

Admission neutrophil-to-lymphocyte ratio and postoperative mortality in elderly patients with hip fracture

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ABSTRACT

BACKGROUND: Hip fractures in elderly patients are associated with a high mortality rate. Most deaths associated with hip fracture result from complications after surgery. Recent studies suggest that the neutrophil-to-lymphocyte ratio (NLR), which is a laboratory marker used to evaluate systemic inflammation, may be useful to estimate excess mortality. This study aimed to investigate the prognostic value of admission NLR in elderly patients with hip fracture.

METHODS: We evaluated patients admitted to the Orthopaedic Surgery Department of Balıkesir-Edremit State Hospital. Inclusion criteria were female gender, age between 65 and 80 years, ASA score of 3, unstable intertrochanteric fracture treated with hemiarthroplasty, and time between fracture and surgery less than 72 h. Patients with multiple fracture, previous same side or other side hip surgery, pathological fracture, such as fracture caused by tumor or metabolic bone disease (e.g., Paget's disease), and malignancies were excluded from this study (purposive sampling technique). Finally, "case" (group 1) was defined as patients who died within 1 year after surgery, whereas "control" (group 2) was defined as patients who survived. Patients in group 1 and 2 were statistically compared in terms of NLR value on hospital admission. A total of 22 patients (44%) were included in group 1, and 28 (56%) were included in group 2.

RESULTS: We found that the admission NLR values of patients in the mortality group were significantly higher than those of patients in the control group ($p<0.001$). The cutoff value of NLR was calculated as 4.7 on ROC analysis.

CONCLUSION: We believe that the NLR value at admission could be used for risk stratification of mortality in elderly patients with hip fracture.

Keywords: Elderly; hip fracture; neutrophil-to-lymphocyte ratio.

INTRODUCTION

Hip fractures in the elderly are associated with high postoperative complications and mortality.^[1] It was previously reported that 1-year mortality ranges from 8.4% to 36%.^[2] Most deaths result from cardiovascular events and inflammatory complications, such as pneumonia, cardiac failure, myocardial infarction, and pulmonary embolism.^[1,3]

Studies indicated that some laboratory findings, such as high potassium, low hemoglobin, and low albumin could be associated with increased risk of mortality in patients with hip

fracture.^[4] Serum inflammation markers such as C-reactive protein (CRP) could also be a predictor of excess mortality.^[5] Recent studies suggest that the neutrophil-to-lymphocyte ratio (NLR), which is a laboratory marker used to evaluate systemic inflammation, may be useful to estimate excess mortality and poor prognosis in clinical conditions such as breast cancer, colorectal-gastric cancer, and coronary heart disease.^[6-8] The preoperative NLR also reflects patients' survival in lung and liver cancer.^[8] In orthopedic literature, the relationship between high NLR and excess mortality has been scarcely studied. Therefore, we aimed to investigate the prognostic value of preoperative NLR in elderly patients with hip

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fracture. We hypothesized that if an elderly patient with hip fracture had a high NLR value on admission, the postoperative 1-year mortality risk increases.

MATERIALS AND METHODS

Study Design

This retrospective case control study was approved by the ethics committee of Balikesir University Faculty of Medicine University, School of Medicine. We evaluated elderly patients with hip fracture admitted to the Orthopaedic Surgery Department of Edremit State Hospital between January 2008 and March 2014. Because age, gender, fracture type, ASA score, and time between fracture and surgery have been reported as risk factors for mortality in patients with hip fracture,^[1] a purposive sampling design was used to better evaluate the prognostic value of high NLR. Inclusion criteria were female gender, age between 65 and 80 years, ASA score of 3, unstable intertrochanteric fracture treated with hemiarthroplasty, and time between fracture and surgery less than 72 h. Patients with multiple fracture, previous same side or other side hip surgery, pathological fracture, such as fracture caused by tumor or metabolic bone disease (e.g., Paget's disease), and malignancies were excluded. Patients with a history of another surgery or infectious disease in the last 30 days prior to admission and current use of immunosuppressants such as corticosteroids were also excluded. The postoperative mortality status of the study population was detected by phone call. Finally, "case" (group 1) was defined as patients who died within 1 year after surgery, whereas "control"(group 2) was defined as patients who survived (Fig. 1).

Patients and Care

All patients were operated under local anesthesia. Calcar replacement, cemented stem was used via posterior exposure in all patients. A second-generation cementing technique was utilized. A similar postoperative protocol comprising early ambulation with weight bearing was performed. Enoxaparin sodium 0.4 ml once a day was initiated on admission and continued for 4 weeks postoperatively. Cefazolin sodium 1 g was intravenously administered three times a day only on postoperative day 1. Clinical follow-up was conducted by a multidisciplinary medical team that included orthopedic surgeons, anesthesiologists, a general internist, and physiotherapists.

Laboratory Measurements

NLR on admission was established as the main variable in this study. In each patient, venous blood samples were obtained, and complete blood cell count (CBC) was assessed at our biochemical laboratory. An automated blood cell counter was used for CBC measurement (Beckman Coulter® LH 780, California, USA). NLR was calculated as the simple ratio between absolute neutrophil and absolute lymphocyte counts on admission.

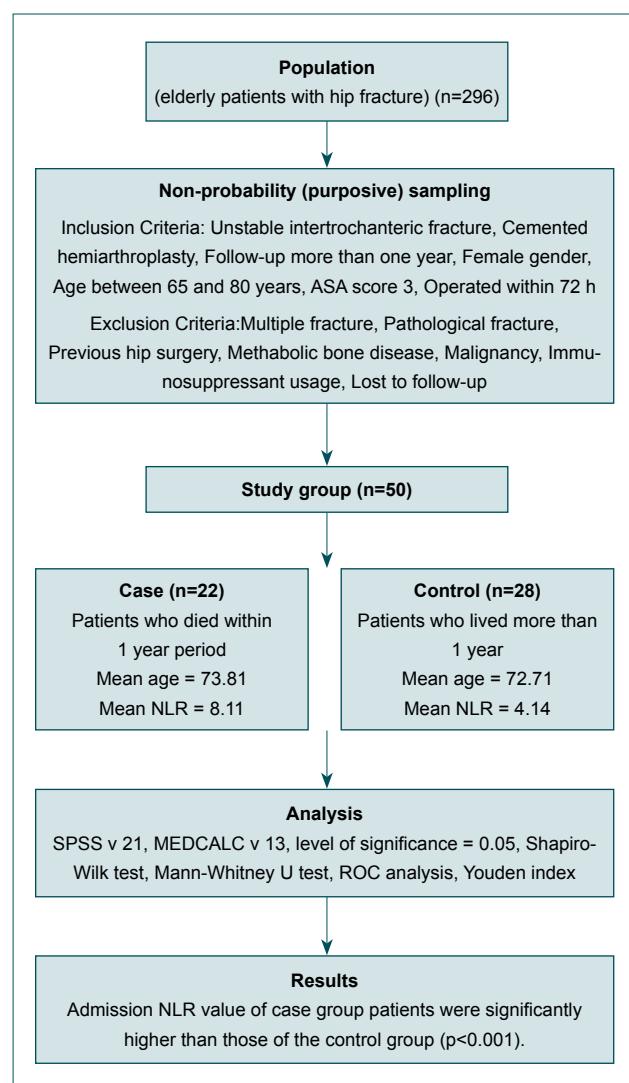


Figure 1. Diagram showing the study design and results.

Statistical Analysis

Group 1 and 2 patients were statistically compared in terms of NLR value on hospital admission. Statistical analysis was performed using SPSS v.21 and MEDCALC v.13 package. The level of significance was defined as $\alpha=0.05$. The normal distribution of data was tested using Shapiro–Wilks test. The Mann–Whitney U-test was used to compare the groups. The ROC analysis and Youden index were used to determine the cutoff value.

RESULTS

Of 296 patients with hip fracture who were treated during this time period, 50 patients who met the inclusion and exclusion criteria were defined as the study group. A total of 22 patients (44%) were included in group 1, and 28 (56%) patients were included in group 2. The mean age of patients was 73.81 (65–80) for group 1 and 72.71 (67–80) for group 2 ($p>0.05$). The mean NLR value was calculated as 8.11 for group 1 and 4.14 for group 2 (Table 1).

Table I. The neutrophil-to-lymphocyte ratio value of each group

Group	n	Median	Minimum	Maximum	Mean	Standard deviation
Control	28	3.730000	1.0000	11.7000	4.140714	1.9744177
Mortality	22	7.51500	1.8500	22.0000	8.118182	4.9131501
Total	50	4.740000	1.0000	22.0000	5.890800	4.0584509

We found that the admission NLR values of the mortality group patients were significantly higher than those of the control group ($p<0.001$). The cutoff value of NLR was calculated as 4.7 on ROC analysis (area under the curve: 0.839, standard error: 0.0635, 95% confidence interval: 0.708–0.928, z statistic: 5.345, $p<0.0001$, sensitivity: 86.4, specificity: 78.6, and Youden index J: 0.65) (Fig. 2).

DISCUSSION

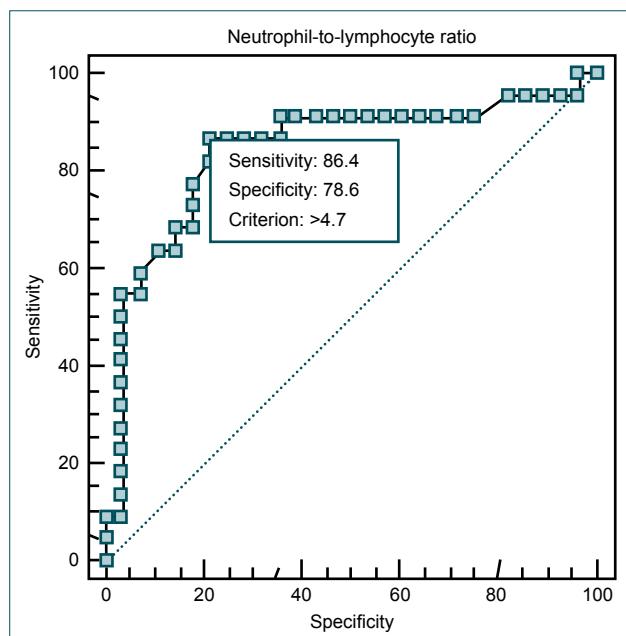
The most important result of our study is that patients who died within 1 year after hip fracture surgery have a higher admission NLR value than those in the control group. As a new risk factor for mortality in patients with hip fracture, NLR was first evaluated by Forget et al.^[2] in 2015. In their study, NLR was investigated at admission and at postoperative days 2 and 5. They reported that if postoperative day 5 NLR >5, excess mortality can be expected, but preoperative NLR is not predictive of postoperative mortality. Fisher et al.^[9] assessed the prognostic value of admission NLR for short-term outcomes in ortho-geriatric patients. They found that high NLR on admission is a significant risk factor of postoperative myocardial injury, high inflammatory response, and in-hospital death.

Inflammatory changes induced by hip trauma and surgery can affect survival.^[10] It has been suggested that acute inflamma-

tory response assessed by some inflammatory markers, such as tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and IL-10 can predict the 12-month outcome of patients with hip fracture.^[11] NLR is also described as a new potential marker of systemic inflammation.^[12] Therefore, it can be associated with the prognosis of patients with hip fracture. Forget et al.^[2] reported that the prognostic value of NLR is more prominent after surgery. They reported that this finding can be explained by the cumulative effect of persistent acute inflammatory response and persisting stress status in frail older patients.^[2] However, acute inflammatory response during the postoperative period can be affected by different factors, such as type of surgery. Sedlár et al.^[13] reported that elevation of CRP, WBC, and IL-6 levels was highest in patients treated with hemiarthroplasty compared with patients treated with osteosynthesis. Del Prete et al.^[14] found that secretion of inflammatory markers, especially IL-6, is less marked when minimally invasive techniques are used compared with traditional surgery for the fixation of pertrochanteric fracture via dynamic hip screw. Accordingly, we focused on the evaluation of the prognostic value of admission NLR rather than postoperative NLR. Preoperative estimation of excess mortality risk may be more useful for determining the treatment modality. If the patient has high admission NLR, less invasive surgical techniques can be selected to prevent excess postoperative inflammatory response. Hypothetically, to reduce systemic inflammation, some pharmacological agents, such as statins and aspirin, can be used in the postoperative treatment of patients with hip fracture with high NLR value. Further investigations are needed in this subject.

Our study is a retrospective analysis of single-center patients, and it has all the inherent limitations of a retrospective study. We used a non-probability, purposive sampling technique to construct a study group, and this technique has some advantages and disadvantages. We believe that the primary advantage of purposive sampling in this study is to reduce the confounding effect of previously reported risk factors of mortality (age, gender, fracture type, surgical time, and ASA score). Additionally, malignancies and recent steroid therapies can affect the inflammatory status and NLR value of patients. The primary disadvantages of purposive sampling are the high probability of selection bias and sampling error. For this reason, the generalizability of our findings is low.

Despite these limitations, we conclude that high NLR value on admission can be a risk factor for excess 1-year mortality in elderly patients with hip fracture. We believe that this sim-

**Figure 2.** Graphics of ROC analysis.

ple and inexpensive biomarker could be used for risk stratification of mortality in this patient population.

Conflict of interest: None declared.

REFERENCES

- Fahy AS, Wong F, Kunasingam K, Neen D, Dockery DNF, Ajuied A, Back DL. A Review of Hip Fracture Mortality—Why and How Does Such a Large Proportion of These Elderly Patients Die? *Surgical Science* 2014;5:227–32. [CrossRef]
- Forget P, Moreau N, Engel H, Cornu O, Boland B, De Kock M, et al. The neutrophil-to-lymphocyte ratio (NLR) after surgery for hip fracture (HF). *Arch Gerontol Geriatr* 2015;60:366–71. [CrossRef]
- Hu F, Jiang C, Shen J, Tang P, Wang Y. Preoperative predictors for mortality following hip fracture surgery: A systematic review and meta-analysis. *Injury* 2012;43:676–85. [CrossRef]
- Mosfeldt M, Pedersen OB, Riis T, Worm HO, Mark Sv, Jørgensen HL, et al. Value of routine blood tests for prediction of mortality risk in hip fracture patients. *Acta Orthop* 2012;83:31–5. [CrossRef]
- Forasassi C, Golmard JL, Pautas E, Piette F, Myara I, Raynaud-Simon A. Inflammation and disability as risk factors for mortality in elderly acute care patients. *Arch Gerontol Geriatr* 2009;48:406–10. [CrossRef]
- Azab B, Bhatt VR, Phookan J, Murukutla S, Kohn N, Terjanian T, et al. Usefulness of the neutrophil-to-lymphocyte ratio in predicting short- and long-term mortality in breast cancer patients. *Ann Surg Oncol* 2012;19:217–24. [CrossRef]
- Malietzis G, Giacometti M, Askari A, Nachiappan S, Kennedy RH, Faiz OD, et al. A preoperative neutrophil to lymphocyte ratio of 3 predicts disease-free survival after curative elective colorectal cancer surgery. *Ann Surg* 2014;260:287–92. [CrossRef]
- Shimada H, Takiguchi N, Kainuma O, Soda H, Ikeda A, Cho A, et al. High preoperative neutrophil-lymphocyte ratio predicts poor survival in patients with gastric cancer. *Gastric Cancer* 2010;13:170–6. [CrossRef]
- Fisher A, Sriksulanukul W, Fisher L, Smith P. The Neutrophil to Lymphocyte Ratio on Admission and Short-Term Outcomes in Orthogeriatric Patients. *Int J Med Sci* 2016;13:588–602. [CrossRef]
- Sedlář M, Kvasnička J, Krška Z, Tománková T, Linhart A. Early and subacute inflammatory response and long-term survival after hip trauma and surgery. *Arch Gerontol Geriatr* 2015;60:431–6. [CrossRef]
- Sun T, Wang X, Liu Z, Chen X, Zhang J. Plasma concentrations of pro- and anti-inflammatory cytokines and outcome prediction in elderly hip fracture patients. *Injury* 2011;42:707–13. [CrossRef]
- Ahsen A, Ulu MS, Yuksel S, Demir K, Uysal M, Erdogan M, Acarturk G. As a new inflammatory marker for familial Mediterranean fever: neutrophil-to-lymphocyte ratio. *Inflammation* 2013;36:1357–62. [CrossRef]
- Sedlář M, Kudrnová Z, Erhart D, Trča S, Kvasnicka J, Krška Z, et al. Older age and type of surgery predict the early inflammatory response to hip trauma mediated by interleukin-6 (IL-6). *Arch Gerontol Geriatr* 2010;51:e1–6. [CrossRef]
- Del Prete F, Nizegorodcew T, Regazzoni P. Quantification of surgical trauma: comparison of conventional and minimally invasive surgical techniques for pertrochanteric fracture surgery based on markers of inflammation (interleukins). *J Orthopaed Traumatol* 2012;13:125–30.

ORİJİNAL ÇALIŞMA - ÖZET

Kalça kırıklı yaşlı hastalarda nötrofil-lenfosit oranı ve ameliyat sonrası mortalite

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AMAÇ: Kalça kırıklı yaşlı hastalarda ameliyat sonrası mortalitenin yüksek olduğu bildirilmiştir. Bunun nedeni genellikle ameliyat sonrası gelişen komplikasyonlardır. Güncel çalışmalarla nötrofil-lenfosit oranının (NLR), yüksek mortalite oranı ile ilişkili olduğu belirtilmektedir. Çalışmamızda amaç, kalça kırıklı yaşlı hastalarda, hastaneye yataş esnasındaki NLR'nın, ameliyat sonrası mortalite ile ilişkisi olup olmadığını araştırmak idi.

GEREÇ VE YÖNTEM: Balıkesir Edremit Devlet Hastanesi Ortopedi ve Travmatoloji Kliniği'nde 65–80 yaş arası, ASA puanı 3 olan, stabil olmayan trokanterik kırık nedeniyle çimentolu bipolar kalça protezi uygulanan kadın hastalar çalışmaya dahil edildi. Tüm hastalar kırık sonrası ilk 72 saat içinde ameliyat edilmiş idi (amaç yönelik örnekleme tekniği). Grup 1 hastalar ameliyat sonrası birinci yıl içinde ölenler ($n=22$, %44), grup 2 hastalar ($n=28$, %56) ise yaşayanlar idi. Her iki grup ameliyat öncesi NLR değerleri açısından istatistiksel olarak karşılaştırıldı.

BULGULAR: Gruplar arasında ameliyat öncesi NLR değeri açısından anlamlı fark tespit edildi ($p<0.001$). ROC analizinde kesim değeri 4.7 bulundu.

TARTIŞMA: Buna göre ameliyat öncesi NLR değerinin kalça kırıklı yaşlı hastalarda mortalite ile ilişkili olduğu kanaatindeyiz.

Anahtar sözcükler: Kalça kırığı; nötrofil-lenfosit oranı; yaşlı hasta.

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