

Association between Increased Neutrophil-To-Lymphocyte Ratio and Postoperative 1-Year Mortality in Elderly Patients with Pertrochanteric Hip Fracture

Pertrokanterik Kalça Kırığı Geçiren Yaşlı Hastalarda Yüksek Nötrofil-Lenfosit Oranı ile Postoperatif 1 Yıllık Mortalite Arasındaki İlişki

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ÖZ

Amaç: Araştırma, yaşlı hastalarda kalça kırığı ameliyatı geçiren bireylerde perioperatif nötrofil/lenfosit oranının (NLR) mortalite üzerindeki prognostik değerini incelemeyi amaçlamaktadır.

Araçlar ve Yöntem: Çalışmaya dahil edilen 236 hasta (%68.6 kadın ve %31.4 erkek), belirlenen kriterlere uyan ve kalça kırığı ameliyatı geçiren bireylerden oluşmaktadır. Hastaların kabul anındaki tam kan sayımı ve beşinci postoperatif günlük değerleri kaydedilmiştir. Kabul anındaki (NLR-D0) ve beşinci postoperatif günlük (NLR-D5) NLR değerleri ana değişken olarak belirlenmiştir.

Bulgular: Hastaların yaş ortalaması 80.1±7.9 yıldır (65-99). Hayatta kalan hastaların ortalama NLR-D0 ve NLR-D5 değerleri sırasıyla 6.54 ve 4.55'tir. Vefat eden hastaların ise ortalama NLR-D0 ve NLR-D5 değerleri sırasıyla 6.99 ve 8.90'dır. Hayatta kalanlar ve vefat edenler arasında NLR açısından anlamlı bir fark bulunmuştur. NLR-D0 değerlerinin yaşayanlar ve ölenler arasında anlamlı bir fark oluşturmadığı, ancak NLR-D5 değerinin ölenlerde belirgin şekilde yüksek olduğu görülmüştür. Birinci postoperatif yıl sonundaki mortalite oranı %35.2'dir.

Sonuç: Kalça kırığı ameliyatı geçiren yaşlı hastalarda beşinci postoperatif gündeki yüksek NLR değeri (NLR-D5>7.85), 1 yıllık mortaliteyi öngörmeye bir belirleyici olabilir.

Anahtar Kelimeler: biyobelirteçler; geriatri; kırılmalık; sağkalım; travma

ABSTRACT

Purpose: This study aimed to examine the prognostic value of perioperative NLR level in terms of mortality in the first postoperative year in elderly patients undergoing hip fracture surgery.

Materials and Methods: The study included 236 patients (68.6% female and 31.4% male) who met the specified criteria and had undergone hip fracture surgery. Complete blood counts were recorded at admission and on the fifth postoperative day. Neutrophil-to-lymphocyte ratios (NLR) at admission (NLR-D0) and on the fifth postoperative day (NLR-D5) were identified as the primary variables.

Results: The mean age of the participants was 80.1±7.9 years (min: 65 years to max: 99 years). The mean NLR-D0 and mean NLR-D5 values of surviving patients were 6.54 and 4.55, respectively. The mean NLR-D0 and mean NLR-D5 values of patients who died were 6.99 and 8.90, respectively. A significant difference was found in the NLR variability of the patients who survived and those who died. The examination of the effects of NLR-D0 and NLR-D5 parameters on mortality revealed no significant difference in NLR-D0 values between the patients who lived and those who died ($p>0.05$), but the NLR-D5 value was significantly higher in the patients who died. The mortality rate at the end of the first postoperative year was 35.2%.

Conclusion: A high NLR value (NLR-D5>7.85) on the fifth postoperative day in elderly patients undergoing hip fracture surgery may be a predictor of 1-year mortality after hip fracture surgery.

Keywords: biomarkers; frailty; geriatric; survival; trauma

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INTRODUCTION

Numerous epidemiological studies have highlighted a rising incidence of hip fractures, attributable to the increasing life expectancy of the population in recent decades. These fractures exert significant adverse effects on both the healthcare system and society at large. Geriatric patients, often burdened with multiple comorbidities, face an elevated risk of mortality during the postoperative recovery period following hip fracture surgery.¹⁻³ Therefore, the death rate in this patient group is very high within the first year after the surgery. Tajeu et al. reported a death rate of 12–37% within the first year after hip fracture surgery.¹ Despite the high incidence, predicting which patients have a high risk of complications and high mortality rates remains a challenge. The use of a simple and inexpensive biomarker derived from a complete blood count may be a prognostically effective and cost-efficient approach.

The neutrophil/lymphocyte ratio (NLR) has become increasingly popular as an indicator calculated using relevant values in the complete blood count. NLR is widely recognized as a marker of subclinical inflammation.⁴ Many studies have reported that NLR can be used to assess the risk of mortality in certain medical procedures such as angiography or appendectomy and to predict prognosis in some types of cancer.⁵

The number of studies examining the relationship between NLR levels after hip fracture surgery and mortality is limited, and the results of existing studies are controversial. This study aimed to investigate the prognostic value of perioperative NLR levels in predicting one-year mortality among patients undergoing hemiarthroplasty following hip fracture. The study utilized a more homogeneous patient group compared to previous studies.

MATERIALS and METHODS

This retrospective cohort study was approved by Kırşehir Ahi Evran University Clinical Research Ethics Committee with the date 09.04.2020 and decision number 2020-06/44. Elderly patients who applied to our clinic due to hip fracture between January 2015 and January 2020 were evaluated. The inclusion criteria were as follows: (1) patients aged 65 years and older, (2) having an ASA score of 3, (3)

having an unstable pertrochanteric fracture treated with cemented hemiarthroplasty, and (4) undergoing surgical treatment within two days after injury. Patients with multiple traumas, those who had undergone any hip arthroplasty surgery previously, those with malignancy or a pathological fracture, those who had undergone another surgical operation within the last 30 days, and patients using corticosteroids or with active infections were excluded. All surgeries were carried out under spinal anesthesia by senior surgeons. The standard posterior approach was used during the surgery. Calcar replacement cemented partial prosthesis was applied using the second-generation cementing technique. All patients were given antibiotic prophylaxis with first-generation cephalosporin (cefazolin sodium 1 g) for 3 days. For pharmacological and mechanical thromboprophylaxis, 0.4 mg/day subcutaneous low-molecular-weight heparin (Enoxiparine) was administered for 35 days to the patients. The postoperative follow-up of the patients was done and documented by an interdisciplinary team comprising anesthesiologists, orthopedic surgeons, internal medicine specialists, and physiotherapists. After discharge, the patients were called for a check-up in the 1st, 3rd, 5th, and 12th months.

The details on patients' demographic characteristics, preoperative comorbidities, ASA scores, surgical time and type, anesthesia type, complications, and CBC taken at the time of admission and on the fifth postoperative day were obtained from the digital databank and recorded. Whether patients died in the first postoperative year was determined using the central population management system (MERNIS) (using the patients' national ID numbers). Complications developed in 55 patients (23.3%). Among these patients, cardiovascular complications (52.7%) and infectious complications (12.7%) were the most common.

The venous blood samples taken from all patients on the day of admission and on the fifth postoperative day were anticoagulated with EDTA (Ethylenediamine tetraacetic acid) and processed in an analysis device (Sysmex; TOA-Med, Japan) used in the biochemistry laboratory for determining CBC. The NLR value was calculated by dividing the absolute total neutrophil count by the absolute number of lymphocytes. In this study, the NLR values at admission and on the 5th postoperative day were selected as the main

variables because these periods reflect the most pronounced inflammatory and immunological changes. The NLR-D0 value represents the patient's preoperative inflammatory status, while the NLR-D5 value indicates the postoperative inflammatory response and recovery process. Previous studies have shown a strong association between NLR-D5 values and postoperative complications and mortality. Therefore, these two time points were chosen to examine changes in the inflammatory response over time and their impact on mortality.

Statistical Analysis

Data were analyzed with the SPSS v.21 program. The kurtosis and skewness values obtained from within-item scales between +3 and -3 were considered sufficient for distributions. The difference in the measurements according to the variables with two groups was examined with the *t* test, and the difference according to the variables with three or more groups was examined with Analysis of Variance (ANOVA). The relationship between the measurements was analyzed using the Pearson correlation test. The change in NLR-D0-NLR-D5 measurements was analyzed using the repeated-measures ANOVA. The effect of NLR-D5 on mortality was analyzed using the binary logistic regression test. ROC curve analysis was applied to determine a cut-off value of the NLR-D5 parameter in determining mortality.

RESULTS

A total of 236 patients (68.6% female and 31.4% male) who met the inclusion criteria out of 346 patients admitted to the hospital with unstable pertrochanteric fractures were included in the study (Fig. 1). The mean age was 80.1±7.9 years (min:65 to max:99 years). The mortality rate at the end of the first postoperative year was 35.2%. The patients' mean NLR-D0 value was 6.70±2.10 and the mean NLR-D5 value was 6.08±2.9. The Pearson correlation test carried out to examine the relationship between age and NLR-D0 and NLR-D5 values showed a positive relationship ($r=0.458, r=0.318$).

The mean values of the patients who survived were 6.54 and 4.55, respectively. The mean NLR-D0 and NLR-D5

values of the patients who died was 6.99 and 8.90. A significant difference was found in the NLR variability of the patients who survived and those who died ($p<0.05$) (Fig. 2).

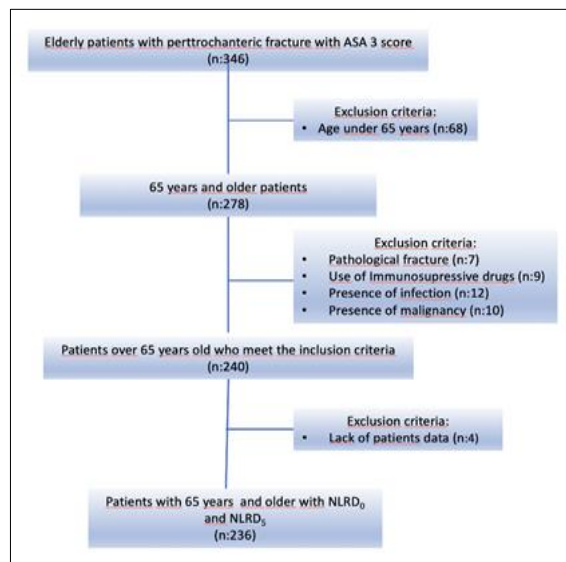


Figure 1. Patient flow chart.

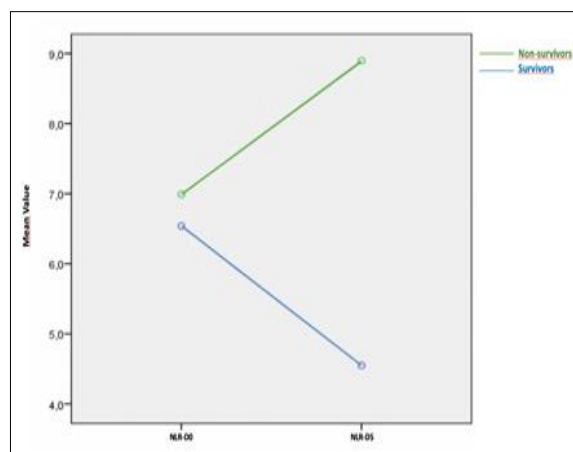


Figure 2. NLR values according to survival status.

Similarly, no significant difference was found in NLR-D0 values between the survivors and non-survivors ($p>0.05$), but the NLR-D5 value was significantly higher in the patients who died (Table 1).

Table 1. NLR values of survivors and nonsurvivors.

	Survivors		Nonsurvivors		P value
	Mean	Standard deviation	Mean	Standard deviation	
NLR-D0	6.54	1.99	6.99	2.28	0.115
NLR-D5	4.55	1.41	8.90	2.84	0.000

In the ROC curve analysis for predicting postoperative mortality with the NLR-D5 value, an area under the curve

of 0.939 was observed ($p < 0.05$). The cut-off value for NLR-D5 was determined to be 7.85 (sensitivity:0.58, specificity:0.993). (SE:0.015, 95% CI:0.909–0.969) (Fig. 3).

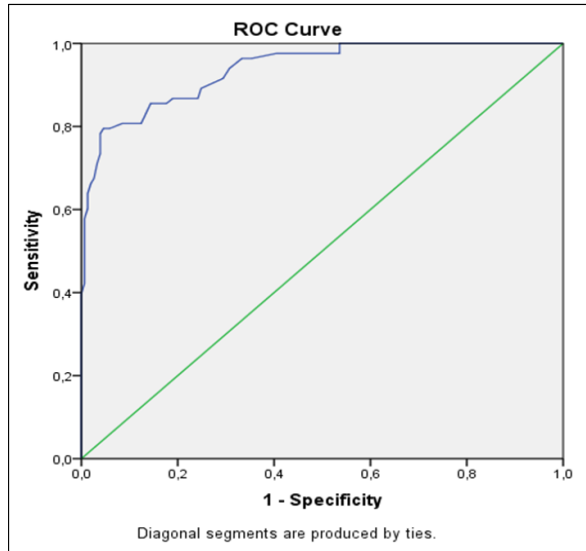


Figure 3. Graphics of ROC analysis.

DISCUSSION

Laboratory tests are utilized in the diagnosis and prognosis monitoring of diseases, as well as in diversifying medical treatments. Many parameters are used as laboratory tests, including the NLR value. Fisher et al. reported that elderly traumatic patients with high NLR values at admission had an increased risk of postoperative myocardial injury and mortality.⁶ The studies examining the relationship between NLR and fractures in orthopedics are limited, and mostly focused on hip fracture surgery.⁷⁻¹³ The relationship between NLR values in geriatric patients diagnosed with this fractures and risk of mortality in the first postoperative year was evaluated for the first time by Forget et al.¹³ The mortality rate for the first year was determined as 27.2% in the study conducted with 247 patients aged 65 years and above. The comparison of the patients who survived and those who died showed that the NLR value significantly decreased on the fifth postoperative day in the patients who survived. The mean NLR value of the patients who survived was 8.1 ± 4.58 at the time of admission, but it dropped to a mean of 5.6 ± 4.3 on the fifth postoperative day, leading to a significant difference. The mean NLR value of the patients who died was 8.4 ± 7.2 at the time of admission, which was similar to that in the other groups. However, the mean NLR value on the fifth postoperative

day was calculated as 8.8 ± 8.6 , and no significant difference was found between the two values. The ROC curve for predicting postoperative mortality with the NLR value on day 5, Forget et al. observed an area under the curve of 0.61 ($P = 0.01$).¹³ The most discriminant NLR value was 4.9 (sensitivity:%62.9, specificity:%57.6). All elderly patients with hip fractures (heterogeneous group), regardless of the type of fractures, type of surgery performed, and additional diseases, were included in the study, which was stated as the most important limitation of their study.¹³ Temiz et al. investigated the preoperative NLR values in terms of 1-year mortality.¹⁴ They included 50 patients who underwent hemiarthroplasty due to unstable intertrochanteric fractures meeting the inclusion criteria. The mean NLR value of the patients who died and those who survived was 8.11 and 4.14, respectively. They observed an area under the curve of 0.839 ($p < 0.0001$). The most discriminant NLR value was 4.7.¹⁴ However, the most important limitation of their study was that the number of cohort was insufficient, although the patient group included in the study was homogeneous.

In our study, while there was no significant difference in NLR-D0 values between the two groups ($p > 0.05$), NLR-D5 values were higher in patients who died ($p < 0.05$) (Table 1).

In addition, the NLR-D5 value was significant in predicting 1-year postoperative mortality. The most distinctive NLR value was calculated as 7.85 in predicting mortality in ROC analysis performed for NLR-D5 values.

In this study, unlike most studies in the literature, a more homogeneous patient group was evaluated using broader exclusion criteria. The most discriminant NLR value in this study compared with other studies might be due to the selection of a bigger patient group with a narrower spectrum and homogeneity, and the differences in NLR values between populations as mentioned in another previous study.^{15,16}

It is not correct to evaluate the NLR alone as a definitive predictor of postoperative mortality.^{17,18} However, the reason for considering this as a significant risk of mortality may be attributed to the variability in the body's endocrine and immunological response to stress caused by events

such as surgical trauma. The stress response induced by events like surgical trauma may entail metabolic and immunological changes. The release of stress hormones and cytokines plays a role in the occurrence of post-traumatic reactions. One of the important hormonal response systems to stress is the stress hormone known as cortisol. A stress response occurs in the body with the mixing of cortisol into the blood.²⁰ Strong elderly patients, who can effectively cope with stress after fractures and surgical trauma, can normalize cortisol secretion in the following days after surgery and therefore their NLR in the postoperative days. In frail older patients, however, the mortality rate is high due to persistent acute inflammatory response and stress status.²¹ This may explain why the NLR values in patients who died were significantly higher on the fifth postoperative day compared with the values in surviving patients, although the NLR values at admission did not differ significantly in patient groups. Less invasive surgical techniques and pharmacological agents may be used in the postoperative treatment of patients with a postoperative NLR-D5>7.85 to prevent postoperative inflammatory and excessive stress response. Knowing the patient group with a high mortality risk after hip fracture surgery offers a different approach to physicians in both postoperative follow-up and hospitalization process.

In interpreting the results, the presence of comorbidities could also be considered. This is because postoperative inflammatory response can either increase or decrease NLR values, thereby potentially altering the relationship between NLR, postoperative complications, and mortality. Evaluating our cohort, which exhibits non-homogeneous characteristics in terms of comorbidity, from this perspective has not been feasible. However, we acknowledge that these factors could have potential effects on our results.

The main limitations of this study include its retrospective nature and single-center design, as well as the reliance on data obtained solely from the hospital's records system. In addition, other external factors that could affect the inflammatory level of the patients were not included in the study. The inflammatory markers, besides the NLR, were not evaluated.

Conclusion

Our study demonstrated that elevated NLR values (NLR-D5>7.85) on the fifth postoperative day in elderly patients undergoing pertrochanteric hip fracture surgery might serve as a predictor of one-year mortality after surgery. More comprehensive and prospective studies are needed in this regard.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

The study was approved by Kırşehir Ahi Evran University Clinical Research Ethics Committee (date: 09.04.2020 and number: 2020-06/44).

Authors' Contributions

Concept/Design: HS, ÖÖ. Data Collection and/or Processing: ÖÖ, HS. Data analysis and interpretation: ÖÖ, HS. Literature Search: EÇ, FE. Drafting manuscript: EÇ, FE. Critical revision of manuscript: FE, EÇ.

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