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The role of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, crp and albumin to predict postoperative one-year mortality in patients with hip fractures

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Abstract

Elderly patients are espcialy at high risk for postoperative complications. This is even more important following hip fracture surgery due to its fragility and comorbidities. Using certain biomarkers may be an interesting way of tackling the question of optimal patient management. In this study we aimed to determine the status of values such as NLR, PLR, albumin, and CRP, which can be easily accessed from blood tests that we routinely use, in predicting mortality in patients who underwent partial prosthesis after hip fractures. Patients over 70 years of age with intertrochanteric femur and collum femoris fractures and who underwent partial endoprosthesis were included in the study. The neutrophil lymphocyte and platelet lymphocyte ratios, albumin values, and CRP values were recorded by examining the hemogram and biochemistry tests taken routinely at the time of admission to the hospital, 1 day before the surgery and on the 1st post-operative day. The distribution of clinical and socio-demographic characteristics of individuals according to their survival within the scope of the study has elaborated that there is a statistically significant difference in terms of age, gender, diagnosis, time to surgery (days) of the deceased and surviving individuals. It is observed that the majority of the patients who died were women and were diagnosed with collum femoris. It was determined that there was a statistically significant difference only in CRP and albumin values between the two groups in postoperative parameters. According to the outcomes of this analysis one can conclude that NLR and PLR values measured preoperatively on the hemogram panel can be used to predict 1-year mortality. Regardless of the fracture period, low albumin value is seen as an independent variable in predicting mortality.

Keywords: Hip fracture, NLR, PLR, crp, albumin, mortality

Introduction

Elderly patients are espcialy at high risk for postoperative complications. This is even more important following hip fracture (HF) surgery due to its fragility and comorbidities. According to this published data, 1year mortality rate after HF surgery ranges from 12% to 37% [1]. The high rate observed in this era drives the clinician to be more proactive in decision making.

Up to date, several postoperative mortality scores has been developed for this specific purpose. On the contrary these scores are usually misinterpreting in analyzing the risk of orthogeriatric patients [2-4]. Hip fractures are one of the main morbidities in elderly patients. Mortality risk after hip fracture is significantly increased compared to the normal population. While a small proportion of deaths after hip fractures are directly related to hip fractures, the remainder is probably due to morbidities that increase with age. Scales and tests that can be used to predict mortality after hip fracture can be used to prevent mortality.

In previous literature, the risk of hip fracture has been found >15 times higher in individuals aged 90 years or above when compared to the risk in individuals under 65 years of age [5]. Intertrochanteric hip fractures are important cause of morbidity and mortality in older patients due to osteoporosis and significantly affect the survival of patients aged >90 years [6]. Surgery and rehabilitation plays a major role in the successful treatment of intertrochanteric fractures. The mortality of hip fractures in the postoperative period depends on multipl factors such as age, surgery, gender, anemia and nutrition [7].

Using certain biomarkers may be an interesting way of tackling the question of optimal patient management. Neutrophil-to-lymphocyte ratio (NLR) has been utilized as regular follow up option in the postoperative regular care [8]. Forget et al. (2014), have reported that NLR levels in the 5th postoperative day could

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be considered as a beneficial prognostic factor [9]. However, using NLR alone may have some limitations and should be evaluated as a composite factor taking age, gender, general status, surgery success into account [10].

In previous research is has been denoted that certain parameters such as low albumin levels, CRP and NLR are not only used for detecting systemic inflammation but also may be utilized for predicting mortality and morbidity [11-13]. On the other hand preoperative NLR can also be used to estimate survival [13].

Study Hypothesis

Among the treatment options applied after elderly hip fractures, proximal femur nail and partial prosthesis are the most commonly used techniques. Between these two, partial prosthesis is a more major surgery than proximal femur nail.

Increased neutrophil/lymphocyte ratio and platelet/lymphocyte ratio are convenient and easily accessible markers that can be used to predict mortality in recent studies. Considering the fact that association between high NLR and excessive mortality has not been excessively investigated in the orthopedic literature, in this study, we aimed to determine the status of values such as NLR, PLR, albumin, and CRP, which can be easily accessed from blood tests that we routinely use, in predicting mortality in patients who underwent partial prosthesis after hip fractures.

Materials and Methods

The medical records of 556 patients aged 70 years and over who underwent partial hip arthroplasty due to collum femoris fracture and intertrochanteric femur fracture between January 2014 and July 2019 were retrospectively reviewed. The study was conducted under the Declaration of Helsinki by obtaining the approval of our local ethics committee and informed consent has been obtained from all participants. Patient data were obtained from hospital records. The ethics committee approval has been granted in 2020 (protocole number: 48670771-514.10). All patients were followed for at least 1 year. Patients with missing medical records, pathological fractures, high-energy trauma, complications such as dislocation-infection during their follow-up, patients with additional infection findings during hospitalization, patients who underwent albumin replacement during hospitalization, patients who died after the first 1 year after surgery were excluded from the analysis. A total of 499 patients were included in the study.

The patients were diagnosed with X-ray, other parameters such as hemogram, biochemistry, coagulation and ELISA tests were obtained. These were recorded as the admission state blood parameters. Hemogram and biochemistry blood tests have been routinely taken from the patients one day before the surgery and were recorded as preoperative parameters and the hemogram and biochemistry blood tests taken routinely on the 1st day after the surgery were recorded as postoperative blood parameters. The time from admission to the emergency room to the day of surgery was taken as the time to surgery.

The neutrophil lymphocyte and platelet lymphocyte ratios, albumin values, and CRP values were recorded by examining the hemogram and biochemistry tests taken routinely at the time of admission to the hospital, 1 day before the surgery and on the 1st post-operative day. The dates of admission to the hospital and the dates of surgery were obtained from the hospital records, and the dates of death were obtained from the national records. Hip fracture surveys were recorded and additional diseases of the patients were obtained from the hospital records.

The fractures were divided into intracapsular and extracapsular according to the region. All patients were operated under spinal anesthesia in the lateral decubitus position, using a posterolateral approach. All patients were applied antibiotic prophylaxis as described by R Sevimli et al [14]. Cemented partial hip prosthesis was applied to all patients using a bipolar head (TST, Istanbul, Turkey).

Patients' age, gender, fracture type, additional diseases, time to surgery, blood tests taken at the time of admission to the hospital, preoperative and postoperative blood tests, NLR, PLR, CRP, albumin values, and mortality times from medical records were recorded.

Statistical Analysis

Patient data collected were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 23.0 package program. Frequency and percentage were given for categorical data, and median and deviations were given as descriptive values for continuous data. "Mann Whitney U-Test" was used for the comparison of two groups, and "Pearson's Chi-Square Test" was utilized for comparison of categorical variables. Examining the factors affecting survival was evaluated with "Logistic Regression Analysis". The results were considered statistically significant when the p value was less than 0.05.

Results

The distribution of clinical and socio-demographic characteristics of individuals according to their survival within the scope of the study is given in Table 1. When the table is examined, it is seen that there is a statistically significant difference in terms of age, gender, diagnosis, time to surgery (days) of the deceased and surviving individuals. It is observed that the majority of the patients who died were women and were diagnosed with collum femoris.

When the clinical results of the individuals were examined, it was seen that there was a difference between the two groups in terms of NLR, PLR, CRP and albumin values on admission and postoperative NLR, PLR, CRP and albumin values. Individuals with exitus were higher in all parameters except the albumin value. The low levels of albumin have been found to be associated with mortality. It was determined that there was a statistically significant difference only in CRP and albumin values between the two groups in postoperative parameters.

The results of the Logistic Regression Analysis performed to examine the risk factors affecting the survival of individuals are given in Table 2. In the analysis of risk factors, the parameters that were found to be significant in Table 1 were included in the univariate model, and the parameters that were found to be significant in the univariate model were included in the multivariate model.

In terms of age, gender, diagnosis, NLR, PLR, CRP and albumin values at admission and before the operation and CRP and albumin values after the operation had an effect on survival in univariate analysis. It was determined that one unit increase in age, increases the risk of death by 1.06 times, and the risk of death for women is 1.5 times higher than for men. The risk of death in individuals diagnosed with intertrochanteric femur was 0.62 times lower than those diagnosed with collum femoris, and a one-unit increase in other laboratory parameters, excluding the albumin parameter, increased the risk of death.

When the variables that were observed to be significant in the univariate model were included in the multivariate model, age, arrival albumin and preoperative NLR were significant in the model created. It was observed that a one-unit increase in age and NLR values increased the risk of death, while an increase in albumin value decreased the risk of death.

Table 1. The clinical and baseline demographics of the study popoulation

Variables*	Total (n=499)	Alive (n=308)	Exitus (n=191)	p-value
Age (years)	**82 (38)**	**82 (27)**	**84 (37)**	**<0.001**
Gender				**0.037**
Male	**163 (32.7)**	**90 (29.2)**	**73 (38.2)**	
Female	**336 (67.3)**	**218 (70.8)**	**118 (61.8)**	
Diagnosis				
Collum femoris	**297 (59.5)**	**197 (64.0)**	**100 (52.4)**	
Interthrocanterical femur	**202 (40.5)**	**111 (36.0)**	**91 (47.6)**	
Comorbidity				0.614
None	127 (25.5)	75 (24.4)	52 (27.2)	
1-2	268 (53.7)	165 (53.6)	103 (53.9)	
≥3	104 (20.8)	68 (22.0)	36 (18.8)	
DM	136 (27.3)	89 (28.9)	47 (24.6)	0.296
HT	340 (68.1)	217 (70.5)	123 (64.4)	0.158
COPD-Asthma	85 (17.0)	55 (17.9)	30 (15.7)	0.535
CAD	180 (36.1)	116 (37.7)	64 (33.5)	0.348
CRF	23 (4.6)	14 (4.5)	9 (4.7)	1.000
Duration to operation, days	**8 (77)**	**7 (76)**	**9 (40)**	**0.005**
Admission NLR	**6.96 (95.46)**	**6.43 (47.73)**	**8.14 (95.46)**	**0.002**
Admission PLR	**190.1 (1265.16)**	**177.68 (959.75)**	**213.79 (1265.16)**	**0.003**
Admission CRP	**18.9 (324.6)**	**14.3 (324.4)**	**24.77 (300.0)**	**0.001**
Admission Albumin	**3.7 (2.5)**	**3.8 (2.2)**	**3.5 (2.5)**	**<0.001**
Pre-op NLR	**4.68 (75.91)**	**4.19 (40.22)**	**5.55 (75.91)**	**<0.001**
Pre-op PLR	**195.2 (3594.27)**	**175.28 (1270.91)**	**220.45 (3594.27)**	**<0.001**
Pre-op CRP	**75.5 (420.5)**	**70.37 (273.4)**	**85.9 (412.9)**	**0.003**
Pre-op Albumin	**3.0 (8.1)**	**3.14 (8.1)**	**2.9 (2.0)**	**<0.001**
Post-op NLR	9.1 (64.57)	8.84 (42.06)	9.61 (64.57)	0.076
Post-op PLR	238.24 (2549.35)	229.31 (1334.92)	250.0 (2549.35)	0.246
Post-op CRP	**76.0 (330.4)**	**71.7 (330.4)**	**85.2 (295.7)**	**0.002**
Post-op Albumin	**2.7 (3.3)**	**2.8 (3.3)**	**2.5 (2.2)**	**<0.001**

* n (%) or Median (deviation)

Table 2. Risk factors effecting survival

Variables*	Univariate Analyses		Multivariate Analyses	
	Odds Ratio (%95 CI)	p-value	Odds Ratio (%95 CI)	p-value
Age (years)	**1.06 (1.03-1.09)**	**<0.001**	**1.03 (1.00-1.07)**	0.038
Gender				
Male	Ref.	-	Ref.	-
Female	1.50 (1.02-2.20)	0.038	1.53 (0.97-2.41)	0.065
Diagnosis				
Collum femoris	Ref.	-	Ref.	-
Interthrocanterical femur	**0.62 (0.43-0.89)**	**0.010**	**0.78 (0.51-1.20)**	0.267
Duration to operation, days	1.02 (0.99-1.05)	0.336		
Admission NLR	**1.04 (1.01-1.06)**	**0.011**	1.02 (0.98-1.06)	0.473
Admission PLR	**1.002 (1.001-1.003)**	**0.003**	1.00 (0.99-1.01)	0.996
Admission CRP	**1.003 (1.000-1.007)**	**0.039**	0.99 (0.98-1.01)	0.459
Admission Albumin	**0.24 (0.16-0.37)**	**<0.001**	**0.34 (0.19-0.62)**	**<0.001**
Pre-op NLR	**1.10 (1.05-1.15)**	**<0.001**	**1.07 (1.00-1.15)**	**0.047**
Pre-op PLR	**1.002 (1.001-1.004)**	**0.002**	1.00 (0.99-1.01)	0.907
Pre-op CRP	**1.005 (1.002-1.008)**	**0.001**	1.00 (0.99-1.01)	0.681
Pre-op Albumin	**0.18 (0.11-0.30)**	**<0.001**	0.47 (0.22-1.01)	0.051
Post-op CRP	**1.005 (1.002-1.007)**	**0.002**	1.00 (0.99-1.01)	0.345
Post-op Albumin	**0.27 (0.17-0.43)**	**<0.001**	0.83 (0.44-1.56)	0.559

Discussion

The results of the current study elaborated that NLR, PLR, CRP and albumin levels measured at the time of admission have been more predictive than the post-operative values. This comparison regarding admission values indicated an association with mortality rates. On the other hand we did not detect a significant cut off value for the investigated paramaeters.

The prevalence of hip fractures has been extensively studied in the elderly in previous research. Pande et al. (2006), have found that 1-year mortality after hip fractures was 45% [15] and a very close rate has been reported by Torruella et al. (2005) as 40% [16]. Similar mortality rates have all been published by Roche et al. (2005) as 33% [17], McLeod et al. (2005) as 24.9% [18], Franzo et al. (2005) as 25.3% [19]. Three or more hip fractures in women than in men is known to occur more frequently [12,17]. In this study, the 1-year mortality rate was 38%. The incidence of hip fracture in women was 2 times higher. The 1-year mortality risk was 1.5 times higher in women than in men.

Kim BG. et al. evaluated 772 hip fracture patients over 65 years of age in a retrospective analysis. The predictability of 1-year mortality of preoperative CRP elevation was examined. The patients were divided into two groups as CRP level (10 mg/dl) above and below. Preoperative CRP was also found to be significant in 1-year mortality logistic regression analysis [20]. Fakler JK. et have conducted a study in 209 patients with femoral neck fractures. They have stated that the effect of preoperative CRP on mortality was significant (p=0.002). In addition, regression analysis was also performed in the study, concluding that CRP at admission was an independent predictor of one-year mortality [21]. Niessen R. et al. conducted a study in 782 patients with hip fractures. CRP measurements have been obtained before surgery or at the time of admission in order to predict in-hospital death. In that study, CRP was not associated with in-hospital mortality [22]. They have analyzed CRP values among patients who developed postoperative hospital discharge or mortality and concluded that preoperative CRP did not have a statistically significant role in predicting mortality in a short time. In our study, CRP values were significantly higher in patients who died within 1 year at the time of first admission to the hospital, preoperatively and postoperatively, compared to patients who were alive.

Bohl DD. et al. conducted a multicenter retrospective cohort study of albumin to predict 1-year mortality, length of hospital stay, and complications. The limit value of albumin was taken as 3.50 g/dl, values above this were considered as normal and values below as hypoalbuminemia. Compared to patients with normal albumin levels, patients with hypoalbuminemia had a higher mortality rate (p=0.001) [23]. Harrison SJ et al. have tried to interprete the effect of albumin changes on 1-year mortality in a retrospective single-center study of 471 subjects. The mean preoperative albumin level was 2.95 g/dl in patients who died and 3.28 g/dl in patients who survived during the study period [24]. In this study we have found that low levels of albumin at hospital admission period have been associated with mortality. The post-operative albumin levels were certainly lower in all individuals.

Aldebeyan et al. have conducted a retrospective study with 10.117 people and investigated 1 month mortality, hospital stay and complications of preoperative hypoalbunemia. Albumin levels have been found below 3.5 g/dl in 4.703 of 10.117 patients. A statistical significance was found between hypoalbunemia and mortality [25] Pimlott BJ. et al. have performed a prospective study on mortality and complications of preoperative albumin values in 583 hip fracture patients. Patients aged 65 and over with hip fracture were included in the study. Albumin level below 3.50 g/dl was accepted as hypoalbuminemia. A statistically significant association was found between low albumin level and mortality [26]. Aldebeyan and Pimlott conducted similar trials with shorter follow-up compared to other studies. Miyanishi et al. performed a 4 year follow up study on factors affecting mortality in a group of 23 men and 103 women with hip fractures. According to their results low serum albumin level (p=0.004) has been found to affect mortality in multiple regression analysis. Patients with an albumin level of 3.60 g/dl on the ROC curves were found to have significantly lower survival rates [27].

Bone tissue is a very important structure that constitutes the frame in human body in order for the organs to work properly, and the disruption of its integrity is defined as fracture. This pathology formation negatively affects neighboring soft tissues and organ systems [28]. Hip fracture is a geriatric health issue and cardiovascular complication and chest infections are the main serious complications of surgery [17]. NLR is a natural denomitor of these complications where these postoperative complications are often associated with postoperative mortality. The clinical utilization of NLR as a predictive risk factor of mortality since 2015. It was first interpereted by Forget et al. and they declared that preoperative NLR is not predictive of postoperative mortality [9]. Fisher et al. investigated the prognostic value of NLR at the time of hospital admission and elaborated that high NLR on admission is a significant risk factor of postoperative myocardial injury, high inflammatory response, and in-hospital death in ortho-geriatric patients [29]. In our study, preoperative NLR value was statistically significantly higher in patients who died within 1 year.

Wang et al. (2020) recently published an article elaborating that high PLR (≥189) is associated with increased one year all-cause mortality in elderly hip fracture patients. This was an important claim as PLR has not been clearly analyzed in hip fractures although it was extensively studied in many different disesases. PLR is a simple and easy to obtain indicator during routine blood tests. Wang et al. have also found that deceased patients had significantly higher platelet counts and PLR [30]. In our study we have found a statistically significant difference during univariate analysis of pre-operative PLR as odds ratio (OR) 1.002 (1.001-1.004) and p value 0.002. Pre-operative PLR were significantly lower for the whole enrolled subjects p<0.001.

Limitations of the Study

There are certain limitations of this study and the most important ones could be elaborated as the lack of data on patients who underwent PFN after hip fracture. The lack of consecutive analysis of blood damples after the 1st post-operative day and long duration until surgery could be stated as additional factors.

Conclusion

According to the outcomes of this analysis one can conclude that NLR and PLR values measured preoperatively on the hemogram panel can be used to predict 1-year mortality. Regardless of the

fracture period, low albumin value is seen as an independent variable in predicting mortality.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical approval
The ethics committee approval has been granted in 2020 (protocole number: 48670771-514.10).

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