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Performance of preoperative inflammatory and immunonutritional indices in predicting periprosthetic joint infection after total knee arthroplasty

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Periprosthetic joint infection (PJI) remains a serious complication after total knee arthroplasty (TKA), with an incidence of 0.5 to 2%.[1-3] It represents one of the leading indications for revision arthroplasty. It is associated with prolonged hospital stay, the need for multiple procedures, increased healthcare costs, and a considerable negative impact on patient function and survival.[4]

The development of PJI is multifactorial, involving interactions between host immunity, systemic inflammation, nutritional status, microbial factors, and comorbidities.[5] In recent years, interest has grown in simple laboratory indices reflecting systemic immune-inflammatory balance. Ratios such as the neutrophil-to-

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ABSTRACT

Objectives: This study aims to evaluate the predictive value of preoperative inflammatory and immunonutritional indices for early periprosthetic joint infection (PJI) following primary total knee arthroplasty (TKA).

Patients and methods: This study included patients undergoing primary TKA between January 2011 and December 2024 in a retrospective case-control design. Patients who developed PJI within 90 days postoperatively were defined as the infection group (n = 64). A control group (n = 128) was selected using a 1:2 matching ratio based on age, sex, and body mass index (BMI). Preoperative laboratory parameters obtained within 30 days before surgery were used to calculate neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), pan-immune-inflammation value (PIV), prognostic nutritional index (PNI), C-reactive protein-to-albumin ratio (CAR), and C-reactive protein-albumin-lymphocyte (CALLY) index. Demographic and clinical variables were recorded. Receiver operating characteristic (ROC) curve analysis and multivariate logistic regression were performed.

Results: Of the patients, 54 of the patients were male and 138 were females with a mean age of 69.4 ± 8.2 (range, 37 to 86) years. Patients who developed PJI demonstrated significantly lower albumin and lymphocyte levels and higher C-reactive protein (CRP) values. NLR, MLR, SIRI, and CAR were significantly elevated, whereas PNI and CALLY were decreased in the PJI group. The ROC analysis revealed moderate discriminative performance for most biomarkers (area under the curve [AUC] = 0.65-0.71). Multivariate analysis identified low albumin, low PNI, elevated CAR, and general anesthesia as independent predictors of early PJI.

Conclusion: Preoperative inflammatory and immunonutritional indices seem to be associated with early PJI following TKA, with albumin, PNI, and CAR emerging as the most consistent biomarker-based predictors. Although their predictive performance is moderate, these readily available biomarkers may support risk stratification when integrated into comprehensive clinical assessment models.

Keywords: C-reactive protein-to-albumin ratio, inflammatory biomarkers, periprosthetic joint infection, prognostic nutritional index, risk prediction, total knee arthroplasty.

lymphocyte ratio (NLR),[6] platelet-to-lymphocyte ratio (PLR),[7] and monocyte-to-lymphocyte ratio (MLR),[8] as well as more complex indices including the systemic immune-inflammation index (SII),[9] systemic inflammation response index SIRI,[10] and pan-immune-inflammation value (PIV)[11] have been investigated in various clinical settings and shown to have potential prognostic value.[12]

In addition, indices integrating inflammatory and nutritional parameters, including the prognostic nutritional index (PNI),[13] C-reactive protein-to-albumin ratio (CAR),[14] and C-reactive protein-albumin-lymphocyte (CALLY) index,[15] provide a more comprehensive representation of both systemic inflammation and immunonutritional status. These markers may better reflect the biological environment predisposing to complications.[16] Most previous research on PJI biomarkers has focused on parameters measured after infection onset.[17] However, identifying high-risk patients before surgery is more clinically relevant, as it may allow optimization of risk factors and improved perioperative management.

Despite the growing number of proposed inflammatory and immunonutritional biomarkers, evidence regarding their comparative performance in predicting PJI remains limited. Although these indices can be readily calculated from routine preoperative laboratory parameters without requiring specialized testing and collectively capture complementary dimensions of systemic inflammation, immune response, and nutritional status,[12,17-19] studies evaluating these indices simultaneously within the same TKA population remain limited, making it difficult to determine their relative predictive value. In the present study, we hypothesized that preoperative inflammatory and immunonutritional indices could be associated with the development of PJI following primary TKA and could serve as useful predictors of early PJI. We, therefore, aimed to evaluate and compare the predictive value of these nine indices for early PJI following primary TKA.

PATIENTS AND METHODS

This single-center, retrospective, case-control study was conducted at Antalya Training and Researh Hospital, Department of Orthopedics and Traumatology between January 2011 and December 2024. Hospital records of a total of 6,560 patients who underwent primary TKA were reviewed. Patients who developed PJI within the first 90 days after surgery were identified and included in the infected group. Patients were included if they underwent primary TKA and had complete preoperative clinical and laboratory data available within 30 days before surgery. Exclusion criteria were as follows: revision TKA, ongoing systemic infection at the time of surgery, history of hematological malignancy, intraoperative femoral condyle or proximal tibial fracture resulting in prolonged operative time, aseptic loosening, unicompartmental knee arthroplasty, hinged knee prosthesis, and prior high tibial osteotomy. Patients with elevated preoperative C-reactive protein (CRP) levels underwent additional clinical evaluation and laboratory assessment before surgery to exclude active systemic or local infection. Patients with elevated preoperative CRP levels were included after medical record review confirmed the absence of clinical or laboratory evidence of active infection at the time of surgery. A total of 64 patients met the diagnostic criteria for PJI. A control group was selected from patients who underwent primary TKA during the same period and did not develop PJI postoperatively. Control patients were matched to the infected group at a 1:2 ratio based on age, sex, and body mass index (BMI) using a nearest-neighbor matching approach, resulting in a total of 128 control patients. In our study, a 1:2 matching ratio was used, as recommended in the literature on control-to-case ratios, since it provides a significant increase in statistical power compared to a 1:1 design.[20,21] Age, sex, and BMI were selected as matching variables, as they are established risk factors for PJI and may also influence inflammatory and immunonutritional biomarkers. A written informed consent was obtained from each participant. The study protocol was approved by the Antalya Training and Research Hospital Scientific Research Ethics Committee (Date: 23.10.2025, No: 18/10). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Diagnosis and definitions Periprosthetic joint infection was diagnosed in accordance with the 2018 International Consensus Meeting (ICM) criteria, based on the Musculoskeletal Infection Society (MSIS) definition.[22] All infected patients underwent reoperation during the acute postoperative period due to infection and were treated with debridement, debridement with insert exchange, or two-stage revision surgery. The diagnosis of PJI was supported by a combination of clinical, laboratory, microbiological, and intraoperative

findings, including elevated preoperative CRP and erythrocyte sedimentation rate (ESR) levels, intraoperative purulence, and positive intraoperative culture results.

A 90-day postoperative period was used to define early PJI. Although no universal consensus exists regarding the optimal definition of early PJI, the 90-day threshold has been widely adopted in studies evaluating acute postoperative PJI, biomarker performance, risk factors, and prediction models. This time window is considered clinically relevant, as it captures infections most likely related to perioperative factors and early host responses while remaining consistent with previous PJI research.[23-25]

Clinical and demographic variables

Demographic and clinical characteristics age, sex, BMI, diabetes mellitus (DM), coronary artery disease (CAD), hypertension (HT), cerebrovascular disease (CVD), chronic obstructive pulmonary disease (COPD), malignancy, hypothyroidism, chronic kidney disease (CKD), rheumatic diseases and American Society of Anesthesiologists (ASA) scores were recorded and analyzed to assess their potential confounding effects.

Laboratory data were obtained from routine preoperative blood tests taken in 30 days prior to surgery. The recorded parameters included serum albumin (g/dL), CRP (mg/L), platelet count ($\times 10^9$/L), neutrophil count ($\times 10^9$/L), lymphocyte count ($\times 10^9$/L), and monocyte count ($\times 10^9$/L). All measurements were obtained from the same preoperative blood sample and analyzed using standardized laboratory methods.

Inflammatory and immunonutritional indices

Nine inflammatory and immunonutritional indices were calculated using preoperative laboratory parameters. All indices were calculated using values derived from the same preoperative blood sample, in accordance with standard formulas.[18,19,26-28] The definitions and formulas of the indices are presented in Table I.

These indices were selected, as they are derived from routine preoperative laboratory testing, have been previously associated with systemic inflammation, immune response, and nutritional status, and have increasingly been investigated as potential predictors of postoperative complications and PJI in the orthopedic literature.[12,17-19]

Statistical analysis

Statistical analysis was performed using the SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Normality was assessed by visual methods and Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous variables were presented in mean ± standard deviation (SD) or median (min-max), while categorical variables were presented in number and frequency. The Mann-Whitney U test was used for non-normally distributed data, and the independent samples t-test for normally distributed data. Categorical variables were compared using the chi-square test. Given that several inflammation-based indices were derived from overlapping hematological parameters, the risk of multicollinearity was carefully assessed. Receiver operating characteristic (ROC) curve analysis was performed, and variables with an area under the curve (AUC) approaching or exceeding

TABLE I
Definitions and formulas of inflammatory and immunonutritional indices

Parameter	Abbreviation	Formula
Neutrophil-to-lymphocyte ratio	NLR	Neutrophil ($\times 10^9$/L) / Lymphocyte ($\times 10^9$/L)
Platelet-to-lymphocyte ratio	PLR	Platelet ($\times 10^9$/L) / Lymphocyte ($\times 10^9$/L)
Monocyte-to-lymphocyte ratio	MLR	Monocyte ($\times 10^9$/L) / Lymphocyte ($\times 10^9$/L)
Systemic immune-inflammation index	SII	Platelet ($\times 10^9$/L) × Neutrophil ($\times 10^9$/L) / Lymphocyte ($\times 10^9$/L)
Systemic inflammation response index	SIRI	Neutrophil ($\times 10^9$/L) × Monocyte ($\times 10^9$/L) / Lymphocyte ($\times 10^9$/L)
Pan-immune-inflammation value	PIV	Platelet ($\times 10^9$/L) × Neutrophil ($\times 10^9$/L) × Monocyte ($\times 10^9$/L) / Lymphocyte ($\times 10^9$/L)
Prognostic nutritional index	PNI	Albumin (g/dL) × 10 + 5 × Lymphocyte ($\times 10^9$/L)
C-reactive protein-to-albumin ratio	CAR	CRP (mg/L) / Albumin (g/dL)
CALLY Index	CALLY	Albumin (g/dL) × Lymphocyte ($\times 10^9$/L) / CRP (mg/L)

CRP, C-reactive protein; Albumin values were recorded in g/dL. For the calculation of the Prognostic Nutritional Index, albumin values were converted to g/L by multiplying by 10; CALLY, C-reactive protein-albumin-lymphocyte.

0.70 were selected for further evaluation. The AUC values were interpreted as follows: 0.9-1.0 as excellent, 0.8-0.9 as good, 0.7-0.8 as fair, 0.6-0.7 as poor, and 0.5-0.6 as failed.[29] The optimal cut-off value was determined using the Youden index (sensitivity+specificity–1). To identify independent predictors of PJI, multivariate logistic regression analysis was performed. Variables showing statistically significant associations in the univariate analyses ($p < 0.05$) were entered into the multivariate models. Anesthesia type was also included, as it differed significantly between the PJI and non-PJI groups in the univariate analysis. Since several inflammation-based indices were derived from overlapping laboratory parameters, variables with a correlation coefficient greater than 0.6 were not included in the same model to minimize multicollinearity. Accordingly, three separate multivariate logistic regression models were constructed: (1) anesthesia type, albumin, and CRP; (2) anesthesia type, CALLY, and PNI; and (3) anesthesia type, CAR, and PNI. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A p value of <0.05 was considered statistically significant.

RESULTS

Of a total of 192 patients included in the study, 128 (66.7%) were in the non-PJI group and 64 (33.3%) were in the PJI group. Overall, 54 of the patients were male and 138 were females with a mean age of 69.4 ± 8.2 (range, 37 to 86) years. No significant difference was found between the groups regarding sex distribution ($p = 1.000$), age ($p = 0.498$), or BMI ($p = 0.876$). Similarly, the distribution of operated side ($p = 0.238$) and smoking status ($p = 0.130$) did not differ between the groups. The prevalence of comorbidities, including DM, CAD, HT, CVD, COPD, malignancy, hypothyroidism, CKD, rheumatologic disease was comparable between the groups (all $p > 0.05$). Anticoagulant ($p = 0.549$) and antiplatelet use ($p = 0.428$) were similar between the groups (Table II).

The ASA score (p = 0.828) and blood transfusion units ($p = 0.208$) were similar between the groups.

TABLE II
Demographic characteristics of all patients

	Non PJI group (n = 128)			PJI group (n = 64)			
Variables	n	%	Mean ± SD	n	%	Mean ± SD	*p*
Age (year)			69.3 ± 7.6			69.6 ± 9.3	0.498*
Sex							1.000#
Male	36	28.1		18	28.1		
Female	92	71.9		46	71.9		
Body mass index (kg/m²)			32.6 ± 4.8			32.8 ± 6.3	0.876*
Side							0.238#
Unilateral	104	81.2		57	89.1		
Bilateral	24	18.8		7	10.9		
Smoker	6	4.7		7	10.9		0.130#
Comorbidities	97	75.8		53	82.8		0.355#
Coronary artery disease	23	18.0		13	20.3		0.845#
Diabetes mellitus	33	25.8		18	28.1		0.729#
Hypertension	79	61.7		45	70.3		0.311#
Cerebrovascular disease/stroke	3	2.3		2	3.1		1.000#
Chronic obstructive pulmonary disease	3	2.3		2	3.1		1.000#
Malignancy	3	2.3		3	4.7		0.402#
Hypothyroidism	10	7.8		3	4.7		0.549#
Chronic kidney disease	0	0.0		2	3.1		0.110#
Rheumatic disease	1	0.8		2	3.1		0.258#
Anticoagulant use	10	7.8		3	4.7		0.549#
Antiplatelet use	21	16.4		14	21.9		0.428#

PJI, periprosthetic joint infection; SD, standard deviation; *, Independent Samples t-test; #, Chi-square test.

Anesthesia type differed significantly between the groups (p = 0.013). The proportion of patients receiving spinal anesthesia was higher in the non-PJI group (84.4% *vs.* 73.4%), whereas general anesthesia was more common in the PJI group (10.9% *vs.* 1.6%). The distribution of epidural anesthesia was similar between the groups (15.6% *vs.* 14.1%).

Preoperative laboratory parameters and inflammation-based indices are presented in Table III. The PJI group had significantly lower serum albumin levels compared to the non-PJI group. (3.8 ± 0.5 *vs.* 4.1 ± 0.4 g/dL, $p < 0.001$), while CRP levels were significantly higher in the PJI group (6.0 [0.2-32.0] *vs.* 3.0 [0.3-46.8] mg/L, $p < 0.001$). Lymphocyte count was significantly lower in the PJI group (2.08 [0.60-4.10] *vs.* 2.36 [0.90-4.85] $\times 10^9$/L, $p = 0.019$). Among inflammation-based indices, NLR ($p = 0.015$), MLR ($p = 0.030$), and SIRI ($p = 0.042$) were significantly higher in the PJI group. In contrast, PNI (48.2 ± 6.7 *vs.* 52.8 ± 5.9, $p < 0.001$) and CALLY (0.14 [0.01-2.87] *vs.* 0.30 [0.02-2.65], $p < 0.001$) were significantly lower, while CAR was significantly higher in the PJI group (1.48 [0.06-9.70] *vs.* 0.72 [0.09-11.70], $p < 0.001$). Other laboratory parameters and indices were comparable between the groups (all $p > 0.05$) (Table III).

Variables showing significant differences in Table III were analyzed using the ROC curves. (Figure 1). The ROC curve analysis demonstrated that all evaluated biomarkers showed moderate discriminative ability for predicting PJI (Figure 1). Serum albumin had an AUC of 0.705 (95% CI: 0.623-0.787), PNI 0.699 (95% CI: 0.620-0.779), CALLY 0.701 (95% CI: 0.617-0.784), CRP 0.660 (95% CI: 0.577-0.744), and CAR 0.684 (95% CI: 0.601-0.766). Optimal cut-off values were determined for variables with AUC values approximately ≥ 0.70 and using the maximum Youden index. Accordingly, the cut-off values were ≤ 4.0 g/dL for albumin, ≤ 50.0 for PNI, ≥ 1.2 for CAR, and ≤ 0.20 for CALLY (Table IV).

Multivariate logistic regression analysis identified several inflammatory and nutritional parameters as independent predictors of PJI (Table V). In Model 1, low serum albumin (OR = 4.31, 95% CI: 2.19-8.49, $p < 0.001$), high CRP levels (OR = 2.67, 95% CI: 1.36-5.25, $p = 0.005$), and general anesthesia compared to spinal anesthesia (OR = 7.61, 95% CI: 1.39-41.75, $p = 0.019$) were independently associated with PJI. In Model 2, low CALLY (OR = 2.97, 95% CI: 1.49-5.91, $p = 0.002$), low PNI (OR = 2.83, 95% CI: 1.42-5.63, $p = 0.003$), and general anesthesia (OR = 7.97, 95% CI: 1.46-43.56,

TABLE III
Preoperative laboratory parameters and inflammation-based indices

	Non PJI group (n = 128)			PJI group (n = 64)			
Variables	Mean ± SD	Median	Min-Max	Mean ± SD	Median	Min-Max	*p*
Serum albumin (g/dL)	4.1 ± 0.4			3.8 ± 0.5			**< 0.001***
CRP (mg/L)		3.0	0.3-46.8		6.0	0.2-32.0	**< 0.001****
Platelet count ($\times 10^9$/L)		265.0	122.0-608.0		254.0	110.0-442.0	0.339**
Neutrophil count ($\times 10^9$/L)		4.4	1.62-11.2		4.7	2.0-8.9	0.416**
Lymphocyte count ($\times 10^9$/L)		2.36	0.90-4.85		2.08	0.60-4.10	**0.019****
Monocyte count ($\times 10^9$/L)		0.55	0.20-1.21		0.60	0.20-1.29	0.354**
NLR		1.92	0.81-11.20		2.62	0.59-5.86	**0.015****
PLR		116.1	50.3-399.0		126.8	43.4-368.3	0.147**
MLR		0.24	0.09-0.64		0.30	0.09-0.79	**0.030****
SII		547.9	168.9-4468.8		605.1	104.2-2155.0	0.076**
SIRI		1.11	0.31-4.79		1.41	0.21-5.52	**0.042****
PIV		294.6	78.6-1417.2		351.9	39.6-1589.3	0.179**
PNI	52.8 ± 5.9			48.2 ± 6.7			**< 0.001***
CAR		0.72	0.09-11.70		1.48	0.06-9.70	**< 0.001****
CALLY		0.30	0.02-2.65		0.14	0.01-2.87	**< 0.001****

PJI, periprosthetic joint infection; SD, standard deviation; CRP, C-reactive protein; NLR, Neutrophil-to-lymphocyte ratio; PLR, Platelet-to-lymphocyte ratio; MLR, Monocyte-to-lymphocyte ratio; SII, Systemic immune-inflammation index; SIRI, Systemic inflammation response index; PIV, Pan-immune-inflammation value; PNI, Prognostic nutritional index; CAR, C-reactive protein-to-albumin ratio; CALLY, C-reactive protein-albumin-lymphocyte; *, Independent Samples t-test; **, Mann-Whitney U test.

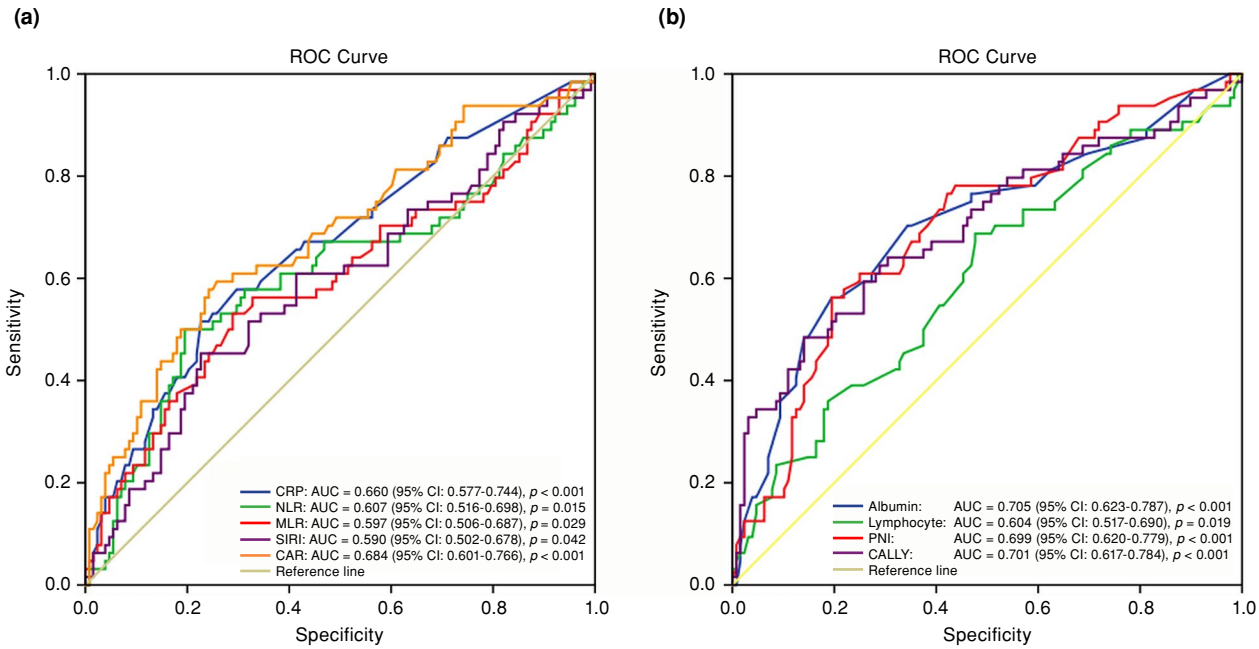


FIGURE 1. ROC curves of inflammatory and nutritional biomarkers for predicting PJI. **(a)** ROC curves for CRP, NLR, MLR, SIRI, and CAR. Higher values indicate a greater likelihood of PJI. **(b)** ROC curves for albumin, lymphocyte count, PNI, and CALLY index. Lower values indicate a greater likelihood of PJI. Higher AUC values indicate better discriminatory performance.

CRP, C-reactive protein; AUC, area under the curve; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SIRI, systemic inflammatory response index; CAR, C-reactive protein-to-albumin ratio; PNI, prognostic nutritional index; CALLY, C-reactive protein-albumin-lymphocyte index; PJI, periprosthetic joint infection; ROC, receiver operating characteristic.

TABLE IV
Optimal cut-off values of preoperative biomarkers for PJI

	Cut-off	Sensitivity (%)	Specificity (%)	+LHR	PPV (%)	NPV (%)	Max Youden Index
Serum albumin	≤ 4.0	70.3	65.6	2.0	50.6	81.6	0.34
CRP	≥ 4.0	65.6	58.6	1.6	44.2	77.3	0.25
PNI	≤ 50.0	60.9	75.0	2.4	51.3	78.4	0.36
CAR	≥ 1.2	60.9	71.1	2.1	50.7	77.8	0.32
CALLY	≤ 0.20	64.1	68.8	2.1	50.6	79.3	0.33

PJI, periprosthetic joint infection; +LHR, positive likelihood ratio; PPV, positive predictive value; NPV, negative predictive value; CRP, C-reactive protein; PNI, prognostic nutritional index; CAR, C-reactive protein-to-albumin ratio; CALLY, C-reactive protein-albumin-lymphocyte index.

$p = 0.017$) remained significant predictors. In Model 3, high CAR (OR = 3.45, 95% CI: 1.76-6.76, $p < 0.001$), low PNI (OR = 3.60, 95% CI: 1.83-7.06, $p < 0.001$), and general anesthesia (OR = 8.52, 95% CI: 1.54-47.06, $p = 0.014$) were independently associated with PJI.

DISCUSSION

In the present study, we examined preoperative inflammatory and immunonutritional indices for predicting early PJI after TKA. Our study results showed that several inflammatory and nutritional biomarkers were significantly related to PJI. In particular, markers reflecting systemic inflammation (CRP, CAR, and CALLY), as well as nutritional status (serum albumin and PNI) consistently appeared as significant factors across different models. Among these, low serum albumin and low PNI were repeatedly identified as independent predictors. These findings suggest that preoperative immunonutritional status may play a key role in infection susceptibility. From a clinical standpoint, these results are not unexpected. In orthopedic cases, patients with malnutrition and elevated inflammatory markers face an increased

TABLE V
Multivariate logistic regression models for predictors of PJI

Model	Variables	OR	95% CI	*p*
Model 1	Low albumin	4.31	2.19-8.49	< 0.001
	High CRP	2.67	1.36-5.25	0.005
	Anesthesia type			
	Epidural *vs.* spinal	1.37	0.55-3.44	0.498
	General *vs.* spinal	7.61	1.39-41.75	0.019
Model 2	Low CALLY	2.97	1.49-5.91	0.002
	Low PNI	2.83	1.42-5.63	0.003
	Anesthesia type			
	Epidural *vs.* spinal	1.56	0.61-3.98	0.349
	General *vs.* spinal	7.97	1.46-43.56	0.017
Model 3	High CAR	3.45	1.76-6.76	< 0.001
	Low PNI	3.60	1.83-7.06	< 0.001
	Anesthesia type			
	Epidural *vs.* spinal	1.46	0.57-3.76	0.434
	General *vs.* spinal	8.52	1.54-47.06	0.014

OR, odds ratio; CI, confidence interval; CRP, C-reactive protein; CALLY: CRP-albumin-lymphocyte index; PNI, prognostic nutritional index; CAR, CRP-to-albumin ratio; ROC, receiver operating characteristic; AUC, area under the curve. Cut-off values were determined using ROC curve analysis and the maximum Youden index. Cut-off values were calculated for variables with acceptable discriminative ability (AUC approximately ≥ 0.70): CRP ≥ 4.0 mg/L, albumin ≤ 4.0 g/dL, PNI ≤ 50.0, CAR ≥ 1.2, and CALLY ≤ 0.20. To minimize multicollinearity arising from shared biological components, variables with pairwise correlation coefficients greater than 0.6 were not entered into the same model. Accordingly, separate multivariate models were constructed using variables with lower intercorrelation.

risk of complications.[30] Our findings support this observation. It has been demonstrated that systemic inflammation and impaired nutritional status facilitate the development of infections.[31]

The association between hypoalbuminemia and postoperative complications has been reported in many studies. Serum albumin reflects both nutritional status and systemic inflammation. Low albumin levels may impair wound healing and weaken the immune response.[32-34] Of note, PNI, which combines albumin and lymphocyte count, may provide a more comprehensive assessment of immune status.[35,36] Previous studies reported high predictive values for CAR and PNI, with some studies demonstrating AUC values above 0.90.[12] In our cohort, the performance was lower (AUC ~0.65-0.71). This finding suggests that, although these markers are associated with infection risk, their predictive value as standalone markers may be limited. Several factors may account for this observation. We only evaluated early PJI within 90 days, while many studies included a broader range of infections. In addition, differences in patient populations may also have affected the results.

The diagnostic utility of inflammatory biomarkers has been investigated in several studies evaluating their performance in detecting infection. Shi et al.[19] found that CAR had high diagnostic accuracy for PJI, with an AUC of 0.941, and performed better than CRP. In the present study, CAR was likewise identified as a significant predictor; however, its predictive performance was comparatively lower. This discrepancy may reflect differences in the clinical application of these biomarkers. Specifically, inflammatory biomarkers may demonstrate greater utility in identifying an established infection, in which systemic inflammatory responses are already present, than in predicting the subsequent development of infection before its clinical manifestation.

Recent studies have shown that inflammatory indices may have roles beyond prediction. To illustrate, changes in markers such as SIRI and

MLR have been linked to treatment success after revision surgery.[17] This suggests that these markers may also be useful for monitoring disease course and treatment response. Similarly, Moldovan[16] reported that several inflammatory indices showed good diagnostic performance in distinguishing PJI from aseptic failure, with AUC values above 0.80. In our study, the predictive performance was more moderate. This difference likely reflects the clinical setting. Their study focused on diagnosis in revision cases, while we evaluated preoperative risk in primary arthroplasty patients. Overall, our findings suggest that inflammatory and immunonutritional indices are associated with PJI. However, their clinical value depends on how they are used. In the preoperative setting, they may help identify higher-risk patients. Still, they should not be used alone and should be part of a broader risk assessment.

The higher AUC values reported in previous studies can be explained by several factors. Most of these studies evaluated diagnostic performance by comparing cases of existing PJI with aseptic conditions; in such cases, the AUC may be higher, as inflammatory differences are more pronounced. This study, however, focused on predicting early PJI within 90 days, which is a more challenging task. Additionally, while our cohort consists of a more homogeneous patient group, other studies may include more heterogeneous populations, such as revision cases and late infections, which could increase the AUC. Sample size, the single-center design, and the optimization of cut-off values or the use of combined models in some studies may also have influenced the results. Therefore, these differences should be taken into account while comparing the AUC values reported in the literature with the results of our study.

From a practical perspective, these cut-off values may help support clinical decisions. These include serum albumin ≤ 4.0 g/dL, PNI ≤ 50, CAR ≥ 1.2, and CALLY ≤ 0.20. However, since the predictive performance in our study was moderate, these values should be used with caution. They are easy to obtain and low-cost, but should not be used alone and are better considered together with other clinical factors.

Although the primary objective of this study was to evaluate the predictive value of preoperative inflammatory and immunonutritional indices, general anesthesia also emerged as an independent predictor of PJI in all multivariate models. This finding is consistent with several recent studies suggesting that spinal or neuraxial anesthesia may be associated with a lower risk of postoperative infection, including PJI, compared with general anesthesia.[37-40] One proposed explanation is that general anesthesia may induce greater perioperative immunosuppression and inflammatory activation, resulting in higher postoperative inflammatory marker levels.[41-43] However, the available evidence remains inconclusive. Some studies have reported no significant differences between general and spinal anesthesia with respect to inflammatory responses or postoperative clinical outcomes.[44-46] Therefore, although our findings are broadly consistent with part of the existing literature, they should be interpreted cautiously. The present study was not specifically designed to compare anesthetic techniques, and the number of patients receiving general anesthesia was relatively small. Accordingly, the observed association cannot be interpreted as establishing a causal relationship and should be considered preliminary. Future prospective studies specifically designed to investigate the impact of anesthesia type on PJI risk are needed to confirm this finding.

This study has several clinical implications. It highlights the importance of preoperative immunonutritional assessment. Additionally, it supports the use of composite biomarkers in perioperative risk assessment. However, due to the moderate predictive performance, these findings should not be used directly as an independent clinical decision-making tool. Instead, these parameters may provide supportive information when used in conjunction with other clinical factors.

Several limitations should be considered when interpreting the findings of this study. First, due to the retrospective design, selection bias and residual confounding cannot be completely excluded. Important intraoperative variables such as operative time, tourniquet duration, surgical technique, and timing of antibiotic prophylaxis were not evaluated and may have influenced the risk of PJI. Moreover, the 12-year study period may have introduced variability in surgical techniques, perioperative protocols, and infection prevention strategies over time. As this was a single-center study, the generalizability of the findings may also be limited. In addition, multiple inflammatory and immunonutritional indices were evaluated simultaneously. The large number of statistical comparisons may have increased the risk of type 1 error. Therefore, the observed associations should be interpreted cautiously and confirmed

in independent cohorts. Finally, the moderate predictive performance observed suggests that factors beyond laboratory parameters, such as surgical technique and intraoperative variables, also play a critical role. Future prospective and multicenter studies may help to further clarify the role of these indices and improve their integration into clinical prediction models.

In conclusion, preoperative inflammatory and immunonutritional indices, particularly albumin, PNI, CALLY and CAR, seem to be associated with early PJI following TKA. While their standalone predictive performance is moderate, they offer practical value as accessible and readily available tools within a comprehensive risk stratification framework. Integration of these biomarkers into clinical decision-making may support personalized perioperative management, although further prospective validation is required.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Shahi A, Parvizi J. Prevention of periprosthetic joint infection. Arch Bone Jt Surg 2015;3:72-81.
2. Buyukarslan V, Yapar A, Yapar D, Dogruoz F, Kose O, Citak M. Impact of temperature and humidity on periprosthetic joint infections following total knee arthroplasty: A 12-year study in a Mediterranean climate. Arch Orthop Trauma Surg 2025;145:469. doi: 10.1007/s00402-025-06081-7.
3. Ma T, Jiao J, Guo DW, Lv SZ, Zhang D, Hou DC. Incidence of periprosthetic joint infection after primary total knee arthroplasty shows significant variation: A synthesis of meta-analysis and bibliometric analysis. J Orthop Surg Res 2024;19:649. doi: 10.1186/s13018-024-05099-8.
4. Atik OŞ. Surgical treatment of periprosthetic joint infection: Two stage or one stage? Jt Dis Relat Surg 2025;36:1-2. doi: 10.52312/jdrs.2025.57926.
5. McMaster Arthroplasty Collaborative (MAC). Risk factors for periprosthetic joint infection following primary total hip arthroplasty: A 15-year, population-based cohort study. J Bone Joint Surg Am 2020;102:503-9. doi: 10.2106/JBJS.19.00537.
6. Ustaalioglu İ, Aydoğdu Umaç G. Neutrophil/lymphocyte ratio as a predictor of mortality among aortic dissection patients in the emergency department. Ulus Travma Acil Cerrahi Derg 2024;30:644-9. doi: 10.14744/tjtes.2024.78241.
7. Celik B, Nalcacioglu H, Ozcatal M, Altuner Torun Y. Role of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in identifying complicated appendicitis in the pediatric emergency department. Ulus Travma Acil Cerrahi Derg 2019;25:222-8. English. doi: 10.5505/tjtes.2018.06709.
8. Gong P, Liu Y, Gong Y, Chen G, Zhang X, Wang S, et al. The association of neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and lymphocyte to monocyte ratio with post-thrombolysis early neurological outcomes in patients with acute ischemic stroke. J Neuroinflammation 2021;18:51. doi: 10.1186/s12974-021-02090-6.
9. Liu B, Wang J, Li YY, Li KP, Zhang Q. The association between systemic immune-inflammation index and rheumatoid arthritis: Evidence from NHANES 1999-2018. Arthritis Res Ther 2023;25:34. doi: 10.1186/s13075-023-03018-6.
10. Ma R, Cui L, Cai J, Yang N, Wang Y, Chen Q, et al. Association between systemic immune inflammation index, systemic inflammation response index and adult psoriasis: Evidence from NHANES. Front Immunol 2024;15:1323174. doi: 10.3389/fimmu.2024.1323174.
11. Jin C, Li X, Luo Y, Zhang C, Zuo D. Associations between pan-immune-inflammation value and abdominal aortic calcification: A cross-sectional study. Front Immunol 2024;15:1370516. doi: 10.3389/fimmu.2024.1370516.
12. Liu Y, Sun L, Liu Z, Ma Y, Li C, Liang M, et al. Validating Mini Nutritional Assessment-Short Form thresholds for postoperative mortality and complications in geriatric hip fracture patients with compromised nutritional status. Jt Dis Relat Surg 2026;37:351-9. doi: 10.52312/jdrs.2026.2417.
13. Zhang L, Ma W, Qiu Z, Kuang T, Wang K, Hu B, et al. Prognostic nutritional index as a prognostic biomarker for gastrointestinal cancer patients treated with immune checkpoint inhibitors. Front Immunol 2023;14:1219929. doi: 10.3389/fimmu.2023.1219929.
14. Aydın A, Kaçmaz O. CRP/albumin ratio in predicting 1-year mortality in elderly patients undergoing hip fracture surgery. Eur Rev Med Pharmacol Sci 2023;27:8438-46. doi: 10.26355/eurrev_202309_33770.
15. Yang M, Lin SQ, Liu XY, Tang M, Hu CL, Wang ZW, et al. Association between C-reactive protein-albumin-lymphocyte (CALLY) index and overall survival in patients with colorectal cancer: From the investigation on nutrition status and clinical outcome of common cancers study. Front Immunol 2023;14:1131496. doi: 10.3389/fimmu.2023.1131496.
16. Moldovan F. Role of serum biomarkers in differentiating periprosthetic joint infections from aseptic failures after total hip arthroplasties. J Clin Med 2024;13:5716. doi: 10.3390/jcm13195716.

17. Vitiello R, Smimmo A, Matteini E, Micheli G, Fantoni M, Ziranu A, et al. Systemic Inflammation Response Index (SIRI) and Monocyte-to-Lymphocyte Ratio (MLR) Are predictors of good outcomes in surgical treatment of periprosthetic joint infections of lower limbs: A single-center retrospective analysis. Healthcare (Basel) 2024;12:867. doi: 10.3390/healthcare12090867.
18. Kürüm H, Key S, Tosun HB, Yılmaz E, Kürüm KO, İpekten F, et al. Relationship between the clinical outcomes and the systemic inflammatory response index and systemic immune inflammation index after total knee arthroplasty. Musculoskelet Surg 2024;108:323-32. doi: 10.1007/s12306-024-00825-1.
19. Shi W, Wang Y, Zhao X, Yu T, Li T. CRP/Albumin has a promising prospect as a new biomarker for the diagnosis of periprosthetic joint infection. Infect Drug Resist 2021;14:5145-51. doi: 10.2147/IDR.S342652.
20. Iwagami M, Shinozaki T. Introduction to matching in case-control and cohort studies. Ann Clin Epidemiol 2022;4:33-40. doi: 10.37737/ace.22005.
21. Taylor JM. Choosing the number of controls in a matched case-control study, some sample size, power and efficiency considerations. Stat Med 1986;5:29-36. doi: 10.1002/sim.4780050106.
22. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: An evidence-based and validated criteria. J Arthroplasty 2018;33:1309-14.e2. doi: 10.1016/j.arth.2018.02.078.
23. Chou CM, Chuang TC, Chiang CH. Factors that increase the risk of prosthetic joint infection within 90 days after THA and TKA: A nationwide population-based study. Clin Orthop Relat Res 2026;484:109-16. doi: 10.1097/CORR.0000000000003592.
24. Bülow E, Hahn U, Andersen IT, Rolfson O, Pedersen AB, Hailer NP. Prediction of early periprosthetic joint infection after total hip arthroplasty. Clin Epidemiol 2022;14:239-53. doi: 10.2147/CLEP.S347968.
25. Löwik CAM, Parvizi J, Jutte PC, Zijlstra WP, Knobben BAS, Xu C, et al. Debridement, antibiotics, and implant retention is a viable treatment option for early periprosthetic joint infection presenting more than 4 weeks after index arthroplasty. Clin Infect Dis 2020;71:630-6. doi: 10.1093/cid/ciz867.
26. Baki H, Aydın ÖF. C-reactive protein -albumin-lymphocyte (CALLY) index as a predictor of early mortality in elderly patients with hip fractures. Ulus Travma Acil Cerrahi Derg 2025;31:1011-7. doi: 10.14744/tjtes.2025.78553.
27. Gurpinar A, Erdal H, Kalayci H. Association of SII and AISI in patients with sepsis: A retrospective study. Med Sci 2025;14:6. doi:10.5455/medscience.2024.10.117
28. Telang S, Mayfield CK, Palmer R, Liu KC, Wier J, Hong K, et al. Preoperative laboratory values predicting periprosthetic joint infection in morbidly obese patients undergoing total hip or knee arthroplasty. J Bone Joint Surg Am 2024;106:1317-27. doi: 10.2106/JBJS.23.01360.
29. Ağababaoğlu İ, Yildiz OO, Yapar D, Ersöz H, Hazer S, Helvacı Ö, et al. Mediastinal lymphnode positivity clinical scoring system for lung adenocarsinoma-mediastinal lymph node evaluation and staging. J Health Sci Med 2022;5:831-8. doi: 10.32322/jhsm.1061755
30. Phillips JLH, Ennis HE, Jennings JM, Dennis DA. Screening and management of malnutrition in total joint arthroplasty. J Am Acad Orthop Surg 2023;31:319-25. doi: 10.5435/JAAOS-D-22-01035.
31. Almeida PR, Mokete L, Sikhauli N, Mota A, Ndindwa B, Pietrzak JRT. Malnutrition in total joint arthroplasty: What should the orthopaedic surgeon consider? EFORT Open Rev 2024;9:615-24. doi: 10.1530/EOR-23-0192.
32. Bohl DD, Shen MR, Kayupov E, Della Valle CJ. Hypoalbuminemia independently predicts surgical site infection, pneumonia, length of stay, and readmission after total joint arthroplasty. J Arthroplasty 2016;31:15-21. doi: 10.1016/j.arth.2015.08.028.
33. Llombart R, Mariscal G, Barrios C, de la Rubia Ortí JE, Llombart-Ais R. The impact of hypoalbuminemia on postoperative complications in patients undergoing shoulder arthroplasty: A meta-analysis. J Nutr Health Aging 2023;27:1248-54. doi: 10.1007/s12603-023-2050-6.
34. Kishawi D, Schwarzman G, Mejia A, Hussain AK, Gonzalez MH. Low preoperative albumin levels predict adverse outcomes after total joint arthroplasty. J Bone Joint Surg Am 2020;102:889-95. doi: 10.2106/JBJS.19.00511.
35. Guo H, Yang L, Liu J, Yu X, Chen L, Huang Y. Prognostic nutritional index and the risk of postoperative complications after spine surgery: A meta-analysis. World Neurosurg 2024;185:e572-81. doi: 10.1016/j.wneu.2024.02.077.
36. Ushirozako H, Hasegawa T, Yamato Y, Yoshida G, Yasuda T, Banno T, et al. Does preoperative prognostic nutrition index predict surgical site infection after spine surgery? Eur Spine J 2021;30:1765-73. doi: 10.1007/s00586-020-06622-1.
37. Scholten R, Leijtens B, Hannink G, Kamphuis ET, Somford MP, van Susante JLC. General anesthesia might be associated with early periprosthetic joint infection: An observational study of 3,909 arthroplasties. Acta Orthop 2019;90:554-8. doi: 10.1080/17453674.2019.1644069.
38. Chong YY, Lau CML, Jiang T, Wen C, Zhang J, Cheung A, et al. Predicting periprosthetic joint infection in primary total knee arthroplasty: A machine learning model integrating preoperative and perioperative risk factors. BMC Musculoskelet Disord 2025;26:241. doi: 10.1186/s12891-025-08296-6.
39. Aljuhani WS, Alanazi AM, Saeed AI, Alhadlaq KH, Alhoshan YS, Aljaafri ZA. Patient-related risk factors of prosthetic joint infections following total hip and knee arthroplasty at King Abdulaziz Medical City, a 10-year retrospective study. J Orthop Surg Res 2023;18:717. doi: 10.1186/s13018-023-04210-9.
40. Liu J, Ma C, Elkassabany N, Fleisher LA, Neuman MD. Neuraxial anesthesia decreases postoperative systemic infection risk compared with general anesthesia in knee arthroplasty. Anesth Analg 2013;117:1010-6. doi: 10.1213/ANE.0b013e3182a1bf1c.
41. Kim HJ, Roychoudhury P, Lohia S, Kim JS, Kim HT, Ro YJ, et al. Comparison of general and spinal anaesthesia on systemic inflammatory response in patients undergoing total knee arthroplasty: A propensity score matching analysis. Medicina (Kaunas) 2021;57:1250. doi: 10.3390/medicina57111250.
42. Genç A, Astan S, Gürler Balta M, Kölükçü V, Şahin AT, Tapar H, et al. Comparison of systemic inflammatory markers in total knee arthroplasty under spinal vs general anesthesia:

A retrospective study. BMC Anesthesiol 2025;25:518. doi: 10.1186/s12871-025-03399-y.

43. Jacobs LMC, Bijkerk V, van Eijk LT, Joosten LAB, Keijzer C, Visser J, et al. The effect of general versus spinal anesthesia on perioperative innate immune function in patients undergoing total hip arthroplasty. BMC Anesthesiol 2025;25:10. doi: 10.1186/s12871-024-02883-1.
44. Eroğlu M, Kokulu S, Koca HB, Demirboğan ME, Baki ED, Özcan Ö. The effects of general and spinal anesthesia on systemic inflammatory response in patients undergoing total knee arthroplasty. Eklem Hastalik Cerrahisi 2016;27:153-9. doi: 10.5606/ehc.2016.31.
45. Wang Q, Lin F, Huang B, Pan LH. The effectiveness and safety of general and spinal anesthesia on systemic inflammatory response in patients with tumor-type total knee arthroplasty. Oncol Res Treat 2020;43:428-34. doi: 10.1159/000507892.
46. Johnson RL, Kopp SL, Burkle CM, Duncan CM, Jacob AK, Erwin PJ, et al. Neuraxial vs general anaesthesia for total hip and total knee arthroplasty: A systematic review of comparative-effectiveness research. Br J Anaesth 2016;116:163-76. doi: 10.1093/bja/aev455.