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Can C-Reactive Protein-Lymphocyte Ratio Be Used as a Screening Tool to Confirm the Diagnosis of Periprosthetic Joint Infection?

Orhan Balta, MD, Sezer Astan, MD*, Harun Altınayak, MD†, Cihan Uçar, MD‡, Feyza Yildiz Aytekin, MD§, Recep Kurnaz, MD‖

Department of Orthopaedics and Traumatology, Gaziosmanpasa University Hospital, Tokat,
**Department of Orthopaedics and Traumatology, Tokat State Hospital, Tokat,*
†Department of Orthopedics and Traumatology, Samsun Training and Research Hospital, Health Sciences University, Samsun,
‡Department of Orthopedics and Traumatology, Trabzon Kanuni Training and Research Hospital, Trabzon,
§Department of Infectious Diseases and Clinical Microbiology, Ministry of Health Prof. Dr. A. Ilhan Özdemir State Hospital, Giresun,
‖Department of Orthopaedics and Traumatology, Acıbadem State Hospital, Eskişehir, Türkiye

Background: This study aimed to investigate whether periprosthetic joint infection (PJI) can be predicted by the C-reactive protein-to-lymphocyte ratio (CLR), whether this ratio increases the accuracy of PJI diagnosis, and whether it is more sensitive than other blood values and ratios.

Methods: The patients were divided into two groups: the septic revision (SR) group and the aseptic revision (AR) group. In cases of septic revision, the diagnosis of PJI was made based on the criteria proposed by the European Bone and Joint Infection Society (EBJIS). The groups were compared in terms of age, sex, body mass index, comorbidity, and preoperative laboratory results. The sensitivity, specificity, and diagnostic performance of the values and ratios were analyzed and compared.

Results: The receiver operating characteristic (ROC) analysis for the CLR gave a diagnostic value of 15.52, which provided a sensitivity of 91.1% and a specificity of 64.2% for PJI. The CLR gave lower specificity and higher sensitivity compared to the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values. The ROC analysis showed that the CLR had a similar area under the curve (AUC) with the ESR and CRP (0.808). The CLR had a higher specificity than other ratios (platelet volume ratio, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and monocyte-to-lymphocyte ratio) and a higher value of the AUC. In the multivariate analysis, the CLR (hazard ratio, 1.088; 95% confidence interval, 1.063–1.113; $p < 0.001$) was found to be a significant risk factor. As CLR increased by one unit, the risk of PJI increased by 1.088 times, and it was statistically significant ($p < 0.001$).

Conclusions: The findings of this study suggest that CLR can serve as a valuable screening tool for diagnosing PJI. CLR demonstrated higher sensitivity in predicting PJI compared to ESR and CRP, and it exhibited greater specificity than other infection markers.

Keywords: *Erythrocyte sedimentation rate, C-reactive protein, Periprosthetic joint infection, C-reactive protein-to-lymphocyte ratio*

Total hip or knee arthroplasty is known to improve patients' quality of life, but complications such as aseptic failure and periprosthetic joint infection (PJI) can still occur.[1] PJI is a highly concerning complication, impacting patients' well-being and even increasing mortality risk.[2] Due to the significant morbidity and mortality associated with PJI, early and accurate diagnosis is crucial. However,

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Correspondence to: Orhan Balta, MD
Department of Orthopaedics and Traumatology, Gaziosmanpasa University Hospital, Kaleardı District Muhittin Fisunoglu St, Tokat 60100, Türkiye
Tel: +90-50-5938-8019, Fax: +90-35-6212-9500
E-mail: drorhanbalta@hotmail.com

diagnosing PJI can be challenging as there is no definitive gold standard test, and the interpretation of serum inflammatory markers lacks standardization.

Diagnosis of PJI typically involves clinical evaluation, physical examination, and laboratory results, including synovial fluid analysis, serum inflammatory markers, and culture data. Various criteria have been defined to predict PJI, such as the 2021 European Bone and Joint Infection Society (EBJIS) criteria,[3] the 2018 International Consensus Meeting (ICM) criteria,[4] the 2013 ICM criteria,[5] and the 2013 Infectious Diseases Society of America and 2011 Musculoskeletal Infection Society (MSIS) criteria.[6,7] Recently, the EBJIS proposed a three-level diagnostic approach based on classic clinical, laboratory, and radiographic findings.[3] This definition divides cases into unlikely infection and confirmed infection and proposes a novel third group as likely but not confirmed PJI. Diagnostic criteria developed by the MSIS and the Infectious Diseases Society have helped surgeons improve the accuracy of PJI diagnosis.[7,8] The EBJIS definition has been suggested to have increased sensitivity compared to previously proposed criteria without negatively impacting specificity. It has also been shown to be better in preoperatively ruling out PJI when serological and synovial biomarkers yield negative results.[9]

Serum inflammatory markers, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), D-dimer, procalcitonin, and interleukin-6, can provide important information in cases where a definitive diagnosis cannot be made.[10-12] However, these markers should be interpreted with caution, especially in patients with other chronic inflammatory diseases that may affect the results. CRP, commonly used as a first-line screening test for late PJI, can yield false-negative results in cases of late PJI, low-virulence pathogens, and prior antibiotic use.[6,13] CRP elevation may not always be evident in infections caused by low-virulence bacteria, leading to potential misdiagnosis.[6,13] Therefore, alternative serum biomarkers like monocyte-to-lymphocyte ratio (MLR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and platelet count ratio-to-mean platelet volume (PVR) have been investigated for their potential role in diagnosing PJI, offering simple predictors of inflammation from complete blood count data.[14-18]

The C-reactive protein-to-lymphocyte ratio (CLR) is one such marker that reflects the balance between systemic inflammatory and immune responses. A high CLR indicates an increased systemic inflammatory response and a reduced immune response.[19,20] This study aimed to investigate whether PJI can be predicted by CLR, whether this ratio increases the accuracy of PJI diagnosis, and whether it is more sensitive than other blood values and ratios.

METHODS

The study plan was to conduct a single-center, retrospective cohort study in which research data obtained from the patients who underwent revision total hip arthroplasty (THA) or total knee arthroplasty (TKA) in our clinic from July 2006 to November 2020 for any reason were retrospectively analyzed using the electronic medical record system (ENLIL Hospital information management system, version v2.19.46 20191118). Ethical approval was obtained from the Clinical Research Ethics Committee of Tokat Gaziosmanpaşa Universty (No. 20-KAEK-095). As the study was designed retrospectively, no written informed consent form was obtained from patients.

The patients were assessed by two orthopedic surgeons who were not involved in the study (OB and SA). The patients were then divided into two groups: those who underwent surgery for septic revision (SR group) and those who underwent surgery for aseptic revision (AR group). In cases of septic revision, the diagnosis of PJI was made according to the EBJIS criteria by McNally et al.[3] All definitions classified the presence of a sinus tract or two positive cultures as evidence of infection. According to the EBJIS definition, infection was also confirmed when the total white blood cell count was > 3,000 cells/μL, the percentage of polymorphonuclear neutrophils was > 80%, there were more than > 50 CFU grown from any organism, or histology was positive for infection. At our hospital, patients scheduled for revision TKA and THA undergo regular screenings for ESR and CRP. For patients with a high suspicion of PJI or elevated serological markers, synovial fluid aspiration is performed. The samples obtained through aspiration are sent to the laboratory for culture and synovial fluid analysis, including cell count and polymorphonuclear differentiation. Perioperative antibiotics were not routinely used in this study. Moreover, in all revision cases, 2 to 5 intraoperative cultures were obtained. Preoperative complete blood counts were performed in all patients who underwent revision TKA and THA. Based on our clinical and laboratory results, patients who met the EBJIS criteria under the category of "infection confirmed" were included in the SR group. Patients with acute PJI occurring within 3 months from the index surgery were excluded from the study due to the inherent difficulty associated with confounding causes of inflammation. Aseptic revisions were considered as cases revised

in a single session due to a noninfectious diagnosis (loosening, instability), which did not develop into PJI within 1 year after surgery and those that did not require reoperation for any reason.

Following the evaluations, 102 patients who underwent surgery for septic revision were designated as the SR group, and 162 patients who underwent surgery for aseptic revision were designated as the AR group. Patients with inflammatory arthritis, hematological diseases, periprosthetic fractures, antibiotic use within 2 weeks before the revision surgery, revision surgery performed within 4 weeks after the index procedure, preexisting infections or malignant tumors in other areas, undergoing chemotherapy, using steroids or immunosuppressants, and patients with diseases affecting the production/modulation of inflammatory markers were excluded from the study. Blood samples were collected before the revision surgery and within the month of the revision procedure. Samples obtained within the last month were included in the study. Blood samples taken 30 days before the revision

Table 1. Patient Characteristics According to Revision Surgery

Variable		Revision surgery		*p*-value*
		Septic revision group	Aseptic revision group	
Group	Knee	62 (60.8)	82 (50.6)	0.106
	Hip	40 (39.2)	80 (49.4)	
Sex	Female	73 (71.6)	126 (77.8)	0.254
	Male	29 (28.4)	36 (22.2)	
Hypertension	Absent	47 (46.1)	61 (37.9)	0.188
	Present	55 (53.9)	100 (62.1)	
Coronary artery disease	Absent	76 (74.5)	116 (71.6)	0.606
	Present	26 (25.5)	46 (28.4)	
Heart failure	Absent	82 (80.4)	139 (85.8)	0.246
	Present	20 (19.6)	23 (14.2)	
Diabetes mellitus	Absent	80 (78.4)	119 (73.5)	0.361
	Present	22 (21.6)	43 (26.5)	
Chronic lung disease	Absent	86 (84.3)	123 (75.9)	0.102
	Present	16 (15.7)	39 (24.1)	
Chronic renal failure	Absent	89 (87.3)	145 (89.5)	0.575
	Present	13 (12.7)	17 (10.5)	
Presence of cerebrovascular event	Absent	86 (84.3)	138 (85.2)	0.848
	Present	16 (15.7)	24 (14.8)	
Arrhythmia	Absent	92 (90.2)	148 (91.4)	0.749
	Present	10 (9.8)	14 (8.6)	
Thyroid dysfunction	Absent	97 (95.1)	150 (92.6)	0.419
	Present	5 (4.9)	12 (7.4)	
Parkinson disease	Absent	102 (100)	160 (98.8)	0.260
	Present	0	2 (1.2)	

Values are presented as number (%).
*Pearson chi-square test.

Table 2. Comparison of the Hematologic and Biochemical Parameters of Revision

Parameter	Septic revision group	Aseptic revision group	*p*-value*
Age	66.84 ± 10.13	65.29 ± 10.87	0.247
Leukocyte	10.02 ± 4.65	8.93 ± 4.12	0.048
Neutrophil percentage	68.95 ± 11.65	64.7 ± 13.71	0.010
Lymphocyte percentage	21.19 ± 9.29	25.38 ± 11.98	0.003
Monocyte percentage	6.95 ± 2.58	7.13 ± 2.52	0.584
Eosinophil percentage	2.12 ± 3.14	2.11 ± 2.14	0.986
Basophil percentage	0.56 ± 0.37	0.69 ± 0.41	0.012
Neutrophil count	7.12 ± 4.3	6.14 ± 4.16	0.068
Lymphocyte count	1.88 ± 0.77	1.96 ± 0.85	0.442
Monocyte count	0.65 ± 0.31	0.6 ± 0.3	0.255
Eosinophil count	0.17 ± 0.28	0.15 ± 0.15	0.589
Basophil count	0.05 ± 0.03	0.05 ± 0.03	0.540
Red blood cell	4.15 ± 0.57	4.45 ± 0.68	< 0.001
Hemoglobin	11.01 ± 1.58	12.19 ± 1.94	< 0.001
Hematocrit	33.94 ± 4.62	37.13 ± 5.66	< 0.001
Mean red cell volume	82.19 ± 6.49	83.72 ± 5.39	0.038
Mean corpuscular hemoglobin	26.69 ± 2.62	27.48 ± 2.23	0.009
Mean corpuscular hemoglobin concentration	32.45 ± 1.35	32.8 ± 1.12	0.022
Red blood cell distribution width	15.38 ± 2.06	14.88 ± 1.87	0.044
Platelet count	286.55 ± 98.41	255.63 ± 59.6	0.002
Mean platelet volume	9.14 ± 1.73	9.23 ± 1.5	0.639
Erythrocyte sedimentation rate	62.82 ± 71.26	12.49 ± 30.88	< 0.001
Serum C-reactive protein	61.21 ± 28.17	25.62 ± 20.55	< 0.001
C-reactive protein to lymphocyte ratio	40.29 ± 33.35	17.24 ± 19.25	< 0.001
Platelet count ratio-to-mean platelet volume	33.33 ± 16.01	28.62 ± 8.64	0.002
Neutrophils to lymphocytes ratio	4.8 ± 4.66	4.22 ± 4.55	0.320
Platelet-to-lymphocyte ratio	179.74 ± 108.16	154.94 ± 76.33	0.030
Lymphocyte to monocyte ratio	3.43 ± 2.08	4.07 ± 2.87	0.051
Charlson comorbidity index	1.44 ± 0.97	1.69 ± 1.25	0.094
Weight (kg)	73.31 ± 6.15	73.89 ± 6.24	0.464
Height (m)	1.67 ± 0.03	1.66 ± 0.03	0.312
Body mass index (kg/m^2)	26.36 ± 2.37	26.68 ± 2.22	0.264

Values are presented as mean ± standard deviation.
*Independent samples *t*-test; a *p*-value < 0.05 was considered significant.

surgery and any blood samples taken more than a month before the surgery were excluded from the study. All blood samples were collected from the patients' veins on the day of hospital admission, stored in tubes containing ethylenediaminetetraacetic acid (EDTA), and later automatically analyzed using internationally certified equipment.

A descriptive analysis was performed to obtain information on the general characteristics of the study population. Quantitative data were analyzed by arithmetic mean and standard deviation. Independent-sample *t*-tests or one-way analysis of variance were applied to compare continuous data between/within groups. The receiver operating characteristic (ROC) analysis was conducted to determine the significance of the whole-blood picture in predicting PJI. A p-value < 0.05 was considered significant. In the multivariate analysis, we examined the independent predictors of treatment outcomes using logistic regression analysis. The SPSS ver. 22 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

RESULTS

A total of 264 patients who had undergone TKA and THA revision surgery were evaluated. Based on the EBJIS criteria, 102 patients were in the SR group (40 hips and 62 knees), and 162 patients were in the AR group (80 hips and 82 knees). The demographic characteristics of the patients are shown in Table 1. There were no statistically significant differences between the two groups in terms of age, comorbidity, body mass index, Charlson comorbidity

Table 3. Effect of Premorbid Condition on CLR

Variable		CLR		*p*-value*
		n	Mean ± SD	
Hypertension	Absent	108	23.92 ± 25.10	0.264
	Present	155	27.84 ± 29.76	
Coronary artery disease	Absent	192	25.50 ± 26.17	0.542
	Present	72	27.86 ± 32.33	
Heart failure	Absent	221	25.20 ± 26.70	0.212
	Present	43	31.02 ± 33.54	
Diabetes mellitus	Absent	199	26.51 ± 29.57	0.713
	Present	65	25.04 ± 22.40	
Chronic lung disease	Absent	209	28.01 ± 29.49	0.034
	Present	55	19.06 ± 19.68	
Chronic renal failure	Absent	234	26.05 ± 26.65	0.881
	Present	30	26.86 ± 37.02	
Presence of cerebrovascular event	Absent	224	26.57 ± 29.10	0.563
	Present	40	23.78 ± 20.37	
Arrhythmia	Absent	240	25.29 ± 26.26	0.116
	Present	24	34.71 ± 40.92	
Thyroid dysfunction	Absent	247	26.42 ± 28.11	0.540
	Present	17	22.12 ± 25.73	
Parkinson disease	Absent	262	26.15 ± 27.97	0.980
	Present	2	25.65 ± 33.68	

CLR: C-reactive protein-to-lymphocyte ratio, SD: standard deviation.
*Independent samples *t*-test; a p-value < 0.05 was considered significant.

index, and sex (Table 2). The effect of premorbid condition on CLR is presented in Table 3.

While LY% ($p = 0.003$), red blood cells ($p < 0.001$), hemoglobin ($p < 0.001$), and hematocrit ($p = 0.001$) were significantly lower in the SR group, platelet count ($p < 0.001$), ESR ($p < 0.001$), CRP ($p < 0.001$), CLR ($p < 0.001$), and platelet count ($p = 0.002$) values were statistically significantly higher (Table 2).

The CLR and PVR values were significantly higher in the SR group than in the AR group, whereas there were no statistically significant differences in terms of the NLR, PLR, and MLR values. The distribution of these values is shown in Fig. 1. Table 4 shows the ROC analysis results. The ROC analysis for the CLR showed a diagnostic value of 15.52, which had a sensitivity of 91.1% and a specificity of 64.2% for PJI. The CLR showed lower specificity and higher sensitivity compared to the ESR and CRP values. The ROC analysis indicated that the CLR had a similar area under the curve (AUC; 0.808) with ESR and CRP. The CLR had a higher specificity than the other ratios (PVR, NLR, PLR, and LMR) and a higher value under the curve. The ROC curve is shown in Fig. 2. As a result of the ROC analysis performed, hemoglobin, sedimentation, CRP, CLR, and NLR were found to be significant parameters in PJI diagnosis.

According to the results obtained in the ROC analysis, there was a difference between hip and knee PJI diagnostic CLR value for PJI in terms of the cutoff values, sensitivity, and specificity (knee CLR: cutoff ≥ 15.42, AUC = 0.770, sensitivity = 90.32%, specificity 58.5%, $p < 0.001$; hip CLR: cutoff ≥ 13.82, AUC = 0.857, sensitivity 95.0%, specificity 67.5%, $p < 0.001$) (Fig. 3)

Female sex was more prone to have infection; the sex distribution was equal in both groups ($p = 0.254$). The ROC analysis provided that the difference in the cutoff of diagnostic CLR value was significant between men and women (CLR in women: cutoff ≥ 16.49, AUC = 0.789, sensitivity = 87.6%, specificity = 62.7%, $p < 0.001$; CLR in men: cutoff ≥ 13.82, AUC = 0.866, sensitivity = 96.5%, specificity = 77.7%, $p < 0.001$) (Fig. 4).

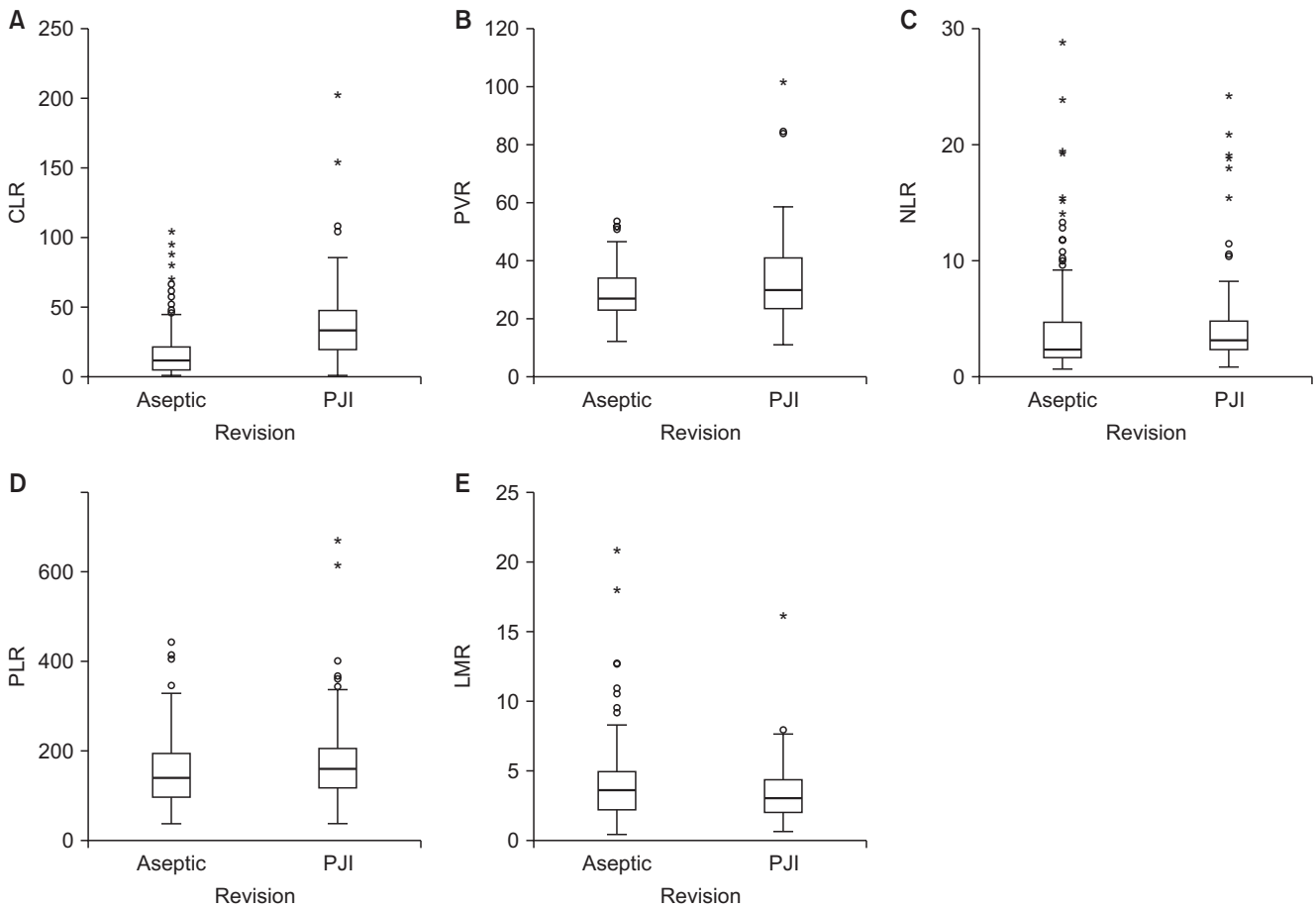

Fig. 1. Boxplot of the distribution of C-reactive protein to lymphocyte ratio (CLR; A), platelet count ratio-to-mean platelet volume (PVR; B), neutrophil-to-lymphocyte ratio (NLR; C), platelet-to-lymphocyte ratio (PLR; D), and lymphocyte-to-monocyte ratio (LMR) (E). PJI: periprosthetic joint infection.

Table 4. Receiver Operating Characteristic Curve Analysis of Serum Biomarkers in the Diagnosis of Periprosthetic Joint Infection

Variable	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	*p*-value*
C-reactive protein to lymphocyte ratio	> 15.52	0.808	0.912	0.642	0.616	0.920	< 0.001
Platelet count ratio-to-mean platelet volume	≥ 35.75	0.574	0.382	0.803	0.549	0.674	0.044
Neutrophil-to-lymphocyte ratio	≥ 2.53	0.606	0.706	0.543	0.493	0.746	0.002
Platelet-to-lymphocyte ratio	≥ 157.60	0.584	0.559	0.654	0.504	0.702	0.019
Lymphocyte-to-monocyte ratio	≤ 3.94	0.564	0.696	0.457	0.447	0.705	0.074
Erythrocyte sedimentation rate	≥ 13.9	0.821	0.735	0.821	0.721	0.831	< 0.001
C-reactive protein	≥ 31	0.850	0.853	0.704	0.644	0.884	< 0.001
Hemoglobin	≤ 11.62	0.689	0.735	0.592	0.531	0.780	< 0.001
Platelet	> 3 21	0.590	0.352	0.870	0.631	0.681	0.018
Mean platelet volume	≤ 9.5	0.518	0.617	0.481	0.428	0.666	0.617

AUC: area under the curve, PPV: positive predictive value, NPV: negative predictive value.
*A *p*-value < 0.05 was considered significant.

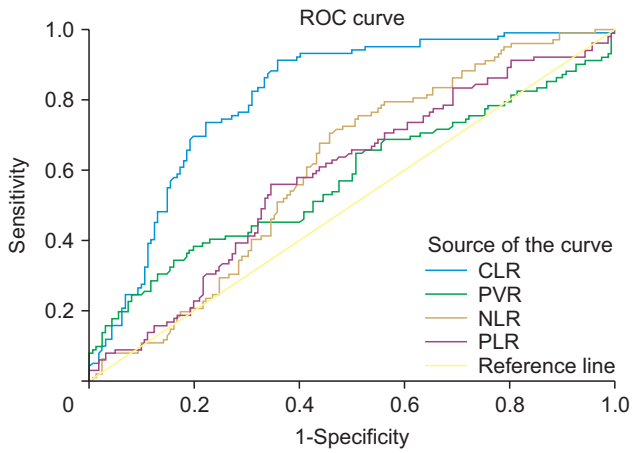

Fig. 2. Comparison of receiver operating characteristic (ROC) curves of C-reactive protein to lymphocyte ratio (CLR), platelet count ratio-to-mean platelet volume (PVR), neutrophil-to-lymphocyte ratio (NLR), and neutrophil-to-lymphocyte ratio (PLR) for predicting periprosthetic joint infection.

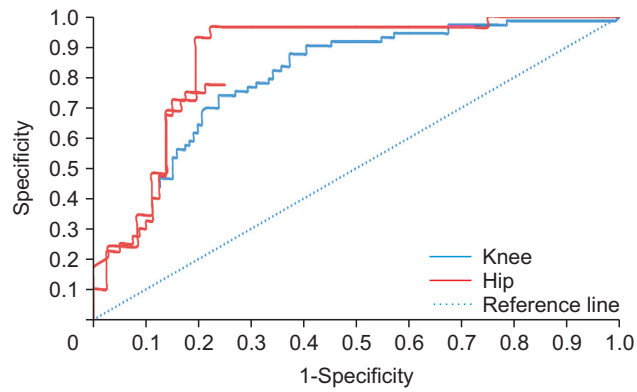

Fig. 3. Receiver operating characteristic curves of C-reactive protein to lymphocyte ratio in knee and hip groups.

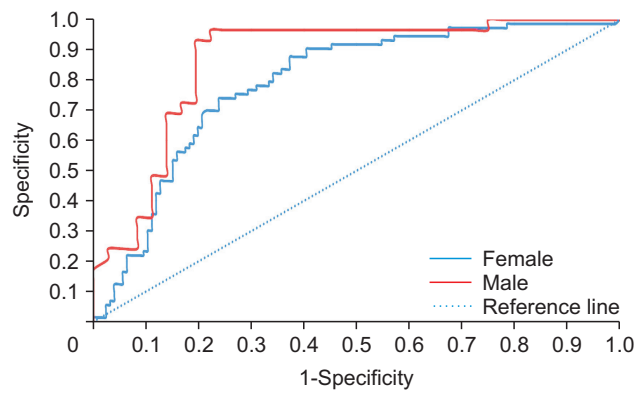

Fig. 4. Receiver operating characteristic analysis for sex.

The results of univariate and multivariate logistic regression analysis performed to determine the effective parameters causing PJI, odds ratios (ORs), and 95% confidence intervals (CIs) for each statistically significant parameter are shown in Table 5. In the multivariate model, the OR value was 0.794 (95% CI, 0.657–0.960; $p = 0.018$) for hemoglobin and 1.051 (95% CI, 1.032–1.069; $p < 0.001$) for CRP.

The ratios other than CLR and PVR were not significant. The OR (95% CI) of CLR was 1.046 (1.030–1.061;

Table 5. Results of Logistic Regression for Revision Variables

Model	Univariate			Multivariate		
	p-value	Crude OR	95% CI for OR	Adjusted *p*-value	Adjusted OR	95% CI for OR
C-reactive protein to lymphocyte ratio	< 0.001	1.046	1.030–1.061	< 0.001*	1.088	1.063–1.113
Platelet count ratio-to-mean platelet volume	0.004	1.033	1.011–1.056	< 0.001*	1.093	1.054–1.134
Platelet-to-lymphocyte ratio	0.036	1.003	1.000–1.006	< 0.001*	0.982	0.976–0.989
Lymphocyte-to-monocyte ratio	0.056	0.896	0.801–1.003	0.087	0.881	0.761–1.019
Hemoglobin	< 0.001	0.693	0.595–0.807	0.018	0.794	0.657–0.960
Platelet	0.002	1.005	1.002–1.009	0.704	0.999	0.995–1.004
Erythrocyte sedimentation rate	< 0.001	1.034	1.021–1.046	0.061	1.010	1.000–1.020
C-reactive protein	< 0.001	1.057	1.042–1.071	< 0.001*	1.051	1.032–1.07

OR: odds ratio, CI: confidence interval.
*Statistical significance.

$p < 0.001$) in the univariate model and 1.088 (1.063–1.113; $p < 0.001$) in the multivariate model. The PVR ratio was significant in both the univariate and multivariate analyses ($p = 0.004$ and $p < 0.001$, respectively). The PLR ratio was not significant in the univariate analysis, but significant in the multivariate analysis ($p = 0.036$ and $p < 0.001$, respectively).

DISCUSSION

In summary, this study demonstrated that the CLR had higher sensitivity compared to ESR, CRP, and other indices in diagnosing PJI. Additionally, the CLR showed higher specificity than other ratios such as PLR, NLR, PVR, and LMR, resulting in a higher AUC value. The regression analysis revealed that the CLR (hazard ratio, 1.088; 95% CI, 1.063–1.113; $p < 0.001$) was a significant risk factor for PJI.

This study aimed to investigate the potential of CLR as a novel biomarker for diagnosing PJI in patients undergoing TKA and THA. While CLR is used as an inflammatory marker in various fields of medicine,[21-23] there is a lack of literature evaluating its diagnostic value in predicting PJI in orthopedic patients. Recently, CLR has been introduced in some studies as a new parameter for determining the prognosis of malignancy.[24] It is easily calculated based on the ratio of CRP-to-lymphocytes. Both CRP elevation and lymphocyte reduction in peripheral blood have been associated with poor prognoses in patients with malignancies. CLR elevation has also been linked to inflammatory diseases, such as appendicitis.[23]

While various inflammatory markers can be used to confirm the diagnosis of PJI, the optimal combination of inflammatory factors remains uncertain.[25,26] Recently, new inflammatory markers such as NLR, PLR, and MLR have been recognized as useful indicators for the diagnosis and prognosis of various infectious diseases.[27] However, their use in orthopedic studies is still limited.[28] This study demonstrated that CLR is more effective than other markers in diagnosing PJI in TKA and THA patients. CLR levels were significantly higher in PJI patients, and it showed higher accuracy in detecting PJI cases compared to other indices. Therefore, CLR is considered a cost-effective and readily available biomarker for diagnosing PJI. Further research is needed to confirm the effectiveness of this new marker and assess its clinical applicability in PJI diagnosis. Combining these markers with existing standard indicators may lead to more accurate and reliable results in diagnosing PJI. Early and accurate diagnosis is of great importance for patient treatment and outcomes.

Increased peripheral leukocytes, ESR, and CRP are neither sensitive nor specific to PJI. After surgery, the ESR and CRP levels may remain elevated for weeks. Therefore, serial postoperative measurements are more informative than single values. In addition, CRP and ESR may be elevated due to other inflammatory conditions or, conversely, false negative in the context of suppressive antimicrobial therapy or organisms with low virulence. However, a normal ESR combined with a normal CRP level indicates a very low probability of infection. The role of new markers, including interleukin-6, procalcitonin, and tumor necrosis factor-α, remains to be defined.[29]

Serum ESR and CRP are markers that are routinely collected and analyzed in the evaluation of patients with PJI. In our study, serum CRP showed a sensitivity of 85% and a specificity of 70%. These results are similar to the data reported in the literature, where sensitivity ranges from 68% to 90% and specificity ranges from 71% to 88%.[14,30-32] In our study, serum ESR yielded a sensitivity of 73% and a specificity of 82%. Although both ESR and CRP have shown limited prognostic values for predicting PJI, recent studies have shown that ESR has the potential to diagnose infections in non-orthopedic specialties.[33]

Both serum and synovial biomarkers have demonstrated encouraging results in the diagnosis of PJI and can be used as diagnostic tools to support bacteriological culture and perioperative and intraoperative clinical findings. Several new tests and markers, such as synovial leukocyte esterase, D-dimer, synovial alpha-defensin, and synovial CRP, have recently been reviewed in the literature for their accuracy in diagnosing PJI.[34,35] However, a single gold standard stepwise approach for the detection of PJI remains unclear. Many of these tests and markers mentioned above are expensive or time-consuming to obtain. In addition, some diagnostic tests, such as synovial alpha-defensin, require equipment and expertise that may not be readily available or accessible at all facilities. Therefore, more studies are needed to investigate readily available and inexpensive serum and synovial fluid markers to be used for the diagnosis of PJI.[36]

This study has limitations due to its retrospective design and data from a single center. Therefore, the results need to be confirmed by prospective multicenter studies. Another important shortcoming was the lack of synovial fluid results of the same laboratory markers. Since the study was retrospective, indirect measurements, that is, blood values, were used. Besides, the fact that certain pathogen species might affect CLR can be regarded as a limitation of the study. This study may indicate higher sensitivity of CLR over ESR and CRP or other ratios; however, there is not a direct association established because the data were obtained from blood samples and not from synovial fluid of the knee joint. Synovial fluid analysis/culture is considered the gold standard in the evaluation of patients with suspected PJI. A prospective study evaluating joint fluid can be planned in the future. A study including more patients in which synovial fluid is efficiently and elaborately investigated in patients with inflammation post-replacement can be recommended to be conducted.

This study demonstrates that CLR is a valuable tool for confirming the diagnosis in patients with PJI. It has been found to have higher sensitivity than ESR and CRP and higher specificity than other infection markers such as PVR, NLR, PLR, and MLR. CLR is a useful diagnostic tool for confirming PJI in patients with suspected periprosthetic infection, especially those with high ESR and CRP levels.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Orhan Balta https://orcid.org/0000-0002-4398-827X
Sezer Astan https://orcid.org/0000-0003-2435-3874
Harun Altınayak https://orcid.org/0000-0002-1915-5665
Cihan Uçar https://orcid.org/0000-0001-6191-4824
Feyza Yildiz Aytekin https://orcid.org/0000-0002-9526-0707
Recep Kurnaz https://orcid.org/0000-0002-8311-047X

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