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Comparison of Preoperative Serum Albumin and C-Reactive Protein Levels in Relation to Surgical Site Infection Following Femoral Implant Placemen

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A B S T R A C T

Introduction: Surgical site infections following femoral implant placement cause severe morbidity, often driven by host malnutrition and baseline inflammation. Serum albumin and C-reactive protein (CRP) reflect metabolic reserve and systemic inflammatory tone, respectively. Therefore, this study aimed to compare preoperative serum albumin and CRP levels in relation to surgical site infection incidence following femoral implant placement.

Material and methods: This analytical cross-sectional study enrolled 125 consecutive patients undergoing primary femoral implant surgery at shohada Hospital, Tabriz. Baseline preoperative serum albumin and C-reactive protein concentrations were quantified alongside comprehensive clinical and operative variables. Patients underwent systematic surveillance over a 90-day postoperative period to adjudicate surgical site infections based on CDC/NHSN criteria, evaluating biomarker predictive performance through comparative and multivariable regression analyses.

Results: Patients developing surgical site infections demonstrated significantly reduced preoperative serum albumin (3.12±0.46 versus 3.89±0.49 g/dL; P<0.001) and elevated hs-CRP concentrations (20.38±6.84 versus 7.31±4.58 mg/L; P<0.001). Multivariable logistic regression identified preoperative hypoalbuminemia (aOR=7.845, 95% CI: 1.614 to 38.128; P=0.011), elevated hs-CRP (aOR=9.132, 95% CI:1.684 to 49.524; P=0.010), low albumin-to-CRP ratio (aOR=11.418, 95% CI: 1.925 to 67.726; P=0.007), and prolonged operative duration (aOR=4.892; P=0.044) as independent infection predictors.

Conclusion: Preoperative hypoalbuminemia and elevated C-reactive protein levels are potent independent predictors of postoperative surgical site infections following femoral hardware fixation. Preoperative screening with these cost-effective biomarkers, particularly the composite albumin-to-CRP ratio, facilitates early risk stratification and enables targeted nutritional and anti-inflammatory interventions to mitigate implant infection rates.

Introduction

Orthopedic reconstructive and trauma procedures involving the femur represent some of the most frequently performed and biomechanically demanding interventions in contemporary surgical practice. Whether indicated for high-energy traumatic fractures, pathological osseous lesions, osteoarthritic joint destruction, or avascular necrosis of the femoral head, internal fixation and arthroplasty using metallic or composite implants have revolutionized functional restoration and patient mobility.

Despite advances in perioperative care, surgical techniques, sterile processing, and laminar airflow operating environments, surgical site infection (SSI) remains among the most devastating and refractory

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complications encountered in orthopedic surgery. SSIs involving femoral implants range from superficial incisional disruptions to profound periprosthetic joint infections and chronic osteomyelitis, frequently necessitating prolonged intravenous antimicrobial therapy, repeated surgical debridement, implant removal, and complex staged revision reconstructions [1].

The physical, psychological, and socioeconomic consequences of surgical site infections following femoral instrumentation are profound and far-reaching. Patients who develop post-fixation or post-arthroplasty infections endure protracted hospital stays, secondary mechanical failure, compromised ambulatory function, chronic pain syndromes, and substantially heightened perioperative mortality rates. From an institutional and public health perspective, the clinical management of an infected femoral implant imposes an exorbitant economic burden on tertiary healthcare infrastructures, involving costly diagnostic modalities, multidisciplinary infectious disease consultations, and prolonged critical care dependency. Consequently, the identification of reliable, reproducible, and easily accessible preoperative risk stratification tools has become a paramount priority in contemporary orthopedic research, with an increasing emphasis on modifiable host-related physiological factors rather than operative variables alone [2].

The pathogenesis of surgical site infections surrounding permanent metallic hardware is intimately tied to the unique local biological microenvironment created by the foreign body itself. The introduction of an artificial substrate, such as titanium, stainless steel, or cobalt-chromium alloys, creates a localized zone of acquired immune compromise characterized by impaired neutrophil bactericidal function and decreased macrophage phagocytic capacity. Bacterial pathogens, predominantly staphylococcal species such as Staphylococcus aureus and Staphylococcus epidermidis, adhere to the implant surface and elaborate a structured, exopolysaccharide-rich extracellular matrix termed a biofilm. Within this sessile biofilm architecture, microcolonies exhibit profound phenotypic resistance to host humoral and cellular defense mechanisms as well as systemic antimicrobial agents. Because eradication of established biofilm-associated infections without hardware explanation is rarely achievable, mitigating baseline host vulnerability prior to the initial incision represents the most effective strategy for infection prevention [3].

Among the multitude of host-related systemic determinants influencing postoperative infection susceptibility, systemic nutritional compromise has emerged as a critical yet frequently underappreciated factor. Adequate nutritional reserve is essential for orchestrating the complex sequence of cellular events required for primary surgical wound healing, including fibroblast proliferation, collagen cross-linking, local angiogenesis, and the physiological resilience that

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places the surgical patient at an elevated risk of infectious complications [6].

In parallel with nutritional derangements, chronic low-grade or acute systemic inflammation represents another major determinant of postoperative infectious risk. C-reactive protein (CRP), a prototypical positive acute-phase reactant belonging to the pentraxin superfamily, is rapidly synthesized by hepatocytes in response to circulating inflammatory cytokines, most notably IL-6. Under physiological resting conditions, serum CRP levels remain minimal; however, upon the onset of systemic tissue injury, occult infectious processes, autoimmune activation, or persistent systemic distress, circulating CRP concentrations rise precipitously within several hours. Elevated baseline CRP concentrations signal a state of systemic immunological priming and cytokine-driven stress, which can lead to dysregulated immune responses and impaired local pathogen clearance following major surgical trauma [7].

Sustained elevation of preoperative CRP levels is frequently observed in patient populations undergoing femoral implant procedures, including elderly patients with underlying chronic inflammatory joint disorders, metabolic syndrome, peripheral vascular disease, or those experiencing occult systemic tissue injury following low-energy fragility fractures. This preexisting state of systemic inflammation compromises postoperative immune equilibrium, leading to premature immune cell exhaustion, dysregulated cytokine signaling, and attenuated oxidative burst capacity in circulating neutrophils. When an invasive procedure involving extensive soft-tissue dissection, intramedullary reaming, and foreign material implantation is superimposed on an already inflamed host, the impaired immune response creates a permissive environment for opportunistic microbial colonization along the freshly prepared bone-hardware interface [8].

Recognizing that nutritional status and inflammatory activity are interconnected biological processes has driven significant interest in combined nutritional-inflammatory assessment tools. Evaluating either serum albumin or CRP in isolation often fails to capture the full spectrum of a patient's systemic vulnerability, as an isolated low albumin level might reflect acute systemic stress rather than true starvation, while an isolated high CRP may indicate transient systemic irritation. In contrast, the concurrent evaluation of both biomarkers provides a comprehensive profile of metabolic reserves and inflammatory tone. This combined approach has proven valuable across diverse surgical disciplines, notably in oncology and gastrointestinal surgery, where ratios and indexes integrating albumin and CRP—such as the Glasgow Prognostic Score—have demonstrated strong prognostic accuracy for adverse outcomes, anastomotic breakdown, and deep infectious morbidity [9].

Despite the growing recognition of nutritional and inflammatory biomarkers in general and gastrointestinal surgical specialties, their specific combined utility in major orthopedic implant surgery remains insufficiently characterized. Femoral instrumentation involves distinctive anatomical and biomechanical considerations, including the presence of an extensive vascularized muscular envelope, large intramedullary and periosteal surface areas, and the introduction of substantial metallic biomaterials that are susceptible to hematogenous and direct peroperative bacterial seeding. Although several individual investigations have suggested separate links between either hypoalbuminemia or elevated CRP and orthopedic complications, existing literature remains fragmented, with conflicting cut-off thresholds, disparate patient populations, and variable surgical indications, leaving the comparative and synergistic predictive value of these two routine biochemical parameters incompletely defined [10].

Establishing clear, evidence-based preoperative thresholds for serum albumin and CRP holds substantial clinical utility for risk stratification and individualized perioperative care in femoral implant surgery. Identification of high-risk patients during the preoperative workup offers an actionable window for multidisciplinary intervention, including targeted preoperative nutritional supplementation, careful glycemic control, optimization of underlying chronic inflammatory conditions, and tailored antimicrobial stewardship. Furthermore, accurate risk profiling can guide surgical decision-making regarding the timing of elective procedures, the choice of fixation construct, the duration of closed-suction drainage, and the intensity of postoperative clinical and serological monitoring for early signs of wound breakdown [11].

Given the devastating physical, functional, and financial burdens of deep surgical site infections following femoral hardware fixation, comprehensive research is needed to determine the predictive capacity of routine preoperative laboratory parameters. Understanding how baseline metabolic reserves and subclinical inflammatory states correlate with postoperative septic complications will help clinicians implement proactive risk-reduction protocols. Therefore, the present study was designed to compare preoperative serum albumin and C-reactive protein levels in relation to the incidence of surgical site infection following femoral implant placement.

Material and methods

Study Design:

This investigation was conducted as an analytical cross-sectional study at Shahid Madani Educational and Medical Center, affiliated with Tabriz University of Medical Sciences, Tabriz, Iran, spanning from March 2024 to February 2025. The primary objective was to evaluate and compare preoperative baseline concentrations of serum albumin and C-reactive protein (CRP) in patients undergoing major femoral implant placement procedures and to assess their direct correlation with the subsequent manifestation of surgical site infections (SSIs). The clinical environment of Shohada Hospital functioning as a tertiary academic referral center equipped with specialized orthopedic traumatology wards, advanced operating suites, dedicated intensive care units, and a centralized clinical chemistry laboratory provided a standardized and controlled setting for patient recruitment, uniform surgical care pathways, and systematic post-intervention surveillance.

Sampling and Sample Size Estimation

Participant enrollment was executed utilizing a non-probability convenience sampling technique among all eligible consecutive candidates presenting to the department of orthopedic surgery for femoral implant instrumentation. The requisite sample size was determined a priori using the standard single-population proportion formula (Cochran's formula) for observational studies: $n=Z1-\alpha/22 \cdot p(1-p)$ d2was set at 1.96 corresponding to a two-sided 95% confidence interval ($\alpha=0.05$). Based on cumulative data from published regional and international literature indicating an anticipated post-fixation femoral surgical site infection incidence (p) of approximately 8.5%, and establishing an absolute precision margin (d) of 0.05, the initial mathematical calculation yielded an optimal target cohort of approximately 120 patients. To account for potential post-discharge attrition, missing biochemical panels, or voluntary withdrawal during the 90-day clinical monitoring timeline, the target population was definitively adjusted upward to finalize an analytical cohort of exactly 125 patients.

Inclusion and Exclusion Criteria

Rigorous eligibility criteria were applied during the preoperative outpatient consultation or immediate emergency trauma admission to construct a well-defined study cohort. Eligible participants comprised adult patients aged 18 years or older who were scheduled to undergo primary open femoral implant placement including cephalomedullary nailing, dynamic hip screw (DHS) fixation, proximal or distal femoral anatomical locking compression plates, or hemi/total femoral arthroplasty and who agreed to provide written informed consent alongside adhering strictly to the designated postoperative follow-up protocol. Conversely, individuals were rigorously excluded if they met any of the following clinical conditions: preexisting systemic active infectious foci (such as osteomyelitis, pneumonia, or complicated urinary tract infections), prior revision or staged hardware reconstruction on the ipsilateral femur, pathological fractures secondary to primary bone malignancies or widespread skeletal metastases, advanced hepatic cirrhosis (Child-Pugh Class B or C) causing intrinsic hypoalbuminemia, end-stage renal disease necessitating maintenance hemodialysis, chronic autoimmune or inflammatory rheumatologic diseases (e.g., systemic lupus erythematosus, active rheumatoid arthritis), recent therapeutic administration of systemic corticosteroids, immunosuppressive agents, or antineoplastic chemotherapy within the preceding six months, human immunodeficiency virus (HIV) seropositivity, or pre-admission administration of exogenous human serum albumin infusions within four weeks prior to surgery.

Study Procedure and Variables

Upon formal admission, comprehensive baseline demographic, anthropometric, and clinical features were prospectively retrieved and entered into an electronic case record form. Evaluated variables comprised biological age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared), tobacco smoking habits, and American Society of Anesthesiologists (ASA) physical status classification, alongside major metabolic and systemic comorbidities including type 2 diabetes mellitus, essential arterial hypertension, chronic obstructive pulmonary disease, and ischemic cardiovascular disease. Detailed perioperative parameters were recorded directly from surgical logs, capturing primary surgical indications (acute traumatic subtrochanteric, intertrochanteric, or shaft fracture versus primary hip joint osteoarthritis), exact implant architecture utilized (intramedullary nail versus plate-screw construct versus modular arthroplasty stem), scheduled or emergency procedural status, net operative duration from initial skin incision to completed wound closure (minutes), estimated intraoperative total blood loss (milliliters), requirement for allogeneic red blood cell transfusions, closed-suction intra-articular or subfascial drainage usage, and the precise timing of intravenous prophylactic antibiotic administration (cefazolin 2 g given within 60 minutes prior to surgical incision).

Venous blood samples were collected under resting morning conditions within 24 hours prior to surgery to profile baseline nutritional and acute-phase inflammatory indices. Collected specimens were processed immediately at the central hospital laboratory using automated analyzer platforms;

quantitative serum albumin concentrations were measured spectrophotometrically via the bromocresol green (BCG) dye-binding method and expressed in grams per deciliter (g/dL), while quantitative high-sensitivity C-reactive protein (hs-CRP) concentrations were determined using particle-enhanced immunoturbidimetric assays and expressed in milligrams per liter (mg/L). Complete hemograms (total leukocyte counts, absolute neutrophil and lymphocyte counts, hemoglobin, and platelets), serum creatinine, blood urea nitrogen, and fasting plasma glucose were recorded concurrently. Following surgery, patients were followed throughout their index hospitalization and at protocolized outpatient intervals (at 2,4,8 and 12 weeks postoperatively) to identify the occurrence of surgical site infections, strictly adjudicated according to the standard surveillance criteria established by the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) for deep and superficial incisional infections involving surgical implants within 90 days of the primary operation.

Statistical Analysis

Statistical computation was performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous demographic, laboratory, and operative variables were verified for distribution properties and demonstrated satisfactory adherence to normality assumptions via visual assessment of standard histogram curves, Q-Q plots, and formal Shapiro-Wilk testing (P>0.05P > 0.05P>0.05); these data are expressed as means with standard deviations (Mean ± SD). Nominal and ordinal categorical variables are summarized as absolute counts and corresponding percentages (nnn, %). Comparative analyses between patients who developed surgical site infections and those who remained uninfected were executed using the two-tailed Independent Samples ttt-test for continuous variables, whereas the Pearson Chi-Square test or Fisher's exact test was applied for cross-tabulated categorical variables as appropriate. Receiver operating characteristic (ROC) curve analysis was generated to determine the diagnostic discriminative capability and optimal cutoff values of preoperative albumin, CRP, and the albumin-to-CRP ratio for predicting infection, reporting the area under the curve (AUC), 95% confidence intervals (CI), sensitivity, and specificity. Univariate and multivariable binary logistic regression analyses were computed to calculate crude and adjusted odds ratios (aOR) with 95% CIs to identify independent predictors of postoperative implant infection, with statistical significance set at a two-tailed PPP-value of <0.05.

Ethical Considerations

The institutional protocol and experimental methodology governing this study received formal review and unanimous clearance from the Regional Ethics Committee of Tabriz University of Medical Sciences (Ethics Code: IR.TBZMED.REC.1404.008). The trial was conducted in strict compliance with the ethical tenets delineated in the Declaration of Helsinki (1975 revision and its subsequent amendments) as well as national clinical research guidelines. Prior to study entry, written informed consent was acquired from all conscious, legally competent participants or their authorized legal surrogates after delivering an explicit verbal and written explanation regarding the study's investigative nature, voluntary participation, and freedom to withdraw without compromising routine medical care. All patient-identifying clinical records and laboratory parameters were fully anonymized and assigned encrypted numerical identification codes to safeguard absolute patient confidentiality throughout data handling, statistical computation, and manuscript preparation.

Results

As presented in Table 1, out of the 125 evaluated patients undergoing femoral implant surgery, 11 individuals (8.80%) developed postoperative surgical site infections within the 90-day follow-up period. Patients who developed surgical site infections exhibited a significantly higher mean body mass index (29.34 ± 4.81 kg/m2 versus 26.61 ± 3.98 kg/m2; P=0.033) and a greater proportion of obesity (54.55% versus 19.30%; P=0.007) compared with the uninfected cohort. Additionally, higher rates of American Society of Anesthesiologists physical status class III or greater (72.73% versus 33.33%; P=0.008) and preexisting type 2 diabetes mellitus (54.55% versus 21.93%; P=0.016) were recorded among infected cases. Regarding intraoperative parameters, the infected group demonstrated significantly prolonged operative duration (136.82 ± 31.42 minutes versus 105.71 ± 26.85 minutes; P=0.001), increased estimated intraoperative blood loss (493.64 ± 138.71 mL versus 371.40 ± 118.25 mL; P=0.002), and a higher rate of allogeneic blood transfusions (45.45% versus 19.30%; P=0.043), whereas baseline age, sex distribution, fracture anatomical configuration, and specific implant architecture did not differ significantly between groups (P>0.05).

Table 1. Baseline Demographic, Clinical, and Perioperative Characteristics of the Study Population Stratified by Surgical Site Infection (SSI) Status

Characteristic	Overall Cohort (N=125)	Non-SSI Group (N=114)	SSI Group (N=11)	Test Statistic (t / Chi-Square)	P-Value
Age (years), Mean ± SD	58.64 ± 14.32	58.12 ± 14.28	64.09 ± 13.91	t = 1.332	0.185
Sex (Male / Female), n (%)	71 (56.80) / 54 (43.20)	65 (57.02) / 49 (42.98)	6 (54.55) / 5 (45.45)	Chi-Square = 0.025	0.874
Body Mass Index (kg/m2), Mean ± SD	26.85 ± 4.12	26.61 ± 3.98	29.34 ± 4.81	t = 2.152	0.033
Body Mass Index >= 30 kg/m2, n (%)	28 (22.40)	22 (19.30)	6 (54.55)	Chi-Square = 7.173	0.007
Current Tobacco Smoking, n (%)	33 (26.40)	29 (25.44)	4 (36.36)	Chi-Square = 0.627	0.428
ASA Physical Status >= III, n (%)	46 (36.80)	38 (33.33)	8 (72.73)	Chi-Square = 7.126	0.008
Type 2 Diabetes Mellitus, n (%)	31 (24.80)	25 (21.93)	6 (54.55)	Chi-Square = 5.753	0.016
Essential Arterial Hypertension, n (%)	52 (41.60)	46 (40.35)	6 (54.55)	Chi-Square = 0.844	0.358
Coronary Artery Disease, n (%)	24 (19.20)	21 (18.42)	3 (27.27)	Chi-Square = 0.521	0.470
Chronic Obstructive Pulmonary Disease, n (%)	15 (12.00)	13 (11.40)	2 (18.18)	Chi-Square = 0.456	0.499
Fracture Location / Surgical Indication, n (%)	-	-	-	Chi-Square = 0.488	0.921
Intertrochanteric Femoral Fracture	58 (46.40)	53 (46.49)	5 (45.45)	-	-
Subtrochanteric Femoral Fracture	29 (23.20)	26 (22.81)	3 (27.27)	-	-
Femoral Shaft Fracture	26 (20.80)	24 (21.05)	2 (18.18)	-	-
Femoral Neck Fracture / Arthroplasty	12 (9.60)	11 (9.65)	1 (9.09)	-	-
Type of Implant Architecture, n (%)	-	-	-	Chi-Square = 0.354	0.838
Cephalomedullary / Intramedullary Nail	74 (59.20)	68 (59.65)	6 (54.55)	-	-
Locking Plate and Screw Construct	39 (31.20)	35 (30.70)	4 (36.36)	-	-
Hemiarthroplasty / Total Hip Stem	12 (9.60)	11 (9.65)	1 (9.09)	-	-
Operative Duration (minutes), Mean ± SD	108.45 ± 28.64	105.71 ± 26.85	136.82 ± 31.42	t = 3.612	0.001
Operative Duration > 120 minutes, n (%)	38 (30.40)	30 (26.32)	8 (72.73)	Chi-Square = 10.973	0.001
Estimated Blood Loss (mL), Mean ± SD	382.16 ± 124.50	371.40 ± 118.25	493.64 ± 138.71	t = 3.204	0.002
Intraoperative Blood Transfusion, n (%)	27 (21.60)	22 (19.30)	5 (45.45)	Chi-Square = 4.092	0.043
Closed-Suction Drainage Usage, n (%)	49 (39.20)	44 (38.60)	5 (45.45)	Chi-Square = 0.207	0.649

As detailed in Table 2, significant differences in baseline nutritional and inflammatory biomarkers were observed between the study cohorts. Patients who subsequently developed surgical site infections exhibited markedly lower preoperative serum albumin concentrations (3.12 ± 0.46 g/dL versus 3.89 ± 0.49 g/dL; P<0.001) and a significantly higher prevalence of preoperative hypoalbuminemia (72.73% versus 15.79%; P<0.001) compared with uninfected individuals. Conversely, baseline high-sensitivity C-reactive protein levels were substantially elevated in the infected group (20.38 ± 6.84 mg/L versus 7.31 ± 4.58 mg/L; P<0.001), with 81.82% of infected patients demonstrating levels of

10.0 mg/L or greater (P<0.001). Consequently, the composite albumin-to-CRP ratio was profoundly reduced in the surgical site infection cohort (0.19 ± 0.11 g/mg versus 0.87 ± 0.46 g/mg; P<0.001). Furthermore, the infected cohort demonstrated significantly decreased baseline hemoglobin (10.98 ± 1.35 g/dL versus 12.48 ± 1.61 g/dL; P=0.003), higher absolute leukocyte counts (9.98 ± 3.12 x10^3/uL versus 7.94 ± 2.31 x10^3/uL; P=0.008), elevated neutrophil-to-lymphocyte ratios (5.48 ± 1.86 versus 2.91 ± 1.25; P<0.001), and higher fasting plasma glucose levels (143.27 ± 43.16 mg/dL versus 111.85 ± 29.80 mg/dL; P = 0.002), whereas baseline renal function indices showed no statistically significant variations (P>0.05).

Table 2. Preoperative Laboratory Parameters, Nutritional Biomarkers, and Inflammatory Indices Stratified by Surgical Site Infection (SSI) Status

Laboratory Parameter	Overall Cohort (N=125)	Non-SSI Group (N=114)	SSI Group (N=11)	Mean Difference (95% CI)	Test Statistic (t / Chi-Square)	P-Value
Serum Albumin (g/dL), Mean ± SD	3.82 ± 0.54	3.89 ± 0.49	3.12 ± 0.46	0.77 (0.46 to 1.08)	t = 5.016	< 0.001
Preoperative Hypoalbuminemia (< 3.5 g/dL), n (%)	26 (20.80)	18 (15.79)	8 (72.73)	Not Applicable	Chi-Square = 20.835	< 0.001
High-Sensitivity C-Reactive Protein (mg/L), Mean ± SD	8.46 ± 6.12	7.31 ± 4.58	20.38 ± 6.84	-13.07 (-16.14 to -10.00)	t = -8.912	< 0.001
Elevated hs-CRP (>= 10.0 mg/L), n (%)	33 (26.40)	24 (21.05)	9 (81.82)	Not Applicable	Chi-Square = 20.932	< 0.001
Albumin-to-CRP Ratio (g/mg), Mean ± SD	0.81 ± 0.48	0.87 ± 0.46	0.19 ± 0.11	0.68 (0.40 to 0.96)	t = 4.864	< 0.001
Albumin-to-CRP Ratio < 0.35 g/mg, n (%)	29 (23.20)	20 (17.54)	9 (81.82)	Not Applicable	Chi-Square = 25.437	< 0.001
Hemoglobin (g/dL), Mean ± SD	12.35 ± 1.64	12.48 ± 1.61	10.98 ± 1.35	1.50 (0.49 to 2.51)	t = 3.008	0.003
Preoperative Anemia (Hb < 12.0 g/dL), n (%)	45 (36.00)	37 (32.46)	8 (72.73)	Not Applicable	Chi-Square = 7.428	0.006
Total Leukocyte Count (x10^3/uL), Mean ± SD	8.12 ± 2.45	7.94 ± 2.31	9.98 ± 3.12	-2.04 (-3.52 to -0.56)	t = -2.714	0.008
Absolute Neutrophil Count (x10^3/uL), Mean ± SD	5.24 ± 1.88	5.08 ± 1.76	6.89 ± 2.41	-1.81 (-2.99 to -0.63)	t = -3.122	0.002
Absolute Lymphocyte Count (x10^3/uL), Mean ± SD	1.86 ± 0.62	1.91 ± 0.61	1.34 ± 0.45	0.57 (0.19 to 0.95)	t = 3.015	0.003
Neutrophil-to-Lymphocyte Ratio, Mean ± SD	3.11 ± 1.42	2.91 ± 1.25	5.48 ± 1.86	-2.57 (-3.52 to -1.62)	t = -6.175	< 0.001
Fasting Plasma Glucose (mg/dL), Mean ± SD	114.62 ± 32.45	111.85 ± 29.80	143.27 ± 43.16	-31.42 (-50.64 to -12.20)	t = -3.226	0.002
Serum Creatinine (mg/dL), Mean ± SD	1.02 ± 0.28	1.01 ± 0.27	1.12 ± 0.34	-0.11 (-0.29 to 0.07)	t = -1.246	0.215
Blood Urea Nitrogen (mg/dL), Mean ± SD	17.84 ± 5.62	17.65 ± 5.51	19.81 ± 6.45	-2.16 (-5.64 to 1.32)	t = -1.218	0.226

As outlined in Table 3, multivariable logistic regression analysis demonstrated that baseline inflammatory and nutritional markers served as significant independent predictors of surgical site infection following femoral hardware instrumentation. After adjusting for potential confounding factors, preoperative serum hypoalbuminemia (< 3.5 g/dL) was independently associated with a nearly eightfold increase in the likelihood of postoperative infection (Adjusted OR = 7.845, 95% CI:1.614 to 38.128; P=0.011). Similarly, elevated preoperative high-sensitivity C-reactive protein (>= 10.0 mg/L) conferred an independent ninefold elevation in infection risk

(Adjusted OR=9.132, 95% CI:1.684 to 49.524; P=0.010), while an impaired composite albumin-to-CRP ratio (<0.35 g/mg) exhibited the strongest predictive capacity (Adjusted OR=11.418, 95% CI:1.925 to 67.726; P=0.007). Among procedural metrics, prolonged operative duration exceeding 120 minutes remained an independent surgical risk factor (Adjusted OR=4.892, 95% CI:1.042 to 22.964; P=0.044), whereas preexisting diabetes mellitus, elevated body mass index, ASA physical class, preoperative anemia, and intraoperative blood loss did not achieve statistical significance in the final multivariable equation (P>0.05).

Table 3. Univariate and Multivariable Logistic Regression Analyses of Predictors for Postoperative Surgical Site Infection Following Femoral Implant Placement

Variable	Univariate Analysis: Crude OR (95% CI)	Univariate Analysis: P-Value	Multivariable Analysis: Adjusted OR (95% CI)	Multivariable Analysis: P-Value
Preoperative Serum Albumin < 3.5 g/dL	14.222 (3.468 to 58.324)	< 0.001	7.845 (1.614 to 38.128)	0.011
Preoperative hs-CRP >= 10.0 mg/L	16.875 (3.424 to 83.178)	< 0.001	9.132 (1.684 to 49.524)	0.010
Albumin-to-CRP Ratio < 0.35 g/mg	21.150 (4.262 to 104.945)	< 0.001	11.418 (1.925 to 67.726)	0.007
Operative Duration > 120 minutes	7.467 (1.854 to 30.065)	0.005	4.892 (1.042 to 22.964)	0.044
Type 2 Diabetes Mellitus	4.272 (1.205 to 15.138)	0.024	3.654 (0.842 to 15.861)	0.083
Body Mass Index >= 30 kg/m2	5.018 (1.403 to 17.948)	0.013	2.915 (0.638 to 13.324)	0.167
ASA Physical Status >= III	5.333 (1.339 to 21.242)	0.018	2.418 (0.472 to 12.385)	0.289
Preoperative Anemia (Hb < 12.0 g/dL)	5.550 (1.385 to 22.242)	0.016	2.184 (0.416 to 11.468)	0.354
Estimated Blood Loss > 450 mL	4.125 (1.142 to 14.901)	0.031	1.842 (0.362 to 9.384)	0.461
Intraoperative Blood Transfusion	3.485 (0.978 to 12.418)	0.054	1.412 (0.264 to 7.552)	0.687
Age >= 65 years	2.145 (0.605 to 7.608)	0.238	Not Included	Not Applicable
Male Sex	0.905 (0.261 to 3.136)	0.8.385)	0.289	-
Preoperative Anemia (Hb < 12.0 g/dL)	5.550 (1.385 to 22.242)	0.016	2.184 (0.416 to 11.468)	0.354
Estimated Blood Loss > 450 mL	4.125 (1.142 to 14.901)	0.031	1.842 (0.362 to 9.384)	0.461
Intraoperative Blood Transfusion	3.485 (0.978 to 12.418)	0.054	1.412 (0.264 to 7.552)	0.687
Age >= 65 years	2.145 (0.605 to 7.608)	0.238	Not Included	Not Applicable
Male Sex	0.905 (0.261 to 3.136)	0.874	Not Included	Not Applicable

Discussion

The primary objective of this prospective clinical investigation was to evaluate the prognostic utility of preoperative serum albumin, high-sensitivity C-reactive protein, and their composite ratio in forecasting surgical site infections among patients undergoing major femoral implant instrumentation. Our principal findings established an overall infection incidence of 8.80% within the 90-day postoperative surveillance timeline, reflecting the challenging biological milieu of complex orthopedic traumatology and reconstruction. Patients who subsequently suffered incisional or deep periprosthetic complications exhibited markedly depressed baseline serum albumin concentrations alongside profound elevations in circulating C-reactive protein. Multivariable logistic regression modeling corroborated that baseline hypoalbuminemia below 3.5 g/dL, systemic inflammatory activation evidenced by C-reactive protein levels exceeding 10.0 mg/L, and an impaired albumin-to-CRP ratio below 0.35 g/mg served as

robust, independent determinants of hardware infection, operating independently of conventional host factors such as adiposity, diabetic dysregulation, and baseline physical performance status. Furthermore, prolonged operative duration exceeding two hours stood out as an independent procedural risk factor, underscoring the synergistic interplay between preoperative systemic physiological vulnerability and intraoperative technical burden [12,13].

The profound association between depressed baseline serum albumin and the escalated risk of surgical site infections observed in our cohort highlights the foundational role of systemic nutritional status in supporting host defense integrity and orchestrating tissue regeneration. Serum albumin constitutes the most abundant circulating plasma protein, serving not merely as a passive oncotic regulator but as an active physiological carrier for vital micronutrients, hormones, and antimicrobial therapeutics. In states of biological depletion, the marked reduction in albumin concentration impairs the cellular translational machinery required for the de novo synthesis of granulation tissue, collagen matrices, and extracellular structural proteins essential for prompt wound closure. Concurrently, systemic hypoalbuminemia induces microvascular hyperpermeability and interstitial edema around freshly dissected peri-implant muscular beds, creating stagnant fluid collections that compromise local tissue perfusion, depress microcirculatory oxygen tension, and establish an optimal niche for bacterial seeding and biofilm colonization. Furthermore, sustained protein malnutrition induces widespread cellular immunodeficiency, characterized by blunt macrophage phagocytic competence, diminished natural killer cell cytotoxicity, impaired lymphocyte proliferation, and attenuated bactericidal oxidative burst capacity. Consequently, individuals admitted with depleted protein reserves are biochemically compromised in mounting an effective barrier defense against transient perioperative bacteremia, resulting in uninhibited bacterial proliferation around devascularized cortical surfaces and metallic hardware interfaces [14,15].

In sharp contrast to the suppressive effects of protein depletion, the pronounced baseline elevation of circulating high-sensitivity C-reactive protein identified among our infected patients demonstrates the insidious influence of a pre-existing subclinical systemic inflammatory state. Synthesized predominantly by hepatic hepatocytes under the upstream transcriptional command of pro-inflammatory cytokines, specifically interleukin-6, interleukin-1beta, and tumor necrosis factor-alpha, C-reactive protein functions as a classical acute-phase reactant reflecting unperceived tissue stress, vascular inflammation, or subclinical cellular senescence. Elevated baseline levels indicate that the host biological system is already entrenched in a dysregulated inflammatory state prior to the physical trauma of orthopedic instrumentation. This pre-existing systemic priming leads to premature systemic leukocyte degranulation, pathological endothelial activation, and impaired cellular signaling pathways. When subjected to the severe physiological stress of extensive surgical dissection, femoral reaming, and rigid implant positioning, these primed immune effector cells exhibit exhausted or aberrant antimicrobial functional responses. Instead of orchestrating a directed, localized immunological countermeasure against perioperative microbiological inocula, circulating neutrophils demonstrate dysfunctional chemotaxis, aberrant extravasation, and premature netosis, leaving periprosthetic surgical hematomas unprotected against opportunistic pathogens introduced during open exposure [16,17].

The biological coupling of low serum albumin and elevated C-reactive protein epitomized by the striking prognostic capacity of the composite albumin-to-CRP ratio demonstrated in our multivariable modeling illustrates the concept of inflammation-driven metabolic catabolism. Emerging evidence indicates that circulating albumin and C-reactive protein represent two reciprocal facets of the same acute-phase physiological phenomenon: albumin acts as a negative acute-phase protein whose hepatic gene expression is directly suppressed by high circulating concentrations of interleukin-6, while C-reactive protein functions as the prototypical positive acute-phase marker. When patients experience occult chronic systemic inflammation, transcapillary escape of albumin increases substantially, while hepatic ribosomal priority shifts decisively from anabolic protein synthesis toward the mass production of defensive inflammatory mediators. This hypercatabolic state triggers systemic sarcopenia, impairs endogenous antioxidant reserves, and leaves the peripheral soft-tissue envelope vulnerable to mechanical and infectious breakdowns. Therefore, an abnormally depressed albumin-to-CRP ratio serves as an integrated molecular fingerprint identifying an unfavorable physiological state characterized simultaneously by active immunological consumption and profound metabolic depletion. Evaluating this composite metric provides superior predictive accuracy over either parameter alone, identifying individuals whose endogenous homeostatic capacity is exhausted before entering the operative suite [18,19].

Beyond humoral and biochemical host parameters, our statistical analysis demonstrated that an operative duration surpassing 120 minutes remained an independent procedural risk factor for hardware infection. Prolonged procedural time exponentially

amplifies the cumulative duration of wound exposure to ambient surgical theater air, laminar flow turbulence, and airborne desiccation, thereby compounding the volumetric load of settling pathogenic bioaerosols directly into the deep operative field. Simultaneously, prolonged surgical exposure necessitates sustained mechanical tissue retraction, which induces local compressive ischemic necrosis along vulnerable femoral muscle bellies and subperiosteal margins. Devascularized muscular tissue devoid of capillary perfusion is incapable of clearing bacterial inocula and provides an anaerobic substrate rich in iron and cellular debris, greatly accelerating bacterial replication. Repeated instrument re-entry, extensive electrocautery thermal injury, prolonged intramedullary canal instrumentation, and late-case fatigue further degrade host-tissue resistance around the implant. When prolonged mechanical trauma is inflicted upon a patient who is already biochemically compromised by hypoalbuminemia and sustained inflammation, the localized periprosthetic biological defense fails entirely, enabling microbial attachment, polysaccharide matrix elaboration, and irreversible biofilm maturation over the hardware surface [20,21].

The convergence of biological frailty and extensive operative trauma is particularly critical in the presence of foreign metallic implants. Femoral instrumentation requires the introduction of substantial metallic biomaterials, such as intramedullary nails, dynamic hip screws, and modular prosthetic components, which inherently disrupt local vascularity and alter bone hemodynamics. Bacteria introduced during surgery can adhere to these artificial abiotic surfaces via nonspecific physicochemical interactions, rapidly forming organized biofilms protected from circulating host immunoglobulins and standard parenteral antibiotic regimens. In patients with normal nutritional reserves and balanced baseline inflammatory status, effective early neutrophil migration and intact local opsonization eliminate low-inoculum bacterial contamination before surface adhesion occurs. Conversely, the combined presence of hypoalbuminemia and elevated C-reactive protein reflects an impaired humoral and cell-mediated microenvironment where opsonizing complement proteins are deficient and bacterial clearance is delayed. Consequently, the minimum infective dose of common opportunistic pathogens, such as Staphylococcus aureus and coagulase-negative staphylococci, is reduced by several orders of magnitude, converting minor intraoperative bacterial contamination into fulminant periprosthetic infection [22,23].

These pathophysiological observations carry profound clinical implications for modern orthopedic care pathways and patient optimization algorithms. Given that routine pre-admission laboratory panels already incorporate serum albumin and C-reactive protein, computing their absolute levels and composite ratio offers a rapid, low-cost risk-stratification protocol that requires no specialized hardware or costly diagnostic platforms. In elective or semi-elective femoral reconstructive procedures, identifying a patient with marked hypoalbuminemia and systemic inflammation warrants a structured preoperative optimization period. This window allows for targeted oral nutritional supplementation enriched with high-quality protein, immunotargets, and micronutrients, alongside rigorous screening and clearance of occult inflammatory foci, such as periodontal pathology, asymptomatic bacteriuria, or decompensated metabolic syndromes. Postponing hardware implantation to achieve biomarker normalization or improvement could substantially diminish postoperative morbidity, shorten hospital length of stay, and avert catastrophic implant failures that necessitate complex revision surgery [24,25].

Nevertheless, the present investigation possesses certain structural limitations that must be acknowledged. First, the study design was analytical and cross-sectional with observational prospective follow-up, conducted at a single tertiary academic medical center with a relatively modest sample size of 125 patients, which may limit the external generalizability of our findings across diverse healthcare settings and community hospitals. Second, while serum albumin and high-sensitivity C-reactive protein were systematically quantified at baseline, dynamic serial measurements during the immediate postoperative trajectory were not incorporated into the primary analytical model, precluding the longitudinal assessment of biomarker kinetics following surgical stress. Third, despite comprehensive adjustment for major surgical indicators and comorbidities, residual unmeasured confounding including precise preoperative functional frailty indices, occult microvascular insufficiency, and variations in surgeon-specific technical nuances cannot be completely ruled out. Future research endeavors should prioritize large-scale, prospective, multicenter randomized trials designed to investigate whether preoperative protocolized nutritional replenishment and anti-inflammatory medical interventions can successfully reverse abnormal baseline biomarker thresholds and definitively reduce the actual incidence of implant-associated surgical site infections [26,27].

Conclusion

Preoperative hypoalbuminemia and elevated C-reactive protein levels are potent independent predictors of postoperative surgical site infections following femoral hardware fixation. Preoperative screening with these cost-effective biomarkers, particularly the composite albumin-to-CRP ratio,

facilitates early risk stratification and enables targeted nutritional and anti-inflammatory interventions to mitigate implant infection rates.

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Authors' Contributions

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