

The effect of neutrophil-lymphocyte ratio on admission to postoperative intensive care and mortality in elderly patients undergoing hip fracture surgery with spinal anesthesia

Ökkeş Hakan Miniksar¹, Osman Kaçmaz²

¹Department of Anesthesiology and Reanimation, Yozgat Bozok University, Faculty of Medicine, Yozgat, Turkey

²Department of Anesthesiology and Reanimation, Turgut Özal University, Malatya Training and Research Hospital, Malatya, Turkey

ABSTRACT

Objectives: Hip Fractures (HF) affect the elderly in particular, and are associated with high mortality rates. Most geriatric patients are admitted to Intensive Care Unit (ICU) after HF surgery. In this study, the purpose was to investigate the prognostic value of preoperative NLR (Neutrophil-to-Lymphocyte Ratio) on postoperative ICU admission and mortality in elderly patients with HF.

Methods: In the present study, the data of 188 geriatric patients who underwent surgery because of isolated HF (i.e. femur neck and intertrochanteric fracture) were examined retrospectively. The patients over 65 years of age, ASA score 3/4, whose preoperative duration was less than 72 hours, and who underwent spinal anesthesia were included in the study. The patients were divided into two groups as ICU admission (ICU, n = 58), and Non-ICU (Non-ICU, n = 130). The patients were also grouped as Survival (n = 168) and Non-survival (n = 20) according to postoperative mortality rates. NLR values were statistically compared between the groups.

Results: The preoperative NLR values of the patients in the ICU Group were significantly higher than those in the Non-ICU Group ($p < 0.001$). The cut-off value of NLR for ICU admission was found to be 9.65 with 89% sensitivity and 67% specificity in the ROC analysis. The median NLR value was 6.42 (3.55-9.44) in the Survivor Group, and 9.5 (7.23-11.02) in the Non-Survivor Groups ($p = 0.015$).

Conclusions: It was shown in the study that high NLR values in elderly patients may be a risk factor for ICU admission, and for postoperative mortality after HF.

Keywords: Geriatrics; hip fracture; neutrophil-to-lymphocyte ratio; intensive care unit; mortality

The population of the world is aging rapidly, and the number of Hip Fractures (HF) is increasing at the same rate. HF is a serious injury affecting the elderly in particular, and causes high mortality and morbidity. The mortality rate of patients after HF is approximately 15-20% [1-3].

Most of deaths following HFs are caused by cardiovascular events, such as heart failure, myocardial

infarction, pulmonary thromboembolism, and infectious complications [1, 2]. It is seen that these high-risk patients, who are older and have comorbidities, are often admitted to ICUs whether in a planned or in an unexpected way according to their preoperative clinical status after HF surgery [3]. However, it is also known that patients who are admitted directly to the ICU in the postoperative period have better results

Received: December 3, 2020; Accepted: June 2, 2021; Published Online: November 4, 2021



How to cite this article: Miniksar ÖH, Kaçmaz O. The effect of neutrophil-lymphocyte ratio on admission to postoperative intensive care and mortality in elderly patients undergoing hip surgery with spinal anesthesia. Eur Res J 2021;7(6):628-XXX. DOI: 10.18621/eurj.835339

Address for correspondence: Ökkeş Hakan Miniksar, MD., Associate Professor, Yozgat Bozok University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Atatürk Road 7. Km., 66100 Yozgat, Turkey. E-mail: hminiksar@yahoo.com, Tel: +90 354 2127060

©Copyright 2021 by The Association of Health Research & Strategy
Available at <http://dergipark.org.tr/eurj>

compared to those who are not [4]. For this reason, the planned admission of patients to ICU help to prevent negative complications, minimizing the likelihood of adverse outcomes [4]. No standard protocol was detected in the literature that will guide the decision of these patients for admission to ICUs. The decision for admitting a patient to ICU is complex, and it is important to identify preoperative predictors that will affect this decision.

Some laboratory findings, such as high urea/creatinine, high glucose, high potassium, low hemoglobin and low albumin were shown in clinical trials to be associated with increased mortality and admission to ICUs in patients with HF [5-7]. It was also reported that inflammation markers, such as C-Reactive Protein (CRP) are associated with mortality [8]. Neutrophil-Lymphocyte Ratio (NLR) is an easily measured, inexpensive and widespread hematological parameter, which can be used as an indicator of systemic inflammation [8-10]. It has been argued in recent years that NLR can be used as an indicator of postoperative mortality and poor prognosis in oncological and emergency abdominal surgeries [9]. It has also been shown that preoperative NLR is the predictor of negative outcomes and mortality following HF surgery in orthogeriatric patients [1, 8, 10].

Identifying patients who have the highest risk of life-threatening complications in the preoperative period is important in preventing the onset of postoperative negative outcomes. As a hematological parameter, the NLR value can help as a guide to the clinician in the controversial ICU admission decision after hip surgery. For this reason, in the present study, the purpose was to investigate the prognostic value of preoperative NLR on postoperative ICU admission and mortality rates in elderly patients undergoing hip fracture surgery with spinal anesthesia.

METHODS

Study Design

The present study was conducted by retrospectively examining the files of geriatric patients who underwent surgery because of isolated HF (e.g. femur neck and intertrochanteric fracture) in the Orthopedic Clinic of our hospital between January 2017 and May 2019.

The inclusion criteria of the study were being over 65 years of age, ASA score 3/4, spinal anesthesia, and less than 72 hours preoperative duration. Exclusion criteria of the study were being under 65 years of age, under general anesthesia, having hematological, infectious and inflammatory disease, history of severe liver disease and malignancy, intraoperative mortality, revision surgery, multitrauma patients, and incomplete records.

The Patients

ASA score, intervention time, surgery duration, and preoperative laboratory parameters (NLR) of the patients were evaluated. The surgery duration was calculated by adding the anesthesia procedure to the duration of the surgical procedure. The time to operation was defined as the day from hospitalization to surgical intervention.

The patients who were operated under regional anesthesia were included in the study. The patients were divided into two groups as those admitted to ICU (ICU), and those who were not (Non-ICU). The decision to admit to ICU was made by the anesthesiologist according to the preoperative clinical condition of the patient. Also, the duration of the stay in ICU and postoperative mortality of the patients were recorded. The patients were also divided further into two groups as the Survivor and Non-Survivor Group according to Intensive Care Unit mortality. The first admissions of all the patients who were admitted to ICU were accepted. All patients were routinely consulted for medical departments (cardiology, respiratory disease or internal medicine) in the preoperative period.

Laboratory Measurements

Venous blood samples (full blood count (CBC)) that were taken from each patient at the Emergency Department were examined. All venous blood samples were processed by the Blood Analyzer (Beckman Coulter®, LH 780, California, USA). The ratio between neutrophil and lymphocyte values was calculated and recorded as NLR.

Ethical Declaration

This retrospective study was approved by the Local Committee for Clinical Research in line with the Helsinki Declaration (Date: 24.07.2019, No: 2019/141).

Statistical Analysis

Admission and mortality groups of ICU were statistically compared in terms of preoperative NLR value. Statistical analysis was performed using SPSS V.21 and MedCalc V.13 package. The significance level was described as $p < 0.05$. The descriptive statistics were given as mean, standard deviation, median, number and percentage. The Kolmogorov–Smirnov test was used to assess the normal distribution of the variables. Non-parametric parameters were analyzed using the Mann-Whitney U test. To determine the cut-off values of the NLR between the ICU and Non-ICU groups, a receiver operating characteristic (ROC) curve was generated, and the area under curve (AUC) was calculated.

RESULTS

Among the 250 patients who were operated with HF diagnosis during the study period, 188 patients who met the inclusion criteria were included in the study for statistical analyses. A total of 111 (59%) of

the patients were female, and the median age (min-max) of all patients was 78 (65-103) years; and 58 patients (30.9%) were included in the ICU Group and 130 patients (69.1%) were included in the Non-ICU Group. The median age of the patients was 79 (65-96) for the ICU Group, and 78 (66-103) for the Non-ICU Group ($p > 0.05$). A total of 168 patients (89.4%) were included in the Survivor Group and 20 patients (10.6%) were included in the Non-Survivor Group. The median age of the patients was 78 (65-94) for the Survivor Group, and 78 (65-103) for the Non-Survivor Group ($p > 0.05$) (Table 1).

Homogeneity was found between the groups, the mean age, gender, ASA score, and time to operation did not differ at significant levels between the groups ($p > 0.05$) (Table 1).

The preoperative NLR values of the patients in the ICU Group were significantly higher compared to those of the Non-ICU Group ($p < 0.001$). The median NLR value was calculated to be 7.59 (4.75-10.43) for the ICU-Group and 4.45 (2.29-7.86) for the Non-ICU Group (Table 2). The cut-off NLR was obtained according to the differences between the ICU and Non-

Table 1. Demographic and clinical data of patients

Variables	ICU group	Non-ICU group	p value	Survivor group	Non survivor group	p value
Age (years)	77.25 ± 7.5	78.5 ± 7.6	0.428 ^a	78.1 ± 7.5	78.3 ± 8.37	0.920 ^a
Sex (female), n (%)	35 (60.3)	76 (58.5)	0.808 ^b	102 (60.7)	9 (45.0)	0.177 ^b
ASA score, n (%)			0.694 ^b			0.118 ^b
3	27 (46.6)	79 (60.8)		98 (58.3)	8 (40)	
4	31 (53.4)	51 (39.2)		70 (41.7)	12 (60)	
Time to operation (days)	2.33 ± 1.7	2.24 ± 1.6	0.899 ^a	2.19 ± 1.6	2.85 ± 1.7	0.073 ^a

Data are presented as mean±standard deviation for continuous variables and number and percentage for categorical variable. ^aCompared by Independent Sample T-Test; ^bChi-square test

Table 2. The neutrophil-lymphocyte ratio value of each group (Admission to ICU)

Group	Median	Interquartile range 25	Interquartile range 75	p value*
ICU group (n = 130)	7.59	4.75	10.43	< 0.001
Non-ICU group (n = 58)	4.45	2.29	7.86	
Total (n = 188)	6.99	3.79	9.68	

*Compared by Mann Whitney U Testi

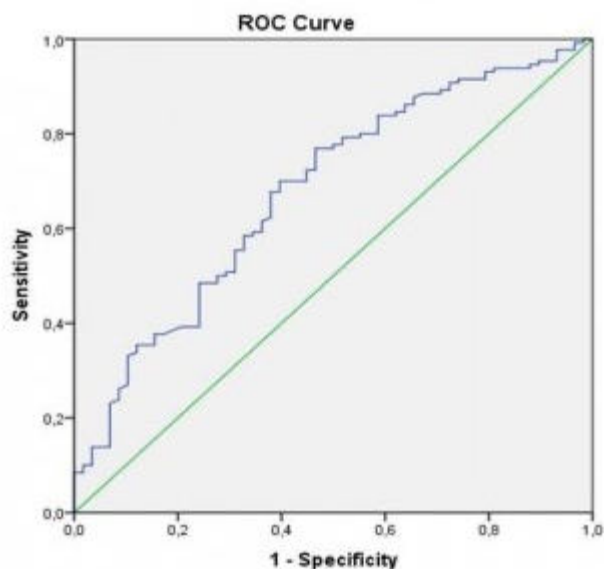


Fig. 1. Sensitivity and specificity assessment with ROC curve of the relationship between neutrophil-lymphocyte ratio and admission of ICU.

ICU Group by using the ROC Analysis. For ICU admission NLR, the cut-off point was determined as 9.65 (AUC of 0.67 [95 % CI 0.59-0.76] with 89% sensitivity and 67% specificity ($p < 0.001$)) (Fig. 1).

When the NLR values of the patients were compared according to intensive care mortality of the patients, significant differences were detected ($p < 0.05$). The Survivor Group had a median NLR value of 6.42 (3.55-9.44), and the Non-Survivor Group had a median NLR value of 9.5 (7.23-11.02) ($p = 0.015$) (Table 3).

DISCUSSION

In the present study, the prognostic value of preoperative NLR value on ICU admission and mortality

was examined in geriatric patients who underwent HF surgery. The results of our study showed that higher NLR value was associated with ICU admission and postoperative mortality after HF in elderly patients.

In elderly patients, hip fractures are among the most common traumatic diseases [1-3], which can cause postoperative ICU requirement, with a high risk of complications and an incidence of mortality. These patients are quite susceptible to inflammation, dehydration, malnutrition, cardiovascular and respiratory problems, which might develop as a result of fractures as well as surgical stress [2-4, 11]. For these reasons, it is important to consider that postoperative care treatments of geriatric HF patients are a featured issue. Also, the planned follow-up of high-risk geriatric trauma patients in ICU after surgery decreases negative outcomes [4, 6]. In elderly patients, multidisciplinary evaluation of patients and planning of postoperative care treatments are mandatory in the preoperative period to minimize the negative outcomes of HF [4].

There are no clear and objective criteria regarding the decision for the admission of geriatric patients with HF, which is high risk, to ICUs. In addition to many clinical factors that affect the ICU admission, laboratory disorders, such as anemia, hypoalbuminemia, and high urea/creatinine levels also plays role in this decision [5, 12]. As a measure of inflammatory response, elevated CRP and NLR values are also associated with postoperative poor clinical outcomes [13, 14]. However, recent studies argue that preoperative high NLR value can be used as an indicator for high risk of complications and mortality after cardiovascular, oncological surgery, and HF surgery [9, 14-16]. For these reasons, the purpose of the present study was to test our hypothesis that higher NLR value, which was found to be associated with negative outcomes after surgery, may also be associated with admission to

Table 3.The neutrophil-lymphocyte ratio value of each group (ICU mortality)

Group	Median	Interquartile range 25	Interquartile range 75	p value*
Survivor group (n = 168)	6.42	3.55	9.44	0.015
Non-survivor group (n = 20)	9.36	7.23	11.02	
Total (n = 188)	7.35	3.79	9.68	

*Compared by Mann Whitney U Testi

ICU. As far as we are concerned, the relation of high NLR with postoperative negative results was studied by many studies in the literature [13-16], and its contribution to ICU admission was not investigated adequately.

Biomarkers, such as neutrophil and lymphocyte values, WBC count, acute phase reactants, adhesion molecules, and cytokines are used to determine the inflammatory response in the body. The CBC Test, which is used widely in practice, is very inexpensive and the result is obtained quickly [10, 17]. NLR value is a very simple and easy-to-calculate parameter. Many studies conducted in recent years have shown it to be a parameter determining the degree of stress and inflammation [1, 8-10].

Recent studies have been found in the literature examining the effects of high NLR on postoperative prognosis in various surgical patients [8-10, 13]. Forget *et al.* [8] conducted a study with 82 patients undergoing major abdominal surgery, and found that higher NLR values were associated with postoperative acute complications, but were not associated with CRP, which is an inflammatory parameter. Vaughan-Shaw *et al.* [16] conducted a study with elderly patients who underwent non-traumatic emergency abdominal surgery, and found that higher NLR was associated with increased mortality. Dilektasli *et al.* [15] reported that high NLR value was associated with mortality in 1.356 critical trauma patients in surgical Intensive Care Unit. These studies also show that higher NLR parameter is determined as a prognostic factor in many surgical and trauma patients.

The clinical characteristics of the patients (i.e. advanced age, high preoperative ASA score, comorbid diseases), type and duration of surgery, preoperative duration, anesthesia method, and factors, such as the ICU capacity of the hospital, surgeon and anesthesiology preference also play roles in postoperative ICU and complications [3, 6, 18-21]. Our study was conducted in a restricted geriatric population with ASA 3/4 and with surgical intervention time of < 72 hours, who underwent spinal anesthesia due to femur neck and intertrochanteric fracture. As a reflection of the severity of preoperative comorbidity, the elevated ASA physical condition is one of the most reliable prognostic indices for perioperative mortality, and is also used to predict postoperative complications [3, 6, 18]. In our study; however, no significant differences

were detected in inter-group ASA score comparisons. Akbas *et al.* [19] reported that HF patients undergoing general anesthesia over 80 years of age were admitted more to ICU, and mortality was higher in these patients. However, there are also several other studies reporting that the anesthesia method has no effects on admission to the ICU [18, 20]. In our study, homogeneity was ensured in the study population by including only geriatric patients who were operated under spinal anesthesia. Although time to operation was reported as an important risk factor in HF patients for perioperative complications [21], it was found that it did not differ at significant levels between the groups in our study.

Forget *et al.* [8] conducted a study with 237 patients who had HF, and found that the patients had an NLR cut-off value of 4.9 (sensitivity: 62.9%, specificity: 57.6%) for 1 year of mortality after the surgery. Fisher *et al.* [10] conducted a study with 415 patients who had HF, and reported that the elevated NLR (≥ 5.1) value at the time of admission was an important risk factor for postoperative myocardial damage, high inflammatory response/infection, and death in hospital. Temiz *et al.* reported that high NLR values after HA (hemi arthroplasty) were associated with mortality; and the cut-off value was 4.7 in elderly patients [1]. In the same study, the authors also reported that less invasive surgical techniques can be selected elevated NLR values to prevent inflammatory response, as well as using pharmacological agents, such as statins and aspirin to reduce systemic inflammation after surgery [1]. However, these prophylactic treatment recommendations should be examined with extensive clinical trials. Uzbek *et al.* [9] conducted another study with 55 patients who underwent proximal femoral nail surgery alone, and found that the cut-off value of preoperative NLR was 5.25 (sensitivity: 84.6%, specificity: 78.6%); and argued that it was predictive for the risk of postoperative death. In our study, NLR cut-off value (9.65) that was found for admission to ICU was higher than the cut-off values of mortality reported by studies in the literature. However, as far as we are concerned, no other studies were detected in the literature, which were planned with a similar patient population for the admission to ICUs. Similar to our results, Slate *et al.* [22] found that NLR 9.2 cut-off value (HR, 3.60 (1.44-9.18 CI 95%, $p = 0.006$)) might be a predictor for 30-day short-term mortality

in acute pulmonary embolism. Similarly, Dilektasli *et al.* [15] reported that an NLR greater than 8.19 was independently associated with in-hospital mortality on the 2nd day of surgery ICU in trauma patients.

When the literature was reviewed, it was found that there were various mechanisms to explain the effect of NLR on the prognosis after orthopedic surgery in the geriatric population [11, 13, 23, 24]. One of them, aging is associated with a high level of proinflammatory cytokines [11]. However, it was also reported that inflammatory markers were independent predictors of postoperative adverse outcomes in elderly trauma patients with reduced physiological reserves [13]. Also, it is considered that the inflammatory response after surgery probably plays roles in organ dysfunction in patients [11, 13, 23]. Lymphocytes are the main components of the humoral and cellular immune system, playing central roles in immune response. Although lymphopenia reflects the weakness of cellular immunity after multitraumas, Neutrophilia can occur due to unbalanced systemic inflammatory response [11, 13, 15]. In addition, previous studies reported that the increase in the neutrophil count in some diseases (e.g. pulmonary embolism, coronary artery disease, deep vein thrombosis) is associated with an increase in thrombus formation [22, 25]. Another mechanism might be the development of the inflammatory response with hormonal changes caused by post-traumatic stress (i.e. increases in serum cortisol levels), which also increases the number of neutrophils, reducing the number of lymphocytes [8, 11, 13, 24]. For these reasons, the inflammatory response that is already increased is expected to increase more with additional surgical trauma. These mechanisms are important in the intensive care management of elderly HF patients, and it is important to identify preventive planning.

Limitations

The study had some limitations. First of all, it was a retrospective and single-centered study; and therefore, we can only rely on the results of the patients in our center. Secondly, there were many factors that affected patient admission to the Intensive Care Unit. For this reason, the deduction of the causal relation between NLR and the results is limited although we kept the patient population limited.

CONCLUSION

Despite the limitations of the study, it was concluded that high admission NLR value may be a risk factor for postoperative ICU admission and mortality in elderly patients with hip fractures. NLR can be used as a prognostic parameter in the perioperative management of this critically ill patient population. The repeatability and generalizability of the results must be investigated with multi-centered further clinical trials.

Authors' Contribution

Study Conception: ÖHM, OK; Study Design: ÖHM, OK; Supervision: ÖHM, OK; Funding: ÖHM; Materials: ÖHM; Data Collection and/or Processing: ÖHM; Statistical Analysis and/or Data Interpretation: ÖHM; Literature Review: ÖHM; Manuscript Preparation: ÖHM, and Critical Review: ÖHM.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

Ethics Committee Approval

Approval was obtained from the Yozgat Bozok University ethics committee (2019 / 137). Helsinki Declaration guidelines were followed throughout the study.

REFERENCES

1. Temiz A, Ersözlü S. Admission neutrophil-to-lymphocyte ratio and postoperative mortality in elderly patients with hip fracture. *J Trauma Acute Care Surg* 2019;25:71-4.
2. Barbosa TA, Souza AMF, Leme FCO, Grassi LDV, Cintra FB, Lima RM, et al. [Perioperative complications and mortality in elderly patients following surgery for femoral fracture: prospective observational study]. *Brazilian J Anesthesiol* 2019;69:569-79. [Article in Portuguese]
3. 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.
4. Onwochei DN, Fabes J, Walker D, Kumar G, Moonesinghe SR. Critical care after major surgery: a systematic review of risk

- factors for unplanned admission. *Anaesthesia* 2020;75(S1):e62-74.
5. Zeyneloğlu P, Pirat A, Candan S, Canikli Ş. Predictors of intensive care unit admission in geriatric patients undergoing hip replacement. *J Turk Soc Intens Care* 2006;6:108-11.
 6. Jang IY, Lee YS, Jung HW, Chang JS, Kim JJ, Kim HJ, et al. Clinical outcomes of perioperative geriatric intervention in the elderly undergoing hip fracture surgery. *Ann Geriatr Med Res* 2016;20:125-30.
 7. Mosfeldt M, Pedersen OB, Riis T, Worm HO, Mark S Van Der, Jørgensen HL, et al. Value of routine blood tests for prediction of mortality risk in hip fracture patients. *Acta Orthop* 2012;83:31-5.
 8. Forget P, Dillien P, Engel H, Cornu O, De Kock M, Yombi JC. Use of the neutrophil-to-lymphocyte ratio as a component of a score to predict postoperative mortality after surgery for hip fracture in elderly subjects. *BMC Res Notes* 2016;9:1-6.
 9. Özbek EA, Ayanoğlu T, Olçar HA, Yalvaç ES. Is the preoperative neutrophil-to-lymphocyte ratio a predictive value for postoperative mortality in orthogeriatric patients who underwent proximal femoral nail surgery for pertrochanteric fractures? *Turk Assoc Trauma Emerg Surg* 2020;26:607-12.
 10. Fisher A, Srikusalanukul 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.
 11. Keel M, Trentz O. Pathophysiology of polytrauma. *Injury* 2005;36:691-709.
 12. Kaplan C, Araz C, Candan S, Pirat A, Zeyneloğlu P, Ayhan A, et al. Predictors of intensive care unit admission following cytoreductive surgery for Stage III-IV ovarian carcinoma. *J Turk Soc Intens Care* 2012;8:102-9.
 13. 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.
 14. Niessen R, Bihin B, Gourdin M, Yombi JC, Cornu O, Forget P. Prediction of postoperative mortality in elderly patient with hip fractures: a single-centre, retrospective cohort study. *BMC Anesthesiol* 2018;18:5-7.
 15. Dilektasli E, Inaba K, Haltmeier T, Wong MD, Clark D, Benjamin ER, et al. The prognostic value of neutrophil-to-lymphocyte ratio on mortality in critically ill trauma patients. *J Trauma Acute Care Surg* 2016;81:882-8.
 16. Vaughan-Shaw PG, Rees JRE, King AT. Neutrophil lymphocyte ratio in outcome prediction after emergency abdominal surgery in the elderly. *Int J Surg* 2012;10:157-62.
 17. Emektar E, Corbacioglu SK, Dagar S, Uzunozmanoglu H, Safak T, Cevik Y. Prognostic value of the neutrophil-lymphocyte and platelet-lymphocyte ratios in predicting one-year mortality in patients with hip fractures and aged over 60 years. *Eurasian J Emerg Med* 2017;16:165-70.
 18. Aslan A, Atay T, Aydoğan NH. Risk factors for mortality and survival rates in elderly patients undergoing hemiarthroplasty for hip fracture. *Orthop Traumatol Turc* 2020;54:138-43.
 19. Akbas S, Ozkan A. Regional versus general anesthesia in patients underwent hip fracture surgery over 80 years old: a retrospective cohort study. *Ann Med Res* 2018;25:698.
 20. Daşar U. One-year retrospective evaluation of hip fracture patients aged more than 80 years and postoperatively monitored in the intensive care unit. *Turk Geriatr Derg* 2018;21:81-6.
 21. Anthony CA, Duchman KR, Bedard NA, Gholson JJ, Gao Y, Pugely AJ, et al. Hip fractures: appropriate timing to operative intervention. *J Arthroplasty* 2017;32:3314-8.
 22. Kayrak M, Erdoğan HI, Solak Y, Akilli H, Gül EE, Yildirim O, et al. Prognostic value of neutrophil to lymphocyte ratio in patients with acute pulmonary embolism: a retrospective study. *Hear Lung Circ* 2014;23:56-62.
 23. Bruunsgaard H, Pedersen M, Pedersen BK. Aging and proinflammatory cytokines. *Curr Opin Hematol* 2001;8:131-6.
 24. Karahan MA. The effect of spinal anesthetic technique on neutrophil to lymphocyte ratio and postoperative mortality in elderly patients with coronary artery disease undergoing hip replacement surgery. *Turk Geriatr Derg* 2019;22:305-14.
 25. Afari ME, Bhat T. Neutrophil to lymphocyte ratio (NLR) and cardiovascular diseases: an update. *Expert Rev Cardiovasc Ther* 2016;14:573-7.



This is an open access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.