

## Evaluation of Inflammation Markers in Elderly Patients Undergoing Hip Fracture Surgery

### Kalça Kırığı Cerrahisi Geçiren Yaşlı Hastalarda İnflamasyon Belirteçlerinin Değerlendirilmesi

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#### ABSTRACT

**Objective:** High inflammatory markers are thought to be important in evaluating poor postoperative outcomes in older orthopedic patients. We aim to investigate the effect of inflammatory markers in patients over 80 who have undergone a hip fracture surgery regarding 30-day mortality and preoperative evaluation.

**Materials and Methods:** Patients over 80 who had undergone hip fracture surgery were included. Age, gender, type of anesthesia, comorbidities, anticoagulant, intensive care unit (ICU) admission, hospitalization period, 30-day mortality rates, were recorded and platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR) and systemic immune inflammation index (SII) values were calculated.

**Results:** The mean age was 85.48±4.07 years old. Postoperative ICU admission was found to be 41.1%, and the 30-day mortality rate was 3.3%. The PLR value was 191±105, the NLR value was 6.4±4.5, and the SII value was 1410±1210. A significant correlation was found between ICU hospitalization and mortality, preoperative and postoperative hospital stay.

**Conclusions:** While there was a positive correlation between intensive care hospitalization and mortality, although no statistically significant correlation was found between the PLR, NLR and SII values and mortality rates, high values close to those stated in the literature were found.

**Keywords:** Anesthesia, hip fracture, inflammation marker, intensive care unit admission, mortality

#### ÖZ

**Amaç:** İleri yaş ortopedik hastalarda yüksek inflamatuvar belirteçlerin kötü postoperatif sonuçların değerlendirilmesinde önemli olduğu düşünülmektedir. Amacımız 80 yaş üstü kalça kırığı ameliyatı geçirmiş hastalarda 30 günlük mortalite ve ameliyat öncesi değerlendirme açısından inflamatuvar belirteçlerin etkisini araştırmaktır.

**Materyal ve Metot:** Kalça kırığı ameliyatı geçiren 80 yaş üstü hastalar çalışmaya dahil edildi. Yaş, cinsiyet, anestezi türü, komorbiditeler, antikoagülan kullanımı, yoğun bakım ünitesinde (YBÜ) yatış süresi, hastane yatış süresi, 30 günlük mortalite oranları kaydedilerek trombosit/lenfosit oranı (PLR), nötrofil/lenfosit oranı (NLR) ve sistemik immün inflamasyon indeksi (SII) değerleri hesaplandı.

**Bulgular:** Yaş ortalaması 85,48 ± 4,07 idi. Postoperatif YBÜ yatışı % 41,1 idi ve 30 günlük mortalite oranı ise % 3,3 idi. PLR değeri 191 ± 105, NLR değeri 6,4 ± 4,5, SII değeri ise 1410 ± 1210 olarak saptandı. YBÜ yatışı ile mortalite, preoperatif ve postoperatif yatış süreleri arasında anlamlı korelasyon saptandı.

**Sonuç:** Yoğun bakıma yatış ile mortalite arasında pozitif bir ilişki bulunurken, PLR, NLR ve SII değerleri ile mortalite oranları arasında istatistiksel olarak anlamlı bir ilişki bulunmamasına rağmen literatürde belirtilen değerlere yakın yüksek değerler bulunmuştur.

**Anahtar Kelimeler:** Anestezi, inflamasyon belirteci, kalça kırığı, mortalite, yoğun bakım yatışı

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#### Yayın Bilgisi / Article Info:

Gönderi Tarihi/ Received: 06/12/2023  
Kabul Tarihi/ Accepted: 12/02/2024  
Online Yayın Tarihi/ Published: 11/03/2024

**Atf / Cited:** Şahin F and et al. Evaluation of Inflammation Markers in Elderly Patients Undergoing Hip Fracture Surgery. *Online Türk Sağlık Bilimleri Dergisi* 2024;9(1):61-65. doi: 10.26453/otjhs.1401020

## INTRODUCTION

A hip fracture is a serious orthopedic problem that becomes more prevalent with advancing age, and it is associated with both short-term and long-term mortality in affected individuals.<sup>1,2</sup> In elderly patients who underwent hip fracture surgery, the mortality rate was found to be 24.7% during the postoperative follow-up period.<sup>3</sup> In a systematic review, it has been shown that the postoperative one-year mortality rate ranges from 8.4% to 36%, and this condition has been associated with arrhythmia, pneumonia, cardiac disease, elevated leukocyte count, and low albumin levels.<sup>4</sup> In another study, it has been revealed that elevated inflammatory marker levels are associated with 30-day mortality following a hip fracture.<sup>5</sup>

Platelets (PLT) are blood cells that have important roles in clotting and have also been shown to have functions in the inflammation process.<sup>6,7</sup> The PLT/lymphocyte ratio (PLR) and the neutrophil/lymphocyte ratio (NLR) are calculated values based on hemogram parameters and are used in studies as indicators of inflammation.<sup>7,8</sup> It is believed that elevated NLR values in elderly orthopedic patients may moderately predict adverse postoperative outcomes such as in-hospital mortality.<sup>9</sup> Systemic immune inflammation index (SII) is another inflammatory marker used as a prognosis-determining factor in many diseases.<sup>10-12</sup> Additionally, it has been demonstrated that elevated SII values serve as a good risk indicator in distinguishing fracture risk in postmenopausal osteoporosis patients.<sup>13</sup>

In this study, we aim to investigate the effect of inflammatory markers on 30-day mortality and the development of the need for an intensive care unit (ICU) in preoperative evaluation in patients over 80 who have undergone a hip fracture surgery.

## MATERIALS AND METHODS

**Ethics Committee Approval:** In the study, after obtaining approval from the Local Ethics Committee of the Sakarya University Faculty of Medicine (Date: 02/02/22, Decision no: E-71522473-0.50.01.04-102134-26), patients aged 80 and over who underwent a hip fracture surgery between January 2017 and January 2022 were screened. The study was carried out by the Helsinki Declaration.

Data on 160 consecutive patients over 80 who underwent hip fracture surgery were obtained from the hospital's electronic data program. Nine patients with preoperative ICU admission were excluded from the study. A total of 151 patients were included in the study. Age, gender, type of anesthesia, comorbidities, anticoagulant use, need for preoperative

ICU admission, postoperative ICU admission, preoperative hospitalization period, postoperative hospitalization period and 30-day mortality rates of the patients included were recorded. Biochemical parameters were recorded, including neutrophil, lymphocyte, platelet, and monocyte count. The PLR, NLR, and SII values were calculated using these parameters. SII is calculated as platelet count x neutrophil count/lymphocyte count. It has been shown that the normal NLR value is between 0.37 and 2.87, and the PLR value is between 36.63 and 172.68 in healthy patients.<sup>14</sup>

Patients aged 80 and over, with an American Society of Anesthesiologists I–III, who underwent hip fracture surgery were included in the study. Patients under 80 and those monitored in the ICU during the preoperative period were excluded from the study. Preoperative anesthesia evaluations were conducted within the last 72 hours before the operation and the preoperative laboratory parameters used during this evaluation were utilized.

**Statistical analysis:** Statistical analysis of the data was conducted using the SPSS 20 software package. Qualitative data were presented as counts and percentages. Quantitative data were indicated as mean and standard deviation (SD). The correlation of quantitative data was assessed using the Pearson correlation test. A statistical significance level (p) of 0.05 was adopted for all tests.

## RESULTS

In this study, when patients over 80 who underwent a hip fracture surgery were scanned, the data of 151 patients who met the study criteria were obtained. While the average age was  $85.48 \pm 4.07$  (elder: 96 years, youngest: 80 years), it was observed that 70.2% (n = 106) were female and 29.8% (n = 45) were male. Regional anesthesia was preferred for 93.38% (n=141) of the patients, while general anesthesia was administered to 6.62% (n=10) of them. The regional anesthesia techniques comprised 72.0% spinal anesthesia, 26.3% combined spinal-epidural anesthesia, and 0.7% peripheral nerve blocks. The most common comorbidities were hypertension (58.9%), neurological diseases (27.2%), and diabetes mellitus (22.5%), with acetylsalicylic acid being the most frequently used medication for anticoagulant and antiplatelet therapy at 27.2%, the second most common being clopidogrel at 6%. Postoperative ICU admission was present in 41.1% of the patients. While the preoperative stay length averaged 4.8 days, the postoperative stay length was 4.5 days. The 30-day mortality rate was 3.3% (Table 1).

**Table 1.** Demographic and operational characteristics of patients.

Specifications		Data
<b>Age</b>		85.48±4.07
<b>Gender, n (%)</b>	Female	106 (70.2%)
	Male	45 (29.8%)
<b>Anesthesia Type, n (%)</b>	Spinal anesthesia	103 (68.2%)
	Combined spinal-epidural anesthesia	37 (24.5%)
	General anesthesia	10 (6.6%)
	Peripheral Block	1 (0.7%)
<b>Comorbidity, n (%)</b>	Coronary Artery Disease	24 (15.9%)
	Diabetes Mellitus	34 (22.5%)
	Hypertension	89 (58.9%)
	Neurological	41 (27.2%)
	Renal	7 (4.6%)
	Malignancy	3 (2.0%)
<b>Anticoagulant, anti-aggregant, n (%)</b>	Acetylsalicylic Acid	41 (27.2%)
	Warfarin	5 (3.3%)
	Clopidogrel	9 (6.0%)
	New-generation oral anticoagulant	4 (2.6%)
<b>Intensive care unit admission, n (%)</b>		62 (41.1%)
<b>Preoperative length of hospital stay, days</b>		4.8 ± 3.0
<b>Postoperative length of hospital stay, days</b>		4.5 ± 2.8
<b>Mortality, n (%)</b>		5 (3.3%)

The calculated PLR value was recorded as 191 ± 105, the NLR value was 6.4 ± 4.5, and the SII value was 1410 ± 1210 (Table 2).

A significant correlation was detected between ICU admission and mortality, and the preoperative and postoperative stay length (p=0.006, p=0.017,

p=0.006, respectively). However, no significant correlation was found between ICU admission and NLR, PLR, and SII. Similarly, no significant correlation was found between mortality, preoperative and postoperative stay length, NLR, PLR, and SII (Table 3).

**Table 2.** PLR, NLR, and SII scores.

Parameters	Data
<b>PLR, Mean±SD</b>	191 ± 105
<b>NLR, Mean±SD</b>	6.4 ± 4.5
<b>SII score, Mean±SD</b>	1410 ± 1210
	1120 (667-1768)*

\*: Interquartile range (IQR); PLR: Platelet/lymphocyte ratio; NLR: Neutrophil/lymphocyte ratio; SII: Systemic immune inflammation index.

**Table 3.** Correlation of infection parameters with ICU admission and mortality.

Specifications		Intensive Care Unit Admission	Mortality	Preoperative Admission Duration	Postoperative Admission Duration	NLR	PLR	SII
<b>Intensive care unit admission</b>	r	1	0.222	0.194	0.222	0.092	0.053	0.115
	p	-	0.006*	0.017*	0.006*	0.262	0.522	0.161
<b>Mortality</b>	r	0.222	1	0.050	0.136	0.021	0.050	0.040
	p	0.006*	-	0.545	0.097	0.796	0.540	0.622

\*: p<0.005; PLR: Platelet/lymphocyte ratio; NLR: Neutrophil/lymphocyte ratio; SII: Systemic immune inflammation index.

## DISCUSSION AND CONCLUSION

Our study, which evaluated the 30-day mortality and ICU admission after a hip fracture surgery, found no correlation between inflammatory parameters and mortality or ICU admission. However, a significant correlation was found between ICU admission and preoperative and postoperative hospital stays.

The association of systemic inflammation with cardiovascular disease, abdominal disease, surgical site infections, and orthopedic disease has been revealed.<sup>8,10-13</sup> The relationship between several inflammatory markers and 30-day mortality in hip fractures has been demonstrated.<sup>5</sup> An experimental animal study has shown that hip fracture causes significant systemic inflammation and acute lung injury, and elderly rats were found to experience more pronounced acute lung injury compared to young rats.<sup>15</sup> A 30-day postoperative mortality rate was 9.9% in hip fracture patients.<sup>5</sup> Another study reported that the 30-day mortality rate in patients was 6%.<sup>16</sup> In a previous study conducted in our clinic, Palabiyik et al.<sup>7</sup> found a 30-day postoperative mortality rate of 10.4% in patients operated on for hip fractures. However, our current study's 30-day mortality rate was 3.3%. Perioperative conditions and medical comorbidities are important in determining risk factors for developing complications after hospitalization. These conditions, if managed well, have the potential to reduce postoperative morbidity and mortality.

In a comprehensive meta-analysis examining elderly hip fracture patients, it has been reported that a low lymphocyte count is valuable data in predicting increased mortality.<sup>17</sup> On the other hand, a high PLT count is a risk factor for the development of postoperative pressure ulcers in patients with hip fractures.<sup>18</sup> A PLR value exceeding 189 is associated with mortality in elderly hip fractures.<sup>19</sup> In our study, similarly to other studies, the mean PLR value was found to be 191; however, a correlation was not found between PLR and mortality.

Fisher et al.<sup>9</sup> have shown a significant association between high NLR values and hip fractures. Furthermore, it has been demonstrated that elevated NLR at the time of admission is not only associated with the presence of fractures and comorbidities but also closely linked to significant adverse outcomes such as postoperative myocardial injury, high inflammatory response, and in-hospital mortality. In patients with fractures, the reasons for elevated NLR at the time of admission can be multifactorial. It may be related to various pre-existing comorbid conditions, concurrent clinical or subclinical infections, and the process of responding to the fracture. Forget et al.<sup>20</sup> have reported that preoperative high NLR values, while insufficient as a standalone predictor for mortality, can be considered as one of the risk factors.

Although the NLR value was 6.4 in our study, no significant correlation was observed between mortality and ICU admission. In our study, NLR and PLR rates were significantly higher than in normal healthy individuals. Mortality rates are lower than other studies. The decision-making process for admitting patients to intensive care after surgery may vary between physicians. Many factors, in addition to inflammatory markers, have an impact on intensive care unit admission and mortality of patients with hip fractures in the elderly. For such reasons, no significant difference was detected between inflammatory markers and mortality.

A high SII value has been identified as a good predictor factor for osteoporotic fractures.<sup>13</sup> Wang et al.<sup>19</sup> demonstrate that in elderly adults who experience and undergo surgery for hip fractures, the SII is significantly associated with mortality and could be a good indicator for predicting prognosis. Wang et al.<sup>21</sup> reported an association between the SII and mortality in patients undergoing hip fracture surgery in another study where they examined 290 patients. It has been indicated that the SII can be easily applied in routine clinical practice due to its simplicity and cost-effectiveness.<sup>19</sup> In this study, while the SII value was approximately 1410, no correlation or significant difference was found in mortality and ICU admission.

The most significant limitation of this study is the small sample size. The use of short-term mortality rates has posed challenges in interpreting the data. The absence of preadmission laboratory parameters for patients has limited a thorough assessment of the baseline impact of inflammation caused by a hip fracture.

In conclusion, a positive correlation was observed between ICU admission and mortality. Statistically, no significant correlation was found between the PLR, NLR, SII values and mortality rates. However, the inflammatory markers of the patients were found to be above normal levels, similar to those stated in the literature. Larger-scale studies with a higher number of patients are needed for a more comprehensive investigation.

**Ethics Committee Approval:** Our study was approved by the Ethics Committee at the Sakarya University Faculty of Medicine (Date: 02/02/22, Decision no: E-71522473-0.50.01.04-102134-26). The study was carried out following the international declaration and guidelines.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Author Contributions:** Concept – FŞ, OP; Supervision – OP, HK, AK; Materials – FŞ, MHT; Data Collection and Processing – FŞ, MHT; Analysis and Interpretation – HK, AK; Writing –FŞ, HK, MHT.

**Peer-review:** Externally peer-reviewed.

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