Infection and Drug Resistance

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Blood Cell Ratio Combinations for Diagnosing Periprosthetic Joint Infections: A Preliminary Study

Yali Yu[1], Yanan Wen[2], Jiaxuan Xia[3], Guixiang Dong[1], Yanli Niu[4]

[1]Department of Clinical Laboratory, Zhengzhou Orthopaedic Hospital, Zhengzhou, People's Republic of China; [2]Department of Blood Transfusion, Huaihe Hospital, Henan University, Kaifeng, People's Republic of China; [3]School of Mathematics and Statistic, Henan University, Kaifeng, People's Republic of China; [4]Laboratory of Cell Signal Transduction, Henan Provincial Engineering Centre for Tumor Molecular Medicine, School of Basic Medical Sciences, Henan University, Kaifeng, People's Republic of China

Correspondence: Yanli Niu, School of Basic Medical Sciences, Henan University, Kaifeng, People's Republic of China, Email nyl0925@henu.edu.cn

Background: Periprosthetic joint infection (PJI) is a serious complication following total joint arthroplasty (TJA), which requires prompt and accurate diagnosis for effective management. Many biomarkers have been used for PJI diagnosis; however, the identification of the most effective inflammatory biomarker combination for optimal diagnostic accuracy may be poorly reported.

Methods: In this prospective, multi-center study, a total of 269 individuals undergoing knee or hip revision arthroplasty were recruited and subsequently categorized based on 2018 ICM PJI criteria into two groups: 93 with periprosthetic joint infection (PJI) and 176 with aseptic failure (AF). Various preoperative biomarkers were analyzed and compared, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), neutrophil-to-lymphocyte ratio (NLR), CRP-to-albumin ratio (CAR), CRP-Albumin-lymphocyte ratio (CALLR), platelet-to-lymphocyte ratio (PLR), platelet-to-albumin ratio (PAR), and neutrophil-to-albumin ratio (NAR). The diagnostic performance of these biomarkers was evaluated using ROC curve analysis and the area under the curve (AUC). Additionally, the Youden index was used to determine optimal threshold values, and positive predictive value (PPV) and negative predictive value (NPV) were calculated to evaluate diagnostic precision.

Results: In the PJI group, levels of PAR, CAR, and CALLY were notably higher compared to the AF group, reaching statistical significance ($P < 0.05$). PAR and CAR were confirmed to have high diagnostic values, with AUC values of 0.779 and 0.718, respectively. CALLY exhibited moderate diagnostic effectiveness, with an AUC of 0.647. When PAR was combined with CRP and ESR, sensitivity and specificity notably improved to 93.8% and 92.5%, respectively. However, subgroup analysis revealed no significant differences in combined inflammatory biomarker levels between the two groups.

Conclusion: PAR and CAR prove to be effective combined inflammatory biomarkers for PJI diagnosis, whereas other markers exhibited limited diagnostic utility for PJI.

Keywords: prosthetic joint infection, blood cell ratio combinations, PAR, CAR, MSIS

Introduction

Periprosthetic joint infection (PJI) represents a significant challenge for patients undergoing total joint arthroplasty (TJA), substantially affecting morbidity and mortality rates.[1] With both primary and revision TJA surgeries increasing annually, the prevalence of PJI-related complications is expected to increase correspondingly.[2–4] Experts project that by 2030, the financial burden of PJI will increase to an alarming $1.85 billion.[5] Hence, prompt and accurate identification of PJI is crucial for effective management and treatment.

The Musculoskeletal Infection Society (MSIS) criteria, a widely accepted standard for PJI diagnosis, integrates findings from blood and synovial fluid analyses, clinical examinations, and histological and microbiological evaluations of intraoperative specimens.[6] These criteria underwent revisions during the 2018 International Consensus Meeting (ICM) on PJI.[7] However, no single blood or synovial fluid examination currently provides a definitive diagnosis of PJI. While

Received: 30 July 2024
Accepted: 12 January 2025
Published: 1 February 2025

advancements such as the identification of biomarkers, including synovial alpha-defensin and the application of next-generation sequencing have improved the accuracy of preoperative PJI detection, these methods are limited by high costs and logistical challenges, particularly for outpatient services and smaller medical facilities.[8,9] Conversely, blood-based biomarkers offer a more reliable initial screening approach for PJI due to their affordability, rapid processing, and widespread availability.[10]

A combination of inflammatory biomarkers, including the CRP-to-albumin ratio (CAR), platelet-to-lymphocyte ratio (PLR), CRP-to-lymphocyte ratio (CLR), neutrophil-to-albumin ratio (NAR), CRP-albumin-lymphocyte index (CALLY), and platelet-to-albumin ratio (PAR), plays a crucial role in assessing the severity and predicting outcomes of inflammatory conditions beyond orthopaedic.[11–15] For PJI, the neutrophil-to-lymphocyte ratio (NLR) and PLR have been identified as potentially beneficial markers.[16–18] However, previous studies have reported varying results on the definitive biomarkers or their combinations for PJI detection. Yu et al reported that NLR (0.802) had higher diagnostic accuracy for early PJI than CRP (0.793) and ESR (0.744).[19] Similarly, Zhao et al reported a high diagnostic value of NLR (0.93).[20] Conversely, Sigmund et al reported that NLR (0.68) was less diagnostically effective compared with traditional indicators such as CRP.[21] Therefore, it is essential to evaluate how these biomarkers and their combinations perform compared to traditional ones such as serum CRP and ESR. It is important to identify the most precise biomarkers, either alone or in combination, to enhance the diagnosis of PJI, despite the potential complexities introduced by their combined use in a clinical setting. Based on this, we performed a prospective, two-center analysis to determine the diagnostic efficacy of different biomarker combinations for PJI. We evaluated NLR, PLR, CAR, CALLY, NAR, and PAR and compared them with established inflammatory markers, CRP and ESR, to assess their prospective diagnostic capabilities in identifying PJI.

Patients and Methods

Study Design

In this prospective, multicenter study, we analyzed patients who underwent hip or knee revision arthroplasty at Zhengzhou Orthopaedic Hospital and Huaihe Hospital of Henan University between January 2020 and December 2023. The study protocol was approved by the local ethics committees of both institutions, and all patients provided written informed consent. A total of 269 patients were included in the study, with 205 patients enrolled from Zhengzhou Orthopaedic Hospital and 64 patients from Huaihe Hospital of Henan University. These patients were categorized into two groups: the PJI group (n = 93), comprising patients who met the updated periprosthetic joint infection (PJI) diagnostic criteria established by the 2018 International Consensus Meeting (ICM), and the aseptic failure (AF) group (n = 176), which included patients with non-infectious prosthetic joint failure.

To ensure accuracy, patients with any of the following conditions were excluded: periprosthetic fractures or prosthetic dislocations, concurrent conditions affecting biomarker levels (eg, malignancies, other joint infections, traumas, or hematologic disorders), autoimmune diseases (eg, rheumatoid arthritis or ankylosing spondylitis), recent use of anticoagulant medications, or incomplete data. This rigorous screening ensured that only patients meeting the inclusion criteria were analyzed.

Data Extraction

We obtained baseline information, including age, sex, height, weight, infection timing, and affected joint, for each patient from the hospital's electronic health records. On the admission day or the following day, nurses collected fasting venous blood samples, which were analyzed in the laboratory within an hour. We documented levels of CRP, ESR, neutrophils, lymphocytes, platelets, and albumin, and calculated the NLR, PLR, CAR, CALLR, NAR, and PAR. To enhance the diagnostic accuracy for PJI, we developed a composite test by combining PAR, CAR, and traditional biomarkers (CRP and ESR). Furthermore, during surgery, we obtained synovial fluid, pus, periprosthetic tissues, or bone for aerobic and anaerobic bacterial cultures.

Bacterial Culture

Synovial fluids collected from the surgery were incubated in BD BACTEC vials for aerobic, anaerobic, fungal, and acid-fast bacilli cultures at 35 °C for 14 days. Periprosthetic tissue samples obtained intraoperatively underwent 1-min homogenization in 3 mL of BHI broth. Then, the resulting homogenate was cultured on Columbia blood agar with selective medium, chocolate agar, and 5% sheep blood, under anaerobic and aerobic conditions for 7 days at 35 °C. Additionally, an identical volume of homogenate (1 mL) was inoculated into BD BACTEC bottles for aerobic, anaerobic, fungal, and acid-fast bacilli cultures for 14 days.

Statistical Analysis

Statistical results are presented as mean ±SD for continuous data and median (25th percentile and 75th percentile) for categorical data. We compared the clinical parameters between the PJI and non-PJI groups. Continuous data across different categories were analyzed using either the Student's *t*-test or the Mann–Whitney *U*-test, whereas categorical variables were analyzed using Pearson's chi-square (χ^2) test. In the ROC analysis, optimal cut-off points for biomarkers, such as NLR, PLR, CAR, CALLY, NAR, and PAR were identified using Youden's index, calculated as the maximum value obtained from the formula: sensitivity + specificity - 1, to determine the probability of PJI. Statistical analyses were performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA), with p-values < 0.05 considered statistically significant, employing two-tailed tests.

Results

Patient Characteristics

In this study, initially, 398 individuals were considered for revision knee or hip arthroplasty between January 2020 and December 2023. Based on the exclusion criteria, 129 patients were excluded. Of the remaining 269 patients, 93 were included in the PJI group based on the 2018 ICM PJI criteria, whereas 176 were included in the AF group (Figure 1). The average body mass index (BMI) was significantly higher in the PJI group than in the AF group (26.9 ±2.37 kg/m^2 vs 25.2 ±1.93 kg/m^2, P = 0.003). Additionally, the incidence of knee infections in the PJI cohort was notably higher than that in the AF group (P < 0.001; Table 1).

Accuracy and ROC Curve of PJI Diagnosis of These Blood Biomarkers

Table 1 and Table 2, along with Figure 2, highlight that the PJI group exhibited significantly higher levels of CAR (0.78 ±0.81 vs 0.35 ±0.65), CALLR (0.97 ±1.51 vs 3.41 ±2.85), and PAR (7.79 ±1.02 vs 5.26 ±1.24) compared with

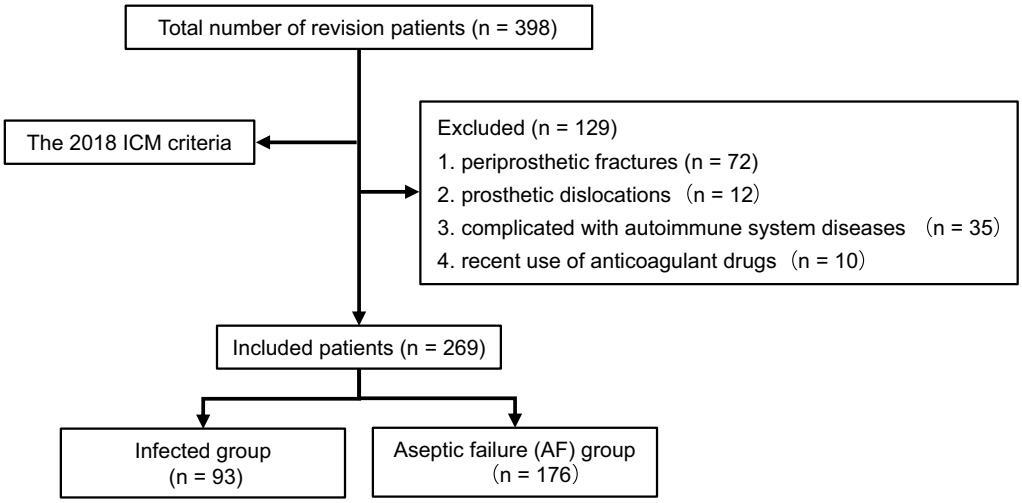

Figure 1 Flowchart of patient inclusion.

https://doi.org/10.2147/IDR.S489201

Table 1 Basic Characteristics of All Patents in the PJI and AF Groups

	Entire Cohort (N = 269)	PJI[a] Group (N = 93)	AF[b] Group (N =176)	*P* value
Age (years)	65.5 ±13.13	63.9 ±12.21	67.29 ±10.07	0.721
Male (% total)	136 (50.6%)	36 (37.5%)	100 (29%)	0.005
BMI[c] (kg/m^2)	29.6 ±3.57	26.9 ±2.37	25.2 ±1.93	0.003
Comorbidities				
Diabetes	19 (4.9%)	11 (11.5%)	8 (2.8%)	0.479
Potential Biomarker				
NLR[d]	2.85 ±2.01	3.29 ±1.22	2.49 ±2.51	0.121
CAR[e]	0.58 ±0.73	0.78 ±0.81	0.35 ±0.65	0.031
CALLY[f]	2.10 ±2.01	0.97 ±1.51	3.41 ±2.85	0.018
PLR[g]	171.89 ±70.81	188.24 ±78.84	153.81 ±62.81	0.078
PAR[h]	6.59 ±1.13	7.79 ±1.02	5.26 ±1.24	0
NAR[i]	0.10 ±0.03	0.11 ±0.05	0.10 ±0.04	0.762
ESR	27.74 ±23.33	35.06 ±21.21	19.33 ±16.14	0.009
CRP	22.18 ±28.62	30.60 ±31.91	12.52 ±17.06	0.015
Joint				0
Hip (%)	193 (71.7%)	51 (54.8%)	142 (80.7%)	
Knee (%)	76 (28.3%)	42 (45.2%)	34 (19.3%)	

Notes: [a] PJI, periprosthetic joint infection; [b] AF, aseptic failure; [c] BMI, body mass index; [d] neutrophil-to-lymphocyte ratio; [e] C-reactive protein-to-albumin ratio; [f] C-reactive protein -Albumin-lymphocyte ratio; [g] platelet-to-lymphocyte ratio; [h] platelet-to-albumin ratio; [i] neutrophil-to-albumin ratio.

Table 2 Diagnostic Value of CRP, ESR, NLR, CAR, CALLR, PLR, PAR and NAR

	AUC	95% CI	Youden Index	Optimal Cutoff Value	Sensitivity (%)	Specificity (%)	PPV[g] (%)	NPV[h] (%)
NLR[a]	0.431	(0.275, 0.587)	0.201	2.73	41.9	42.7	44.8	40
CAR[b]	0.718	(0.579, 0.857)	0.466	0.27	64.5	85.7	81.8	68.7
CALLY[c]	0.647	(0.495, 0.800)	0.428	0.82	64.4	64.3	66.7	62.1
PLR[d]	0.628	(0.479, 0.777)	0.295	170.56	58.1	72.6	70.2	60.6
PAR[e]	0.779	(0.659, 0.899)	0.424	5.36	77.4	71.4	76.4	72.1
NAR[f]	0.524	(0.370, 0.678)	0.271	0.14	51.6	50	53.33	48.3
CRP	0.722	(0.585, 0.859)	0.465	11.21	61.3	85.7	81.8	64.9
ESR	0.706	(0.559, 0.854)	0.525	24.5	70.1	82.1	81.5	71.9

Notes: [a] neutrophil-to-lymphocyte ratio; [b] C-reactive protein-to-albumin ratio; [c] C-reactive protein -Albumin-lymphocyte ratio; [d] platelet-to-lymphocyte ratio; [e] platelet-to-albumin ratio; [f] neutrophil-to-albumin ratio; [g] positive predictive rate; [h] Negative predictive value.

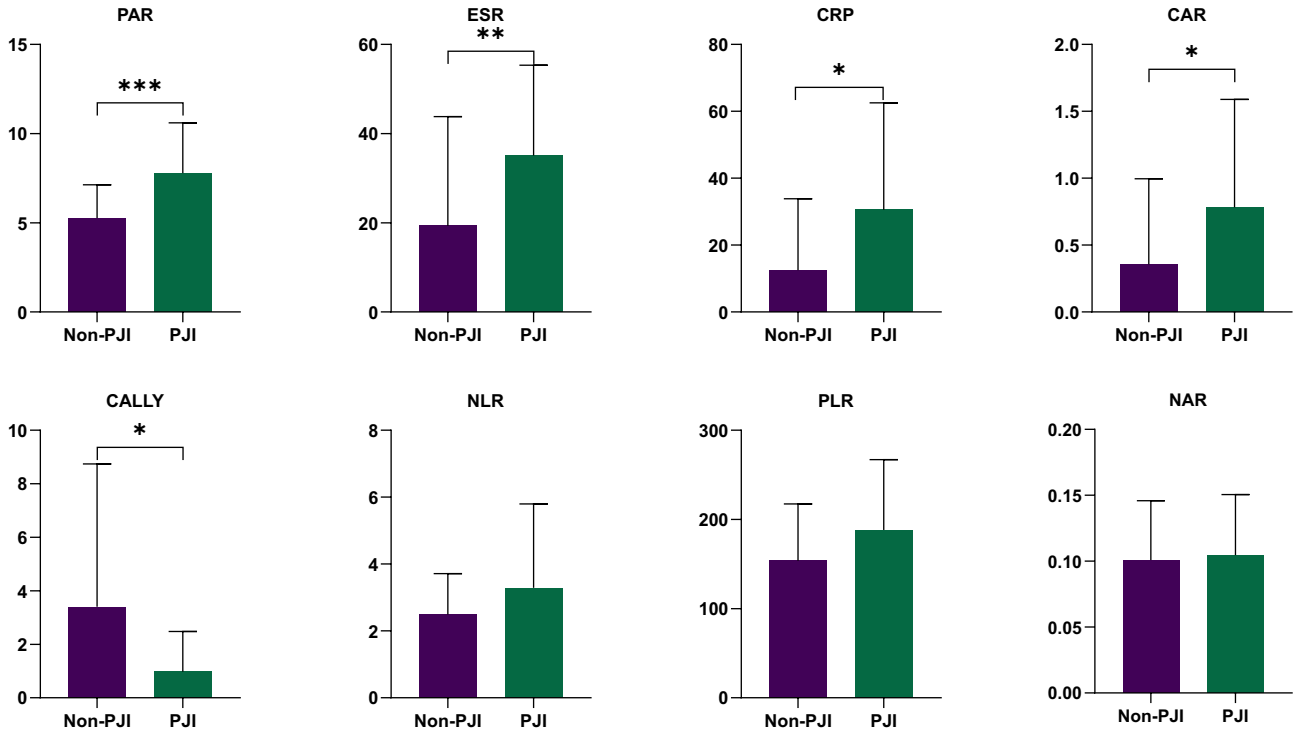

Figure 2 Comparison of combined inflammatory biomarkers levels between the PJI group and the AF group.
Notes: Statistical significance: *P < 0.05, **P < 0.01, ***P < 0.001.
Abbreviations: NLR, neutrophil-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio; CALLY, C-reactive protein -Albumin-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; NAR, neutrophil-to-albumin ratio.

the AF group, with P-values below 0.05. NLR, PLR, and NAR did not exhibit significant variations between the two groups, with P-values of 0.121, 0.078, and 0.762, respectively. The ROC curve analysis indicated that PAR had superior diagnostic accuracy (AUC = 0.779) compared with CRP (AUC = 0.722) and ESR (AUC = 0.706), whereas CAR's AUC was 0.718. The optimal threshold for PAR was identified at 5.36, obtaining a sensitivity of 77.4% and specificity of 71.4%. The optimal cut-off of CAR was 0.48, with 64.5% sensitivity and 85.7% specificity. CALLY and PLR offered moderate diagnostic values, with AUCs of 0.647 and 0.628 and optimal thresholds of 0.82 and 170.56, respectively. However, NLR and NAR showed negligible diagnostic utility, with AUCs of 0.431 and 0.524, respectively. According to Youden's index, the predictive values for CAR, CALLY, PAR, NLR, PLR, and NAR were also calculated, with PPVs of 81.8%, 66.7%, 76.4%, 44.8%, 70.2%, and 53.3%, and NPVs of 64.9%, 62.1%, 72.1%, 40.0%, 60.6%, and 48.3%, respectively (Figure 3 and Table 2).

Subgroup analyses revealed no significant differences in biomarker levels when categorized by culture results or infected joint (Table 3). To improve the diagnostic accuracy for PJI, we combined PAR, CAR, and traditional biomarkers (CRP and ESR) into a composite test. The results showed a significant improvement in sensitivity, specificity, PPV, and NPV for PJI detection (Table 4). Interestingly, the highest diagnostic precision was obtained when ESR was used sequentially with PAR and concurrently with CAR, implicating ESR's potential value in this combined diagnostic approach.

Microbiological Findings

In this cohort, each patient underwent at least two culture tests that identified the same pathogen. Among the 93 individuals in the PJI group, 61 tested positive for cultures, resulting in a positivity rate of approximately 65.59% (61/

https://doi.org/10.2147/IDR.S489201

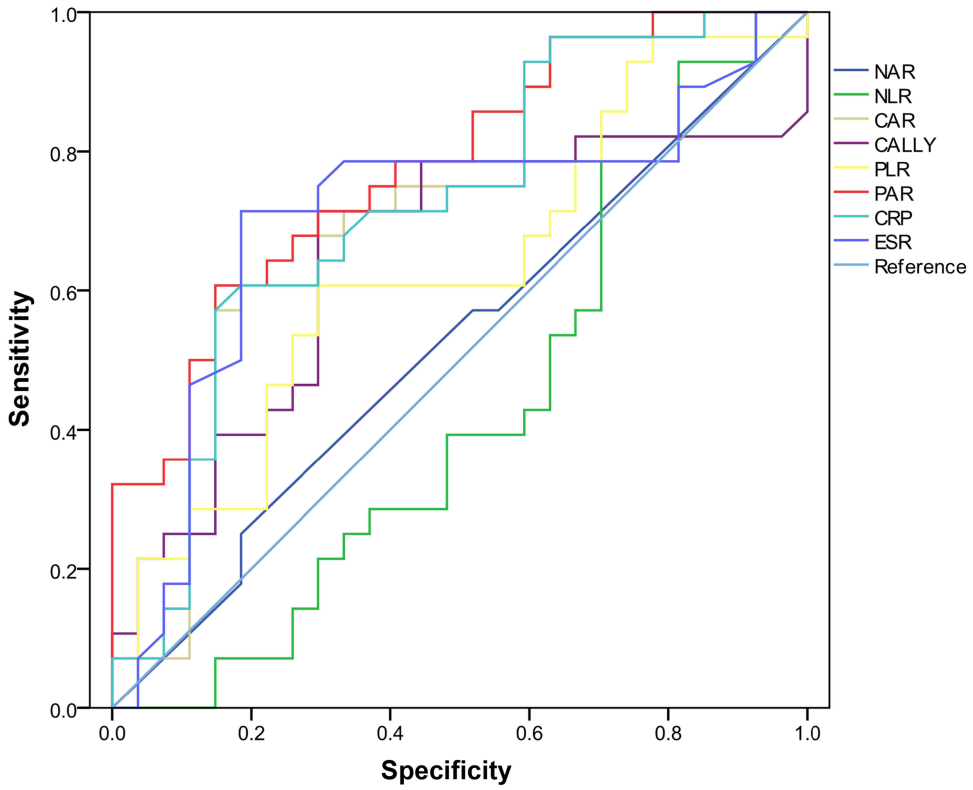

Figure 3 The ROC curves of ESR, CRP, PAR, PLR, CALLY, CAR, NLR, and NAR.

93). The most frequently isolated bacteria were *Staphylococcus epidermidis* (24/61, 39.3%) and *Staphylococcus aureus* (14 out of 60, 23.3%). Additionally, one case involved a polymicrobial culture, which included a combination of *S. epidermidis* and *Brucella* (Table 5).

Table 3 Comparison of All Inflammatory Biomarker Combination in the Different PJI Subgroups

	Culture-Positive PJI (n = 61)	Culture-Negative PJI (n = 32)	*P* value	Knee PJI (n = 42)	Hip PJI (n = 51)	*P* value
NLR[a]	2.57 ±1.28	2.54 ±1.21	0.947	2.41 ±1.28	2.33 ±1.21	0.879
CAR[b]	0.83 ±0.82	0.87 ±0.75	0.904	0.85 ±0.82	0.84 ±0.75	0.934
CALLY[c]	0.84 ±1.71	1.20 ±1.63	0.559	0.93 ±1.49	1.05 ±1.57	0.659
PLR[d]	185.40 ±72.84	197.96 ±75.62	0.686	188.20 ±72.67	191.35 ±75.31	0.664
PAR[e]	7.46 ±2.4	8.29 ±1.82	0.463	7.51 ±1.91	8.03 ±1.82	0.442
NAR[f]	0.10 ±0.04	0.11 ±0.03	0.647	0.09 ±0.03	0.11 ±0.03	0.573
CRP	31.9 ±32.23	34.42 ±2.23	0.85	30.8 ±30.17	32.12 ±2.53	0.752
ESR	36.73 ±16.76	38 ±16.76	0.877	36.54 ±16.82	37.8 ±16.53	0.952

Notes: [a] neutrophil-to-lymphocyte ratio; [b] C-reactive protein-to-albumin ratio; [c] C-reactive protein -Albumin-lymphocyte ratio; [d] platelet-to-lymphocyte ratio; [e] platelet-to-albumin ratio; [f] neutrophil-to-albumin ratio.

 https://doi.org/10.2147/IDR.S489201

Table 4 Combinational Diagnostic Value of the PAR Combined With CRP and ESR for PJI

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PAR or CRP	80.6	88.9	89.7	82.8
PAR or ESR	93.8	85.1	88.2	95.8
PAR or ESR or CRP	93.8	92.5	90.9	92.6
CAR or CRP	64.5	89.3	83.3	68.7
CAR or ESR	71	92.9	89	75.3
CAR or ESR or CRP	71	96.4	89	78.9
PAR or CAR or ESR	96.7	96.4	93.5	96.1

Table 5 Culture Results of Patients in the PJI Group

Culture Results	No. of Patients
Staphylococcus epidermidis	24
Staphylococcus aureus	13
Methicillin-resistant Staphylococcus aureus	3
Coagulase-negative Staphylococcus	2
Streptococcus species	2
Enterococcus faecalis	2
Escherichia coli	2
Brucella	2
Staphylococcus lugdunensis	1
Enterobacter cloacae	1
Streptococcus agalactiae	1
Pseudomonas aeruginosa	1
Acinetobacter baumannii	1
Candida albicans	1
\Mycobacterium tuberculosis	1
Aeromonas hydrophila	1
Serratia marcescens	1
Corynebacterium striatum	1
Corynebacterium	1
Nontuberculosis mycobacteria	1
Negative	32

https://doi.org/10.2147/IDR.S489201

Discussion

In this study, we evaluated the diagnostic potential of combined inflammatory biomarkers for detecting PJI. We found that PAR and CAR exhibit remarkable diagnostic accuracy. When compared with traditional markers such as CRP and ESR, these novel biomarkers exhibit improved sensitivity and specificity, suggesting their potential for broader adoption in future diagnostic protocols. The diagnostic value of PLR and CALLY appears limited and considerably lower than that of conventional markers. Interestingly, our analysis indicates that NLR and NAR do not significantly contribute to the diagnosis of PJI, which contrasts with previous research findings.[11,22,23]

Recent research suggests that platelets play a crucial role beyond hemostasis, significantly influencing immune and inflammatory responses.[24,25] When platelets interact with bacteria during immune reactions, they become activated, enabling them to interact with other cells through surface receptors and secrete various proteins, such as cytokines and chemokines, helping regulate the immune system. Albumin, a protein produced by the liver, is commonly used to evaluate nutritional status.[26] However, emerging evidence indicates a strong association between albumin levels and inflammation, where decreased albumin levels often indicate heightened inflammatory activity.[27,28] This inverse correlation during infections likely highlights the significant diagnostic relevance of PAR. Given its increasing recognition as an inflammatory marker, the use of PAR in diagnosing various infectious diseases has garnered considerable attention.[29–31] Our study, which expanded the patient cohort with PJI and AF, is consistent with earlier findings by establishing the superior diagnostic efficacy of PAR among various combinations of inflammatory biomarkers.[32] With an AUC of 0.779 and sensitivity and specificity of 77.4% and 71.4%, respectively, PAR emerges as a standout marker. Its diagnostic performance is further improved when combined with ESR and CRP, increasing sensitivity and specificity to 93.8% and 92.5%, respectively. These results position PAR as a potent diagnostic tool for PJI, a conclusion supported by recent work by Shi et al, which attributed a high diagnostic accuracy to PAR, reflected in an AUC of 0.785.[11]

CRP, an acute-phase protein synthesized by the liver, increases in response to inflammation or infection, whereas serum ALB decreases during immune activation.[33,34] This inverse correlation makes CAR a valuable prognostic indicator in conditions such as acute pancreatitis and surgical site infections following major abdominal operations.[35,36] While some studies have reported CAR's superiority over traditional markers such as CRP and ESR, demonstrating its robust diagnostic capability among various combinations of inflammatory biomarkers,[37–39] our analysis revealed that CAR's AUC (0.718) was comparable to that of CRP (0.722) and ESR (0.706). The Youden index also indicated that CAR's sensitivity and specificity were similar to those of CRP and ESR, suggesting that CAR's overall diagnostic performance in PJI is equivalent to these conventional markers. Improvements in sensitivity and specificity to 71.0% and 92.9%, respectively, were observed when CAR was used in conjunction with ESR and CRP, highlighting its effectiveness as a diagnostic marker for PJI.

Lymphocytes, crucial for the body's specific immune response, become activated upon exposure to pathogens. In conditions such as sepsis, lymphocyte counts decrease significantly due to marginalization, increased apoptosis, and cell redistribution, mirroring the behavior of albumin.[40] Consequently, CALLY, an emerging inflammatory marker, may serve a purpose similar to CAR. Historically, research on CALLY has focused on predicting cancer prognoses and assessing the severity of COVID-19.[14,41] Iida et al reported that preoperative CALLY levels could predict outcomes in patients undergoing surgery for hepatocellular carcinoma (HCC).[42] However, the association between CALLY and PJI remains unexplored in the existing literature. Our investigation revealed a notable increase in CALLY levels within the PJI cohort compared with the AF group, suggesting its potential relevance in PJI scenarios.

The efficacy of NLR as a diagnostic tool for PJI is still debatable While two studies have reported its good diagnostic performance with AUC values of 0.80,[19,43] a majority indicate its limited utility, with AUCs ranging from 0.656 to 0.740, suggesting NLR's inadequacy as a standalone biomarker for PJI diagnosis.[44] In the present study, NLR exhibited suboptimal performance in diagnosing PJI, evidenced by a low AUC of 0.431, a sensitivity of 41.9%, and a specificity of 42.7%. These findings are consistent with the results from a recent meta-analysis, reinforcing the notion that NLR may not be a dependable marker for PJI detection.

This study systematically evaluates the diagnostic potential of combined inflammatory biomarkers, such as PAR and CAR, for detecting PJI. By comparing these novel biomarkers with traditional ones like CRP and ESR, it

provides a comprehensive understanding of their relative efficacy and valuable insights for clinical application. However, the present study has some limitations. Although it is a prospective study conducted across two centers, the relatively small sample size may still limit the generalizability of the findings. Consequently, our results should be further validated through larger, multi-center studies involving more extensive cohorts. Additionally, the homogeneity in the racial background of our study participants is a limitation. The impact of racial diversity on biomarker efficacy remains uncertain, underscoring the need for future research to explore this aspect across different racial groups.

Conclusion

Our findings indicate that PAR offers comparable diagnostic excellence to CRP and ESR in identifying PJI; therefore, it can be a valuable asset in the screening process for patients with PJI. A broader adoption of this biomarker combination can improve diagnostic accuracy in the clinical setting.

Ethical Approval

This study protocol was approved by the Institutional Review Board of Zhengzhou Orthopaedic Hospital (2019014). This study was conducted in accordance with the declaration of Helsinki and patient data were kept confidential. Informed consent was obtained in written form from all participants involved in the study.

Acknowledgments

We would like to acknowledge the hard and dedicated work of all the staff that implemented the intervention and evaluation components of the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the Program Project of Science and Technology Innovation Guidance of Zhengzhou City [2024YLZDJH175].

Disclosure

All authors declare no conflicts of interest in this work.

References

1. Patel R. Periprosthetic joint infection. *N Engl J Med*. 2023;388(3):251–262. doi:10.1056/NEJMra2203477
2. Eka A, Chen AF. Patient-related medical risk factors for periprosthetic joint infection of the Hip and knee. *Ann Transl Med*. 2015;3(16):233. doi:10.3978/j.issn.2305-5839.2015.09.26
3. Kurtz SM, Lau EC, Son MS, Chang ET, Zimmerli W, Parvizi J. Are we winning or losing the battle with periprosthetic joint infection: trends in periprosthetic joint infection and mortality risk for the medicare population. *J Arthroplasty*. 2018;33(10):3238–3245. doi:10.1016/j.arth.2018.05.042
4. Zhu Y, Zhang F, Chen W, Liu S, Zhang Q, Zhang Y. Risk factors for periprosthetic joint infection after total joint arthroplasty: a systematic review and meta-analysis. *J Hosp Infect*. 2015;89(2):82–89. doi:10.1016/j.jhin.2014.10.008
5. Premkumar A, Kolin DA, Farley KX, et al. Projected economic burden of periprosthetic joint infection of the Hip and knee in the United States. *J Arthroplasty*. 2021;36(5):1484–1489.e3. doi:10.1016/j.arth.2020.12.005
6. Parvizi J, Zmistowski B, Berbari EF, et al. New definition for periprosthetic joint infection: from the workgroup of the musculoskeletal infection society. *Clin Orthop Relat Res*. 2011;469(11):2992–2994. doi:10.1007/s11999-011-2102-9
7. Parvizi J, Tan TL, Goswami K, et al. The 2018 definition of periprosthetic Hip and knee infection: an evidence-based and validated criteria. *J Arthroplasty*. 2018;33(5):1309–1314.e2. doi:10.1016/j.arth.2018.02.078
8. Ivy MI, Sharma K, Greenwood-Quaintance KE, et al. Synovial fluid α defensin has comparable accuracy to synovial fluid white blood cell count and polymorphonuclear percentage for periprosthetic joint infection diagnosis. *Bone Joint J*. 2021;103-B(6):1119–1126. doi:10.1302/0301-620X.103B6.BJJ-2020-1741.R1

9. Yu Y, Wang S, Dong G, Niu Y. Diagnostic performance of metagenomic next-generation sequencing in the diagnosis of prosthetic joint infection using tissue specimens. *Infect Drug Resist*. 2023;16:1193–1201. doi:10.2147/IDR.S397260
10. Xu H, Xie J, Zhang S, Wang D, Huang Z, Zhou Z. Potential blood biomarkers for diagnosing periprosthetic joint infection: a single-center, retrospective study. *Antibiotics*. 2022;11(4):505. doi:10.3390/antibiotics11040505
11. Shi W, Jiang Y, Tian H, et al. C-reactive protein-to-albumin ratio (CAR) and C-reactive protein-to-lymphocyte ratio (CLR) are valuable inflammatory biomarker combination for the accurate prediction of periprosthetic joint infection. *Infect Drug Resist*. 2023;16:477–486. doi:10.2147/IDR.S398958
12. Demirkol ME, Bilgin S, Kahveci G, et al. C-reactive protein-to-lymphocyte ratio is a reliable marker in patients with COVID-19 infection: the CLEAR COVID study. *Cir Cir*. 2022;90(5):596–601. doi:10.24875/CIRU.22000124
13. Hu Z, Wang J, Xue Y, et al. The neutrophil-to-albumin ratio as a new predictor of all-cause mortality in patients with heart failure. *J Inflamm Res*. 2022;15:701–713. doi:10.2147/JIR.S349996
14. Tsunematsu M, Haruki K, Taniai T, et al. The impact of C-reactive protein-albumin-lymphocyte (CALLY) index on the prognosis of patients with distal cholangiocarcinoma following pancreaticoduodenectomy. *Ann Gastroenterol Surg*. 2022;7(3):503–511. doi:10.1002/ags3.12637
15. Yang Y, Yuan J, Liu L, Qie S, Yang L, Yan Z. Platelet-to-albumin ratio: a risk factor associated with technique failure and mortality in peritoneal dialysis patients. *Ren Fail*. 2021;43(1):1359–1367. doi:10.1080/0886022X.2021.1977319
16. Zhang J, Zhang HY, Li J, Shao XY, Zhang CX. The elevated NLR, PLR and PLT may predict the prognosis of patients with colorectal cancer: a systematic review and meta-analysis. *Oncotarget*. 2017;8(40):68837–68846. doi:10.18632/oncotarget.18575
17. Gasparyan AY, Ayvazyan L, Mukanova U, Yessirkepov M, Kitas GD. The platelet-to-lymphocyte ratio as an inflammatory marker in rheumatic diseases. *Ann Lab Med*. 2019;39(4):345–357. doi:10.3343/alm.2019.39.4.345
18. Salimi M, Karam JA, Willman M, et al. Neutrophil to lymphocyte ratio and periprosthetic joint infection: a systematic review and meta-analysis. *J Arthroplasty*. 2024;39(3):831–838. doi:10.1016/j.arth.2023.08.067
19. Yu BZ, Fu J, Chai W, Hao LB, Chen JY. Neutrophil to lymphocyte ratio as a predictor for diagnosis of early Periprosthetic joint infection. *BMC Musculoskelet Disord*. 2020;21(1):706. doi:10.1186/s12891-020-03704-5
20. Zhao G, Chen J, Wang J, et al. Predictive values of the postoperative neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and lymphocyte-to-monocyte ratio for the diagnosis of early periprosthetic joint infections: a preliminary study. *J Orthop Surg Res*. 2020;15(1):571. doi:10.1186/s13018-020-02107-5
21. Sigmund IK, Holinka J, Staats K, et al. Inferior performance of established and novel serum inflammatory markers in diagnosing periprosthetic joint infections. *Int Orthop*. 2021;45(4):837–846. doi:10.1007/s00264-020-04889-z
22. Festa E, Ascione T, Bernasconi A, et al. Diagnostic performance of neutrophil to lymphocyte ratio, monocyte to lymphocyte ratio, platelet to lymphocyte ratio, and platelet to mean platelet volume ratio in periprosthetic Hip and knee infections: a systematic review and meta-analysis. *Diagnostics*. 2022;12(9):2033. doi:10.3390/diagnostics12092033
23. Ye Y, Chen W, Gu M, et al. Limited value of serum neutrophil-to-lymphocyte ratio in the diagnosis of chronic periprosthetic joint infection. *J Orthop Traumatol*. 2021;22(1):37. doi:10.1186/s10195-021-00599-3
24. Herter JM, Rossaint J, Zarbock A. Platelets in inflammation and immunity. *J Thromb Haemost*. 2014;12(11):1764–1775. doi:10.1111/jth.12730
25. Von hundelshausen P, Weber C. Platelets as immune cells: bridging inflammation and cardiovascular disease. *Circ Res*. 2007;100(1):27–40. doi:10.1161/01.RES.0000252802.25497.b7
26. Mobarhan S. The role of albumin in nutritional support. *J Am Coll Nutr*. 1988;7(6):445–452. doi:10.1080/07315724.1988.10720260
27. Sheinenzon A, Shehadeh M, Michelis R, Shaoul E, Ronen O. Serum albumin levels and inflammation. *Int J Biol Macromol*. 2021;184:857–862. doi:10.1016/j.ijbiomac.2021.06.140
28. Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: pathogenesis and clinical significance. *JPEN J Parenter Enteral Nutr*. 2019;43(2):181–193. doi:10.1002/jpen.1451
29. Gui Y, Xu Y, Yang P. Predictive value of the platelet-to-albumin ratio (PAR) on the risk of death at admission in patients suffering from severe fever with thrombocytopenia syndrome. *J Inflamm Res*. 2021;14:5647–5652. doi:10.2147/JIR.S335727
30. Huang Z, Zheng Q, Yu Y, et al. Prognostic significance of platelet-to-albumin ratio in patients with esophageal squamous cell carcinoma receiving definitive radiotherapy. *Sci Rep*. 2022;12(1):3535. doi:10.1038/s41598-022-07546-0
31. Bilge H, Başol Ö. The effect of platelet-albumin ratio on mortality and morbidity in peptic ulcer perforation. *Medicine*. 2022;101(31):e29582. doi:10.1097/MD.0000000000029582
32. Sibia RS, Sood A, Subedi A, et al. Elevated serum PAR-1 levels as an emerging biomarker of inflammation to predict the dengue infection severity. *J Med Virol*. 2023;95(1):e28152. doi:10.1002/jmv.28152
33. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. *Front Immunol*. 2018;9:754. doi:10.3389/fimmu.2018.00754
34. Dirajlal-Fargo S, Kulkarni M, Bowman E, et al. Serum albumin is associated with higher inflammation and carotid atherosclerosis in treated human immunodeficiency virus infection. *Open Forum Infect Dis*. 2018;5(11):ofy291. doi:10.1093/ofid/ofy291
35. Haider Kazmi SJ, Zafar MT, Zia BF, et al. Role of serum C-reactive protein (CRP)/Albumin ratio in predicting the severity of acute pancreatitis: a retrospective cohort. *Ann Med Surg Lond*. 2022;82:104715. doi:10.1016/j.amsu.2022.104715
36. Qu S, Sun M, Sun H, Hu B. C-reactive protein to albumin ratio (CAR) in predicting surgical site infection (SSI) following instrumented posterior lumbar interbody fusion (PLIF). *Int Wound J*. 2023;20(1):92–99. doi:10.1111/iwj.13843
37. Seringec Akkececi N, Yildirim Cetin G, Gogebakan H, Acipayam C. The C-reactive protein/albumin ratio and complete blood count parameters as indicators of disease activity in patients with takayasu arteritis. *Med Sci Monit*. 2019;25:1401–1409. doi:10.12659/MSM.912495
38. Katkat F, Kalyoncuoglu M, Ozcan S, et al. C-reactive protein to albumin ratio as a novel inflammatory-based marker for 30-day mortality in patients undergoing transcatheter aortic valve replacement. *Braz J Cardiovasc Surg*. 2022;37(3):292–300. doi:10.21470/1678-9741-2020-0482
39. Tsai CM, Yu HR, Tang KS, Huang YH, Kuo HC. C-reactive protein to albumin ratio for predicting coronary artery lesions and intravenous immunoglobulin resistance in Kawasaki disease. *Front Pediatr*. 2020;8:607631. doi:10.3389/fped.2020.607631
40. de Pablo R, Monserrat J, Prieto A, Alvarez-Mon M. Role of circulating lymphocytes in patients with sepsis. *Biomed Res Int*. 2014;2014:671087. doi:10.1155/2014/671087

41. Özdemir S, Özkan A. The importance of the CALLY index as a non-invasive prognostic biomarker in SARS-CoV-2 infected patients: an analytical study: CALLY index in SARS-CoV-2 Infection. *Med Sci Discov*. 2023;10(7):443–448. doi:10.36472/msd.v10i7.967
42. Iida H, Tani M, Komeda K, et al. Superiority of CRP-albumin-lymphocyte index (CALLY index) as a non-invasive prognostic biomarker after hepatectomy for hepatocellular carcinoma. *HPB*. 2022;24(1):101–115. doi:10.1016/j.hpb.2021.06.414
43. Denyer S, Eikani C, Sheth M, Schmitt D, Brown N. Diagnosing periprosthetic joint infection. *Bone Jt Open*. 2023;4(11):881–888. doi:10.1302/2633-1462.411.BJO-2023-0094.R1
44. Denyer S, Eikani C, Sheth M, Schmitt D, Brown N. Utility of blood cell ratio combinations for diagnosis of periprosthetic joint infection. *Arthroplast Today*. 2023;23:101195. doi:10.1016/j.artd.2023.101195