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RESEARCH

A drop of blood, a hint of risk: neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as early predictors and risk stratifiers in pyogenic spondylodiscitis

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Abstract

Introduction Pyogenic spondylodiscitis (PSD) is a severe spinal infection with potential for significant morbidity. Early identification of patients at risk for poor outcomes is crucial. This study investigated the prognostic value of neutrophil-to-lymphocyte ratio (NLR) and platelet- to-lymphocyte ratio (PLR) at Emergency Department (ED) admission.

Materials and methods This retrospective, single-center cohort study included 187 patients diagnosed with PSD or vertebral osteomyelitis (VO) between January 2017 and December 2023. NLR and PLR were calculated from routine blood tests at admission. Outcomes included prolonged hospitalization (>15 days), 90-day readmission, and one-year mortality. ROC analysis determined optimal cut-offs for NLR (7.78) and PLR (174.2). Multivariate logistic regression assessed the association of elevated ratios with outcomes.

Results Elevated NLR and PLR at admission were significantly associated with adverse outcomes. Patients with NLR > 7.78 had a 2.1-fold increased risk of prolonged hospitalization (95% CI 1.08–4.07), a 1.7-fold higher risk of 90-day readmission (95% CI 1.01–2.94), and a 2.4-fold increased risk of one-year mortality (95% CI 1.18–5.07). Similarly, PLR > 174.2 was associated with a 1.8-fold increased risk of prolonged hospitalization (95% CI 1.01–3.28) and a 1.8-fold increased risk of one-year mortality (95% CI 1.02–3.42). Patients with both elevated NLR and PLR had a 3.4-fold increased risk of prolonged hospitalization, a 2.4-fold increased risk of 90-day readmission, and a 3.3-fold increased risk of one-year mortality.

Conclusions Elevated NLR and PLR at ED admission are independent predictors of adverse outcomes in patients with PSD/VO. These simple hematological markers may serve as valuable tools for early risk stratification and warrant further investigation for integration into clinical management pathways.

Keywords Pyogenic spondylodiscitis · Neutrophil/lymphocyte ratio · Platelet/lymphocyte ratio · Inflammatory markers · Disease severity · Prognosis

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Introduction

Pyogenic spondylodiscitis (PSD) or Vertebral Osteomyelitis (VO) represents a critical infectious pathology affecting the vertebral column and intervertebral discs, and is associated with substantial morbidity and mortality [1]. A significant challenge in the management of PSD lies in its frequent initial misdiagnosis or delayed recognition, which can detrimentally impact patients' clinical and functional recovery. This diagnostic lag can lead to prolonged patient suffering, extended periods of hospitalization, and an elevated risk of developing complications. Consequently, the prompt and accurate identification of PSD, followed by the timely initiation of appropriate therapeutic interventions, is paramount for improving patient prognosis and enhancing their overall quality of life [1, 2]. The etiological agents most commonly implicated in pyogenic spinal infections are Gram-positive and Gram-negative bacteria, with Staphylococcus aureus and members of the Enterobacteriaceae family representing the predominant pathogens [2]. Clinically, patients with PSD typically present with severe axial back pain, which may or may not be accompanied by fever. Furthermore, neurological deficits can arise in certain cases due to the formation of epidural spinal abscesses, leading to radicular or medullary compression [3]. Standard diagnostic evaluations often reveal laboratory findings such as neutrophilic leukocytosis and elevated levels of inflammatory biomarkers, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin (PCT). However, the widespread implementation of these specialized tests can be constrained by their associated costs [1].

In the routine clinical management of patients with suspected PSD, basic hematological analyses are invariably performed. These routine blood tests offer a valuable opportunity to explore readily available inflammatory markers without incurring additional financial burden. Fundamental hematological parameters, such as red blood cell (RBC) count, white blood cell (WBC) count, platelet count, and hemoglobin levels, are routinely assessed. Moreover, composite ratios derived from these basic parameters, specifically the neutrophil-to- lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR), can be easily calculated from the same routine blood samples [4].

It is well-established that various disease states and conditions involving immune responses are characterized by significant alterations in leukocyte populations. Indeed, in pathological conditions, an elevated neutrophil-to-lymphocyte ratio (NLR) and a decreased platelet-to- lymphocyte ratio (PLR) have been frequently reported [5]. These ratios have demonstrated potential as accessible indicators of disease severity and prognostic outcomes across a spectrum of medical conditions. Given the substantial impact of PSD on patient health and well-being, it is noteworthy that the existing body of literature lacks a comprehensive investigation into the potential utility of NLR and PLR in the diagnostic process and subsequent follow-up of this specific infectious entity. To date, only a few studies evaluated NLR and PLR in the context of spondylodiscitis, specifically for differentiating between tuberculous and non-tuberculous infections [6]. However, no prior studies have investigated the prognostic significance of these markers in relation to clinical outcomes in patients with pyogenic spondylodiscitis, making our study the first to address this specific aspect.

Against this backdrop, our present study aims to elucidate the significance of the NLR and PLR as readily accessible and cost-effective inflammatory markers in patients diagnosed with pyogenic spondylodiscitis within an emergency setting. Specifically, this investigation seeks to evaluate their potential role in risk stratification, identifying patients who may be at a higher risk of experiencing adverse outcomes and consequently require more intensive clinical attention. By exploring the utility of these simple hematological ratios, this study intends to contribute to a more refined understanding of inflammatory responses in PSD, thereby paving the way for the development of more accessible and efficient methods for disease assessment. Such advancements hold the promise of ultimately leading to improved patient management strategies and enhanced clinical outcomes in individuals affected by this challenging spinal infection.

Materials and methods

Study design and patient cohort

This retrospective, single-center cohort study adhered to the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines [6]. We meticulously screened all patients admitted to the Emergency Department (ED) of our institution who received a confirmed diagnosis of PSD or VO between January 1, 2017, and December 31, 2023, for eligibility. All study procedures were conducted in accordance with the ethical principles outlined in the 1964 Helsinki Declaration and its subsequent amendments. Informed consent for the scientific utilization of anonymized clinical data was obtained from all patients as per institutional regulations and the guidelines set forth by the Italian Data Protection Authority. All patient data were anonymized to ensure confidentiality in compliance with privacy regulations.

Inclusion and exclusion criteria

The inclusion criteria for this study were: (1) age ≥ 18 years and (2) a confirmed diagnosis of PSD based on imaging findings (Magnetic Resonance Imaging or Computed Tomography) and/or microbiological evidence obtained during the hospitalization period following the ED admission. Patients were excluded if they presented with any of the following: active malignancy, known immunodeficiency disorders, non-pyogenic spinal infections (e.g., tuberculosis or fungal infections), or pregnancy.

Clinical management

Upon initial presentation to the Emergency Department with suspected PSD or VO, all patients underwent a comprehensive diagnostic workup. This included the collection of two sets of blood cultures and standard laboratory panels to evaluate inflammatory markers and organ function. Each case was promptly assessed in collaboration with both spine surgery and infectious disease specialists to ensure coordinated management from the outset. Diagnostic imaging was critical in confirming infection and determining the anatomical extent of involvement. Standard protocol involved performing spinal radiographs followed by contrast- enhanced magnetic resonance imaging (MRI) with gadolinium to identify vertebral involvement, disc space infection, and potential epidural or paravertebral abscesses. In patients contraindicated for MRI, a computed tomography (CT) scan was utilized to detect indirect radiological signs such as cortical endplate destruction, disc space narrowing, or soft tissue collections suggestive of infection. When blood cultures failed to yield a pathogen, a CT- guided percutaneous biopsy of the affected vertebral level was attempted to obtain microbiological specimens. In cases where percutaneous biopsy was non-diagnostic or when patients exhibited neurological deficits, open surgical biopsy combined with decompression was performed to both establish a definitive microbiological diagnosis and address neural element compression. Patients with a confirmed microbiological diagnosis, either through blood cultures or tissue sampling, were started on targeted antimicrobial therapy based on susceptibility profiles. Conversely, patients in whom a pathogen could not be identified received empiric broad-spectrum intravenous antibiotics. The duration of antibiotic therapy typically ranged from 4 to 6 weeks, tailored according to the identified pathogen and clinical response. All patients were prescribed a rigid spinal orthosis, customized to the level of vertebral involvement, to provide segmental immobilization and support during the acute phase of infection. Additionally, a transthoracic echocardiogram was routinely performed in all cases during hospitalization to screen for concomitant infective endocarditis, given the potential for hematogenous dissemination.

Data acquisition

A standardized electronic health record system facilitated the systematic retrieval of data for all patients diagnosed with PSD or VO who were managed in our institution's Emergency Department. The following demographic and clinical variables were extracted, reviewed for accuracy, and compiled into a dedicated database: patient age (in years), sex (male or female), a detailed account of their medical history, the calculated Charlson Comorbidity Index (CCI) as a measure of overall comorbidity burden, the presence or absence of pre-existing diabetes mellitus, the presence or absence of chronic kidney disease, the presence or absence of fever (defined as a body temperature ≥ 38 °C) at the time of ED presentation, the patient's subjective report of pain intensity, and the total length of the index hospital stay (in days). Neurological status at admission was assessed using the Frankel grading system, as this was the standardized format recorded in our institutional electronic health records. Data on the ASIA Impairment Scale were not available for the study cohort.

Furthermore, the initial hematological parameters obtained from blood samples drawn upon the patient's arrival in the ED were meticulously recorded. These parameters included procalcitonin (PCT, ng/L), C-reactive protein (CRP, mg/L), absolute neutrophil count (cells/μL), absolute lymphocyte count (cells/μL), and the platelet count (cells/μL). Subsequently, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated for each patient using the methodology previously described by Vitiello et al. [7]. In all patients with a suspected diagnosis of PSD or VO in our ED, two sets of blood cultures were routinely obtained.

Data regarding all-cause mortality within one year and hospital readmission was assessed through a combination of hospital medical records and direct follow-up contact. Patients treated for pyogenic spondylodiscitis at our institution are enrolled in a structured follow-up program, which includes scheduled outpatient evaluations during the first year after discharge. For patients who did not attend follow-up visits within the defined period, telephone interviews were conducted with the patients themselves, their families, or their primary care physicians to determine their vital status. Hospital records were reviewed to identify in-hospital deaths and verify clinical outcomes during hospitalization.

Outcome measures

The primary outcome of this study was defined as prolonged hospitalization, which was operationalized as a total hospital stay exceeding 15 days. Secondary outcomes included hospital readmission within a 90-day period following the initial discharge and all-cause mortality within one year from the date of the index admission.

Statistical analysis

All statistical analyses were performed using SPSS Statistics software, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as medians with their corresponding interquartile ranges (IQR) due to their non-normal distribution, while categorical variables are expressed as frequencies and percentages. Differences between relevant patient groups were assessed using the non-parametric Mann–Whitney U test for continuous variables and either the chi-squared test or Fisher's exact test for categorical variables, as appropriate based on data distribution and sample size considerations. A post-hoc power analysis was conducted based on the observed incidence of prolonged hospitalization (29.1%) in our cohort. Using an alpha level of 0.05, a statistical power of 80%, and an expected odds ratio of 2.1 (as identified in the univariate analysis for NLR), the minimum required sample size was estimated at 168 patients. With a final cohort of 187 patients, our study meets this threshold, ensuring sufficient power to detect clinically relevant associations.

An initial univariate analysis was conducted to explore potential associations between the calculated NLR and PLR values and the defined clinical outcomes. Subsequently, Receiver Operating Characteristic (ROC) curve analysis was performed to determine the optimal cut-off values for both NLR and PLR in predicting the primary outcome of prolonged hospitalization. The selection of these cut-off points was based on the maximization of the Youden index. The identified optimal thresholds for NLR (7.78) and PLR (174.2) were then utilized to categorize the patient cohort into high-risk and low-risk groups based on these ratios. To assess the independent association of elevated NLR and PLR with the clinical outcomes of interest, multivariate logistic regression models were constructed. These models were adjusted for potential confounding variables, including age, sex, relevant comorbidities (as captured by the Charlson Comorbidity Index, diabetes mellitus, and chronic kidney disease), and the initial severity of the infection (as potentially indicated by clinical presentation and laboratory values). To assess potential multicollinearity between NLR and PLR, Variance Inflation Factor (VIF) values were calculated within the multivariate logistic regression models. Both NLR and PLR demonstrated VIF values below 2 (1.72 and 1.68, respectively), indicating no significant multicollinearity concerns. To further strengthen the study's analytical framework, multivariate logistic regression models were expanded to include the following covariates: age, sex, CCI, diabetes mellitus, chronic kidney disease, body mass index (when available), surgical intervention (yes/no), blood culture positivity, infection by resistant pathogens, and the shift to targeted antibiotic therapy (yes/no).

In addition, propensity score–based approaches (1:1 matching and inverse probability of treatment weighting, IPTW) were employed to reduce bias from observed confounders. Multiple imputation was used to address missing covariate data. Stratified analyses were performed for patients undergoing surgical intervention and for those with resistant pathogens. Finally, to assess the robustness of our findings to potential unmeasured confounding, E-values were calculated for each of the main associations between NLR, PLR, and clinical outcomes. The results of the regression analyses are presented as odds ratios (OR) with their corresponding 95% confidence intervals (CI). A p-value of less than 0.05 was considered to indicate statistical significance for all analyses.

Results

Study cohort characteristics

The final analysis included a total of 187 patients who met the study criteria. The median age of the cohort was 69 (IQR 56–78) years, indicating a predominantly older population. Males constituted the majority of the study participants, accounting for 57.7% of the total sample. No significant differences were found between groups in terms of median BMI, obesity, or major comorbidities such as arterial hypertension, ischemic cardiomyopathy, heart failure, previous stroke/TIA, COPD, hepatic disease, cirrhosis, diabetes, and chronic kidney disease (all $p > 0.05$). A comprehensive summary of the demographic characteristics of the study population is presented in Table 1.

Incidence of clinical outcomes

Prolonged hospitalization, defined as a hospital stay exceeding 15 days, was observed in 29.1% of the patient cohort. Within the 90-day follow-up period, 30.2% of patients experienced hospital readmission. The all-cause mortality rate at one year following the index admission was 15.4%. Surgery, diagnostic or decompressive, was needed in 22.3% of patients.

Table 1 Demographic features of cohort of analysed patients

	All patients (*n*. 187)	NLR > 7.78 and PLR > 174.3 (*n*. 42)	NLR AND/OR PLR below cut- off value (*n*. 145)	*p*
Demographics				
Sex (Male)	108 (57.7%)	28 (66.6%)	80 (55.2%)	0.034
Age (years) (IQR)	69 (56–78)	66 (56–74)	69 (58–78)	0.128
BMI	27.1 (21.2–32.8)	26.9 (21.2–31.4)	27.2 (23.4–32.8)	0.832
Obesity	39 (20.7%)	12(26.4%)	27(18.6%)	0.092
Arterial hypertension	55 (29.15%)	9 (19.8%)	46 (31.7%)	0.929
Ischemic cardiomyopathy	19 (10.1%)	4 (8.8%)	15 (10.4%)	0.987
Heart failure	10 (5.3%)	2 (4.4%)	8 (5.5%)	0.857
Previous stroke or TIA	12 (6.4%)	1 (2.2%)	11 (7.6%)	0.665
COPD	9 (4.8%)	1 (2.2%)	8 (5.5%)	0.359
Hepatic disease	9 (4.8%)	0 (0.0%)	9 (6.2%)	0.716
Cirrhosis	4 (2.1%)	1 (2.2%)	3 (2.1%)	0.519
Diabetes	37 (19.6%)	8 (17.6%)	29 (20%)	0.162
Chronic kidney disease	19 (10.1%)	6 (13.2%)	13 (9%)	0.824
Clinical presentation				
Pain	145 (76.8%)	39 (85.8%)	106 (73.1%)	0.078
Fever	69 (36.6%)	17 (37.4%)	52 (35.9%)	0.35
Neurological deficit	12 (6.4%)	2 (4.4%)	10 (6.9%)	0.085
Sensory deficit	9 (4.8%)	1 (2.2%)	8 (5.5%)	0.098
Neurological status				
Frankel A	2 (1.6%)	0	2 (1.4%)	0.002
Frankel B	3 (1.1%)	1 (2.2%)	2 (1.4%)	0.072
Frankel C	7 (3.7%)	1 (2.2%)	6 (4.2%)	0.437
Frankel D	9 (4.8%)	1 (2.2%)	8 (5.5%)	0.001
Frankel E	166 (88%)	39 (85.8%)	127 (89%)	0.539
Outcomes:				
Prolonged Hospitalization	54 (29.1%)	28 (62.1%)	26 (17.9%)	0.004
90-day Readmission	57 (30.2%)	25 (56.1%)	33 (23%)	0.0012
1 year mortality	29 (15.4%)	15 (34.1%)	14(10.3%)	0.022
Need for surgery	42 (22.3%)	11 (24.2%)	31 (21.7%)	0.067
Treatment informations				
Positive blood colture	85 (45.1%)	24 (55.2%)	61 (41.4%)	0.026
Need for biopsy	102 (54.1%)	18 (44.8%)	84 (58.6%)	0.019
Needle biopsy isolation	39 (20.7%)	4 (14.3%)	35 (23.8%)	0.023
Open biopsy isolation	27 (14.3%)	7 (16.6%)	20 (13.6%)	0.072
No isolation	36 (19.8%)	7 (16.6%)	29 (19.7%)	0.617
Shift to specific antibiotics therapy	151 (80%)	35 (80.5%)	116 (78.9%)	0.582
Pathogen with antibiotics resistance	37 (19.6%)	15 (34.5%)	22 (15%)	0.002

COPD: Chronic Obstructive Pulmonary Disease; CRP: C-reactive-protein; IQR: interquartile range; LoS: Length of stay; NLR: neutrophil-to-lymphocyte ratio; PCT: procalcitonin; PLR: platelet-to-lymphocyte ratio; TIA: transitory ischemic attack

NLR and PLR cut-off value determination

>Univariate analysis followed by ROC curve analysis was performed to identify optimal cut-off values for NLR and PLR in predicting the primary outcome of prolonged hospitalization. This analysis yielded a cut-off value of 7.78 for NLR and 174.2 for PLR. The area under the ROC curve (AUC) for NLR was 0.75 [95% CI 0.67–0.78], indicating good discriminatory power for predicting prolonged hospitalization. The AUC for PLR was 0.71[95% CI 0.62–0.73], suggesting moderate discriminatory ability. These ROC curve findings concerning primary outcome are visually represented in Fig. 1.

Association of NLR and PLR with prolonged hospitalization

An elevated NLR, defined as a value greater than 7.78, was observed in 57 patients (30.5% of the cohort). Among these patients with elevated NLR, 63.2% experienced prolonged hospitalization, in contrast to only 13.8% of patients with NLR values below the identified threshold. The sensitivity

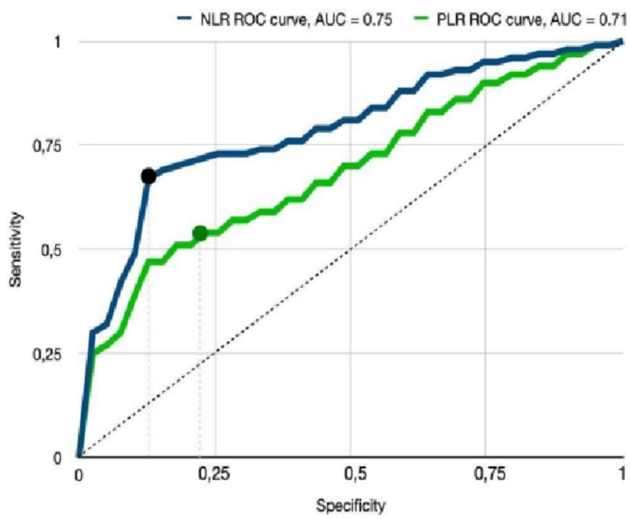

Fig. 1 Receiver Operating Characteristic (ROC) curves illustrating the predictive performance of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) for prolonged hospitalization (>15 days) in patients with pyogenic spondylodiscitis. The area under the curve (AUC) was 0.75 [95% CI 0.67–0.78] for NLR and 0.71 [95% CI 0.62–0.73] for PLR, indicating good and moderate discriminative ability, respectively. The dashed line represents no discrimination (AUC = 0.5). Cut-off values were 7.78 for NLR and 174.2 for PLR, as indicated by the dots on each curve

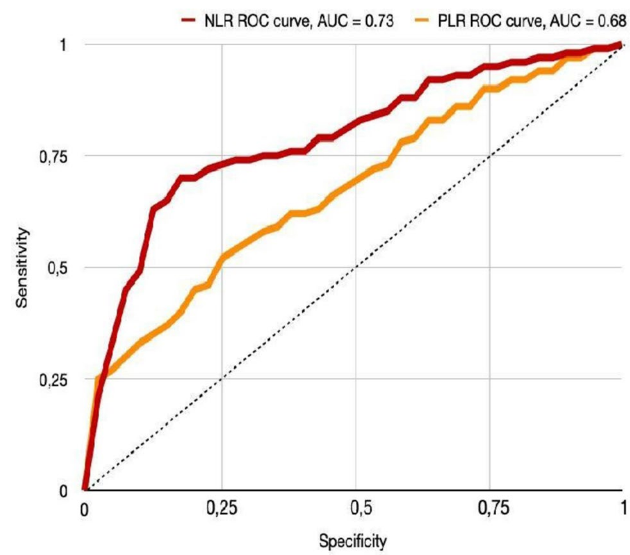

Fig. 2 Receiver Operating Characteristic (ROC) curves for the prediction of 90-day hospital readmission in patients with pyogenic spondylodiscitis based on NLR and PLR. The AUC was 0.73 [95% CI 0.65–0.77] for NLR, indicating moderate discriminative ability, and 0.68 [95% CI 0.61–0.73] for PLR, suggesting modest predictive capacity. The dashed line represents no discrimination (AUC = 0.5). Cut-off values were 7.78 for NLR and 174.2 for PLR

of NLR > 7.78 in predicting prolonged hospitalization was 66.7%, and the specificity was 84.2%. Similarly, 65 patients (34.7% of the cohort) presented with a PLR greater than 174.2. In this subgroup, 53.8% experienced prolonged hospitalization, compared to 15.6% among patients with lower PLR values. For predicting prolonged hospitalization, a PLR > 174.2 demonstrated a sensitivity of 64.7%, a specificity of 77.4%. In terms of risk assessment, an elevated NLR was associated with a 2.1-fold increased odds of prolonged hospitalization (OR 2.1, 95% CI 1.08–4.07). Similarly, an elevated PLR was associated with a 1.8-fold increased odds of prolonged hospitalization (OR 1.8, 95% CI 1.01–3.28).

Association of NLR and PLR with readmission

Patients with an NLR above the threshold of 7.78 exhibited a 1.7-fold higher risk of hospital readmission within 90 days (OR 1.7, 95% CI 1.01–2.94). An elevated PLR showed a borderline significant association with a 1.6-fold increased risk of 90-day readmission (OR 1.6, 95% CI 0.98–2.72). The ROC analysis cut-off value for NLR yielded a sensitivity of 63.2% and a specificity of 83.9% for predicting 90-day readmission, with an estimated AUC of 0.73 [95% CI 0.65–0.77], indicating moderate discriminative ability. However, the ROC curve for PLR cut-off value in predicting 90-day hospital readmission yielded a sensitivity of 52.6% and a specificity of 73.1%. The AUC was estimated at 0.68 [95% CI 0.61–0.73], suggesting a modest ability of PLR to discriminate against patients with higher risk for readmission (Fig. 2).

Association of NLR and PLR with one-year mortality

Regarding one-year mortality, an NLR greater than 7.78 was associated with a 2.4-fold increased risk of death (OR 2.4, 95% CI 1.18–5.07), and a PLR above 174.2 was associated with a 1.8-fold increased risk of one-year mortality (OR 1.8, 95% CI 1.02–3.42). At this threshold, NLR > 7.78 demonstrated a sensitivity of 72.4%, a specificity of 82.3%. The overall diagnostic accuracy was 75.9%, with an AUC of 0.78 [95% CI 0.69–0.82], indicating good discriminative ability. Concerning one-year mortality the PLR > 174.3 demonstrated a sensitivity of 58.6%, a specificity of 69.6%. The overall diagnostic accuracy was 67.9%, with an AUC of 0.68 [95% CI 0.56–0.72], indicating modest discriminative ability.

Association of NLR and PLR with surgery

When evaluating the need for surgical intervention, no statistically significant association was observed between elevated NLR or PLR values and the likelihood of undergoing surgery (NLR and PLR both above the cut-off: 24.2% vs. below cut-off: 21.7%, $p = 0.067$). This suggests that, unlike other adverse outcomes, higher inflammatory ratios at admission did not correlate with an increased probability of surgical treatment in this cohort.

Impact of combined NLR and PLR elevation

A subset of 42 patients (22.5% of the total cohort) presented with both elevated NLR (>7.78) and elevated PLR (>174.2) at admission. This group exhibited significantly worse clinical outcomes compared to the rest of the cohort. Specifically, these patients had a 3.4-fold increased odds of prolonged hospitalization (OR 3.4, 95% CI 2.48–4.66), a 2.4-fold increased odds of hospital readmission within 90 days (OR 2.4, 95% CI 1.62–3.55), and a 3.3-fold increased odds of all-cause mortality within one year (OR 3.3, 95% CI 2.17–5.03). Additionally, patients in this group showed higher rates of positive blood cultures (55.2% vs. 41.4%, $p=0.026$), but were less frequently subjected to biopsy procedures (44.8% vs. 58.6%, $p=0.019$) and had lower rates of pathogen isolation from needle biopsy samples (14.3% vs. 23.8%, $p=0.023$). Of note, the spectrum of isolated pathogens in this subgroup included a higher proportion of multidrug-resistant organisms (21.4% vs. 9.8%, $p=0.017$), particularly methicillin-resistant Staphylococcus aureus (MRSA) and extended-spectrum β-lactamase (ESBL)-producing Enterobacterales, which may have contributed to the observed worse outcomes (Fig. 3).

Sensitivity and multivariable analyses

After adjustment for the expanded set of covariates (age, sex, Charlson Comorbidity Index, diabetes mellitus, chronic kidney disease, body mass index, surgical intervention, blood culture positivity, infection by resistant pathogens, and the shift to targeted antibiotic therapy) elevated NLR (>7.78) and PLR (>174.2) remained independently associated with prolonged hospitalization, 90-day readmission, and one-year mortality. Adjusted odds ratios (aOR) were as follows: for NLR, prolonged hospitalization (aOR = 1.95, 95% CI 1.02–3.84), 90-day readmission (aOR = 1.62, 95% CI 1.01–2.81), and one-year mortality (aOR = 2.18, 95% CI 1.09–4.82); for PLR, prolonged hospitalization (aOR = 1.66, 95% CI 0.97–2.94) and one-year mortality (aOR = 1.71, 95% CI 1.01–3.28).

Propensity score matching and IPTW analyses confirmed consistent directional results, supporting the independence of these associations.

The calculated E-values were 3.62 for the association between NLR and prolonged hospitalization and 4.23 for one-year mortality, suggesting that an unmeasured confounder would need to have a risk ratio of ≥3.6–4.2 with both exposure and outcome to fully account for the observed effect.

These findings indicate that the associations between elevated inflammatory ratios and adverse outcomes are robust to potential residual confounding.

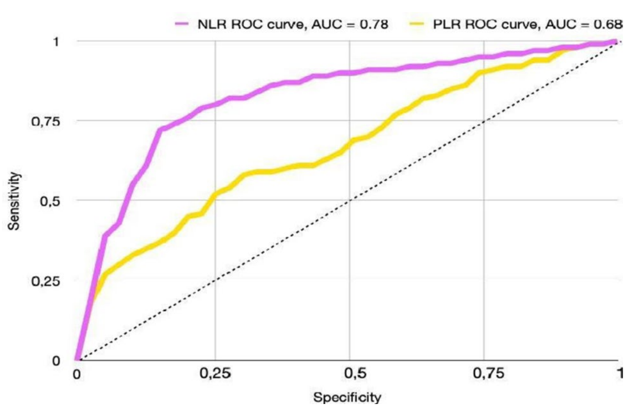

Fig. 3 Receiver Operating Characteristic (ROC) curves for the prediction of one-year mortality in patients with pyogenic spondylodiscitis based on NLR and PLR. For NLR, the AUC was 0.78 [95% CI 0.69–0.82], indicating good discriminative ability; for PLR, the AUC was 0.68 [95% CI 0.56–0.72], indicating modest discriminative ability. Cut-off values were 7.78 for NLR and 174.2 for PLR. The dashed line represents no discrimination (AUC = 0.5)

Antibiotics therapy regimens

In patients presenting with severe symptoms, neurological compromise, or signs of sepsis, empirical antimicrobial therapy was initiated immediately following blood and tissue cultures. The standard regimen consisted of a combination therapy aimed at covering the most prevalent pathogens, primarily Staphylococcus aureus (including potential Methicillin-Resistent *S. aureus*, MRSA) and common Gram-negative organisms. This typically involved Vancomycin (IV, dosed to maintain therapeutic trough levels) combined with either a third-generation Cephalosporin (e.g., Ceftriaxone, 2 g IV every 24 h) or a Fluoroquinolone (e.g., Ciprofloxacin, 400 mg IV every 8–12 h), based on individual patient risk factors.

Upon confirmation of the causative organism and its sensitivity profile, the regimen was switched to targeted therapy. For Methicillin-Sensitive *S. aureus* (MSSA), treatment involved a β-lactam, such as Cefazolin (2 g IV every 8 h). Cases of MRSA were primarily managed with Vancomycin or Linezolid (600 mg IV/oral every 12 h). For Gram-negative infections, targeted monotherapy with a highly active agent, such as a third-generation cephalosporin or a fluoroquinolone, was utilized. All patients received a mandatory initial intravenous phase of 2 to 4 weeks. Following clinical and inflammatory markers improvement, a switch to an oral agent with excellent bone penetration was performed, completing a total antibiotic course of 8 to 12 weeks.

Table 2 Association of elevated Neutrophil-to-Lymphocyte ratio (NLR) and Platelet-to- lymphocyte ratio (PLR) at emergency department admission with clinical outcomes in patients with pyogenic spondylodiscitis

Outcome Measure	Elevated NLR (>7.78) (*n* = 57)	Elevated PLR (> 174.2) (*n* = 65)	Both Elevated NLR & PLR (*n* = 42)
Prolonged Hospitalization (>15 days)	63.2% experienced it	53.8% experienced it	3.4-fold increased odds (OR 3.4, 95% CI 2.48–4.66)
Odds Ratio (vs. lower ratio)	2.1 (95% CI 1.08–4.07)	1.8 (95% CI 1.01–3.28)	–
90-day Readmission	1.7-fold higher risk (OR 1.7, 95% CI 1.01–2.94)	Borderline significant 1.6- fold increased risk (OR 1.6, 95% CI 0.98–2.72)	2.4-fold increased odds (OR 2.4, 95% CI 1.62–3.55)
One-Year Mortality	2.4-fold increased risk (OR 2.4, 95% CI 1.18–5.07)	1.8-fold increased risk (OR 1.8, 95% CI 1.02–3.42)	3.3-fold increased odds (OR 3.3, 95% CI 2.17–5.03)

In our cohort, the shift to pathogen-directed antibiotic therapy following microbiological identification was associated with improved outcomes, demonstrating a protective effect against prolonged hospitalization (OR = 0.58, 95% CI 0.34–0.96), 90-day readmission (OR = 0.62, 95% CI 0.38–0.99), and one-year mortality (OR = 0.55, 95% CI 0.31–0.93).

Discussion

Background and clinical implications

PSD and VO are increasingly recognized infectious conditions, particularly in aging populations with complex comorbidities. Despite their relatively low incidence, these infections are associated with significant morbidity and healthcare resource utilization. Previous studies have highlighted the role of systemic inflammatory markers such as CRP and PCT in the diagnostic and prognostic evaluation of spinal infections [1, 8]. However, the potential prognostic utility of hematological indices such as the NLR and PLR remains less well defined. The NLR and PLR are simple, widely available, and inexpensive biomarkers reflecting the balance between innate and adaptive immune responses [9, 10]. Elevated NLR values indicate a relative increase in neutrophilic inflammation and/or a suppression of lymphocytic activity, both of which have been implicated in poor outcomes across a variety of infectious and non-infectious conditions [7, 11]. Similarly, PLR has emerged as a potential marker of systemic inflammation and has been associated with adverse prognosis in sepsis, malignancy, and cardiovascular disease [12].

Elevations in NLR and PLR reflect a complex interplay between the innate and adaptive immune responses, typically triggered by systemic inflammatory stimuli. Neutrophilia, which drives the numerator in the NLR, is a hallmark of the acute phase reaction and is fueled by increased bone marrow output under the influence of pro-inflammatory cytokines such as IL- 1β, IL-6, and G-CSF [10]. This neutrophil predominance often occurs alongside lymphopenia, which may result from lymphocyte apoptosis, redistribution to lymphoid tissues, or impaired lymphopoiesis, all of which are well-recognized consequences of severe infection and physiological stress [10, 11]. Similarly, elevated platelet counts contributing to a higher PLR can be mediated by thrombopoietin release during inflammation, endothelial activation, and direct platelet–pathogen interactions that promote immune cell recruitment and cytokine amplification [11–13].

Nowadays the accurate and timely identification of factors associated with adverse outcomes in the management of PSD is crucial. Such early risk stratification has the potential to significantly alter the clinical and therapeutic approach to these complex and potentially debilitating infections. Recognizing patients at higher risk upon their initial presentation to the ED allows for more intensive monitoring, expedited specialist consultation, and a more proactive and tailored management strategy [1]. This may include earlier consideration of advanced imaging techniques, more aggressive antimicrobial regimens, closer monitoring for the development of complications such as epidural abscesses or neurological deterioration, and potentially a lower threshold for surgical intervention in selected cases. Ultimately, the goal of early risk stratification is to improve patient outcomes, reduce the length of hospital stays for those at lower risk, and potentially decrease the rates of readmission and mortality in this vulnerable patient population [13]. Our primary objective in this study was to identify readily available and cost-effective biomarkers, specifically the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) obtained at the time of ED admission, that could serve as early indicators of patients at increased risk for poor clinical outcomes. These initial values could act as a trigger for heightened clinical vigilance and potentially influence immediate management decisions (Table 2).

In our cohort, patients with elevated NLR and PLR exhibited a higher rate of positive blood cultures, suggesting that these indices may be more likely to rise in the presence of bacteremia. Moreover, this subgroup also showed a greater prevalence of infections caused by antibiotic- resistant pathogens, potentially indicating that more severe, treatment-resistant infections elicit a stronger and more dysregulated inflammatory response. In addition to hematological ratios, several infection-specific biomarkers and microbiological parameters may provide further insights into disease severity and prognosis in pyogenic spondylodiscitis. In our cohort, C- reactive protein (CRP) and procalcitonin (PCT) levels were systematically measured at admission, but no significant differences were observed between patients with favorable and unfavorable outcomes. This suggests that while CRP and PCT remain valuable diagnostic tools for confirming systemic inflammation and monitoring therapeutic response, their early prognostic utility appears limited compared to the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR).

Moreover, blood culture results were incorporated into the analysis, and patients with positive blood cultures exhibited higher NLR and PLR values, indicating a potential link between systemic inflammatory burden and bacteremia.

However, advanced molecular diagnostics such as next-generation sequencing (NGS), which can increase pathogen detection and characterize microbial diversity, were not routinely available during the study period.

Future studies integrating NGS data and longitudinal biomarker trends may further clarify the interplay between microbial factors and host inflammatory responses, refining prognostic models in this patient population.

In our cohort, looking ahead, we also recognize the potential utility of these markers in monitoring disease progression and response to treatment. Future investigations will explore whether changes in NLR and PLR during the course of antibiotic therapy correlate with treatment efficacy and whether these parameters can serve as valuable tools in the follow-up of patients with PSD to detect early signs of relapse or treatment failure.

Our findings in the context of existing literature

Our findings robustly demonstrate that elevated NLR (> 7.78) and PLR (> 174.2) measured at the time of admission to the Emergency Department are significantly associated with an increased risk of prolonged hospitalization, hospital readmission within 90 days, and one-year mortality in patients diagnosed with pyogenic spondylodiscitis. The moderate discriminatory ability of both NLR and PLR for predicting prolonged hospitalization, as indicated by the ROC curve analysis (AUC 0.75 for NLR and 0.71 for PLR), suggests their potential clinical utility as early prognostic markers. These results are consistent with a growing body of evidence across various medical fields, including other infectious diseases, where elevated NLR and PLR have been shown to correlate with disease severity and adverse outcomes [15–17]. The fact that these simple hematological ratios, derived from routine blood tests, can provide such valuable prognostic information underscores their potential for widespread clinical application, particularly in resource-limited settings where more expensive inflammatory markers like CRP and PCT may not be readily available [18, 19]. The synergistic effect observed when both NLR and PLR were elevated is particularly noteworthy. Patients exhibiting both high NLR and high PLR at admission had a substantially increased risk of all three adverse outcomes studied. This finding suggests that the combined assessment of these two readily available markers may offer a more refined and powerful tool for early risk stratification in PSD than either marker alone. The pathophysiological basis for this observation likely lies in the fact that NLR reflects the balance between pro-inflammatory (neutrophils) and anti-inflammatory (lymphocytes) components of the immune response, while PLR reflects the interplay between inflammation and thrombotic processes. An elevation in both ratios may therefore signify a more pronounced and dysregulated systemic inflammatory state, coupled with increased thrombotic potential, which could contribute to a more severe disease course and poorer outcomes in patients with spinal infections. Our results align with studies in other infectious conditions that have also reported the synergistic prognostic value of combined NLR and PLR [14, 15]. From a clinical standpoint, identifying patients with this dual elevation early in their presentation could trigger a more aggressive and multidisciplinary management approach.

Limitations and strengths of the study

Several limitations inherent to our study design warrant consideration when interpreting the findings. Firstly, the retrospective, single-center nature of our investigation may limit the generalizability of our results to other patient populations and healthcare settings. Variations in local diagnostic and treatment protocols could influence the observed associations. Secondly, while we employed multivariate logistic regression to adjust for several potential confounding factors, including age, sex, comorbidities, and initial severity indicators, the possibility of residual confounding due to unmeasured or unknown variables cannot be entirely excluded. Specifically, important clinical factors such as smoking status, alcohol use, diabetes control, nutritional status (including BMI and serum albumin levels), and pathogen exposure history were not systematically recorded and therefore not incorporated into the analysis. This omission represents a significant limitation that could have influenced the observed associations. For instance, the specific causative microorganism, the extent and location of the spinal infection, and the timing of antibiotic initiation, while important, may not have been fully captured by the variables included in our analysis. Although microbiological data from blood cultures and local biopsies were included, more advanced diagnostic modalities such as PCR-based assays and next-generation sequencing were not routinely utilized during the study period, potentially underestimating pathogen diversity. Thirdly, our analysis focused solely on the initial NLR and PLR values obtained at ED admission. It is plausible that the dynamic changes in these inflammatory markers during the course of hospitalization and treatment could provide additional prognostic information. Future prospective studies incorporating serial measurements of NLR and PLR may offer a more comprehensive understanding of their prognostic utility in PSD. Additionally, while neurological status was considerate at admission (Frankel grade), reliable data regarding neurological recovery during follow-up were not consistently available due to the retrospective design of the study, limiting our ability to analyze functional neurological outcomes. The study did not specifically investigate the relationship between NLR and PLR and the response to antibiotic therapy or their utility in long-term follow-up for detecting treatment failure or relapse. Moreover, antibiotic regimens were highly individualized based on pathogen identification and antimicrobial susceptibility profiles, preventing the standardization of treatment protocols across the cohort. This remains an important area for future research.

Finally, the expanded multivariate adjustment and the use of propensity score–based methods, our analysis remains subject to limitations inherent to retrospective designs. Some potentially relevant variables—such as smoking habits, alcohol use, detailed glycemic control parameters (e.g., HbA1c), and nutritional status—were not systematically recorded in the institutional database. To address this limitation, we calculated E-values, which indicated that unmeasured confounders would need to be strongly associated with both NLR/PLR elevation and adverse outcomes (risk ratio > 3–4) to fully explain the observed effects. This strengthens the likelihood that the reported associations reflect true clinical relationships rather than residual confounding.

Despite these limitations, our study possesses several notable strengths. Firstly, it is one of the first studies to specifically investigate the prognostic value of both NLR and PLR in a well- defined cohort of patients with pyogenic spondylodiscitis. Given the significant morbidity and mortality associated with this condition, the identification of simple and readily available prognostic markers is of considerable clinical importance. Secondly, the relatively large sample size of our study (which met the required threshold based on post-hoc power calculation) provided sufficient statistical power to detect significant associations between the hematological ratios and the clinical outcomes of interest. Thirdly, our rigorous methodology, including the use of ROC curve analysis to determine optimal cut-off values and multivariate regression analysis to assess the independent predictive value of NLR and PLR, strengthens the validity of our findings. Furthermore, the identification of a subgroup of patients with both elevated NLR and PLR who are at particularly high risk for adverse outcomes highlights the potential for a simple combined biomarker approach to improve early risk stratification in this challenging clinical scenario. Our findings contribute valuable insights to the growing body of literature supporting the clinical utility of NLR and PLR as readily accessible and cost-effective prognostic markers in infectious diseases, specifically in the context of spinal infections. Future prospective, multicenter studies are warranted to validate our findings and to further explore the dynamic changes in these markers and their utility in guiding treatment strategies and long- term management of pyogenic spondylodiscitis.

Conclusion

Our findings demonstrate that elevated NLR and PLR measured at the time of ED admission independently correlate with a higher risk of prolonged hospitalization, increased rates of hospital readmission within 90 days, and elevated one-year mortality in patients diagnosed with pyogenic spondylodiscitis and vertebral osteomyelitis. These readily available and inexpensive hematological indices hold promise as valuable tools for the early stratification of patients according to their risk of adverse outcomes, potentially complementing traditional clinical and microbiological evaluations. The simplicity and low cost of obtaining these ratios from routine blood tests make them particularly attractive for widespread clinical application. Moving forward, it is crucial to conduct further prospective, multicenter studies to validate these findings in larger and more diverse patient populations. Additionally, future research should focus on exploring the optimal integration of NLR and PLR into standardized clinical pathways for the management of spinal infections, investigating their dynamic changes during treatment, and assessing their utility in predicting response to therapy and long-term outcomes. The potential for these markers to guide early clinical decision-making and improve patient management warrants further comprehensive investigation.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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