**RESEARCH ARTICLE**

# Are Neutrophil-to-Lymphocyte, Platelet-to-Lymphocyte, and Lymphocyte-to-Monocyte Ratios Predictive of Postoperative Complications and Mortality in Patients with Inflammatory Bowel Disease?

 Gizem Kılınç Tuncer[1],  Korhan Tuncer[2],  Serdar Aydoğan[3],  Kemal Erdinç Kamer[3]

[1]University of Health Sciences Turkey, İzmir Bozyaka Training and Research Hospital, Clinic of General Surgery, İzmir, Turkey
[2]Çiğli Training and Research Hospital, Clinic of General Surgery, İzmir, Turkey
[3]University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, Clinic of General Surgery, İzmir, Turkey

## ABSTRACT

**Aim:** Although clinicians try to control inflammatory bowel diseases with medical treatment, surgical intervention may be required due to complications. Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) could be potential biomarkers of systemic inflammation in chronic diseases. This study aims to determine whether these ratios could be predictive of postoperative complications, mortality, and reoperation in patients operated on for inflammatory bowel disease complications.

**Method:** Patients who were operated on for inflammatory bowel disease between 2010-2021 were analyzed retrospectively. The patients were divided into two groups: the Crohn's disease (CD) group and the ulcerative colitis (UC) group. Descriptive statistics were carried out between the two groups. Moreover, this study analyzed the effects of NLR, PLR, and LMR on short- and long-term postoperative complications, mortality, and reoperation.

**Results:** A total of 42 patients were included in this study, 29 (69%) of them were men and 13 (31%) were women, and 24 (57%) of them were operated on for CD. NLR and PLR were significantly higher in patients with UC (p=0.031, p=0.009). However, none of these ratios were related to postoperative early and delayed complications, mortality, and reoperation in patients who were operated on for inflammatory bowel disease complications.

**Conclusion:** NLR, PLR, and LMR cannot be used to predict postoperative complications, mortality, and reoperation in patients that were operated on for inflammatory bowel disease complications.

**Keywords:** Inflammatory bowel disease, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio

## Introduction

Inflammatory bowel diseases (IBD) have an increasing prevalence worldwide: almost 0.5% in western countries.[1,2] Although clinicians try to control IBDs with medical treatment, surgical intervention may be required as a result of complications.[3] Neuthrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte (LMR) ratios could be potential biomarkers of systemic inflammation in chronic diseases. There are many articles that define NLR as a valuable biomarker that can be used to predict the severity of IBD in patients.[3,4] Although these biomarkers are used to determine the severity and prognosis of the disease, there are limited studies on their use in predicting postoperative complications in IBD.[5] This study aims to determine the effects of NLR, PLR, and LMR in predicting postoperative complications and mortality in patients operated on for IBD.

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## Materials and Methods

This is a single-center retrospective study that was conducted in accordance with the ethical standards of the Helsinki declaration. The protocol of this study was approved by the Local Ethics Committee of the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (approval number: 21, date: 17.01.2022). Informed consent was not provided by the patients as this was a retrospective study.

Patients who underwent emergency operations for IBD complications in Tepecik Training and Research Hospital between January 2010 and January 2021 were analyzed retrospectively. Age, sex, comorbidities, NLR, PLR, LMR, postoperative complications, mortality, and postoperative hospital stays were defined as parameters. Patients under the age of 18 who had a history of previous abdominal surgery were excluded from this study, and 1-year patient follow-ups were examined. The patients were divided into two groups: the Crohn's disease (CD) group and ulcerative colitis (UC) group, and descriptive statistics were carried out between them. Moreover, short-term complications were defined as complications that appeared during the postoperative hospitalization period. Long-term complications were defined as complications that occurred after discharge or at a one-year follow-up. Furthermore, this study analyzed the effects of NLR, PLR, and LMR on short- and long-term postoperative complications, mortality, and reoperation.

### Statistical Analysis

All statistical analyses were performed using the SPSS statistics software, version 25.0. Continuous variables with normal distribution were presented as mean and standard deviation. Variables without normal distribution were presented as the median (Q1-Q3) and compared using the Mann-Whitney U test. Moreover, variables with normal distribution and continuous variables were compared using the $x^2$ test. Univariate analysis was performed to find potential risk factors, and multivariate analysis was used to identify independent factors. Furthermore, p<0.05 was considered statistically significant.

## Results

A total of 42 patients were included in this study, 29 (69%) of them were men and 13 (30%) were women, and 24 (57%) of them were operated on for CD. The most common complication leading to the operation was mechanical bowel obstruction, and other causes are summarized in Table 1 in detail. The median age was 60.5 (40.8-68) years, and the age was significantly higher in patients with UC (p=0.010). In the CD group, 16 (67%) patients underwent right hemicolectomy, five (21%) patients underwent segmental small bowel resection, two (8.3%) patients underwent left hemicolectomy, and one (4.2%) patient underwent subtotal colectomy. In the UC group, nine (50%) patients underwent Hartmann's procedure, eight (44.4%) patients underwent total proctocolectomy, and one (5.5%) patient underwent abdominoperineal resection. The American Society of Anesthesiologists (ASA) score was significantly higher in patients with UC (p=0.042). The median length of hospital stays was 8 (6-12) days. Although the lymphocyte count was significantly higher in patients with CD, NLR was significantly higher in patients with UC (p=0.010, p=0.031). Furthermore, PLR was significantly higher in patients with UC (p=0.009). There were no differences in the lymph node count, postoperative hospital stay, short-term postoperative complications, mortality, reoperation, and long-term postoperative complications between the UC and CD groups (Table 2). The Clavien-Dindo complication score was 1 in all patients with CD who experienced short-term complications. Moreover, the Clavien-Dindo complication score was 1 in one patient, two in one patient, and three in one patient with short-term complications in the UC group. The difference between the two groups for the Clavien-Dindo complication score was not statistically significant (p=0.361). Furthermore, this difference was not associated with the complexity of the surgery, and postoperative complications and their details are defined in Table 3. None of these ratios were found as predictive parameters for postoperative short- and long-term complications, mortality, and reoperation in multivariate analysis (Table 4).

Table 1. Operation indications of the patients

| Operation indications | All patients, n (%) | Crohn's disease, n (%) | Ulcerative colitis, n (%) |
|---|---|---|---|
| Mechanical bowel obstruction | 22 (52.4) | 14 (58.3) | 8 (44.4) |
| Perforation | 12 (28.6) | 8 (33.3) | 4 (22.2) |
| Bleeding | 6 (14.3) | 0 | 6 (33.3) |
| Enterocutaneous fistula | 2 (4.8) | 2 (8.3) | 0 |

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**Table 2.** Factors associated with Crohn's disease and ulcerative colitis

| | All patients (n=42) | Crohn's disease (n=24) | Ulcerative colitis (n=18) | p-value |
|---|---|---|---|---|
| Age, median (Q1-Q3) | 60.5 (40.8-68) | 47.5 (39.3-63.8) | 66.5 (58.3-73) | **0.010** |
| **Sex, n (%)** | | | | 0.700 |
| Male | 29 (69) | 16 (66.7) | 13 (72.2) | - |
| Female | 13 (31) | 8 (33.3) | 5 (27.8) | - |
| Diabetes mellitus, n (%) | 5 (11.9) | 2 (8.3) | 3 (16.7) | 0.636 |
| Hypertension, n (%) | 11 (26.2) | 8 (33.3) | 3 (16.7) | 0.299 |
| **ASA score, n (%)** | | | | **0.042** |
| 1 | 10 (23.8) | 8 (33.3) | 2 (11.1) | |
| 2 | 21 (50) | 13 (54.2) | 8 (44.4) | |
| 3 | 11 (26.2) | 3 (12.5) | 8 (44.4) | |
| WBC (10^3/uL), median (Q1-Q3) | 12.5 (7.3-17.2) | 11.7 (7.1-14.9) | 13.8 (7.5-18.6) | 0.340 |
| NEU# (10^3/uL), median (Q1-Q3) | 9.1 (4.7-14.2) | 9.1 (3.9-11.4) | 9.800 (5.7-18.2) | 0.155 |
| LYM# (10^3/uL), median (Q1-Q3) | 1.3 (0.8-2) | 1.3 (1.1-2.2) | 0.9 (0.7-1.3) | **0.010** |
| MON# (10^3/uL), median (Q1-Q3) | 0.7 (0.4-1) | 0.8 (0.4-1.1) | 0.6 (0.4-1) | 0.655 |
| PLT (10^3/uL), median (Q1-Q3) | 285.5 (225.5-407.3) | 266 (228-400.8) | 336 (213.8-428.3) | 0.741 |
| NLR, median (Q1-Q3) | 6.1 (3.6-14.5) | 5 (1.8-9.2) | 9.4 (4.3-22.5) | **0.031** |
| PLR, median (Q1-Q3) | 259.4 (153.6-462.5) | 186.2 (138.3-310.7) | 331.6 (217.4-676.3) | **0.009** |
| LMR, median (Q1-Q3) | 1.93 (1.36-3.5) | 2.01 (1.45-5) | 1.88 (1.25-2.18) | 0.093 |
| Lymph node count, median (Q1-Q3) | 10 (2.8-25.5) | 10 (3.3-19.8) | 11 (0.8-36.8) | 0.628 |
| Postoperative hospital stay, median (Q1-Q3) | 8 (6-12) | 8 (6.3-9.8) | 8.5 (5.8-16.3) | 0.646 |
| Postoperative short-term complications, n (%) | 6 (14.3) | 3 (12.5) | 3 (16.7) | 1.000 |
| Mortality, n (%) | 3 (7.1) | 0 | 3 (16.7) | 0.071 |
| Postoperative long-term complications, n (%) | 8 (19) | 6 (25) | 2 (11.1) | 0.431 |
| Reoperation, n (%) | 7 (16.7) | 4 (16.7) | 3 (16.7) | 1.000 |

ASA: American Society of Anesthesiologists

**Table 3.** Postoperative complications and their details

| Postoperative complications | Crohn's disease, (n=24) | Ulcerative colitis (n=18) |
|---|---|---|
| **Short-term complications, n (%)** | | |
| Surgical site infection | 2 (8.3) | 1 (5.6) |
| Low-output enterocutaneous fistula | 1 (4.2) | 0 |
| Intraabdominal abscess | 0 | 1 (5.6) |
| Perforation | 0 | 1 (5.6) |
| **Long-term complications, n (%)** | | |
| Brid ileus | 6 (25) | 1 (5.6) |
| Incisional hernia | 2 (8.3) | 0 |
| Surgical site infection | 0 | 1 (5.6) |

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**Table 4.** Multivariate analyses for postoperative short-term complications, reoperation, and postoperative long-term complications

| Variables | Short-term complications Multivariate analyses Odds ratio (95% CI) | p-value | Reoperation Multivariate analyses Odds ratio (95% CI) | p-value | Long-term complications Multivariate analyses Odds ratio (95% CI) | p-value |
|---|---|---|---|---|---|---|
| Age | 1.02 (0.95-1.10) | 0.528 | 0.98 (0.91-1.06) | 0.641 | 1.06 (0.98-1.15) | 0.175 |
| Male | 0.73 (0.09-5.63) | 0.761 | 1.38 (0.17-11.01) | 0.764 | 3.59 (0.30-43.33) | 0.315 |
| NLR | 0.99 (0.95-1.02) | 0.427 | 1.00 (0.92-1.08) | 0.931 | 1.02 (0.96-1.09) | 0.491 |
| PLR | 1.00 (1.00-1.01) | 0.377 | 1.00 (0.99-1.00) | 0.354 | 1.00 (0.99-1.01) | 0.476 |
| LMR | 0.46 (0.16-1.37) | 0.164 | 1.35 (0.84-2.17) | 0.223 | 1.28 (0.81-2.02) | 0.292 |
| Crohn's disease | 1.65 (0.16-17.07) | 0.676 | 0.25 (0.02-2.95) | 0.274 | 3.14 (0.27-36.53) | 0.361 |
| ASA3 | 0.92 (0.06-13.47) | 0.950 | 1.37 (0.13-14.43) | 0.792 | 0.06 (0.00-2.93) | 0.156 |

CI: Confidence interval, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio

## Discussion

Inflammatory bowel disease has an increasing prevalence worldwide, and it is primarily controlled through medical treatment. Intermittent attacks may occur during the course of the disease, and these attacks, for which medical treatment is usually sufficient, may become complicated according to the progression of the disease. In these situations, surgical intervention may be required. Therefore, it is important to keep the disease under control and reduce the attacks as much as possible. While many inflammatory parameters are used in the course of the disease, the ratios formed through these parameters have started to gain popularity recently. Among these, the most common parameter is NLR, and many studies have stated the use of this ratio in determining the severity and course of the disease. In addition, LMR and PLR are popular parameters that began to be used in detecting the severity of the disease. Azab et al.[6] showed that NLR is a more effective parameter than white blood cells in predicting the prognosis of acute pancreatitis. Furthermore, there are studies emphasizing that these rates are not useful in showing the severity of the disease.[7] Although there are many studies that show the relationship between the ratios and the severity of the disease, studies exploring the relationship between these ratios and postoperative complications are limited. Kang et al.[8] showed that an NLR greater than 4.1 increases the risk for postoperative complications by 2.782 times. Moreover, in a study by Nishida et al.[9], NLR was detected as a prognostic marker for the development of pouchitis in patients with UC who underwent ileal pouch-anal anastomosis. Furthermore, in a study by Argeny et al.[10], preoperative NLR levels were not associated with postoperative complications in patients with symptomatic CD. Mullin et al.[11] reported inflammatory markers as predictive parameters in patients who underwent gastrointestinal surgery for CD. Moreover, in a study performed by Tsunoda et al.[12] and published in 2022, it was reported that NLR was a useful marker for predicting postoperative complications in CD. This study could not find any correlation between postoperative complications and these ratios. Singh et al.[13] reported a systematic review and meta-analysis in 2015, and they found no difference in mortality between elective and emergency surgeries for UC. They stated that mortality was higher in patients who underwent emergency surgery in CD. In this study, although the difference was not statistically significant, mortality was higher in patients with UC. This may be a result of the higher age and ASA scores in patients with UC rather than the complexity of the surgery. In addition, the Clavien-Dindo complication scores were higher in patients with UC; however, this difference was not statistically significant.

## Conclusion

NLR, PLR, and LMR are not predictive inflammatory biomarkers for postoperative complications, mortality, and reoperation in patients who underwent emergency surgery for IBD complications.

### Ethics

### Authorship Contributions

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K.T., Literature Search: G.K.T., S.A., Writing: G.K.T., S.A., K.E.K.

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