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The Role of C-Reactive Protein as an Early Detection of Infection in Closed Fractures Following Open Reduction and Internal Fixation (ORIF)

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Abstract

Surgical Site Infection (SSI) remains a significant complication in orthopedic surgery, necessitating reliable early detection biomarkers. This study aims to evaluate the role of C-Reactive Protein (CRP) on the third postoperative day (POD 3) and its correlation with the ASEPSIS score on POD 7 for detecting early infection in patients with closed femoral fractures treated with Open Reduction and Internal Fixation (ORIF). A prospective cohort study was conducted at RSUP H. Adam Malik, Medan, involving 16 patients selected through consecutive sampling. Data collection included laboratory CRP measurements and clinical wound evaluation using the ASEPSIS scoring system. The results

showed that 100% of subjects had normal CRP levels (<10 mg/dL) on POD 3 and achieved "Satisfactory Healing" on POD 7, with a zero infection rate (0%). Statistical analysis revealed no significant correlation between POD 3 CRP levels and POD 7 ASEPSIS scores, attributed to the homogeneity of the positive clinical outcomes. This study concludes that in low-risk patients without comorbidities, early normal CRP levels are highly consistent with uncomplicated wound healing. CRP serves as a valuable negative predictor of infection when integrated into a multimodal monitoring framework.

Keywords: ASEPSIS Score, C-Reactive Protein, Closed Fracture, Femur, Open Reduction Internal Fixation (ORIF)

1. Introduction

Surgical Site Infection (SSI) remains a major postoperative complication, particularly in orthopedics, leading to significant morbidity and increased healthcare costs. While global incidence ranges from 5% to 15%, rates in Indonesian government hospitals have been reported as high as 55.1% [1]. In procedures such as Open Reduction and Internal Fixation (ORIF) for closed fractures, infection can lead to devastating consequences like non-union or osteomyelitis if not detected early. However, clinical signs often appear only after the infection is advanced [2].

C-Reactive Protein (CRP) serves as a crucial systemic indicator for early detection. Unlike Erythrocyte Sedimentation Rate (ESR) or leukocyte counts, which can be influenced by non-infectious factors or react slowly, CRP has rapid kinetics. It typically peaks at 48–72 hours and should decline by day 3; a persistent elevation suggests infection. Therefore, serial CRP measurement offers higher sensitivity for differentiating normal postoperative inflammation from developing sepsis compared to other biomarkers [3–5].

To validate these findings clinically, the ASEPSIS score provides a quantitative method for wound evaluation, optimally assessed on the 7th postoperative day. Despite the high volume of orthopedic surgeries at RSUP H. Adam Malik as a national referral center, data correlating early CRP trends with ASEPSIS scores in this specific population remains limited. Consequently, this study aims to determine the role of CRP in the early detection of infection in closed fractures treated with ORIF and to analyze its correlation with ASEPSIS scores, providing a scientific basis for improved postoperative monitoring protocols.

2. Methods

2.1 Study Design and Setting

This study employed a prospective cohort design to analyze the role of C-Reactive Protein (CRP) in the early detection of infection in closed fracture patients undergoing Open Reduction and Internal Fixation (ORIF). The research was conducted at the Surgical Ward of Haji Adam Malik General Hospital, Medan, Indonesia. Data collection and analysis took place from

November 2025 to December 2025. This study received ethical approval from the Health Research Ethics Commission of the Universitas Sumatera Utara (USU). All participants provided written informed consent, ensuring the principles of confidentiality and anonymity were maintained throughout the study.

2.2 Participants and Sampling

The study population comprised all patients with closed fractures treated with ORIF surgery at the study site. The sample was selected using a consecutive sampling technique, recruiting subjects who met the inclusion and exclusion criteria until the minimum sample size was achieved. Based on the sample size calculation for numerical correlation analysis (assuming $\alpha = 0.05$, $\beta = 0.2$, and an estimated correlation coefficient $r = 0.65$ based on Mercurio *et al.*, 2022), the minimum required sample size was determined to be 16 patients.

2.3 Eligibility Criteria

The inclusion criteria were: (1) patients with closed fractures who had undergone ORIF surgery; and (2) patients willing to participate and sign informed consent. The exclusion criteria included: (1) patients with comorbidities such as Diabetes Mellitus, autoimmune diseases, cancer, cardiovascular diseases, pregnancy, or chronic liver disease; and (2) patients who had undergone debridement at another hospital prior to referral.

2.4 Study Protocol and Data Collection

Participants underwent CRP level examination on postoperative day 3 to capture the physiological peak of the inflammatory response. CRP levels were categorized as normal (<10 mg/dL) or high (≥ 10 mg/dL). Subsequently, on postoperative day 7 when clinical signs of infection typically become apparent the researcher assessed the surgical wound using the ASEPSIS score developed by Wilson *et al.*

The ASEPSIS scoring system evaluates wound conditions based on clinical parameters (serous discharge, erythema, purulent exudate, and separation of deep tissues) and treatment consequences (administration of antibiotics, drainage under local anesthesia, debridement under general anesthesia, isolation of bacteria, and prolonged hospital stay >14 days). The total score was stratified into five categories: Satisfactory Healing (0–10), Disturbance of Healing (11–20), Minor Wound Infection (21–30), Moderate Wound Infection (31–40), and Severe Wound Infection (>40).

2.5 Statistical Analysis

Data were analyzed using statistical software. Descriptive statistics were used to present the frequency distribution of demographic characteristics (age, gender), clinical characteristics (fracture location), and ASEPSIS categories. Numerical data were presented as mean and standard deviation. The normality of the data was tested using the Shapiro-Wilk test. To analyze the correlation between CRP levels on day 3 and ASEPSIS scores on day 7, the Pearson correlation test was used for normally distributed data, while the Spearman rank correlation test was used for non-normally distributed data. Statistical significance was set at $p < 0.05$.

3. Results

3.1 General Characteristics of Study Subjects

The study included a total of 16 patients who underwent Open Reduction and Internal Fixation (ORIF) for closed femoral fractures. As presented in Table I, the majority of subjects were male ($n = 12$; 75%), while females accounted for 25% of the population. In terms of age distribution, the study was dominated by the adult age group (19–65 years), comprising 87.5% of the subjects.

Regarding clinical characteristics, all fractures (100%) were located in the lower extremity, specifically the femur. The most common fracture site was the midshaft/diaphyseal region of the femur (56.2%), followed by the proximal/neck region (25%) and the distal region (18.8%).

3.2 Postoperative C-Reactive Protein (CRP)

Levels CRP levels were measured on the 3rd postoperative day to assess the systemic inflammatory response. The results showed that all 16 subjects (100%) had CRP levels within the normal limit (<10 mg/dL). No patients exhibited elevated CRP levels (≥ 10 mg/dL) at this time point. This finding indicates that while surgical trauma typically triggers an inflammatory response, the systemic inflammation in this study population was well-controlled and did not exceed pathophysiological thresholds associated with infection.

3.3 Clinical Wound Healing (ASEPSIS Score)

Wound healing was evaluated on the 7th postoperative day using the ASEPSIS scoring system. As shown in Table II, all subjects (100%) were categorized as "Satisfactory Healing" with a total score of < 10 . The majority of patients had a score of 0, indicating dry wounds with good approximation. Only one patient recorded a score of 5 due to local erythema; however, this was still classified as satisfactory physiological healing and did not progress to Surgical Site Infection (SSI).

3.4 Correlation Between CRP Levels and ASEPSIS Scores

A Spearman correlation test was conducted to analyze the relationship between CRP levels on day 3 and ASEPSIS scores on day 7. The analysis yielded a correlation coefficient (r) of 0.295 with a p -value of 0.267. However, this statistical result must be interpreted with caution. Since 100% of the sample showed normal CRP levels and satisfactory healing, there was no variance in the data to establish a significant linear relationship. The absence of infection in this study population correlates with the consistently normal CRP levels observed on day 3, suggesting that in the absence of complications, inflammatory markers return to physiological ranges early in the postoperative period.

4. Discussion

The study identified a predominance of male subjects (75%) within the productive age group (87.5%), a demographic profile consistent with epidemiological trends for high-energy trauma in femoral fractures [4]. Anatomically, the femur is surrounded by substantial muscle mass, and surgical procedures like Open Reduction and Internal Fixation (ORIF) typically induce significant soft tissue damage. Physiologically, this trauma triggers an acute

systemic inflammatory response mediated by cytokines such as IL-6, which subsequently stimulates hepatic CRP synthesis [6].

Despite the physiological expectation of an inflammatory surge, laboratory results revealed that all patients (100%) maintained CRP levels within normal limits (<10 mg/dL) on the third postoperative day. This finding contrasts with studies utilizing high cutoffs (>100 mg/L) to predict infection [5] but aligns with Mercurio *et al.* It suggests that in patients without comorbidities, inflammatory markers remain within physiological limits or normalize rapidly in the absence of complications, indicating a well-controlled systemic response [7].

Clinical evaluation using the ASEPSIS score on day 7 confirmed "Satisfactory Healing" (score <10) in all subjects, resulting in 0% a Surgical Site Infection (SSI) rate. This outcome is significantly superior to global figures reported by Liu *et al.*, where deep infection rates in orthopedic trauma range from 5.1% to 8.2%. The absence of infection in this cohort validates the efficacy of standard perioperative management when combined with strict patient selection [8]. The optimal clinical outcomes are likely attributable to the strict exclusion criteria applied in this study, which eliminated high-risk factors such as uncontrolled diabetes mellitus, smoking, and hypoalbuminemia. Literature indicates that these comorbidities significantly impair neutrophil chemotaxis and wound healing. By excluding these confounders, the study minimized the risk of infection from common pathogens like MRSA or Gram-negative bacteria, highlighting the critical role of host status in postoperative recovery [9, 10].

Statistical analysis revealed no significant correlation ($p = 0.0267$) between day 3 CRP levels and day 7 ASEPSIS scores. This lack of significance arises from the homogeneity of the positive results: all patients maintained normal CRP levels and achieved satisfactory healing. Theoretically, this confirms that low CRP levels reliably mirror the absence of infection. However, reliance on a single biomarker should be cautious; multimodal monitoring combining biomarkers with objective scoring remains the gold standard to avoid overtreatment [11].

Several limitations must be acknowledged in this study. The relatively small sample size ($n = 16$) and single-center setting limit the generalizability of the findings. Furthermore, CRP was measured only at a single time point (day 3), preventing the analysis of kinetic trends, and the 7-day follow-up period may not capture late-onset infections. Future research should consider serial measurements and longer observation periods to further validate these findings.

5. Conclusion

In conclusion, this study demonstrates that among patients with closed femoral fractures treated with ORIF, the systemic inflammatory response measured by C-Reactive Protein (CRP) on the third postoperative day remained within physiological limits (<10 mg/dL) for all subjects (100%). This biochemical profile aligned perfectly with clinical outcomes on day 7, where all patients achieved "Satisfactory Healing" based on the ASEPSIS score, with zero incidence of surgical site infection. Although statistical analysis revealed no significant correlation ($p > 0.05$) due to the homogeneity of these positive results, the findings clinically suggest that a normal CRP level in the early postoperative period serves as a reliable indicator of

uncomplicated recovery in low-risk patients. Consequently, while CRP is a valuable negative predictor for infection, it should be utilized within a multimodal monitoring framework alongside objective clinical scoring to guide postoperative management effectively.

6. Acknowledgment

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7. References

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