The Role of Prognostic Nutritional Index and Systemic Immune-Inflammation Index in Determining Ulcerative Colitis Severity

Prognostik Nutrisyonel İndeksin ve Sistemik İmmün-İnflamasyon İndeksin Ülseratif Kolit Hastalığının Sıvvetinin Belirlenmesindeki Rolü

Ibrahim Ethem Guven¹, Batuhan Baspinar¹, Rasim Eren Cankurtaran², Ertugrul Kayacetin²

¹Department of Gastroenterology, Ankara City Hospital; ²Department of Internal Medicine, Department of Gastroenterology, Ankara Yıldırım Beyazit University School of Medicine, Ankara, Turkey

ABSTRACT
Aim: Ulcerative colitis (UC) is a chronic, idiopathic, relapsing inflammatory disease of the gastrointestinal tract. In recent years, biochemical parameters have been widely used to determine the disease activity of UC. The present study aimed to determine the relationship between the prognostic nutritional index (PNI), systemic immune-inflammation index (SII), and disease activity.

Material and Method: All adult patients followed in the IBD unit of the Ankara City Hospital Gastroenterology Department between March 1st, 2019, and March 31st, 2021, were included in this retrospective study. We analyzed the relationship between the SII, PNI, and the endoscopic severity of UC. In addition, PNI and SII were compared between the active and remission group. Disease activity was described by the Rachmilewitz endoscopic activity index (EAI).

Results: The study group consisted of 402 patients. One hundred sixty-five of these patients were in the endoscopic remission group, and 237 were in the endoscopically active group. SII, NLR, and PLR values were significantly higher in the active UC group, and PNI values exhibited a lower mean than inactive UC patients (p<0.05 for all parameters). In addition, the NLR, PLR, and SII were positively, and PNI was negatively correlated with the endoscopic activity index (respectively, R=0.29, R=0.24, R=0.38, R=-0.32; and for all parameters, p<0.001).

Conclusion: PNI and SII were significantly associated with UC activity. PNI and SII may be useful tools for assessing disease activity in UC.

Key words: ulcerative colitis; disease activity; nutrition

ÖZET
Amaç: Ülseratif kolit (ÜK) gastrointestinal sistemin kronik, idiyopatik, tekrarlayan inflamatuar bir hastalığıdır. Son yıllarda ÜK’in hastalığı belirlemek için biyokimyasal parametreler yaygın olarak kullanılmaktadır. Bu çalışmada, prognostik nutrisyonel indeksi (PNİ) ve sistemik immün-inflamasyon indeksi (SII) ile hastalık aktivitesi arasındaki ilişkinin belirlenmesi amaçlanmıştır.

Materyal ve Metot: Bu retrospektif çalışma Ankara Şehir Hastanesi Gastroenteroloji Bölümü IBD ünitesinde 1 Mart 2019 ile 31 Mart 2021 tarihleri arasında takip edilen tüm erişkin hastalar dahil edildi. PNİ ve SII ile ÜK’in endoskopik aktivite şiddetini arasındaki ilişkinin analiz edildi. Ek olarak PNİ ve SII aktiv ve remisyondaki hasta grupları arasında karşılaştırıldı. Hastalık aktivitesinin belirlenmesinde Rachmilewitz endoskopik aktivite indeksi (EAI) kullanıldı.

Bulgular: Çalışma grubu 402 hastadan oluşuyordu. Bu hastaların %165’i endoskopik olarak remisyondu, 237’si endoskopik olarak aktiftir. Aktif ÜK grubunda, SII, NLR, PLR değerleri significantly higher in the active UC group, and PNİ değerleri daha düşük saptandı (p<0.05 tüm parametreler için). Ek olarak, SII, NLR, PLR, PNİ pozitif olarak ve PNİ negatif olarak endoskopik aktivite indeksi ile korele saptandı (srasıyla, R=0.29, R=0.24, R=0.38, R=-0.32; ve tüm parametreler için p<0.001).

Sonuç: PNİ ve SII, ÜK aktivitesi ile önemli ölçüde ilişkilidir. PNİ ve SII, ÜK’de hastalık aktivitesinin değerlendirilmesi için faydalı bir araç olabilir.

Anahtar kelimeler: ülseratif kolit; hastalık aktivitesi; nutrisyon

İletişim/Contact: Ibrahim Ethem Güven, Department of Gastroenterology, Ankara City Hospital, Ankara, Turkey • Tel: 0505 759 66 63 • E-mail: drtheemguen@gmail.com • Geliş/Received: 04.11.2021 • Kabul/Accepted: 20.03.2022 • ORCID: Ibrahim Ethem Güven, 0000-0002-7436-6414 • Batuhan Başpinar, 0000-0003-3143-2642 • Rasim Eren Cankurtaran, 0000-0002-3687-3845 • Ertugrul Kayacetin, 0000-0002-8822-3991
Introduction
Ulcerative colitis (UC) is an immune-mediated bowel disorder characterized by chronic and recurrent inflammation of colonic mucosa \(^1\). There is often rectal involvement, and the inflammation spreads from the rectum to the proximal colon \(^2\). The natural course of the disease is characterized by relapse and remission periods \(^3\). During exacerbations, the main symptoms are bleeding, fever, and abdominal pain \(^4\). Early detection of the disease activity is important for both treatment success and prevention of complications that can affect the quality of life \(^5\).

Colonoscopy is the most sensitive and specific diagnostic step for diagnosing and determining the disease activity and severity. However, the assessment of disease activity by colonoscopy is an invasive procedure and not easily accessible \(^6\). Therefore, noninvasive inflammatory biomarkers are needed for early detection of the disease activity.

White blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are frequently evaluated to assess inflammation severity in UC. However, an optimal test has not yet been developed, and the currently used biomarkers are nonspecific \(^7\). In recent years, the prognostic nutritional index (PNI), the systemic immune-inflammation index (SII), the platelet-lymphocyte ratio (PLR), and neutrophil-lymphocyte ratio (NLR) have been adapted as an indicator of inflammation and have been widely studied to define the severity of inflammation in rheumatic diseases, diabetes mellitus, arterial hypertension, several cardiovascular diseases, and malignancies \(^8\)–\(^11\).

Herein, we aimed to evaluate the relationship between SII, PNI, and endoscopic activity in patients with UC.

Material and Methods

Patients
All adult patients followed in the Inflammatory Bowel Disease Unit of the Ankara City Hospital Gastroenterology Department between March 1st, 2019, and March 31st, 2021, was employed in this retrospective study. The UC diagnosis was made based on clinical, radiological, laboratory, endoscopic, and histological findings. The patient's demographic characteristics, disease duration, medication history, endoscopic activity score, disease localization, and laboratory test results were obtained from hospital records.

Exclusion criteria were hematological disease and malignancy, acute bacterial or viral infection or chronic infectious diseases, autoimmune diseases, steroid usage within the previous week, neoplastic disorders, chronic liver disease, or chronic renal failure. This study was approved by Ankara City Hospital Scientific Research Assessment and Ethics Committee (Approval No: E1/1753/2021).

Laboratory Values
NLR, PLR, SII, and PNI were calculated by the formulas mentioned below:

- NLR: neutrophil count/lymphocyte count
- PLR: platelet count/lymphocyte count
- SII: platelet count × NLR
- PNI: 10 × albumin (g/dL) + 0.005 × lymphocyte count

Disease Activity
The endoscopic disease activity and severity in patients with UC were determined by the Rachmilewitz endoscopic activity index (EAI) based on colonoscopy findings. The EAI score is <4 points for the remission group. Based on the severity of inflammation, the EAI score is regarded as 4–9 points for the mild/moderate active group and 10–12 points for the severe active group.

Statistical Analysis
Statistical analysis was performed with SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA). The normality of distribution was tested using the Kolmogorov-Smirnov test for continuous variables. The results were presented as mean ± standard deviation (SD) for variables with normal distribution and median (interquartile range, IQR 25%–75%) for variables with the abnormal distribution. Statistical comparisons of continuous variables were performed using the independent samples t-test or Mann-Whitney U test regarding the distribution pattern. Comparisons of categorical variables were performed using the chi-square test. Spearman’s or Pearson’s test was used for the correlation analysis. A two-tailed p<0.05 was considered statistically significant.

Results
A total of 402 UC patients were enrolled in the presented study. One hundred sixty-five of these patients...
were in the endoscopic remission group, and 237 were in the endoscopically active group. No significant difference was found in group comparisons regarding age, gender, and lymphocyte counts. The median disease duration of UC patients after diagnosis was 84.0 (48.0–141.0) months. The medication history and disease location of all patients are presented in Table 1.

Platelet, WBC, neutrophil, CRP, and sedimentation values were higher in the active disease group. The mean hemoglobin and albumin values were lower than the remission group (p<0.05 for all parameters). SII, NLR, and PLR values were significantly higher, and PNI values were significantly lower in patients in the severe UC group versus the mild to moderate UC group (p<0.05 for all parameters) (Table 2).

In addition, the NLR, PLR, and SII were positively, and PNI was negatively correlated with EAI (respectively, R=0.29, R=0.24, R=0.38, R=-0.32; and for all parameters p<0.001) (Table 3).

**Discussion**

This retrospective study revealed significantly higher SII, NLR, PLR values, and lower PNI values in the

---

**Table 1. Baseline clinical and laboratory parameters of study population**

| Total (n=402) | Active (n=237) | Remission (n=165) | P value |
|--------------|---------------|------------------|---------|
| Age, (years) | 47.4±13.7     | 47.6±13.7        | 47.2±13.7 | 0.75 |
| Gender male, n (%) | 238 (59) | 148 (62) | 90 (55) | 0.12 |
| Disease duration, month | 84.0 (48.0–141.0) | 84.0 (36.0–142.0) | 84.0 (48.0–132.0) | 0.80 |
| Endoscopic activity index | 5.5±3.8 | 8.3±2.3 | 1.6±1.4 | <0.001 |
| Hemoglobin, g/dl | 13.4±1.7 | 13.2±1.8 | 13.8±1.6 | 0.01 |
| Platelet, x10³/mm³ | 300.5±96.4 | 320.1±109.3 | 272.4±64.7 | <0.001 |
| WBC, x10³/mm³ | 7.4±1.9 | 7.9±2.0 | 6.7±1.5 | <0.001 |
| Neutrophil, x10³/mm³ | 4.6±1.6 | 5.0±1.8 | 4.0±1.1 | <0.001 |
| Lymphocyte, x10³/mm³ | 1.9±0.7 | 2.0±0.7 | 1.9±0.6 | 0.67 |
| Albumin, gr/dL | 4.4±0.4 | 4.3±0.4 | 4.6±0.2 | <0.001 |
| CRP, mg/dL | 2.0 (0.6–10.0) | 7.0 (2.1–16.0) | 0.6 (0.3–0.9) | <0.001 |
| Sedimentation, mm/hour | 11.0 (6.0–20.0) | 15.0 (7.0–23.0) | 8.0 (5.0–12.0) | <0.001 |
| NLR | 2.6±1.5 | 2.9±1.8 | 2.2±0.8 | <0.001 |
| PLR | 152.6 (117.9–187.7) | 159.4 (122.5–205.8) | 148.0 (114.8–173.0) | <0.001 |
| SII x 10³ | 672.2 (468.0–910.6) | 768.3 (525.5–1045.2) | 596.8 (419.0–726.5) | <0.001 |
| PNI | 54.8±5.5 | 53.8±6.2 | 56.2±4.0 | <0.001 |
| Medication history, n (%) | | | | |
| 5-ASA | 291 (72) | 156 (66) | 135 (82) | 0.001 |
| 5-ASA + AZA | 48 (12) | 38 (16) | 10 (6) | 0.002 |
| 5-ASA + anti-TNF | 51 (13) | 37 (16) | 14 (9) | 0.03 |
| 5-ASA + AZA + anti-TNF | 11 (3) | 5 (2) | 6 (4) | 0.36 |
| Localization, n (%) | | | | |
| Proctitis | 76 (19) | 28 (12) | 48 (29) | <0.001 |
| Left-sided colitis | 231 (58) | 141 (60) | 90 (55) | 0.30 |
| Pan-colitis | 94 (23) | 67 (28) | 27 (16) | 0.005 |

Results are expressed as: mean ± SD or median (IQR) or frequency (%). WBC: white blood cell, CRP: C-reactive protein, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, SII: systemic immune-inflammation index, PNI: prognostic nutritional index, 5-ASA: 5-aminosalicylic acid, AZA: azathioprine, TNF: tumor necrosis factor
active UC group compared to the inactive UC group. Also, NLR, PLR, and SII were significantly higher, and PNI was significantly lower in patients in the severe UC group versus the mild to moderate UC group. In addition, the NLR, PLR, and SII were positively, and PNI was negatively correlated with the endoscopic activity index.

UC is a chronic inflammatory disease of the colonic mucosa, and the clinical course of the disease is characterized by remission and relapse. Early activation diagnosis is important as it reduces the need for surgery and enables early treatment modification. Clinical evaluation of disease activation is determined by evaluating the radiological, endoscopic, and pathological findings. Colonoscopy is the standard gold method for assessing the disease activity, allowing direct visibility of the mucosa and biopsy. However, there are some limitations, such as the increased risk of complications and lack of accessibility of the process. Therefore, non-invasive methods to evaluate disease activation have attracted more attention in recent years. In this concept, calprotectine is frequently used as a non-invasive inflammatory marker. However, lack of availability in all clinics and high cost limits the routine use of calprotectine.

### Table 2. Baseline clinical and laboratory parameters according to the severity of the disease

|                          | Mild/Moderate (n=137) | Severe (n=100) | P value |
|--------------------------|-----------------------|----------------|---------|
| Age, (years)             | 47.0±13.7             | 48.5±13.6     | 0.39    |
| Gender male, n (%)       | 84 (61)               | 64 (64)       | 0.68    |
| Disease duration, month  | 84.0 (48.0–145.0)     | 72.0 (24.0–120.0) | 0.16   |
| Endoscopic activity index| 6.6±1.5               | 10.5±0.9      | <0.001  |
| Hemoglobin, g/dl         | 13.7±1.6              | 12.6±1.89     | <0.001  |
| Platelet, x10^9/mm³      | 308.6±110.6           | 335.9±105.9   | 0.027   |
| WBC, x10^9/mm³           | 7.5±1.7               | 8.3±2.3       | 0.006   |
| Neutrophil, x10^9/mm³    | 4.7±1.5               | 5.5±2.0       | 0.001   |
| Lymphocyte, x10^9/mm³    | 2.0±0.6               | 1.9±0.8       | 0.38    |
| Albumin, gr/dL           | 4.5±0.3               | 4.2±0.5       | <0.001  |
| CRP, mg/dL               | 3.1 (0.9–8.3)         | 15.5 (7.5–32.0) | <0.001 |
| Sedimentation, mm/hour   | 11.0 (6.0–18.0)       | 20.0 (10.2–29.7) | <0.001 |
| NLR                      | 2.6±1.7               | 3.2±1.7       | 0.006   |
| PLR                      | 154.4 (115.6–191.5)   | 170.4 (133.5–244.2) | 0.007 |
| SII x 10^3               | 704.2 (480.1–954.3)   | 863.4 (650.8–1386.5) | <0.001 |
| PNI                      | 55.2±4.8              | 51.7±7.2      | <0.001  |

Medication history, n (%)

|          | 5-ASA | 5-ASA + AZA | 5-ASA + anti-TNF | 5-ASA + AZA + anti-TNF |
|----------|-------|-------------|------------------|------------------------|
| 5-ASA    | 97 (71)| 18 (13)     | 19 (14)          | 2 (2)                  |
| 5-ASA + AZA | 59 (59)| 20 (20) | 18 (18) | 3 (3) |
| 5-ASA + anti-TNF | 7 (7) | 62 (62) | 31 (31) |
| 5-ASA + AZA + anti-TNF | 0.048 | 0.16 | 0.40 | 0.65 |

Localization, n (%)

|          | Proctitis | Left-sided colitis | Pan-colitis |
|----------|-----------|--------------------|-------------|
| Proctitis| 21 (15)   | 79 (58)            | 36 (28)     |
| Left-sided colitis | 7 (7) | 62 (62) | 31 (31) |
| Pan-colitis | 0.048 | 0.55 | 0.45 |

Results are expressed as: mean ± SD or median (IQR) or frequency (%), WBC: white blood cell, CRP: C-reactive protein, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, SII: systemic immune-inflammation index, PNI: prognostic nutritional index, 5-ASA: 5-aminosalicylic acid, AZA: azathioprine, TNF: tumor necrosis factor.

### Table 3. Correlation between Endoscopic activity index and different inflammatory variables in study population

| Rho   | P      |
|-------|--------|
| NLR   | 0.294  | <0.001 |
| PLR   | 0.245  | <0.001 |
| SII   | 0.385  | <0.001 |
| PNI   | 0.328  | <0.001 |

NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, SII: systemic immune-inflammation index, PNI: prognostic nutritional index.
In routine clinical practice, WBC count, CRP, and ESR have been widely used in the follow-up of UC. However, due to their low sensitivity and specificity, they don’t accurately reflect the activity of the disease. In recent years, NLR and PLR values have been widely used to determine the disease activity of UC, and it has been shown that there is a significant relationship between the disease activity index and high NLR and PLR values. Moreover, the SII index has been proposed to help determine the disease’s endoscopic severity.

In conclusion, this study demonstrates that SII, PNI, and PLR values were strongly associated with disease activity and endoscopic severity in UC, which can help determine the disease’s endoscopic severity.

References

1. Magro F, Gionchetti P, Eliakim R, et al. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part I: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. Journal of Crohn’s & Colitis. 2017;11(6):649–70.

2. Langholz E, Munkholm P, Nielsen OH, Kreiner S, Binder V. Incidence and prevalence of ulcerative colitis in Copenhagen country from 1962 to 1987. Scand J Gastroenterol. 1991;26:1247–56.

3. DeRoche TC, Xiao SY, Liu X. Histological evaluation in ulcerative colitis. Gastroenterol Rep (Oxf)2014;2(3):178–92.

4. Travis SP. Review article: the management of mild to severe acute ulcerative colitis. Aliment Pharmacol Ther. 2004;20(Suppl. 4):88–92.

5. Cima RR, Pemberton JH. Medical and surgical management of chronic ulcerative colitis. Arch Surg. 2005;140:300–10.

6. Leighton JA, Shen B, Baron TH, Adler DG, Davila R, Egan Jv, et al. Standards of Practice Committee, American Society for Gastrointestinal Endoscopy: endoscopy in the diagnosis and treatment of inflammatory bowel disease. Gastrointest Endosc. 2006;63:558–65.

7. Vermeire S, Van Assche G, Rutgeerts P. Laboratory markers in IBD. Useful, magic, or unnecessary toys? Gut. 2006;55:426–431.

8. Posul E, Yilmaz B, Aktas G, Kurt M. Does neutrophil-to-lymphocyte ratio predict active ulcerative colitis? Wien Klin Wochenschr. 2015;127(7–8):262–5.

9. Seo M, Yamada T, Morita T, Furukawa Y, Tamaki S, Iwasaki Y, et al. Prognostic value of systemic immune-inflammatory index in patients with chronic heart failure (P589). Eur. Heart J. 2018;39:70–10. Jeong Y, Jeon SR, Kim HG, Moon JR, Lee TH, Jang JY, Cho JH, Park JS, Park H, Lee KH, Kim JO, Lee JS, Ko BM, Park S. The role of platelet to lymphocyte ratio and neutrophil to lymphocyte ratio in ulcerative colitis. Intest Res. 2021;19(1):62–70.

10. Choheho T, Uchino M, Sasaki H, Bando T, Takesue Y, Ikeuchi H. Associations Between the Prognostic Nutritional Index and Morbidity/Mortality During Intestinal Resection in Patients with Ulcerative Colitis. World J Surg. 2018;42(7):1949–1959.

11. Naber AH, de Jong DJ. Assessment of disease activity in inflammatory bowel disease; relevance for clinical trials. Neth J Med. 2003;61:105–10.

12. Bohl JL, Sobka K. Indications and Options for Surgery in Ulcerative Colitis. Surg Clin North Am. 2015;95(6):1211–32.

13. Conrad K, Roggenbuck D, Laass MW. Diagnosis and classification of ulcerative colitis. Autoimmun Rev. 2014;13(4–5):463–6.

14. Ungaro R, Mehandru S, Allen PB, Peyrin-Biroulet L, Colombel JF. Ulcerative colitis. Lancet. 2017;389(10080):1756–1770.

15. Yoon JY, Park SJ, Hong SP, Kim TI, Kim WH, Cheon JH. Cor relations of C-reactive protein levels and erythrocyte sedimentation rates with endoscopic activity indices in patients with ulcerative colitis. Dig Dis Sci. 2014;59(4):829–37.

16. Zittan E, Kelly OB, Kirsch R, Milgrom R, Burns J, Nguyen GC, Croitoru K, Van Assche G, Silverberg MS, Steinhart AH. Low Fecal Calprotectin Correlates with Histological Remission and Mucosal Healing in Ulcerative Colitis and Colonic Crohn’s Disease. Inflamm Bowel Dis. 2016;22(3):623–30.

17. Osada T, Ohkusa T, Okayasu I, Yoshida T, Hirai S, Beppu K, Shibuya T, Sakamoto N, Kobayashi O, Nagahara A, Terai T, Watanabe S. Correlations among total colonoscopic findings, clinical symptoms, and laboratory markers in ulcerative colitis. J Gastroenterol Hepatol. 2008;23 Suppl 2:262–7.
19. Chang S, Malter L, Hudesman D. Disease monitoring in inflammatory bowel disease. World J Gastroenterol. 2015;21(40):11246–59.

20. Demir AK, Demirtas A, Kaya SU, Tastan I, Butun I, Sagan M, Sahin S, Tasliyurt T, Yilmaz A. The relationship between the neutrophil-lymphocyte ratio and disease activity in patients with ulcerative colitis. Kaohsiung J Med Sci. 2015;31(11):585–90.

21. Hu B, Yang XR, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Res. 2014;20:6212–22. Yang R, Chang Q, Meng X, Gao N, Wang W. Prognostic value of Systemic immune-inflammation index in cancer: A meta-analysis. J Cancer. 2018;9:3295–302.

23. Ahn SS, Jung SM, Song JJ, Park YB, Lee SW. Prognostic nutritional index is correlated with disease activity in patients with systemic lupus erythematosus. Lupus. 2018;27:1697–7.

24. Peters Jr T. Metabolism: Albumin in the body. In: All About Albumin: Biochemistry, Genetics and Medical Applications. Amsterdam: Elsevier; 1996. p. 188–250.

25. Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. Br J Anaesth. 2000;85:599–610.

26. Moshage HJ, Janssen JA, Franssen JH, Hafkenscheid JC, Yap SH. Study of the molecular mechanism of decreased liver synthesis of albumin in inflammation. J Clin Invest. 1987;79:1635–41.

27. Correa-Rodríguez M, Pocovi-Gerardino G, Callejas-Rubio JL, Fernández RR, Martín-Amada M, Cruz-Caparros MG, Ortega-Centeno N, Rueda-Medina B. The Prognostic Nutritional Index and Nutritional Risk Index Are Associated with Disease Activity in Patients with Systemic Lupus Erythematosus. Nutrients. 2019;11(3):638.

28. Ataş N, Babaoğlu H, Demirel E, Çelik B, Biliç Salman R, Satış H, Karadeniz H, Güler AA, Haznedaroğlu S, Göker B, Tufan A, Öztürk MA. Use of prognostic nutritional index in the evaluation of disease activity in patients with Behçet’s disease. Eur J Rheumatol. 2020;7(3):99–104.