2003;23(11):2063-9.
25. Sakurai T, Saruta M. Positioning and Usefulness of Biomarkers in Inflammatory Bowel Disease. *Digestion.* 2023;104(1):30-41.
26. Herrlinger KR, Dittmann R, Weitz G, Wehkamp J, Ludwig D, Schwab M, et al. Serum procalcitonin differentiates inflammatory bowel disease and self-limited colitis. *Inflamm Bowel Dis.* 2004;10(3):229-33.
27. De Vos M. Joint involvement associated with inflammatory bowel disease. *Dig Dis.* 2009;27(4):511-5.
28. Khan KJ, Ullman TA, Ford AC, Abreu MT, Abadir A, Marshall JK, et al. Antibiotic therapy in inflammatory bowel disease: a systematic review and meta-analysis. *Am J Gastroenterol.* 2011;106(4):661-73.