Retrospective Cohort Study

Effective immune-inflammation index for ulcerative colitis and activity assessments

Meng-Hui Zhang, Han Wang, Hong-Gang Wang, Xin Wen, Xiao-Zhong Yang

ORCID number: Meng-Hui Zhang 0000-0002-8679-386X; Han Wang 0000-0003-3655-7953; Hong-Gang Wang 0000-0003-1025-7734; Xin Wen 0000-0001-8904-1340; Xiao-Zhong Yang 0000-0001-8788-6569.

Author contributions: Zhang MH and Wang H contributed equally to this work by participating in project design, data collection, literature retrieval, data collection and analysis, and drafting of the article; All authors have approved the final version of the manuscript.

Institutional review board statement: The study was approved by the medical ethics committee of The Affiliated Huai’an No.1 People’s Hospital of Nanjing Medical University Institutional.

Conflict-of-interest statement: All of the authors declare that they have no conflicts of interest regarding this paper.

Data sharing statement: No additional unpublished data are available.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

BACKGROUND
The inverse association between systemic immune-inflammation index (SII) and overall survival in tumors has been studied.

AIM
To evaluate the hematological indexes for assessing the activity of ulcerative colitis (UC).

METHODS
In this case-control study, 172 UC patients and healthy participants were included. Comparisons were made among groups of white blood cells, hemoglobin, platelets, neutrophils, lymphocytes, monocytes, SII, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR). The relationship with hematological inflammation was verified by Spearman correlation analyses. The efficiency of SII, NLR, and PLR for distinguishing between UC and severe disease status was assessed by the receiver operator curve and logistic regression analyses.

RESULTS
The values of SII, NLR, and PLR were higher in UC patients than in controls (P < 0.001) and were positively correlated with the Mayo endoscopic score, extent, Degree of Ulcerative Colitis Burden of Luminal Inflammation (DUBLIN) score, and Ulcerative Colitis Endoscopic Index of Severity (UCEIS). The cut-off NLR value of 562.22 predicted UC with a sensitivity of 79.65% and a specificity of 76.16%. Logistic regression analysis revealed that patients with SII and NLR levels above the median had a significantly higher risk of UC (P < 0.05). Risk factors independently associated with DUBLIN ≥ 3 included SII ≥ 1776.80 [odds ratio (OR) = 11.53, 95% confidence interval (CI) OR = 11.53, 95% CI] and NLR value of 2.67-4.23 (OR = 2.96, 95% CI).
multivariate analysis. Compared with the first quartile, SII ≥ 1776.80 was an independent predictor of UCEIS ≥ 5 (OR = 18.46, P = 0.012).

CONCLUSION
SII has a certain value in confirming UC and identifying its activity.

Key Words: Ulcerative colitis; Systemic immune-inflammation index; Endoscopic score; Neutrophil-to-lymphocyte ratio; Platelet-to-lymphocyte ratio; Disease activity

INTRODUCTION
Ulcerative colitis (UC) is a chronic, non-specific inflammatory condition in the colon, which has recently increased in Asia. Etiology may be associated with genetic susceptibility, intestinal flora disorders, multiple environmental factors, and abnormal immune disorders[1]. The overall prevalence exceeds 0.3% in North America, Oceania, and most European countries[2]. Inflammatory bowel disease (IBD) is the third highest risk factor for colorectal cancer (CRC), and 18% of IBD-related CRC cases occur in patients with a history of less than 8 years[3]. Cross-sectional imaging under endoscopy may accurately reflect current inflammation of the intestines. Endoscopy biopsy plays a dominant role in determining a diagnosis, disease severity, treatment response, recurrence, and CRC. However, it is expensive, invasive, and weakly repeatable, and the disease may be aggravated by surgery. Hence, we continued to explore non-invasive measures to determine the severity of UC and the level of inflammatory burden.

Blood, urine, and fecal indicators may prevent these limitations and have been studied to indicate the inflammatory state. Urine markers are rarely studied and have no clinical application[4]. The most important acute phase serological markers are C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR), which are useful for predicting relapse, severity, and response to treatment[5-8]. Fecal calprotectin (FC) can be derived from neutrophils and may reflect the destruction of the epithelial barrier and the inflammatory process of the intestine. Compared to blood markers and symptomatic flare, FC is the best to trace relapse, particularly after colectomy, with values ≤ 100 μg/mg, indicating remission without a need for colonoscopy[9,10]. However, due to the variation in testing methodologies and cut-off values, non-specific markers including ESR, CRP, and FC are vulnerable to various pathological conditions and not generally accepted criteria for disease monitoring[10,11]. Thus, there is a need to identify new indicators to improve diagnostic efficiency, cost performance, safety, and convenience.

Recent studies have shown that the platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) may help to diagnose UC and its activity[12-14]. However, the potential role of PLR and NLR in patients with UC remains controversial. Compared PLR and NLR only consists of two circulating immune cells, the systemic immune-inflammation index (SII) integrates platelets (PLTs), neutrophils, and lymphocytes. SII is a useful biomarker of the inflammatory status and immune response. A higher SII value indicates a relatively low lymphocyte count and high
Zhang MH et al. SII evaluate UC and its activity

neutrophil and PLT counts, demonstrating a stronger inflammatory response and weaker cell-mediated immunity. Elevated SII is a weak prognostic predictor of various malignant solid tumors including digestive system tumor, renal cancer, germ-cell tumors, metastatic castration-resistant prostate cancers, non-small cell lung cancer, and small cell lung cancer[15-17]. Infiltration and metastasis of malignant tumors are inflammatory-mediated processes. However, there is no study in the literature regarding SII in UC.

In this study, we evaluated the diagnostic value of SII and determined if SII is more advantageous for assessing disease severity than NLR or PLR in patients with UC.

MATERIALS AND METHODS

Participants
The data analyzed in this study were from January 2017 to December 2019, and included 172 patients with UC and 172 healthy controls from Huaian No. 1 People’s Hospital. Data on sex, age, duration of illness, frequency of defecation, stool consistency, pulse, and body temperature were extracted from the medical record. The diagnosis of UC was based on consensus for the diagnosis and treatment of IBD as the UC group. Participants with hematological disease, liver, and kidney damage, tumors, certain forms of autoimmune diseases, and infections were excluded. The study was approved by the medical ethics committee of The Affiliated Huai’an No. 1 People’s Hospital of Nanjing Medical University Institutional. Informed consent was waived in this retrospective study.

Laboratory investigation
Venous blood was taken from the fasting state in the morning and then analyzed by the automatic analyzer certified by our hospital. A blood test can yield measurements of white blood cells (WBCs), hemoglobin (HB), PLTs, neutrophils, lymphocytes, and monocytes. Based on the above parameters, SII, PLR, and NLR were determined.

Colonoscopy score
The patient underwent colonoscopy in the endoscopic center of our hospital after intestinal preparation. The endoscopic outputs were documented in detail by professional experts, and then rated based on previous literature. Extent is classified as follows[18]: E1 = proctosigmoiditis, E2 = left-sided colitis (distal to splenic flexure), E3 = pancolitis (proximal to splenic flexure). The Mayo endoscopic score (MES)[19] is considered to be 0 points for normal or inactive lesions, 1 point for mild (redness, the reduced texture of blood vessel, and mildly brittle mucosa), 2 points for moderate (significant erythema, disappeared texture of blood vessel, brittle or eroded mucosa), and 3 points (spontaneous mucosal bleeding or ulceration). The score for Degree of Ulcerative Colitis Burden Luminal Inflammation (DUBLIN) is the MES multiplied by the maximal extent score[20]. The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) includes three parts: Vascular pattern, bleeding, erosions, and ulcer of the mucosa, with each component graded between 0 and 3 (normal to severe)[21].

Statistical analysis
Statistical analysis was performed using SPSS 26.0 software (SPSS Inc., Chicago, IL, United States). The data were stratified according to age and gender. Matching of the propensity score between patients and controls was precise and fuzzy with 1:1.02 age and sex matching. The Kolmogorov-Smirnov test was done to detect normality. Data between groups were compared using the Mann-Whitney U test for continuous variables and the chi-squared test for categorical variables. The relationship between inflammatory markers in blood and extent, MES, DUBLIN score, and UCEIS was verified by Spearman correlation analyses. Receiver operating characteristic (ROC) curves were constructed to evaluate the diagnostic efficiency of SII, NLR, and PLR. Multivariate logistic regression was performed to identify the risk factor of UC and the severe UC status (DUBLIN score 3 and UCEIS 5). The first quartile was set as a reference, and \( P < 0.05 \) was considered statistically significant.
RESULTS

Participants’ clinical characteristics
The median ages of the UC and control groups were 48.00 and 47.50 years, respectively ($P = 0.545$). No statistically significant differences in age and gender between UC patients and controls were observed. The median SII values of active UC patients and controls were 1063.23 and 384.86, respectively ($P < 0.001$). UC patients had lower levels of HB and lymphocytes and higher values of WBC, PLT, neutrophils, NLR, PLR, and SII compared to the healthy subjects ($P < 0.05$) (Table 1).

Correlation of inflammation markers and endoscopic score
SII, NLR, and PLR showed a positive correlation with endoscopic severity scores (extent, MES, DUBLIN score, and UCEIS), whereas SII was the most reliable indicator of inflammation markers (Table 2). The relationship among NLR, PLR, extent, MES, DUBLIN score and UCEIS was weak (all $P > 0.05$). Although Spearman correlation analysis of active UC indicated a significant correlation of SII with extent, DUBLIN score and UCEIS, no correlation was found with MES ($r = 0.124$, $P = 0.106$).

ROC curves of inflammation markers
Analysis of the ROC curve showed that the optimum SII cut-off point for UC was 562.22, with an area under the curve (AUC), sensitivity, and specificity of 0.856, 79.65%, and 76.16%, respectively (Table 3). The AUC value of the NLR was 0.858, and there was no statistical difference relative to SII ($P = 0.86$). The cut-off value of NLR was 2.66, with 75% sensitivity and 82.56% specificity. The AUC of SII and NLR was statistically different from that of PLR ($P < 0.01$).

Inflammation markers for UC and disease severity
Multivariate logistic regression showed that SII and NLR were associated with UC and higher endoscopic scores. Compared to the lowest quartile, SII and NLR levels in the third and highest quartile levels were independent risk factors for UC ($P < 0.05$) (Table 4), but were not the values in other levels. The odds ratio (OR) for DUBLIN 3 was 11.53 and 2.96 at SII 1776.80 and NLR of 2.67-4.23, respectively ($P < 0.05$) (Table 5). Table 6 shows that the OR was 18.46 at SII 1776.80 for UCEIS 5 ($P < 0.05$).

DISCUSSION
Routine blood testing is the most commonly used detection index, but additional studies are required for its use as an indicator of IBD activity. This study determined if SII could diagnose and predict the severity of the UC. The preliminary findings of our study showed elevated levels of neutrophils and PLTs, and reduced levels of leukocytes in patients with UC. Various pathogenic factors may disrupt the balance of the intestinal mucosal immune system, either directly or indirectly. Polymorphonuclear neutrophils are first recruited into the intestine when the body is suffering from an infection or mucosal injury. Activated neutrophils also develop overproduced proteases, including elastase, proteinase, and matrix metalloproteinases, which may reduce the levels of junctional proteins, leading to epithelial barrier defects\cite{22,23}. Lymphocyte subsets are considered to cause IBD ulcers. Abnormal gut-homing lymphocyte has identified endothelial ligands by expressing specific surface receptors, causing an overactive immune response and damage to the intestine\cite{24}. The development and clinical trials of the anti-leukocyte adhesion agent are underway, and the United States Food and Drug Administration approved the powder injection of vedolizumab in 2014 for patients with moderate to severe UC and Crohn’s disease with reduced efficacy of conventional drugs and anti-tumor necrosis factor (anti-TNF) antibodies\cite{25}. Our results confirmed the lower levels of active UC in peripheral blood lymphocytes. Histopathological examination of UC showed diffuse and chronic infiltration of the inflammatory cells\cite{26}. Neutrophils, lymphocytes, plasma cells, monocytes, and eosinophils were seen in the lamina propria, and neutrophils were found in the glandular epithelial cells. Active IBD is characterized by cryptitis and a formation of the crypt abscess. PLTs serve as a bridge between coagulation and inflammation\cite{27,28}. Previous studies have indicated that PLT count, PLT-PLT, and PLT-leukocyte aggregates are increased in blood circulation, and colonic veins are associated with disease activity\cite{29}. Upon activation, PLTs secrete inflammatory molecules derived from PLTs, synthesize a series of mediators, and generate
Table 1 Clinical and laboratory characteristics of patients with ulcerative colitis and healthy controls

|                          | Control, n = 172 | Ulcerative colitis, n = 172 | P value |
|--------------------------|------------------|-----------------------------|---------|
| Male, n (%)              | 96 (55.81%)      | 91 (52.90%)                 | 0.588   |
| Age (yr)                 | 47.50 (37.00-56.00) | 48.00 (35.00-57.00)         | 0.545   |
| WBC (× 10^9/L)           | 5.37 (4.47-6.29)  | 7.26 (5.85-9.23)            | < 0.001 |
| HB (g/L)                 | 138.00 (125.00-152.50) | 131.00 (122.00-143.00)      | 0.001   |
| PLT (× 10^9/L)           | 213.00 (179.50-251.00) | 245.00 (197.00-312.00)      | < 0.001 |
| N (× 10^9/L)             | 3.11 (2.55-3.86)   | 5.48 (4.07-7.25)            | < 0.001 |
| L (× 10^9/L)             | 1.67 (1.35-2.08)   | 1.25 (0.97-1.70)            | < 0.001 |
| M (× 10^9/L)             | 0.30 (0.24-0.37)   | 0.33 (0.18-0.49)            | 0.295   |
| SII (× 10^9/L)           | 384.86 (282.31-557.42) | 1063.23 (587.24-1787.87)    | < 0.001 |
| NLR, %                   | 1.83 (1.45-2.47)   | 4.31 (2.73-6.47)            | < 0.001 |
| PLR, %                   | 127.49 (98.71-156.21) | 191.87 (130.97-263.89)      | < 0.001 |

HB: Hemoglobin; L: Lymphocytes; M: Monocytes; N: Neutrophils; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; PLT: Platelet; SII: Systemic immune-inflammation index; WBC: White blood cell.

Table 2 Correlation analysis between systemic immune-inflammation index and endoscopic score

|                  | MES | Extent | DUBLIN | UCEIS |
|------------------|-----|--------|--------|-------|
|                  | r   | P value | r     | P value | r     | P value | r     | P value |
| SII              | 0.124 | 0.106 | 0.174 | 0.023 | 0.193 | 0.011 | 0.227 | 0.003 |
| NLR              | 0.068 | 0.375 | 0.146 | 0.056 | 0.139 | 0.068 | 0.130 | 0.088 |
| PLR              | 0.043 | 0.577 | 0.060 | 0.432 | 0.074 | 0.336 | 0.108 | 0.158 |

DUBLIN: Degree of Ulcerative Colitis Burden of Luminal Inflammation; MES: Mayo endoscopic score; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; SII: Systemic immune-inflammation index; UCEIS: Ulcerative Colitis Endoscopic Index of Severity.

Table 3 Receiver operating characteristic analyses of systemic immune-inflammation index, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in diagnosing ulcerative colitis

| Variable | Cut-off | AUC (95%CI) | Sensitivity, % | Specificity, % | P value |
|----------|---------|-------------|----------------|----------------|---------|
| SII      | > 562.22 | 0.856 (0.814-0.891) | 79.65 | 76.16 | < 0.001 |
| NLR      | > 2.66   | 0.858 (0.817-0.893) | 75.00 | 82.56 | < 0.001 |
| PLR      | > 156.54 | 0.754 (0.705-0.799) | 65.70 | 76.16 | < 0.001 |

AUC: Area under the receiver operating characteristic curve; CI: Confidence interval; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; SII: Systemic immune-inflammation index.

extracellular vesicles in IBD inflammatory cascades\(^{30}\), PLTs that express P-selectin, glycoprotein IIb/IIIa, CD-40 ligand, and glycoprotein 53 may interact with inflammatory cells that cause tissue injury. Meanwhile, inflammatory mediators such as interleukin-6 (IL-6) stimulate bone marrow thrombopoiesis and accelerate the metabolism of PLT, forming a vicious circle\(^{29,31,32}\). Drugs that inhibit PLT inflammatory makers may alleviate the course of disease in IBD models despite the risk of aggravating ulcer bleeding. For patients with UC, higher SII values result from elevated peripheral blood neutrophils and PLTs, and lower lymphocyte levels. NLR and PLR levels can predict activation of UC and endoscopic mucosal injury\(^{12,13}\). Similar results were found in our study showing that NLR, PLR, and SII levels were higher in UC patients and correlated with the endoscopic score. In distinguishing UC, the AUC of SII and NLR was higher than that of PLR, and the SII...
Table 4 Multivariate logistic regression analyses of the relationship between inflammatory indicators and ulcerative colitis

|     | B    | P value | Odds ratio | 95%CI       |
|-----|------|---------|------------|-------------|
| SII | 346.44 | Reference |            |             |
|     | 346.45-574.88 | 0.56 | 0.241  | 1.76 | 0.69-4.52 |
|     | 574.89-1084.51 | 1.24 | 0.031  | 3.45 | 1.12-10.63 |
|     | 1084.52 | 3.03  | 0.001  | 20.64 | 3.57-119.18 |
| NLR | 1.69 | Reference |            |             |
|     | 1.70-2.53 | 0.64  | 0.163  | 1.91 | 0.77-4.71 |
|     | 2.54-4.60 | 1.32  | 0.010  | 3.73 | 1.37-10.18 |
|     | 4.61  | 2.53  | 0.001  | 12.52 | 2.77-56.60 |
| PLR | 111.93 | Reference |            |             |
|     | 111.94-149.11 | -0.15 | 0.718  | 0.87 | 0.40-1.90 |
|     | 149.11-203.33 | -0.26 | 0.560  | 0.77 | 0.32-1.84 |
|     | 203.34 | -0.38 | 0.517  | 0.68 | 0.21-2.18 |

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; SII: Systemic immune-inflammation index.

Table 5 Multivariate logistic regression analyses of the relationship between inflammatory indicators and degree of ulcerative colitis burden of luminal inflammation

|     | B    | P value | Odds ratio | 95%CI       |
|-----|------|---------|------------|-------------|
| SII | 589.63 | Reference |            |             |
|     | 589.64-1047.18 | 0.51  | 0.372  | 1.66 | 0.55-5.04 |
|     | 1047.19-1776.79 | 0.86  | 0.299  | 2.36 | 0.47-11.98 |
|     | 1776.80 | 2.45  | 0.027  | 11.53 | 1.33-100.15 |
| NLR | 2.66 | Reference |            |             |
|     | 2.67-4.23 | 1.09  | 0.047  | 2.96 | 1.01-8.65 |
|     | 4.24-6.46 | 0.85  | 0.237  | 2.33 | 0.57-9.49 |
|     | 6.47  | -0.20 | 0.820  | 0.82 | 0.15-4.49 |
| PLR | 132.35 | Reference |            |             |
|     | 132.36-190.31 | -0.59 | 0.286  | 0.56 | 0.19-1.63 |
|     | 190.32-263.47 | -0.33 | 0.620  | 0.72 | 0.20-2.65 |
|     | 263.48 | -1.06 | 0.201  | 0.35 | 0.07-1.76 |

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; SII: Systemic immune-inflammation index.
was an independent indicator of UC and for the status of severe disease. SII is a novel inflammatory marker based on neutrophils, lymphocytes, and PLTs. Chronic intestinal mucosal inflammation in patients with UC has been associated with the risk of hospitalization, colectomy, thrombosis, cardiovascular problems, and malignant tumors\(^\text{34}\). Monitoring the burden of intestinal inflammation is, therefore, critical for evaluating the progress of the disease activity and recognizing patients who need to upgrade their treatment regimens. The differential leucocytic ratio is an easily applicable and cost effective test, which could be more helpful for monitoring the inflammatory burden when they are used together with the serum laboratory inflammation index. Other studies have suggested that higher levels of SII predict shorter overall survival or progression-free survival in various malignancies, because the inflammatory reaction is crucial for the tumor progression\(^\text{15,16}\).

The current goal of UC treatment is mucosal healing. While not all endoscopic scores have been thoroughly validated to date, MES and UCEIS are frequently used indicators to measure endoscopic inflammation activity. The DUBLIN score is determined based on the MES. We found that the NLR, PLR, and SII levels were correlated with endoscopic scores. In this context, Akpinar et al\(^\text{12}\) demonstrated that NLR and PLR could identify and predict active diseases under endoscopy, as described by the Rachmilewitz endoscopic activity index. Another study showed that lower levels of both baseline NLR and PLR were associated with mucosal healing in UC patients after 54 wk of anti-TNF therapy\(^\text{35}\). In this study, logistic regression analysis showed that the higher levels of SII were independently associated with UC, DUBLIN ≥ 3, and UCEIS ≥ 5. The risks of treatment failure, colectomy, drug improvement, and enhancement of treatment plan are related to DUBLIN ≥ 3\(^\text{20}\). Four grades of UCEIS scores were stratified: remission (0-1), mild (2-4), moderate (5-6), and severe (7-8)\(^\text{36}\). When UCEIS was ≥ 5, 27/54 (50%) needed rescue therapy, and 18/54 (33%) came to colectomy during the follow-up compared to UCEIS ≤ 4\(^\text{37}\). The results of this study show that SII could be used as brief information on activity and degree of mucosal damage prior to the endoscopic examination, in particular for patients with high responsiveness to invasive investigations or unable to obtain equipment during the active period. Although the promising efficacy needs further study, non-invasive indicators have a supporting role in predicting active lesions.

This study had some limitations. First, this retrospective analysis was not able to remove the possible bias. Second, the cases studied were from a single institution, and it is unknown in their region or country. Third, it is rudimentary to investigate the SII value in the blood, and subsequent studies should be conducted on the relationship between SII and histological injury-related indicators. To conclude, this is the first study to provide evidence that SII can assist with UC diagnosis. Defining a known cut-off value will help determine the diagnosis and severity of UC if the results of this study are further verified.

**CONCLUSION**

Our analysis showed that the SII, NLR, and PLR were significantly elevated and were related to endoscopic severity in UC patients, which can help in diagnosing UC and determining the endoscopic severity of this disease. Moreover, because elevated levels of SII are an independent risk factor for patients with active UC, paying attention to this factor may lead to the early identification of UC and prevent disease progression. In addition, the SII values can be used to track disease severity and provide physicians with information to adjust treatment protocols when colonoscopy is not available. Further research is needed on the correlation between differential leucocytic ratio and histological severity of mucosal injury. This first application of SII was based on evidence to determine the importance of diagnosing UC, and the severity of the disease.
Table 6 Multivariate logistic regression analyses of the relationship between inflammatory indicators and ulcerative colitis endoscopic index of severity

|       | B   | P value | Odds ratio | 95% CI     |
|-------|-----|---------|------------|------------|
| SII   | 589.63 | Reference |           |           |
|       | 589.64-1047.38 | 1.09 | 0.146 | 2.98 | 0.69-12.94 |
|       | 1047.19-1776.79 | 1.57 | 0.129 | 4.81 | 0.63-36.56 |
|       | 1776.80 | 2.92 | 0.012 | 18.46 | 1.89-180.30 |
| NLR   | 2.66 | Reference |           |           |
|       | 2.67-4.23 | 0.06 | 0.934 | 1.06 | 0.27-4.23 |
|       | 4.24-6.46 | 0.05 | 0.954 | 1.05 | 0.20-5.41 |
|       | 6.47 | -0.61 | 0.534 | 0.54 | 0.08-3.71 |
| PLR   | 132.35 | Reference |           |           |
|       | 132.36-190.31 | -1.06 | 0.139 | 0.35 | 0.09-1.41 |
|       | 190.32-263.47 | -0.96 | 0.212 | 0.38 | 0.09-1.73 |
|       | 263.48 | -1.20 | 0.174 | 0.30 | 0.05-1.70 |

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; SII: Systemic immune-inflammation index.

ARTICLE HIGHLIGHTS

Research background
Peripheral blood-derived inflammation-based scores have limited clinical value in ulcerative colitis (UC).

Research motivation
Assess the clinical disease activity.

Research objectives
Explore a simple and readily available predictor.

Research methods
Mann-Whitney U test, spearman correlation analyses, receiver operator curve, and logistic regression analyses.

Research results
Systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio values were correlated with endoscopic score.

Research conclusions
SII could help confirm UC and identify the activity.

Research perspectives
Track the activity of disease and guide adjustment of treatment protocols.

REFERENCES

1 Nirmala M, Smitha SG, Kamath GJ. A Study to Assess The Efficacy of Local Application of Oral Probiotic in Treating Recurrent Aphthous Ulcer and Oral Candidiasis. Indian J Otolaryngol Head Neck Surg 2019; 71: 113-117 [PMID: 31741944 DOI: 10.1007/s12070-017-1139-9]
Zhang MH et al. SII evaluate UC and its activity

2 Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, Panaccione R, Ghosh S, Wu JCY, Chan FKL, Sung JJY, Kaplan GG. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet 2018; 390: 2769-2778 [PMID: 29050646 DOI: 10.1016/S0140-6736(17)32448-0]

3 Klepp P, Brackmann S, Cvanecarova M, Hovik ML, Hovde Ø, Henriksen M, Hupperttz-Hauss G, Bernkleve T, Hoie O, Kempski-Monstad I, Solberg IC, Stray N, Jahnzen J, Vatn MH, Moun B. Risk of colorectal cancer in a population-based study 20 years after diagnosis of ulcerative colitis: results from the IBSEN study. BMJ Open Gastroenterol 2020; 7: e000361 [PMID: 32337058 DOI: 10.1136/bmjgast-2019-000361]

4 Cioffi M, Rosa AD, Serao R, Picone I, Vietti MT. Laboratory markers in ulcerative colitis: Current insights and future advances. World J Gastroenterol 2015; 6: 13-22 [PMID: 25685607 DOI: 10.4291/wjjg.v6.i1.13]

5 Restellini S, Chao CY, Martel M, Barkun A, Kherad O, Seidman E, Wild G, Bitton A, Afif W, Bessissow T, Lakatos PL. Clinical Parameters Correlate With Endoscopic Activity of Ulcerative Colitis: A Systematic Review. Clin Gastroenterol Hepatol 2019; 17: 1265-1275. e8 [PMID: 30583048 DOI: 10.1016/j.cgh.2018.12.021]

6 Mitsuyama K, Niwa M, Takedatsu H, Yamasaki H, Kuwaki K, Yoshioka S, Yamauchi R, Fukunaga S, Torimura T. Antibody markers in the diagnosis of inflammatory bowel disease. World J Gastroenterol 2016; 22: 1304-1310 [PMID: 26811667 DOI: 10.3748/wjg.v22.i3.1304]

7 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: 8235-8247 [PMID: 29290660 DOI: 10.3748/wjg.v23.i46.8235]

8 Derkaç A, Ołczyk P, Komosińska-Vassev K. Diagnostic Markers for Nonspecific Inflammatory Bowel Diseases. Diag Markers 2018; 2018: 7451946 [PMID: 30911750 DOI: 10.18632/oncotarget.18856]

9 Day AS, Leach ST, Lembong DA. An update on diagnostic and prognostic biomarkers in inflammatory bowel disease. Expert Rev Mol Diagn 2017; 17: 835-843 [PMID: 28770636 DOI: 10.1080/14737159.2017.1364160]

10 Sands BE. Biomarkers of Inflammation in Inflammatory Bowel Disease. Gastroenterology 2015; 149: 1275-1285 [PMID: 26166315 DOI: 10.1053/j.gastro.2015.07.003]

11 Mendoza JJ, Abreu MT. Biological markers in ulcerative colitis: disease-related: pathological advances for clinicians. Gastroenterol Clin Biol 2009; 33 Suppl 3: S158-S173 [DOI: 10.1016/S0399-8320(09)73151-3]

12 Akpinar MY, Ozin YO, Kaplan M, Ates I, Kalkan IH, Kilic ZMY, Yuksel M, Kayacetin E. Platelet-to-lymphocyte Ratio and Neutrophil-to-lymphocyte Ratio Predict Mucosal Disease Severity in Ulcerative Colitis. J Med Biochem 2018; 37: 155-162 [PMID: 30581352 DOI: 10.1515/jomb-2017-0050]

13 Nishida Y, Hosomi S, Yamagami H, Yukawa T, Otani K, Nagami Y, Tanaka F, Taira K, Kamata N, Tanigawa T, Shiba M, Watanabe K, Watanabe T, Tominaoka K, Fujiyara Y. Neutrophil-to-lymphocyte Ratio for Predicting Loss of Response to Infliximab in Ulcerative Colitis. PLoS One 2017; 12: e0169845 [PMID: 28076386 DOI: 10.1371/journal.pone.0169845]

14 Cherfane CE, Gessel L, Cirillo D, Zimmerman MB, Polyanuk S. Monocytosis and a Low Lymphocyte to Monocyte Ratio are Effective Biomarkers of Ulcerative Colitis Disease Activity. Inflamm Bowel Dis 2015; 21: 1769-1775 [PMID: 25993688 DOI: 10.1097/MIB.0000000000000427]

15 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: 3295-3302 [PMID: 30271480 DOI: 10.7150/jca.25691]

16 Zhong JH, Huang DH, Chen ZY. Prognostic role of systemic immune-inflammation index in solid tumors: a systematic review and meta-analysis. Oncotarget 2017; 8: 75381-75388 [PMID: 29088873 DOI: 10.18632/oncotarget.18856]

17 Kim Y, Choi H, Jung SM, Song JJ, Park YB, Lee SW. Systemic immune-inflammation index could estimate the cross-sectional high activity and the poor outcomes in immunosuppressive drug-naïve patients with antineutrophil cytoplasmic antibody-associated vasculitis. Nephrol (Carlton) 2019; 24: 711-717 [PMID: 30202901 DOI: 10.1111/nep.13491]

18 Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut 2005; 55: 749-753 [PMID: 16698746 DOI: 10.1136/gut.2005.082909]

19 Schroeder KW, Tremaine WJ, Istrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. N Engl J Med 1987; 317: 1625-1629 [PMID: 3317057 DOI: 10.1056/NEJM198712243172603]

20 Rowan CR, Cullen G, Mulcahy HE, Sheridan J, Moss AC, Ryan EJ, Doherty GA. Dublin [Degree of Ulcerative colitis Burden of Luminal Inflammation] Score, a Simple Method to Quantify Inflammatory Burden in Ulcerative Colitis. J Crohns Colitis 2019; 13: 1365-1371 [PMID: 30911757 DOI: 10.1093/eco-jcc/jj0067]

21 Travis SP, Schnell D, Krzeski P, Abreu MT, Altman DG, Colombel JF, Feagan BG, Hanauer SB, Lèmann M, Lichtenstein GR, Marteau PR, Reinsch W, Sands BE, Yacyshyn BR, Bernhard CA, Mary JY, Sandborn WJ. Developing an instrument to assess the endoscopic severity of ulcerative colitis: the Ulcerative Colitis Endoscopic Index of Severity (UCEIS). Gut 2012; 61: 535-542 [PMID: 21997563 DOI: 10.1136/gutjnl-2011-300486]

22 Arseneau KO, Cominelli F. Targeting leukocyte trafficking for the treatment of inflammatory bowel
acute severe ulcerative colitis. Association between the ulcerative colitis endoscopic index of severity (UCEIS) and outcomes in Corte C

Li H, Huang SY, Shi FH, Gu ZC, Zhang SG, Wei JF. αβ2 integrin inhibitors: a patent review. Expert Opin Ther Pat 2018; 28: 903-917 [PMID: 30444683 DOI: 10.1080/13543776.2018.1549227]

Wallace KL, Zheng LB, Kanazawa Y, Shih DQ. Immunopathology of inflammatory bowel disease. World J Gastroenterol 2014; 20: 6-21 [PMID: 24415853 DOI: 10.3748/wjg.v20.i1.6]

Voudoukis E, Karmiris K, Koutoubakis IE. Multipotent role of platelets in inflammatory bowel diseases: a clinical approach. World J Gastroenterol 2014; 20: 3180-3190 [PMID: 24696603 DOI: 10.3748/wjg.v20.i12.3180]

Danese S, Motte Cd Cde L, Fiocchi C. Platelets in inflammatory bowel disease: clinical, pathogenic, and therapeutic implications. Am J Gastroenterol 2004; 99: 938-945 [PMID: 15128364 DOI: 10.1111/j.1572-0241.2004.04129.x]

Pankratz S, Bittner S, Kehrel BE, Langer HF, Kleinschnitz C, Meuth SG, Göbel K. The Inflammatory Role of Platelets: Translational Insights from Experimental Studies of Autoimmune Disorders. Int J Mol Sci 2016; 17: 1723 [PMID: 27754414 DOI: 10.3390/ijms17101723]

Kayo S, Ikura Y, Suekane T, Shirai N, Sugama Y, Ohsawa M, Adachi K, Watanabe K, Nakamura S, Fujiwara Y, Oshitani N, Higuchi K, Maeda K, Hirakawa K, Arakawa T, Ueda M. Close association between activated platelets and neutrophils in the active phase of ulcerative colitis in humans. Inflamm Bowel Dis 2006; 12: 727-735 [PMID: 16917228 DOI: 10.1097/00054725-200609000-00009]

Senchenkova E, Seifert H, Granger DN. Hypercoagulability and Platelet Abnormalities in Inflammatory Bowel Disease. Semin Thromb Hemost 2015; 41: 582-589 [PMID: 26270113 DOI: 10.1055/s-0035-1556590]

Koutoubakis IE. The relationship between coagulation state and inflammatory bowel disease: current understanding and clinical implications. Expert Rev Clin Immunol 2015; 11: 479-488 [PMID: 25719625 DOI: 10.1586/1744666X.2015.1019475]

Torun S, Tunç BD, Suvaş B, Yıldız H, Baş A, Sayılır A, Özderin YO, Beyazıt Y, Kayacan E. Assessment of neutrophil-lymphocyte ratio in ulcerative colitis: a promising marker in predicting disease severity. Clin Res Hepatol Gastroenterol 2012; 36: 491-497 [PMID: 22841412 DOI: 10.1016/j.clinre.2012.06.004]

Choi CR, Al Bakir I, Ding NJ, Lee GH, Askari A, Warusavitarne J, Moorghen M, Humphries A, Ignjatovic-Wilson A, Thomas-Gibson S, Saunders BP, Rutter MD, Graham TA, Hart AL. Cumulative burden of inflammation predicts colorectal neoplasia risk in ulcerative colitis: a large single-centre study. Gut 2019; 68: 414-422 [PMID: 30158489 DOI: 10.1136/gutjnl-2017-314190]

Bertani L, Rossari F, Barberio B, Demarzo MG, Tapete G, Albano E, Baiano E, Cavalliero B, Ceccarelli L, Mamolo MG, Brornbin C, de Bortoli N, Bellini M, Marchi S, Bodini G, Savarino E, Costa F. Novel Prognostic Biomarkers of Mucosal Healing in Ulcerative Colitis Patients Treated With Anti-TNF: Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio. Inflamm Bowel Dis 2020; 26: 1579-1587 [PMID: 32232392 DOI: 10.1093/ibd/izz062]

Xie T, Zhao C, Ding C, Zhang T, Dai X, Lv T, Li Y, Guo Z, Gong J, Zhu W. Fecal calprotectin as an alternative to ulcerative colitis endoscopic index of severity to predict the response to corticosteroids of acute severe ulcerative colitis: A prospective observational study. Dig Liver Dis 2017; 49: 984-990 [PMID: 28539226 DOI: 10.1016/j.dld.2017.04.021]

Corte C, Fernandopullu N, Catuneanu AM, Burger D, Cesarin M, White L, Keshav S, Travis S. Association between the ulcerative colitis endoscopic index of severity (UCEIS) and outcomes in acute severe ulcerative colitis. J Crohns Colitis 2015; 9: 376-381 [PMID: 25770163 DOI: 10.1093/ecco-jcc/jvy047]
