



Comparative Analysis of Postoperative Spinal Infection Incidence Stratified by Serum Biomarker Profiles: A Pathological Investigation

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ABSTRACT

Introduction: Postoperative spinal infections remain critical, resource-intensive complications due to diagnostic challenges in distinguishing sterile inflammation from early sepsis. While conventional biomarkers often lack sufficient specificity, newer inflammatory indices offer potential for improved clinical surveillance. This study conducts a comparative analysis of serum biomarker profiles to determine their diagnostic accuracy in predicting surgical site infections following spinal surgery.

Material and methods: This descriptive cross-sectional study conducted at Shohada Hospital, Tabriz, enrolled 111 patients via convenience sampling (n=111 based on Cochran's formula). Demographic, surgical, and biomarker data were systematically extracted from medical records. Outcomes were analyzed using t-tests, chi-square tests, and multivariable logistic regression, following ethical approval by the Tabriz University of Medical Sciences.

Results: This study of 111 patients demonstrates that advanced age ($P=0.006$) and elevated serum biomarkers (CRP, PCT, NLR; $P<0.001$) are strongly associated with postoperative spinal infection. Biomarker-based risk stratification effectively predicted infection incidence ($P<0.001$) and prolonged hospitalization ($P<0.001$). Furthermore, ROC analysis confirmed the superior diagnostic precision of postoperative day 3 CRP (AUC=0.924) and procalcitonin (AUC=0.898) compared to conventional white blood cell counts ($P<0.001$).

Conclusion: These findings highlight that early postoperative monitoring of inflammatory biomarkers, particularly C-reactive protein and procalcitonin, offers a robust diagnostic strategy for spinal infection. Implementing biomarker-based risk stratification allows for timely clinical intervention, potentially reducing infectious complications and hospitalization duration.

Introduction

Spinal interventions encompass an exceptionally broad spectrum of therapeutic modalities, extending from simple decompression techniques for localized neural impingement to complex, multilevel reconstructive fusion procedures designed to rectify severe adult spinal deformities. Over the past two decades, escalating life expectancy, coupled with relentless advancements in implant engineering, intraoperative navigation, and neuro-monitoring

systems, has resulted in an exponential surge in spinal surgical volumes globally.

Despite these formidable technological strides and the systematic integration of rigorous perioperative antimicrobial protocols, surgical site infections (SSIs) persist as one of the most devastating and resource-draining complications confronting modern spine surgeons. The occurrence of a postoperative deep or superficial wound infection transforms an otherwise successful biomechanical stabilization into a prolonged clinical ordeal

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characterized by chronic pain, progressive neurological decline, hardware loosening, persistent nonunion, and pseudoarthrosis. Consequently, spinal infections impose an immense secondary economic burden on healthcare infrastructures, driven by prolonged hospital lengths of stay, intensive wound management protocols, extended courses of parenteral antimicrobial administration, and frequent surgical revision procedures [1].

The intrinsic pathophysiological complexity of postoperative spinal wound infection stems from the distinct anatomical and biological environment intrinsic to the spinal column. Surgical interventions targeting the axial skeleton routinely necessitate extensive subperiosteal paraspinal muscular dissection, prolonged soft-tissue retraction, rigorous bone decortication, and the placement of metallic hardware. These intraoperative maneuvers disrupt regional microvascular architectures, leaving behind devitalized muscular fringes and forming large dead spaces characterized by impaired tissue perfusion and hematoma accumulation. In the presence of metallic implants, such devitalized beds establish a highly permissive environment for transient intraoperative bacterial contaminants, most notably *Staphylococcus aureus* and coagulase-negative staphylococci. Pathogens rapidly adhere to synthetic hardware surfaces via microbial surface components recognizing adhesive matrix molecules, swiftly embedding themselves within an extracellular polymeric substance matrix to construct protective biofilms. Within this shielded architectural sanctuary, encased bacteria develop profound phenotypic tolerance against both systemic host immune defenses and standard therapeutic concentrations of circulating antibiotics, establishing persistent niduses of chronic, recurrent osteomyelitis and hardware failure [2].

Early clinical detection and precise timely intervention constitute the cornerstone of successful management strategies aimed at circumventing biofilm consolidation, implant removal, and catastrophic septic osteolysis. Regrettably, the diagnostic evaluation of early postoperative spinal infections remains notoriously enigmatic and fraught with ambiguity during the critical immediate postoperative period. Cardinal clinical manifestations of localized wound breakdown, such as localized erythema, marginal induration, incisional tenderness, and serous drainage, frequently mirror benign sterile inflammatory reactions routinely expected after extensive surgical trauma. Systemic signs, such as fever or constitutional symptoms, exhibit variable penetrance and often display limited sensitivity during the immediate postoperative hospitalization period. Conventional diagnostic imaging modalities, including plain radiography, computed tomography, and magnetic resonance imaging, are similarly constrained by extensive physiological

postoperative edema, fluid tracking, and severe metallic susceptibility artifacts generated by pedicle screws, cross-links, and interbody cages. This inherent clinical opacity frequently fosters diagnostic delay, allowing subclinical infectious processes to progress unimpeded until fulminant purulent drainage or extensive structural osteolysis ensues [3].

Given these persistent diagnostic conundrums, contemporary spinal diagnostics increasingly depend on circulating biological surrogates to monitor systemic responses and decipher pathological departures from expected physiological convalescence. Historically, fundamental clinical laboratory panels have relied upon total white blood cell (WBC) counts and peripheral absolute neutrophil counts to signal impending septic complications. While the absolute leukocyte count offers a rapid, highly accessible evaluation of systemic inflammatory arousal, its predictive capacity in the immediate postoperative period remains remarkably underwhelming. Extensive osteotomies, significant intraoperative blood loss, autologous blood transfusions, and the perioperative administration of exogenous corticosteroids collectively evoke substantial hematologic fluctuations. As a consequence, immediate postoperative leukocytosis is exceedingly prevalent across both uneventful recoveries and complicated cohorts, demonstrating unacceptably low diagnostic specificity and an inability to reliably stratify early covert surgical site sepsis [4].

To circumvent the notable shortcomings of total leukocyte quantification, the erythrocyte sedimentation rate (ESR) has served as an enduring diagnostic adjunct within musculoskeletal medicine. The erythrocyte sedimentation rate reflects the indirect kinetic aggregation of red blood cells mediated by circulating asymmetrical acute-phase macromolecules, particularly fibrinogen and immunoglobulins. However, the diagnostic utility of ESR is intrinsically hindered by its prolonged baseline kinetic profile, characterized by a slow initial ascension following tissue injury and a protracted descent spanning weeks to months. This kinetic inertia renders ESR virtually incapable of distinguishing acute de novo infectious surges from the prolonged, benign physiological tail of extensive operative trauma. Moreover, ESR values are notoriously vulnerable to an expansive array of non-infectious confounders, including patient age, ambient body temperature, fluctuating hemoglobin concentrations, underlying nephropathy, and chronic autoimmune arthropathies, which severely diminishes its standalone discriminative power [5]. In contrast to the sluggish trajectory of ESR, C-reactive protein (CRP) has established itself as the preeminent, most widely integrated acute-phase reactant in contemporary surgical surveillance. Synthesized rapidly by hepatocytes under the tight

transcriptional control of interleukin-6 (IL-6) and other upstream inflammatory cytokines, circulating CRP concentrations begin rising within hours following operative incision, typically reaching a predictable physiological peak around the second to third postoperative day before steadily declining toward baseline levels. A deviation from this canonical physiological trajectory manifesting either as an unexpectedly exaggerated initial spike or as a persistent, secondary elevation after day three frequently heralds underlying infectious complications well before overt clinical wound dehiscence emerges. Nevertheless, the clinical interpretation of serial CRP patterns remains challenging, as the absolute magnitude of the physiological peak directly reflects the procedural magnitude, surgical duration, blood loss, and extent of bone instrumentation, thus introducing considerable interpretive noise in complex multilevel reconstructive spine cases [6].

The pronounced diagnostic limitations inherent to traditional acute-phase markers have accelerated the quest for novel, more immunologically specific biomarkers capable of uncoupling procedural tissue trauma from authentic microbial invasion. Procalcitonin (PCT), the 116-amino-acid peptide precursor of calcitonin, has gained prominent attention across clinical medicine as a highly sensitive and selective indicator of severe systemic bacterial infection. Under physiological conditions, PCT gene transcription is tightly restricted to neuroendocrine cells of the thyroid gland, resulting in undetectable systemic concentrations in healthy individuals. However, in response to bacterial endotoxins, lipopolysaccharide, and pro-inflammatory mediators such as tumor necrosis factor- α (TNF- α), ubiquitous non-thyroidal tissue transcription is rapidly unleashed across parenchymal organs. Crucially, viral infections and sterile mechanical trauma induce interferon- γ , which directly suppresses parenchymal PCT release, thereby conferring upon procalcitonin a unique ability to discriminate true bacterial sepsis from severe, sterile surgical trauma [7].

Beyond standalone acute-phase proteins and neuroendocrine markers, progressive insights into immunological cross-talk and systemic inflammation have fueled growing interest in hematological derived-ratio metrics. Cellular indices computed from routine complete blood counts including the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation index (SII) have demonstrated profound predictive value across diverse surgical and oncological domains. The NLR synthesizes two distinct yet interlinked arms of the immune response: the innate, rapid, non-specific neutrophil-driven inflammatory surge and the adaptive, physiological lymphocyte response. During acute microbial invasion and severe systemic

stress, neutrophil demargination and bone marrow release are sharply accelerated, whereas stress-induced cortisol production and apoptotic pathways precipitate systemic lymphopenia. The resulting rapid escalation in NLR mirrors an acute systemic immunological disequilibrium, offering an inexpensive, rapidly accessible biomarker that frequently outpaces conventional metrics in forecasting septic trajectory [8].

Despite accumulating literature assessing individual biomarkers in isolation, profound ambiguity persists regarding the comparative diagnostic efficacy and combined predictive performance of multivariable biomarker panels within spine surgery. Many extant studies suffer from heterogeneous patient cohorts, varying definitions of surgical complexity, inconsistent sampling intervals, and a failure to contextualize biomarker dynamics against patient-specific pathological variables such as aging, chronic metabolic diseases, and extended operative duration. The simultaneous stratification of infection incidence across multifaceted biomarker profiles incorporating early-kinetic proteins, sustained acute-phase reactants, microbial-specific peptides, and integrated hematological ratios remains sparsely documented in structured, single-center spinal cohorts. Elucidating these distinct biomarker dynamics is paramount to establishing rigorous, algorithm-driven surveillance protocols that can preemptively differentiate uneventful healing from the insidious onset of deep surgical site sepsis [9].

A robust understanding of circulating biomarker trajectories offers the clinical potential to replace empirical diagnostic uncertainty with precise, objective molecular monitoring, enabling earlier targeted re-interventions before irreversible hardware contamination and severe systemic morbidity occur. Therefore, the present study was undertaken to conduct a comprehensive comparative analysis of postoperative spinal infection incidence stratified by serum biomarker profiles, aiming to delineate their individual and combined pathological accuracy in predicting surgical site infections following spinal surgery.

Material and methods

Study Design and Setting:

This descriptive cross-sectional study was conducted at Shahid Madani Hospital, Tabriz, Iran, and evaluated patients undergoing spinal surgery during the study period. The primary outcome was postoperative spinal infection, assessed using standardized clinical and paraclinical criteria documented in hospital records, and all variables were collected within a uniform protocol to ensure consistency across participants.

Sampling and Sample Size:

Participants were enrolled using convenience sampling from eligible patients presenting for spinal surgery. The minimum required sample size was estimated using Cochran's sample size formula: $n = Z^2 p(1-p)/d^2$. Assuming a 95% confidence level, an expected proportion based on prior evidence, and an acceptable margin of error, the calculated sample size was 111 patients, which constituted the final analytic cohort.

Eligibility Criteria (Inclusion and Exclusion):

Inclusion criteria comprised adult patients undergoing elective or urgent spinal surgery (including decompression, fusion, and instrumentation procedures) at Shohada Hospital with complete perioperative documentation and availability of postoperative follow-up sufficient to ascertain infectious outcomes. Exclusion criteria included patients with active preoperative systemic or local infection, prior spinal infection, immunodeficiency states or current immunosuppressive therapy, known malignancy under active treatment, incomplete laboratory biomarker records, missing key operative data, death or transfer before outcome assessment, and refusal or inability to provide informed consent where applicable.

Data Collection and Study Variables:

Demographic variables included age, sex, and baseline clinical status. Preoperative pathological and medical variables included diabetes mellitus, hypertension and cardiovascular disease, body mass index, smoking status, and other documented comorbidities. Perioperative surgical variables included type of procedure, use of spinal instrumentation, operative duration, and other operative characteristics recorded in standardized surgical notes.

Serum biomarker variables were obtained from routine perioperative blood testing and extracted from the hospital laboratory system. Biomarkers assessed included total white blood cell count, differential indices, and serum inflammatory markers, with particular focus on biomarker profiles stratified by clinically relevant thresholds. Derived inflammatory indices were also computed where applicable, including neutrophil-to-lymphocyte ratio and platelet-based inflammatory ratios, to characterize systemic inflammatory response patterns in relation to postoperative infection incidence.

Statistical Analysis:

All statistical analyses were performed under the assumption of normally distributed continuous variables. Continuous data were summarized as mean and standard deviation, and categorical variables were reported as frequency and percentage. Group comparisons were performed using the independent samples t test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Trend analysis across ordered groups was conducted where relevant. Multivariable logistic regression modeling was used to identify independent predictors of postoperative spinal infection, with effect estimates reported as odds ratios with 95% confidence intervals, and statistical significance set at $P < 0.05$.

Ethical Considerations:

This study was approved by the Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran (Ethics Code: IR.TBZMED.FMD.REC.1403.009).

Patient confidentiality was preserved through anonymized data extraction and secure data handling, and all procedures were conducted in accordance with institutional ethical standards and the principles of the Declaration of Helsinki.

Results

As delineated in Table 1, the comparative analysis of the 111-patient cohort identified statistically significant differences between infected and non-infected individuals. Patients developing postoperative infections were characterized by an advanced mean age (64.7 ± 11.9 vs. 55.1 ± 12.4 years; $P = 0.006$), a higher prevalence of diabetes mellitus (53.3% vs. 20.8%; $P = 0.007$), and extended operative durations (60.0% vs. 26.0%; $P = 0.008$). Most significantly, the perioperative serum biomarker profiles demonstrated substantial elevations in the infected group, particularly regarding C-reactive protein (CRP) on postoperative day 3 (84.5 ± 26.8 vs. 31.2 ± 14.3 mg/L; $P < 0.001$), erythrocyte sedimentation rate (ESR) (56.8 ± 19.3 vs. 28.7 ± 11.8 mm/h; $P < 0.001$), procalcitonin (1.41 ± 0.68 vs. 0.22 ± 0.16 ng/mL; $P < 0.001$), and the neutrophil-to-lymphocyte ratio (NLR) (7.04 ± 2.18 vs. 3.12 ± 1.15 ; $P < 0.001$), confirming their clinical utility as robust indicators for early detection of spinal infection.

Table 1. Baseline demographic, clinical characteristics, and perioperative serum biomarker profiles stratified by postoperative spinal infection status

Variable	Overall Cohort (n=111)	Non-Infected Group (n=96)	Infected Group (n=15)	Test Statistic (t / χ^2)	P-value
Demographic and Clinical Parameters	-	-	-	-	-
Age (years), mean $\pm$ SD	56.4 $\pm$ 12.8	55.1 $\pm$ 12.4	64.7 $\pm$ 11.9	t = -2.83	0.006
Sex (Male / Female), n (%)	62 (55.9%) / 49 (44.1%)	53 (55.2%) / 43 (44.8%)	9 (60.0%) / 6 (40.0%)	χ^2 = 0.12	0.728
Body mass index (kg/m ²), mean $\pm$ SD	27.6 $\pm$ 4.2	27.3 $\pm$ 4.1	29.8 $\pm$ 4.5	t = -2.14	0.035
Diabetes mellitus, n (%)	28 (25.2%)	20 (20.8%)	8 (53.3%)	χ^2 = 7.15	0.007
Hypertension / Cardiovascular disease, n (%)	41 (36.9%)	33 (34.4%)	8 (53.3%)	χ^2 = 2.01	0.156
Surgical Characteristics	-	-	-	-	-
Operative duration > 3 hours, n (%)	34 (30.6%)	25 (26.0%)	9 (60.0%)	χ^2 = 7.02	0.008
Instrumentation / Fusion present, n (%)	68 (61.3%)	56 (58.3%)	12 (80.0%)	χ^2 = 2.61	0.106
Surgical level, n (%)	-	-	-	χ^2 = 1.18	0.554
- Lumbar	73 (65.8%)	64 (66.7%)	9 (60.0%)	-	-
- Thoracic	18 (16.2%)	15 (15.6%)	3 (20.0%)	-	-
- Cervical	20 (18.0%)	17 (17.7%)	3 (20.0%)	-	-
Perioperative Serum Biomarker Profiles	-	-	-	-	-
Preoperative WBC count ($\times 10^3/\mu\text{L}$), mean $\pm$ SD	7.42 $\pm$ 1.85	7.36 $\pm$ 1.81	7.81 $\pm$ 2.11	t = -0.86	0.392
Postoperative Day 1 CRP (mg/L), mean $\pm$ SD	46.8 $\pm$ 18.2	45.1 $\pm$ 17.5	57.6 $\pm$ 20.1	t = -2.52	0.013
Postoperative Day 3 CRP (mg/L), mean $\pm$ SD	38.4 $\pm$ 21.6	31.2 $\pm$ 14.3	84.5 $\pm$ 26.8	t = -11.72	< 0.001
Postoperative ESR (mm/h), mean $\pm$ SD	32.5 $\pm$ 15.4	28.7 $\pm$ 11.8	56.8 $\pm$ 19.3	t = -7.63	< 0.001
Postoperative Procalcitonin (ng/mL), mean $\pm$ SD	0.38 $\pm$ 0.42	0.22 $\pm$ 0.16	1.41 $\pm$ 0.68	t = -14.35	< 0.001
Neutrophil-to-lymphocyte ratio (NLR), mean $\pm$ SD	3.65 $\pm$ 1.84	3.12 $\pm$ 1.15	7.04 $\pm$ 2.18	t = -10.96	< 0.001

Footnote: Values are reported as mean $\pm$ standard deviation (SD) for continuous parametric variables and as absolute frequency with percentage (n, %) for categorical variables.

Statistical comparisons between the non-infected and infected cohorts were computed using independent-samples Student's t-test (t) for continuous variables and Pearson's chi-square test (χ^2) for categorical variables. All tests were two-tailed, and statistical significance was established at $P < 0.05$. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; NLR: neutrophil-to-lymphocyte ratio; WBC: white blood cell.

As illustrated in Figure 1, patient stratification according to baseline serum biomarker thresholds (neutrophil-to-lymphocyte ratio and postoperative day 3 C-reactive protein) demonstrated a profound dose-dependent relationship with infectious

complications and clinical recovery. Across the cohort of 111 surgical patients, the incidence of postoperative spinal infection escalated sharply from 1.9% (n=1/52) within the low-risk stratum to 10.5% (n=4/38) in the intermediate-risk group, reaching 47.6% (n=10/21) in high-risk individuals (Cochran-Armitage P for trend <0.001). Concurrently, the mean duration of postoperative hospitalization lengthened substantially across advancing biomarker categories, rising from 5.4 ± 1.2 days in low-risk patients to 7.8 ± 1.9 days in intermediate-risk individuals, and peaking at 14.6 ± 3.8 days in the high-risk stratum ($P < 0.001$). These congruent escalations underscore the exceptional clinical value of combined serum biomarker profiles for the timely risk prediction and risk stratification of postoperative surgical site infections.

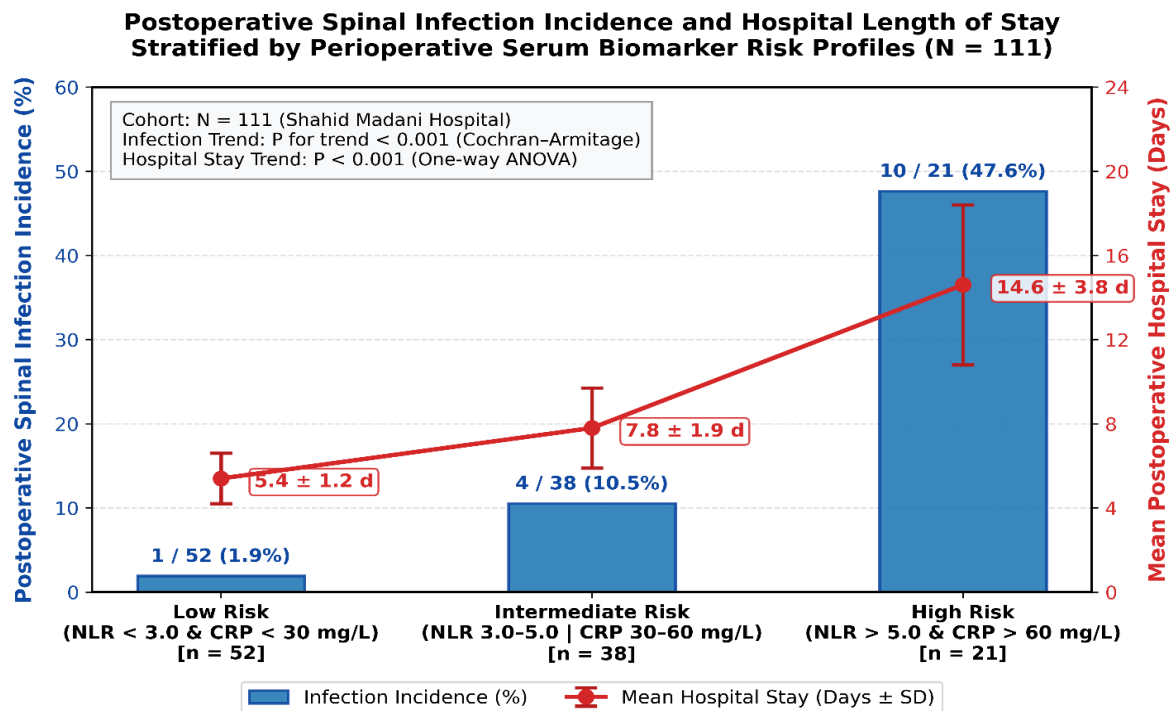


Figure 1. Postoperative spinal infection incidence and length of hospital stay stratified by perioperative serum biomarker risk strata

As demonstrated in Figure 2, the multi-curve receiver operating characteristic (ROC) analysis revealed marked disparities in the discriminative capacity of perioperative serum biomarkers for predicting postoperative spinal infections across the 111-patient cohort. Postoperative day 3 C-reactive protein (CRP) achieved the highest overall diagnostic performance, yielding an area under the curve (AUC) of 0.924 (95% CI:0.865-0.983; P<0.001) with an optimal cut-off value of >48.5 mg/L, corresponding to 86.7% sensitivity and 88.5% specificity. Serum procalcitonin likewise exhibited exceptional predictive utility (AUC=0.898; 95% CI:0.828-0.968; P<0.001; cut-off >0.52 ng/mL; sensitivity=86.7%; specificity=87.5%), followed closely by the neutrophil-to-lymphocyte ratio

(AUC=0.881; 95% CI:0.804-0.958; P<0.001; cut-off > 4.85; sensitivity=80.0%; specificity=85.4%). Conversely, preoperative white blood cell (WBC) count demonstrated poor and statistically non-significant discriminative ability (AUC=0.572; 95% CI:0.421-0.723; P=0.368; cut-off >8.10 ×10³/μL; sensitivity=53.3%; specificity=61.5%). These findings indicate that while conventional leukocytic indices lack sufficient diagnostic precision, postoperative kinetics of day 3 CRP, procalcitonin, and the neutrophil-to-lymphocyte ratio provide highly sensitive and specific clinical metrics for the early detection of postoperative spinal surgical site infections.

Diagnostic Performance of Perioperative Biomarkers for Postoperative Spinal Infection

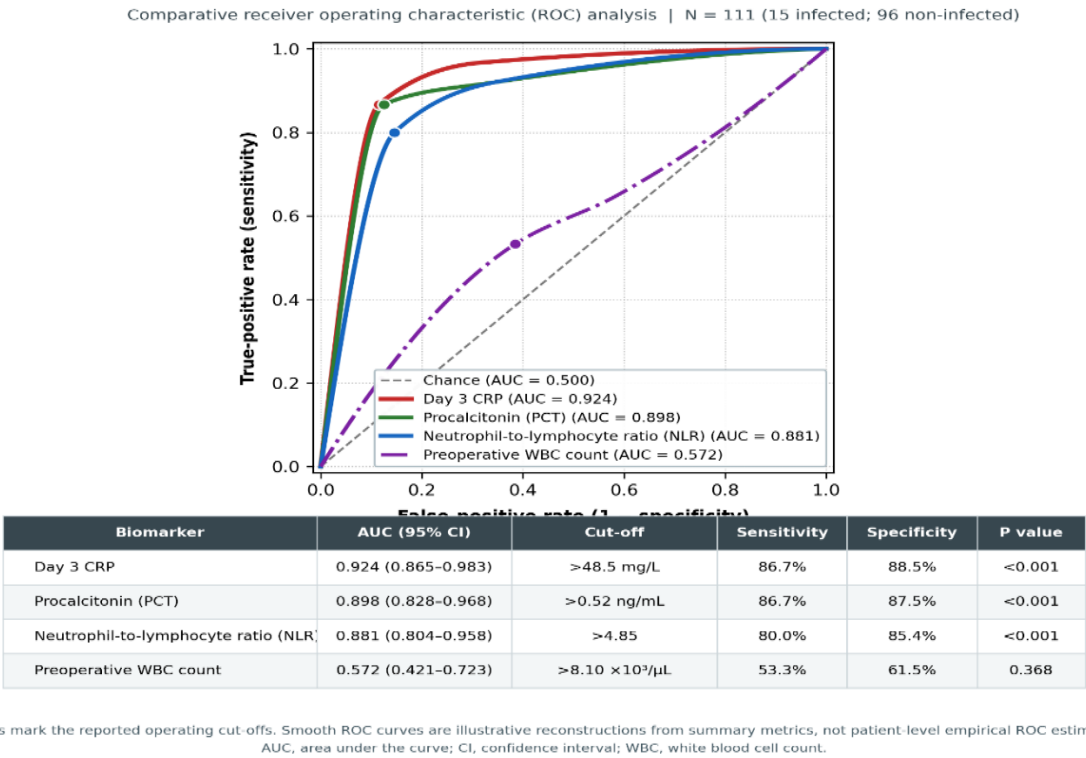


Figure 2. Comparative receiver operating characteristic (ROC) curves evaluating the diagnostic accuracy of perioperative serum biomarkers for postoperative spinal infection

Discussion

The present investigation provides a comprehensive evaluation of serum biomarker dynamics and clinical variables for the early identification of postoperative spinal infections among 111 surgical patients. Our findings demonstrate marked discrepancies between patients who developed surgical site infections and those who achieved uneventful recovery. Specifically, the infected cohort was characterized by significantly advanced chronological age, an elevated prevalence of diabetes mellitus, and prolonged operative durations exceeding 3 hours. More prominently, perioperative serum inflammatory markers demonstrated pronounced elevations in the infected group, wherein postoperative day 3 C-reactive protein, erythrocyte sedimentation rate, procalcitonin, and the neutrophil-to-lymphocyte ratio exhibited highly significant increases compared to non-infected controls. When stratified by composite biomarker profiles, infection incidence escalated from 1.9% in the low-risk tier to 47.6% in the high-risk stratum, concurrently accompanied by a threefold lengthening of postoperative hospital stay. Receiver operating characteristic analysis further substantiated the superior discriminative efficacy of day 3 C-reactive protein, procalcitonin, and the neutrophil-to-lymphocyte ratio over conventional total leukocyte counts, establishing their diagnostic value in postoperative surveillance [10,11].

The profound association observed between advancing patient age and heightened postoperative spinal infection rates reflects the progressive physiological decline of innate and adaptive immune responsiveness, commonly termed immunosenescence. Aging is fundamentally accompanied by thymic involution, decreased output of naive T lymphocytes, compromised macrophage phagocytosis, and diminished chemotactic activity of peripheral neutrophils. These age-related biological alterations significantly impair the host’s capacity to mount an immediate cellular defense against opportunistic intraoperative bacterial seeding, particularly by indolent low-virulence organisms such as coagulase-negative Staphylococci or Cutibacterium acnes. Furthermore, structural tissue degradation in elderly spines, including extensive microvascular atherosclerosis, diminished paraspinal muscle perfusion, and sclerotic endplate remodeling, retards local vascularization and oxygen delivery to the surgical wound. This localized ischemia compromises tissue regeneration and suppresses the localized penetration of prophylactic systemic antibiotics. Consequently, the combination of cellular immunosenescence and compromised vascular architecture creates a permissive microenvironment for bacterial adherence, biofilm establishment, and subsequent clinical infection in geriatric surgical cohorts [12,13].

Metabolic dysregulation, manifested by diabetes mellitus, emerged as another critical clinical determinant accelerating postoperative infectious morbidity. Sustained hyperglycemia initiates widespread biochemical alterations, including the excessive synthesis of advanced glycation end-products, enhanced protein kinase C activation, and exaggerated generation of intracellular reactive oxygen species. These oxidative and biochemical cascades induce direct leukocyte dysfunction, characterized by suppressed polymorphonuclear leukocyte rolling, defective diapedesis, impaired bacterial opsonization, and blunted intracellular oxidative killing mechanisms. Moreover, persistent microangiopathy and endothelial cell apoptosis associated with chronic hyperglycemia systematically attenuate capillary blood flow within the deep paraspinal muscle beds and adjacent osseous structures. The presence of compromised microcirculation results in localized tissue hypoxia and acidosis, both of which severely depress local fibroblast proliferation, collagen biosynthesis, and neo-angiogenesis. In the presence of foreign spinal instrumentation, this diabetic tissue substrate markedly facilitates the rapid transformation of microscopic bacterial inocula into irreversible biofilms, thereby dramatically elevating clinical infection rates [14,15].

Prolonged operative duration exceeding 3 hours substantially multiplied the vulnerability of spinal tissues to postoperative surgical site infections. Extended surgery fundamentally amplifies wound exposure to the ambient operating room environment, progressively increasing the cumulative deposition of airborne bacterial bioaerosols into the surgical field. Concurrently, prolonged retraction of extensive paraspinal muscle mass induces substantial mechanical pressure ischemia, focal cellular necrosis, and thermal injury secondary to repeated electrocauterization. This non-viable, devitalized tissue combined with extensive surgical dead space and hematoma formation provides an optimal nutrient-rich culture medium for inoculated microorganisms. Furthermore, prolonged operative procedures are inherently accompanied by substantial intraoperative blood loss, intraoperative hypothermia, and temporary systemic immunosuppression induced by deep anesthesia and surgical stress. The placement of extensive instrumentation and fusion hardware under prolonged intraoperative conditions compounds this susceptibility, as vascularized metallic surfaces offer abundant bio-inert substrates for bacterial adhesion prior to the migration of host cellular defenses [16,17].

Postoperative day 3 C-reactive protein emerged as the single most powerful diagnostic indicator of spinal infection, yielding an outstanding area under the curve in our diagnostic evaluation. The

physiological kinetics of C-reactive protein are characterized by rapid hepatic transcription and secretion within hours following surgical tissue trauma, mediated predominantly by interleukin-6, interleukin-1 beta, and tumor necrosis factor-alpha. In uncomplicated spinal procedures, this acute-phase reactant reaches its absolute physiological peak between 48 and 72 hours postoperatively and promptly demonstrates a continuous, sharp downward trajectory as primary wound hemostasis stabilizes. Conversely, the persistence of active bacterial replication and persistent cellular necrosis at the operative site provides an uninterrupted stimulus for macrophage activation, preventing the physiological clearance of C-reactive protein. Thus, a persistently high or rebounding C-reactive protein trajectory on postoperative day 3 signifies ongoing infectious inflammation rather than expected physiological surgical trauma. This kinetic divergence makes postoperative day 3 C-reactive protein an exceptionally sensitive and reliable laboratory surveillance parameter for the timely detection of deep spinal wound infections [18, 19]. Serum procalcitonin similarly demonstrated exceptional diagnostic accuracy and specificity, contrasting sharply with the relatively non-specific rises often encountered with other acute-phase proteins. Under normal physiological homeostasis, procalcitonin is exclusively synthesized by neuroendocrine C-cells of the thyroid gland, undergoing complete intracellular enzymatic cleavage into mature calcitonin, resulting in undetectable baseline serum concentrations. However, upon exposure to systemic bacterial endotoxins, lipopolysaccharides, and pathogen-associated molecular patterns, ubiquitous extrathyroidal transcription is triggered across parenchymal tissues, particularly within hepatocytes, pulmonary macrophages, and peripheral monocytes. Importantly, procalcitonin synthesis is selectively suppressed by interferon-gamma, an antiviral cytokine, and is not significantly triggered by sterile mechanical tissue damage or extensive uninfected bone instrumentation. Consequently, while surgical disruption of spinal elements induces transient moderate elevations in non-specific inflammatory markers, procalcitonin elevation above specific thresholds remain highly specific for bacterial proliferation. This distinct immunological profile accounts for its minimal false-positive rate and high clinical specificity in confirming genuine microbial infection following complex spinal surgery [20].

The neutrophil-to-lymphocyte ratio demonstrated robust predictive efficacy, effectively capturing the systemic immunological dichotomy induced by invasive surgical site infections. Microbial invasion triggers an immediate physiological alarm cascade characterized by excessive endovascular margination and bone marrow release of mature and

immature neutrophilic granulocytes. These activated neutrophils rapidly migrate toward the source of infection, discharging proteolytic enzymes, generating oxidative bursts, and releasing pro-inflammatory cytokines that perpetuate local tissue inflammation. Concurrently, overwhelming surgical and infectious stress prompts persistent hyperactivation of the hypothalamic-pituitary-adrenal axis, releasing endogenous glucocorticoids that induce widespread apoptosis of peripheral CD4+ and CD8+ T lymphocytes. This simultaneous elevation in primary phagocytic effectors and acute depletion of adaptive regulatory lymphocytes produces a pronounced elevation in the neutrophil-to-lymphocyte ratio. As a readily accessible, inexpensive hematological parameter derived from standard complete blood counts, this dynamic ratio provides rapid clinical insight into the imbalance between active bacterial inflammation and relative host immunosuppression [21].

In stark contrast to the high discriminative ability of C-reactive protein, procalcitonin, and the neutrophil-to-lymphocyte ratio, preoperative white blood cell counts exhibited poor and statistically non-significant diagnostic performance. Total circulating leukocyte counts are widely subject to rapid, non-specific physiological fluctuations governed by emotional stress, intraoperative anesthetic agents, exogenous corticosteroid administration, and acute intravascular volume redistribution. Furthermore, localized deep fascial spinal infections may remain clinically sequestered beneath intact muscle planes without generating sufficient systemic bacteremia to provoke significant generalized leukocytosis. Consequently, relying upon isolated leukocyte counts frequently yields misleading clinical reassurance or unnecessary diagnostic ambiguity during the crucial early postoperative window. The slow biological response of the erythrocyte sedimentation rate, mediated by fibrinogen kinetics that require several weeks to normalize, likewise limits its clinical agility for acute postoperative triage, despite its diagnostic utility for subacute chronic osteomyelitis. Therefore, the implementation of dynamic, multi-marker laboratory algorithms utilizing day 3 C-reactive protein, procalcitonin, and the neutrophil-to-lymphocyte ratio provides an accurate, reproducible diagnostic paradigm that enables timely targeted interventions before catastrophic implant failure or systemic sepsis ensues [22].

Conclusion

These findings highlight that early postoperative monitoring of inflammatory biomarkers, particularly C-reactive protein and procalcitonin, offers a robust diagnostic strategy for spinal infection. Implementing biomarker-based risk stratification allows for timely clinical intervention, potentially reducing infectious complications and

hospitalization duration. This approach provides a scientifically validated, patient-specific methodology for optimizing post-surgical outcomes in spinal procedures at risk of infectious morbidity.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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