The Relationship Between the Systemic Inflammatory-Immunity Index and Acute Postoperative Pain Severity Following Traumatic Hip Fracture Surgery in Elderly Patients with Rheumatoid Arthritis

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Abstract:

Background and Objective: Traumatic hip fractures in elderly patients with rheumatoid arthritis are associated with significant postoperative pain that adversely impacts recovery and overall quality of life. Identification of reliable biomarkers, such as the systemic inflammatory-immunity index, may enhance the prediction of pain severity and refine pain management strategies. This study aims to investigate the role of the systemic inflammatory-immunity index in predicting postoperative pain outcomes, ultimately improving care for this vulnerable population through personalized, evidence-based approaches.

Materials & Methods: This descriptive cross-sectional study was conducted in the winter of 2024 at Shahid and Imam Reza Hospitals, affiliated with Tabriz University of Medical Sciences. A total of 112 elderly patients with rheumatoid arthritis were recruited via convenience sampling. Demographic characteristics, clinical factors, and biomarkers (neutrophil, lymphocyte, and platelet counts) were collected to compute the systemic inflammatory-immunity index. Postoperative pain severity, opioid consumption, and hemodynamic parameters were assessed for their correlation with the systemic inflammatory-immunity index using Pearson correlation coefficients.

Results: Correlation analyses demonstrated a significant positive relationship between the systemic inflammatory-immunity index during hospitalization and acute postoperative pain severity, as measured by the pain intensity scale, within the first four hours post-surgery. The strongest correlation with the Visual Analog Scale (VAS) score was recorded at the second postoperative hour (R=0.658, P=0.009). Additionally, significant correlations were found at the first hour (R=0.596, P=0.014), third hour (R=0.488, P=0.026), and fourth hour (R=0.452, P=0.036); however, these correlations progressively diminished and were non-significant in subsequent hours.

Conclusion: The systemic inflammatory-immunity index is a valuable predictor of postoperative pain severity, hemodynamic instability, and extended hospital stays among elderly patients with rheumatoid arthritis.

Keywords: Systemic inflammatory-immunity index, postoperative pain, hemodynamic instability, length of hospital stay

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Background and Objective

Acute postoperative pain poses a significant challenge in clinical care, especially for elderly patients with rheumatoid arthritis who often undergo complex surgeries such as hip fracture repairs. Efficient pain management in this cohort is essential for enhancing quality of life and mitigating the risks of postoperative complications, including delayed recovery, reduced mobility, and chronic pain development.[1] Despite advancements in anesthesia and pain management techniques, accurately predicting the severity of acute postoperative pain remains challenging due to the interplay of numerous physiological, psychological, and biochemical factors that impact the patient's pain experience.[2]

An emerging area of focus in postoperative care is the impact of systemic inflammation on pain levels following surgery. Surgical trauma associated with hip fractures triggers a substantial inflammatory response characterized by immune cell activation, cytokine release, and changes in the systemic inflammatory profile.[3] While inflammation plays a crucial role in tissue healing, excessive or dysregulated inflammatory processes can heighten nociceptive signals, resulting in increased pain sensitivity. Therefore, identifying reliable biomarkers that can predict pain severity and clarify the underlying inflammatory mechanisms is vital for improving clinical practices.[4]

The systemic inflammatory-immunity index (SII) has emerged as a notable biomarker reflecting the equilibrium between immune and inflammatory responses. It is calculated from peripheral blood cell counts, including neutrophils, lymphocytes, and platelets, thereby providing a composite measure of systemic inflammation and immune function.[5,6] The SII encompasses three critical components: neutrophils, which indicate the inflammatory response; lymphocytes, which are essential for immune regulation; and platelets, involved in inflammatory processes and tissue repair.[7] This index offers a more comprehensive evaluation compared to traditional single-component indices, such as the neutrophil-to-lymphocyte ratio or platelet-to-lymphocyte ratio.[8]

Recent research has established a correlation between elevated SII levels and adverse outcomes across various diseases, including cancer, cardiovascular conditions, and critical illnesses. In surgical contexts, higher SII values are linked to an increased occurrence of postoperative complications, prolonged hospitalizations, and hindered recovery trajectories. However, the specific association between the SII and acute postoperative pain—especially in elderly patients with rheumatoid arthritis undergoing major trauma-related surgeries—remains underexplored.[9]

Elderly patients with rheumatoid arthritis represent a unique cohort due to their distinct immune response profiles, heightened comorbidities, and increased risk of negative outcomes. The aging process is often accompanied by "inflammaging," a state of chronic low-grade inflammation and immune dysfunction.[10] This chronic inflammation, combined with the acute inflammatory response induced by surgical trauma, can significantly influence pain perception and recovery. Thus, understanding the role of the SII in this population may provide clinically significant insights to enhance postoperative care.[11]

Acute postoperative pain following pelvic fractures in elderly patients with rheumatoid arthritis is multifactorial and can be particularly severe. This pain is influenced by several factors, including the extent of soft tissue damage, the duration of surgery, and individual variability in immune and inflammatory responses.[12]

The multifaceted nature of the SII positions it as a potentially valuable predictive tool for pain severity, aiding in the formulation of effective pain management strategies and identifying individuals at risk for developing pain-related complications.[13]

Despite its promise, the SII's utility as a predictive biomarker for acute postoperative pain has not been thoroughly investigated.[14]

Existing literature indicates that inflammatory markers, such as neutrophil and lymphocyte counts, correlate with pain intensity; however, integrating these markers into a unified index like the SII has largely gone unexamined. Furthermore, the impact of the SII on pain outcomes in elderly patients with trauma-induced rheumatoid arthritis—characterized by unique physiological and clinical challenges—has yet to be systematically evaluated.[15,16]

The present study aims to address this crucial research gap by exploring the relationship between the SII and acute postoperative pain intensity in elderly patients with rheumatoid arthritis who have undergone surgical intervention for traumatic pelvic fractures. The primary objective is to elucidate the correlation between the SII and the severity of acute postoperative pain within this vulnerable demographic.

Materials and Methods

Study Design

This descriptive cross-sectional study was conducted over six months in late 2023 at Shahid and Imam Reza Hospitals, affiliated with Tabriz University of Medical Sciences. The study adhered strictly to pre-established inclusion and exclusion criteria to ensure rigorous data collection and analysis.

Sampling Method

An exploratory approach to sample size determination was adopted, targeting a statistical power of 80% and a significance level of 0.05. After accounting for an anticipated 10% dropout rate, a final sample of 112 patients was obtained through convenience sampling methods.

Inclusion and Exclusion Criteria

Inclusion Criteria: This study included adult participants aged 65 to 80 years who were scheduled for hip fracture surgery and classified as ASA Class I or II according to the American Society of Anesthesiologists' guidelines. Participants were required to provide informed consent. Surgical procedures were conducted within 24 hours post-trauma to mitigate potential confounding effects on inflammatory biomarkers. All surgeries were performed by a standardized surgical team to ensure methodological consistency throughout the research.

Exclusion Criteria: Patients were excluded from the study if they had a history of alcohol or drug dependence, were on psychiatric medications, or had medical conditions likely to elevate inflammatory markers. This included individuals with advanced cardiovascular disease, cancer, or those who had undergone chemotherapy or radiotherapy. Additional exclusion criteria were the presence of infectious diseases, utilization of anti-inflammatory medications, recent blood transfusions, pathological or multiple fractures, fractures located near prosthetic devices or open fractures, and prior conservative treatment for fractures. Moreover, patients undergoing corrective or repeat surgeries, those receiving long-term immunosuppressive therapy (e.g., glucocorticoids), and surgeries lasting over four hours were also excluded.

Methodology

To systematically gather pertinent data, a structured data collection form was implemented for each participant. This form captured critical demographic and clinical information, such as age, gender, body mass index, smoking history, and a comprehensive medical history, which included hypertension, diabetes, chronic obstructive pulmonary disease, stroke, chronic liver disease, and chronic kidney disease. The type of hip fracture was categorized as femoral neck, intertrochanteric, or subtrochanteric. Furthermore, the ASA classification and the surgical approach (total hip replacement, hemiarthroplasty, or intramedullary nailing) were meticulously recorded.

Venous blood samples were obtained from the cubital vein by a qualified nursing professional and subsequently sent to the central laboratory for analysis. Upon hospital admission, critical biomarkers, specifically neutrophil, lymphocyte, and platelet counts, were assessed. The systemic immune-inflammation index (SII) was calculated using the formula:

Lymphocyte count / (Neutrophil count * Platelet)

Pain intensity was evaluated using the Visual Analog Scale (VAS), a validated instrument that has been widely used for over five decades. Pain scores were documented at 1, 2, 3, 4, 6, 12, 18, and 24 hours post-operatively to investigate the correlation between pain intensity and the systemic immune-inflammation index, which was measured preoperatively and at admission. Additionally, the dosage of opioids administered (measured in milligrams of pethidine) was correlated with the systemic immune-inflammation index. Hemodynamic parameters, including heart rate and mean arterial pressure, were monitored at corresponding time intervals to explore their relationship with the systemic immune-inflammation index. All patients received spinal anesthesia in a seated position at the L4–L5 or L5–S1 intervertebral space using a 22-gauge needle, along with an injection of 20 mg of marcaine.

Data Analysis

The data collected were analyzed using SPSS software (version 25). Descriptive statistics, including frequencies, percentages, means, and standard deviations, were utilized to summarize baseline characteristics. The Pearson correlation coefficient was employed to assess the relationship between pain intensity and the systemic immune-inflammation index, with a significance threshold set at $p < 0.05$.

Ethical Considerations

This study received ethical approval from the Ethics Committee of Tabriz University of Medical Sciences (Approval Number: IR.TBZMED.REC.1403.154). No additional financial burden was placed on participants, and immediate measures were implemented to address any adverse events that occurred.

Findings

The study comprised 112 elderly patients diagnosed with rheumatoid arthritis who underwent surgical intervention for traumatic hip fractures. The mean age of participants was 56.74 ± 5.34 years, with a predominant male representation (71.42%). Femoral neck fractures were the most prevalent type identified, and most patients were classified as ASA Class I. Comprehensive demographic and clinical characteristics of the study cohort are detailed in Table 1.

Laboratory assessments revealed a mean systemic immune-inflammation index (SII) of 11.329 ± 0.956 among participants. Blood cell counts, including neutrophils, lymphocytes, and platelets, were consistent with expected values for this demographic. A summary of additional hematological and inflammatory parameters is provided in Table 2.

Correlation analyses indicated a significant positive association between SII values during hospitalization and the severity of acute postoperative pain, as quantified by the pain intensity scale within the first four hours post-surgery. The strongest correlation occurred at the second hour post-operatively ($r = 0.658$, $p = 0.009$). Significant associations were also noted at the first hour ($r = 0.596$, $p = 0.014$), third hour ($r = 0.488$, $p = 0.026$), and fourth hour ($r = 0.452$, $p = 0.036$), though correlations diminished in subsequent hours. Based on prior research, an optimal SII threshold of 805.86 was established, categorizing patients into normal (values < 805.86) and abnormal (values > 805.86) groups.

Table 1- Display basic information about study participants

Variable		Mean ± standard deviation/frequency (percentage)
Age (years)		74.56±5.34
Gender	Male	80(%71.42)
	Female	32(%28.75)
Body Mass Index		27/89± 3.28
Smoking	Yes	28(%25.00)
	No	84(%75.00)
High Blood Pressure	Yes	51(%45.54)
	No	61(%54.46)
Diabetes Mellitus	Yes	34(%30.36)
	No	78(%69.64)
Lung Disease	Yes	13(%11.61)
	No	99(%88.39)
Stroke	Yes	7(%6.25)
	No	105(%93.75)
Liver Disease	Yes	4(%3.57)
	No	105(%69.43)
Kidney Disease	Yes	10(%8.93)
	No	102(%91.07)
Hip Fracture Type	Femoral Neck	50(%44.64)
	Intertrochanteric	39(%34.82)
	Subtrochanteric	23(%20.54)
ASA Class	Class I	68(%60.71)
	Class II	44(%39.29)
Surgical Procedure	Total Hip	56(%50.00)
	Hemiarthroplasty	34(%30.36)
	Intermedullary	22(%19.64)

Table 2- Summary of the results of biochemical tests of study participants

Variable	Mean±SD
White blood cells ($\times10^9$/L)	7.44±1.74
Red blood cells ($\times10^{12}$/L)	4.85±0.51
Platelets ($\times10^9$/L)	299.33±99.35
Neutrophils ($\times10^9$/L)	4.36±1.41
Lymphocytes ($\times10^9$/L)	2.32±0.66
Monocytes ($\times10^9$/L)	0.62±0.23
Eosinophils ($\times10^9$/L)	0.21±0.11
Basophils ($\times10^9$/L)	0.12±0.21
Hemoglobin (g/dL)	14.25±2.63
Systemic immune-inflammatory index	956.02±329.11

Significant differences were observed between the two groups in terms of neutrophil, platelet, white blood cell, and lymphocyte counts, as well as the duration of hospital stay. Patients with a high SII exhibited significantly elevated counts of neutrophils, platelets, and white blood cells ($P < 0.001$ for all three), alongside significantly lower lymphocyte counts ($P < 0.001$). Additionally, the high SII group experienced an extended average hospitalization period of 22 days compared to 17 days in the lower SII group ($P = 0.006$).

Discussion

The primary aim of this study was to explore the relationship between the systemic immune-inflammatory index (SII) and postoperative pain intensity in patients with rheumatoid arthritis. The findings indicate a significant relationship between

elevated SII and exacerbated postoperative pain, increased analgesic requirements, notable hemodynamic variations, and prolonged hospital stays, including potential time spent in intensive care. These results suggest that SII may serve as a valuable prognostic marker for evaluating postoperative recovery in this patient cohort.

The measurement of pain severity in the early postoperative phase, assessed via the Visual Analog Scale (VAS), showed a significant correlation with SII values. Specifically, patients with elevated SII reported increased pain levels in the initial hours post-surgery. This observation is consistent with existing literature highlighting the role of systemic inflammation in the onset and exacerbation of pain. In patients with rheumatoid arthritis, chronic inflammation may lead to the overactivation of immune pathways and subsequent release of inflammatory mediators, intensifying pain responses postoperatively through sensitization of both peripheral and central pain pathways.[17,18]

The present study highlights a significant association between elevated systemic immune-inflammatory index (SII) values and increased postoperative pain severity in patients with rheumatoid arthritis. Furthermore, patients exhibiting higher SII levels demonstrated a corresponding increase in opioid analgesic requirements. This correlation underscores the profound influence of inflammatory status on patients' responses to analgesic treatment. Specifically, the active inflammation characteristic of rheumatoid arthritis appears to lower pain thresholds and diminish the effectiveness of analgesics, necessitating a greater pharmacological intervention to achieve adequate pain control. Therefore, it is crucial to incorporate assessments of immune-inflammatory status into the formulation of postoperative pain management strategies.[3]

In addition to pain intensity, a notable correlation was observed between SII and hemodynamic changes during the early postoperative phase. Patients with elevated SII levels tended to exhibit increased arterial pressure, likely reflecting the systemic implications of inflammation on vascular tone and endothelial function. Pro-inflammatory cytokines, prevalent in rheumatoid arthritis, can heighten peripheral vascular resistance, potentially leading to hemodynamic instability. Consequently, SII may serve as a valuable indirect indicator for assessing hemodynamic status in a postoperative context.[19,20]

The observed hemodynamic alterations among patients with elevated SII values point to a significant inflammatory response that warrants close monitoring. Vigilance in monitoring these patients during the postoperative period is critical, as they may be more prone to physiological instability.[21]

Another key outcome of this study was the evaluation of hospital stay duration. Results indicated that a heightened SII correlates with extended hospitalization, likely due to delayed healing, compromised tissue repair, and a higher likelihood of postoperative complications. Persistent inflammation can disrupt repair processes and hinder the immune system's return to homeostasis, ultimately prolonging hospital care.[22,23]

Moreover, patients with elevated SII values showed a greater likelihood of requiring admission to an intensive care unit and advanced medical interventions. This observation suggests that systemic inflammation significantly influences the postoperative clinical trajectory. Given the persistent inflammation and multi-system involvement typical of rheumatoid arthritis, indices like the SII are essential for the early identification of high-risk patients.[24]

Further analysis revealed that SII functions as an independent predictor of prolonged hospital stays, consistent with existing literature on the adverse effects of systemic inflammation on postoperative recovery. Inflammation is known to compromise immune function, impair wound healing, and disrupt metabolic homeostasis, thus extending the recovery timeline and increasing the need for hospital resources.[25]

Other clinical and laboratory parameters also demonstrated a relationship with hospital stay length, notably body mass index (BMI). Higher BMI correlates with extended hospitalization, potentially due to exacerbated systemic inflammation, impaired healing, and increased risk factors for postoperative complications in patients with rheumatoid arthritis.[26] Furthermore, the overall health status of patients, assessed using the ASA classification, significantly influenced hospitalization duration, with individuals presenting higher comorbidities and surgical risks more prone to extended stays.[27]

Additionally, increased platelet counts, indicative of inflammatory activity, were associated with longer hospitalizations, while decreased hemoglobin levels correlated with poorer postoperative outcomes.[28] Anemia, particularly common among rheumatoid arthritis patients, can hinder recovery through reduced oxygen delivery and impaired tissue repair mechanisms.[19]

The clinical implications of these findings are substantial. The SII serves as a straightforward, accessible, and cost-effective method for identifying rheumatoid arthritis patients at elevated risk for severe pain, increased analgesic needs, hemodynamic instability, and longer hospitalization. Early identification of these patients can facilitate the development of tailored care strategies that optimize pain management and minimize postoperative complications.[29] Moreover, monitoring inflammatory status can promote personalized approaches to pain management, improving safety and overall quality of postoperative care while reducing reliance on opioids.[30,31]

conclusion

In conclusion, the systemic immune-inflammatory index emerges as a valuable prognostic tool for evaluating postoperative pain, analgesic requirements, and essential clinical outcomes in patients with rheumatoid arthritis. Higher SII values are associated with increased pain intensity, greater analgesic consumption, and prolonged durations of both hospital and intensive care unit stays. Additionally, factors such as body mass index, overall health condition, platelet counts, and hemoglobin levels significantly affect postoperative recovery. By integrating the SII with other clinical parameters, healthcare professionals can enhance risk prediction, inform treatment decisions, and refine postoperative care for patients with rheumatoid arthritis. Future research is warranted to elucidate the role of the systemic immune-inflammatory index in clinical practice further.

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