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Research Article

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Neutrophil/lymphocyte and platelet/lymphocyte ratios as a biomarker in postoperative wound infections

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Abstract

Objectives: We aimed to investigate retrospectively the association between the development of surgical wound infection after orthopedic surgery, and neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) obtained from complete blood count results.

Methods: A total of 120 patients who underwent orthopedic surgery between 2018 and 2020 were evaluated retrospectively in our study. Wound culture results, complete blood counts, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) values, orthopedic surgery, and wound types were obtained from the laboratory data administration system. The data were statistically analyzed using SPSS 22.0 software.

Results: A total of 70 patients who experienced surgical wound infection (66% males and 34% females) and 50 patients without wound infection (64% males and 36% females) were included in this study. The mean age was 46.8 ± 11.4 years for the patients with infection after surgery and 50.1 ± 11.7 years for the patients without infection. Preoperative CRP, NLR, and PLR, and post-operative white blood cell (WBC), neutrophils, ESR, CRP, NLR, and PLR values were significantly higher, and lymphocyte concentrations were significantly lower in the group with infection, in comparison with those without infection. In the postoperative period, CRP and ESR were high in patients with and without infection, while NLR was increased in only those with infection. A medium-level correlation was found between NLR and PLR, and CRP and ESR. Sensitivity was 66%, and specificity was 68% with a cut-off of >3.5 for NLR, while sensitivity was 42% and specificity was 71% with a cut-off of >135 for PLR.

Conclusions: We believe that the estimation of NLR and PLR values before the intervention in patients undergoing orthopedic surgery may be advantageous for identifying infection.

Keywords: biomarker; neutrophil/lymphocyte ratio; surgical wound infections.

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Introduction

Complete blood count (CBC), which is one of the most frequently ordered tests from clinical laboratories, is used by surgeons as part of the preoperative evaluation and for the detection of infectious pathologies. CBC indices: neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) are calculated from neutrophil, platelet, and lymphocyte values, and they are inflammatory indicators with a progressively growing popularity. They are generally considered indicators of subclinical inflammation. The fact that they are readily available is a great advantage [1–5]. Also, inflammatory indicators are believed to be associated with the prognosis of bacterial infections [6].

Surgical wound infections still cause considerable morbidity and mortality after orthopedic surgery and create an economical burden on the health system. Cultures and sensitivity tests still constitute the golden standard for both diagnosis and determination of the treatment protocol of wound infections. On the other hand, the requirement for a 48–72 h period to obtain the results of wound cultures underline the need for alternative tests that may be helpful to the clinician for diagnosis [7, 8]. NLR and PLR were investigated in various studies as preoperative biomarkers for the prediction of the complication of postoperative wound infection, and they were found to be better predictor-markers than C-reactive protein (CRP) and leukocyte values. Also, NLR and PLR were used to determine the presence and severity of infection in studies on several infections in adult patients [9, 10].

We aimed to investigate retrospectively the association between the development of surgical wound infection after orthopedic surgery, and NLR and PLR obtained from CBC results.

Materials and methods

Study design and setting

A total of 120 patients who underwent orthopedic surgery between 2018 and 2020 were included in this study. All the patients underwent interventions that did not require preoperative surgical prophylaxis and no patient had taken antibiotics before surgery. Culture-positive 70 patients in whom surgical wound infection had developed and 50 patients in whom no infectious complications had developed were evaluated retrospectively. Complaints had occurred in the first seven postoperative days in all 70 culture-positive patients, and samples for cultures were obtained immediately. Exclusion criteria included patients with a chronic illness such as diabetes mellitus (DM) which could affect the comparison. Patients and controls were matched in terms of age and gender. Wound culture results, CBC, CRP, and erythrocyte sedimentation rate (ESR) values were obtained from the laboratory data administration system. Test results obtained 3–10 days before surgery and those obtained during the infection were used. The surgery wound infection was classified as superficial and deep wound infection. The undergoing orthopedic surgery was categorized as minor (stenosing tenosynovitis, carpal tunnel syndrome, hallux valgus), arthroscopy (shoulder, knee), and major (bone fracture reduction).

Laboratory analysis

Biochemical analysis: Blood samples were analyzed in 1 h. CBC was measured with an automated hematology analyzer (Sysmex 2010, Kobe, Japan). Neutrophil-lymphocyte ratio was calculated for NLR, and platelet/lymphocyte ratio was calculated for PLR. ESR samples were put into tubes containing citrate (3.5 mg/mL) and were measured by the infrared barrier method (Sistat ESR 40, Sistat Diagnostics, Ankara, Turkey). CRP levels were measured with commercial reactive by turbidimetric method in a chemistry autoanalyzer (Cobas 6000 c501, Roche Diagnostic, Mannheim, Germany).

Microbiological analysis: Samples for culture obtained from the wound by an injector or swab were evaluated at the microbiology laboratory. All samples were incubated for 24–48 h at 37 °C after inoculation in blood agar, Eosin Methylene Blue (EMB) agar, and chocolate agar. The organisms that were isolated were identified by conventional methods (colony morphology, gram staining, catalase, coagulase, oxidase, urease tests) and BD Phoenix 100 automated identification system (BD Phoenix System, Beckton Dickinson, USA). *In vitro* antibiotic susceptibility testing of the isolates was done with Phoenix TM 100 automated identification and antibiotic susceptibility testing system (Beckton, Dickinson and Company, USA), in accordance with European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria [11].

Statistical analysis

Statistical analysis of data obtained in this study was done with SPSS 22.0 (SPSS INC, Chicago, IL, USA) software. Kolmogorov Smirnov and Shapiro Wilk tests were used for determining whether the groups showed a normal distribution. Numerical data were expressed as percentages and medians (25th–75th). Mann Whitney *U* test was used in the comparison of groups, at least one of which did not show a normal distribution, and the Wilcoxon test was used in the comparison of two dependent groups. Categorical data were expressed as percentages. The Chi-square test was used in the comparison of independent groups containing categorical variables. The correlation of NLR and PLR values with demographic data and other laboratory measurements were evaluated with the Spearman correlation coefficient. Univariate and multivariate logistic regression analyses were also performed to predict NLR and PLR on surgery wound infections. Variables with a p-value<0.05 in the univariate analysis were then entered into the multivariate analysis. Receiver Operating Characteristic (ROC) analysis was performed to show the diagnostic performance of tests in discrimination between patients with and without infection. Positive predictive values (PPV), negative predictive values (NPV), sensitivity, specificity, and diagnostic accuracy of the tests were calculated. A p-value<0.05 was considered statistically significant.

Results

A total of 70 patients who experienced surgical wound infection (66% males and 34% females) and 50 patients without wound infection (64% males and 36% females) were included in this study. The mean age was 46.8 ± 11.4 years for the patients with infection after surgery and 50.1 ± 11.7 years for the patients without infection. There were no significant differences between the patient group with and without infection in terms of age and gender (p=0.358, p=0.803). The type of surgical wound infection and surgical procedure of the patients are shown in Table 1. When evaluated according to surgery, superficial wound

Table 1: Comparison of demographical measurements in patients with and without infection.

	Total (n = 120)	With infection (n = 70)	Without infection (n = 50)	p-Value
Age, years (X ± SD)[a]	49.0 ± 11.7	46.8 ± 11.4	50.1 ± 11.7	0.358
Gender[b]				
Female, n (%)	42 (35)	24 (34)	18 (36)	0.803
Male, n (%)	78 (65)	46 (66)	32 (64)	
Day of the start of postoperative complaint, mean (min-max)	4 (1–20)	2 (1–13)	4 (1–20)	<0.001
The type of surgery site infection				
Superficial wound infection, %		70	–	
Deep wound infection, %		30	–	
Types of surgery				
Minor surgery, %		53	46	
Arthroscopic surgery, %		34	42	
Major surgery, %		13	12	

p<0.05 was considered significant. [a]Data are expressed as mean ± standard deviation (X ± SD), [b]data are expressed as numbers (percentages).

infection developed in all the minor surgery. Patients who had arthroscopic surgery, 48% had superficial wound infection and 52% had deep wound infection. Deep wound infection was detected in all patients who underwent major surgery. There were also no significant differences between NLR and PLR values in the type of surgical wound infection and surgery procedure.

One single, pure bacterium was detected in each culture of the 70 patients with infection. The bacterium that was most frequently isolated from wound cultures was *Staphylococcus aureus* (52.8%); with 32.4% methicillin resistance. Other organisms were: 12.9% *Proteus* spp., 8.6% *Escherichia coli*, 8.6% *Acinetobacter baumannii*, 5.7% *Pseudomonas aeruginosa*, 4.3% *Klebsiella pneumonia*, 4.3% *Streptococcus pyogenes*, 1.4% *Enterobacter cloaca*, 1.4% *Morganella morganii*.

There were also no significant differences between NLR and PLR values of the two genders (p=0.601, p=0.179). A statistically significant difference was not detected between the sites that the samples were sent, in terms of NLR values (p=0.302).

Preoperative CRP, NLR, and PLR values of patients with infection were significantly higher than those without infection (p=0.029, p=0.035, p=0.001). Postoperative WBC, neutrophil, ESR, CRP, NLR and PLR values of patients with infection were significantly higher, and lymphocyte counts were significantly lower in comparison with patients without infection (p=0.005, p=0.001, p=0.042, p<0.001, p<0.001, p=0.023, p=0.024) (Table 2). A comparison of pre and postoperative laboratory measurements of patients without infection showed significantly higher WBC, ESR, CRP, and PLR values after surgery (p=0.013, p=0.001,

Table 2: Comparison of preoperative and postoperative laboratory measurements in patients with and without infection.

	Preoperative			Postoperative		
	n = 70			n = 70		
	Median (25th–75th)			Median (25th–75th)		
	Without infection	With infection	p-Value	Without infection	With infection	p-Value
WBC, 10^3/μL	7.26 (6.53–8.30)	7.69 (6.2–10.2)	0.329	8.55 (6.85–9.87)	9.88 (7.87–14.42)	0.005
Neutrophil, 10^3/μL	4.20 (3.62–5.05)	4.7 (3.5–6.8)	0.148	4.89 (4.04–6.23)	6.96 (4.89–11.39)	0.001
Lymphocyte, 10^3/L	2.30 (1.68–2.63)	1.9 (1.4–2.4)	0.094	2.04 (1.54–2.52)	1.66 (1.37–2.22)	0.024
PLT, 10^3/μL	258 (200–330)	297 (235–394)	0.072	290 (219–368)	326 (251–403)	0.127
ESR, mm/hour	28 (12–47)	32 (17–77)	0.153	39 (21–64)	46 (31–83)	0.042
CRP, mg/L	5.85 (2.10–12.12)	9.3 (5.0–31.6)	0.029	10.40 (4.44–41.45)	37.90 (15.40–160.3)	<0.001
NLR	1.88 (1.49–2.83)	2.3 (1.7–4.2)	0.035	2.62 (1.79–3.75)	3.94 (2.40–6.97)	<0.001
PLR	116.3 (102.2–180.3)	169.9 (137.5–233.9)	0.001	150.8 (99.90–217.5)	189.9 (129.5–266.6)	0.023

p<0.05 statistically significant. All data are expressed as median (25th–75th). WBC, white blood cell; PLT, platelet; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio.

p<0.001, p=0.050). On the other hand, a comparison of pre and postoperative laboratory values of patients with infection showed significantly higher WBC, neutrophil, ESR, CRP, and NLR levels after surgery (p<0.001, p<0.001, p=0.026, p<0.001, p<0.001).

The correlation analysis of NLR and PLR values with demographic data and other laboratory measurements are shown in Table 3. The logistic regression analysis uses the laboratory parameters as an independent factor associated with wound infections (Supplemental Table 1). In the multivariable analysis, we excluded three variables: neutrophil, lymphocyte, and platelet, to avoid multicollinearity. The univariable analysis results identified as the independent risk factors for wound infection only WBC, neutrophil, lymphocyte, CRP, NLR PLR, and the multivariate analysis yielded similar results as the univariate analysis for CRP and NLR.

A medium-level correlation was found between NLR and WBC, CRP and ESR, and a medium-level correlation was found between PLR and CRP and ESR. The diagnostic performances of NLR (cut-off level of >3.5), PLR (cut-off value of >135 for), and other laboratory measurements are shown in Supplemental Table 2. ROC analysis results of the laboratory tests used in this study are shown in Supplemental Table 3, and ROC graphics are shown in Figure 1. The area under the curve (AUC) for NLR and PLR levels were 0.688 and 0.617, respectively.

Discussion

This study aims to investigate the NLR and PLR parameters in the diagnosis of postoperative surgical wound infection.

Table 3: Correlation analysis of NLR and PLR values and demographic data and other laboratory measurements.

	NLR		PLR	
	Rho	p-Value	Rho	p-Value
Presence or absence of infection	0.326	<0.001	0.208	0.023
Day of the start of the postoperative complaint	0.246	0.007	0.242	0.008
WBC	0.617	<0.001	0.179	0.051
ESR	0.427	<0.001	0.479	<0.001
CRP	0.587	<0.001	0.412	<0.001

p<0.05 statistically significant. Rho <0.3 means low-level relationship and 0.3–0.7 means medium-level relationship. WBC, white blood cell; PLT, platelet; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio.

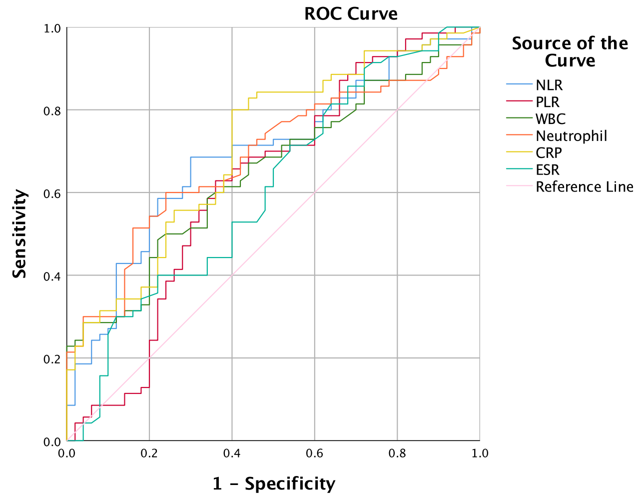

Figure 1: ROC analysis graphic of laboratory measurements of the patients. ROC, receiver operator curve; AUC, area under curve; WBC, white blood cell; PLT, platelet; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio.

We found in our study that especially NLR was significantly associated with the diagnosis of postoperative surgical wound infection. Surgical wound infections are among the important complications of the postoperative period. They cause various negative outcomes such as increasing antibiotic use, delay in wound healing, and increasing duration of hospital stay [12], so a rapid diagnosis and initiation of empirical treatment until results of culture-antibiotic sensitivity are obtained are important. *S.aureus* is frequently isolated from postoperative wound infections in patients undergoing orthopedic surgery, and we also found this organism most frequently from the cultures in our study [13–15].

The considerable time required to obtain the results of cultures and antibiotic sensitiviy tests has caused the use of auxiliary tests of inflammatory markers. As ESR and CRP have been used as biomarkers for a long time, CBC parameters such as NLR and PLR started to be used more frequently [6]. While there are many studies in the medical literature investigating the association between NLR, PLR, and many different diseases such as cancer, cardiovascular disease, renal diseases, inflammatory diseases, and colorectal disorders [2, 8, 15–20], studies investigating the association between these markers and postoperative wound infections in patients who did not receive prophylactic antibiotics are scarce. We believe that our study may contribute to the medical literature in this respect.

In the study by Shen et al. [10] evaluating patients that had undergone posterior lumbar spinal surgery, laboratory data obtained at the postoperative 4th and 7th days were compared in patients with and without infection. The neutrophil percentage and NLR were significantly high, and leukocyte percentage was significantly low in patients in whom infection developed on the postoperative 4th day. There were no significant differences between the two groups in terms of neutrophil and leukocyte counts, WBC, and CRP values. There were significant differences in the group with infection in terms of neutrophil count, neutrophil percentage, and NLR values on the 7th postoperative day. Complaints due to wound infection occurred in the first seven postoperative days in all the patients in whom growth was detected in our study. Laboratory tests and cultures were done simultaneously, and neutrophil and lymphocyte counts were determined, but their percentages were not included in this study. WBC, neutrophil count, ESR, CRP, NLR, and PLR values of patients with infection were significantly higher, and lymphocyte counts were significantly lower than those without infection. Also, a medium-level, statistically significant correlation was found between NLR and PLR values, and ESR and CRP. When we consider these two studies, NLR and PLR seem to be biomarkers that may be used in practice like CRP and ESR, in the detection of postoperative infection.

We compared preoperative and postoperative laboratory values in the patient groups with and without infection. Postoperative WBC, ESR, and CRP values were significantly higher than preoperative values, but neutrophil count and NLR values were also statistically significantly different in only the group with infection. ESR and CRP values were significantly higher after surgery, independent of the presence or absence of infection. In the study by Yombi et al. [21], where the relationship between CRP and NLR values, and postoperative wound infection was investigated in patients who underwent total knee arthroplasty, NLR was found to return to normal values earlier than CRP and was reported to be a better parameter in follow-up for infection in the early period. Zhao et al. [22] have evaluated the correlation between laboratory data and the development of periprosthetic joint infection in patients undergoing total joint arthroplasty and found that CRP and ESR remained high for a long period after arthroplasty, and NLR was more sensitive for early diagnosis. According to these three studies, markers like ESR and CRP may be increased after orthopedic surgery, independent of infection, and NLR may be a better parameter for showing the presence of infection.

Kahramanoglu et al. [6] have evaluated postoperative wound infections in patients who had undergone abdominal hysterectomy and found the preoperative neutrophil count and NLR significantly higher in patients with infection, lymphocyte counts significantly lower, and platelet counts similar to patients without infection. Forget et al. [23] have found preoperative NLR values more beneficial than CRP in early diagnosis of postoperative complications in patients who had undergone major abdominal surgery. In our comparison of preoperative CBC, ESR, and CRP values, only NLR, PLR, and CRP values showed significant differences between the two groups. This suggests that preoperative NLR and PLR values may be used in the prediction of wound infections after surgery.

We did not find a standard use of NLR and PLR cut-off values in our literature search [2, 8, 15–18, 24]. In the study by Maruyama et al. [9] investigating patients undergoing head and neck surgery, a sensitivity of 82.4%, specificity of 48.3% was found with a cut-off of ≥3.5 for NLR, and a sensitivity of 70.5%, specificity of 72.1% with a cut-off of >160 for PLR. Shen et al. have found a sensitivity of 69.2% and specificity of 62.7% with a NLR cut-off value of >3.85. We used a cut-off of >3.5 for NLR, and >135 for PLR, and evaluated diagnostic performance. A sensitivity of 68% and specificity of 66% were found for NLR, and a sensitivity of 71% and specificity of 42% were found for PLR. We also performed performance analysis of the tests as biomarkers. The highest performance was found for CRP, and NLR was the second highest, showing higher performances than ESR, which is frequently used in routine practice. PPV of NLR was higher than CRP, while PPV of PLR was slightly lower than CRP. Yu et al. [25] in their study investigating patients undergoing total knee and hip arthroplasty have found NLR sensitivity and NPV values better than CRP, and PPV values similar to CRP. NLR is independently associated with surgical site infections in multivariate models. These findings show that diagnostic performances of both parameters are good, with NLR better than PLR.

Limitations of our study included retrospective design, small sample size, absence of identical surgical teams, and methods for comparison. In our study, the presence of chronic disease was used as an exclusion criterion, and it should be noted that this situation will bring an important limitation to the tests. In addition, since our evaluation can only be used in orthopedic patients and wound infections, it would be appropriate to re-evaluate the patient in other postoperative infections.

Conclusions

Surgical wound infection is one of the most frequent complication types, with a considerable negative impact on the surgical process for both the surgeon and the patient. Therefore, early diagnosis and swift medical treatment are very important. We found in this study that CBC parameters, especially NLR, can be used in the diagnosis of postoperative surgical wound infection. NLR is more closely associated with surgical wound infection, and NLR may even be helpful in predicting the development of postoperative infection. Thus, we believe that especially NLR from routine blood parameters may be beneficial in terms of diagnosing infection in patients undergoing orthopedic surgery. Nevertheless, in comparison with commonly used infection markers, there is the same for using them alone or combined value of serum NLR and PLR for diagnosing wound infections.

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Author contributions: 1. Hülya Duran: Conduct the study, literature review, data collection, study design, analyze the data, write the manuscript, and final review. 2. Medine Alpdemir: Conduct the study, design of study, literature review, data collection, analyze the data, write the manuscript, and final review. 3. Nihan Çeken: Literature review, data collection, write the manuscript, and review. 4. Mehmet fatih Alpdemir: Data collection, write the manuscript, literature review, and final review. 5. Tugba Kula Atik: Data collection, analyze the data, and literature review. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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Informed consent: Informed consent was obtained from all individuals included in this study.

Ethical approval: Approval from the Ethics Committee was obtained from the Clinical Research Ethics Committee of Balikesir University (Date: 09.12.2020, Decision No: 2020/233).

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