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Investigation of the Relationship Between Prognostic Nutrition Index and Mortality in Patients with Femur Fracture

Femur Kırığı Olan Hastalarda Prognostik Nutrisyon İndeksi ile Mortalite Arasındaki İlişkinin Araştırılması

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Abstract

Aim: The incidence of adverse postoperative outcomes in surgeries for femur fractures is high and is associated with malnutrition. In this study, it was aimed to determine the independent factors for 6-month survival in patients with femur fracture and to evaluate the predictive value of the prognostic nutrition index (PNI).

Material and Method: One hundred and sixteen patients operated on only for femoral fracture were divided into survival and non-survival groups according to mortality.Demographic characteristics of the patients, operation data, fracture sites, need for intensive care unit and length of stay, postoperative hospital stay, and preoperative laboratory values, prognostic nutrition indices and mortality were evaluated.

Results: Twenty-six (22.4%) of 116 patients who were operated for femoral fracture resulted in 6-month mortality. CRP, albumin, prealbumin, crp/albumin ratio and PNI values at admission were independent risk factors for postoperative mortality (p=0.014, p<0.001, p=0.041, p=0.003, p<0.001). The optimal cut-off value for PNI was determined as 29.0. In the group with PNI>29.0, survival rates were found to be higher at the end of the 1st, 3rd and 6th months (94.2%, 89.5%, 89.5%).

Conclusion: Nutritional indices should be evaluated when patients with femoral fractures are admitted to the hospital. A low prognostic nutritional index may a predict mortality in patients with femoral fractures.

Keywords: Prognostic nutrition index, mortality, femur fracture

Öz

Amaç: Femur kırıkları için yapılan ameliyatlarda postoperatif olumsuz sonuçların insidansı yüksektir ve yetersiz beslenme ile ilişkilidir. Bu çalışmada femur kırığı olan hastalarda 6 aylık sağkalım için bağımsız faktörlerin belirlenmesi ve prognostik beslenme indeksinin (PNI) prediktif değerinin değerlendirilmesi amaçlandı.

Gereç ve Yöntem: Sadece femur kırığı nedeniyle opere edilen 116 hasta mortaliteye göre hayatta kalan ve hayatta kalmayan gruplara ayrıldı. Hastaların demografik özellikleri, operasyon verileri, kırık bölgeleri, yoğun bakım ihtiyacı ve kalış süresi, postoperatif hastanede kalış süresi, preoperatif laboratuvar değerleri, prognostik beslenme indeksleri ve mortalite değerlendirildi.

Bulgular: Femur kırığı nedeniyle opere edilen 116 hastanın 26'sı (%22.4) 6 aylık mortalite ile sonuçlandı. CRP, albumin, prealbumin, crp/albumin oranı ve PNI değerleri postoperatif mortalite için bağımsız risk faktörleriydi (p=0.014, p<0.001, p=0.041, p=0.003, p<0.001). PNI için optimal cut-off değeri 29,0 olarak belirlendi. PNI>29.0 olan grupta 1., 3. ve 6. ay sonunda sağkalım oranları daha yüksek bulundu (%94.2, %89.5, %89.5).

Sonuç: Femur kırığı olan hastalar hastaneye kabul edildiğinde beslenme indeksleri değerlendirilmelidir. Düşük bir prognostik beslenme indeksi, femur kırığı olan hastalarda mortaliteyi öngörebilir.

Anahtar Kelimeler: Prognostik beslenme indeksi, mortalite, femur kırığı

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INTRODUCTION

The number of patients with fractures is increasing worldwide, especially with the increase in the elderly population.[1,2] Femoral fractures are one of the most clinically encountered fracture types. It may cause a high complication rate, a severe decrease in the quality of life, morbidity, mortality, and serious economic costs.[2,3] Femoral fractures are generally classified according to the fracture site; proximal, shaft, and distal. The most common type is proximal femur fracture. With the rapid aging of the world population, the increase in osteoporosis will probably continue to increase this incidence.[4,5] Femoral shaft fractures are more common in young patients due to trauma. Distal femur fractures are rare and may be due to traumas and sports injuries.[5]

Surgery is the best treatment for patients with femoral fractures. It is applied frequently. However, it can cause many adverse postoperative outcomes, including deep vein thrombosis, pulmonary embolism, pneumonia, wound infection, chronic disease activation, intensive care unit admission, and death. Age, additional diseases, surgery, stress, trauma, hemorrhage, infection, pain, and immobilization are considered the causes of these results. Such patients may be at risk of protein catabolism and malnutrition. In addition, nutrition has a impact on fracture healing, and impaired fracture healing has been observed among significant malnourished individuals.[6] Meesters et al. In their study stated that protein deficiency causes higher complications and longer hospitalizations in patients with femoral fractures.[6] However, a study showing the negative effects of nutrition on femur fracture has not been found in the literature.

Perioperative malnutrition was found to be an independent risk factor for postoperative complications in orthopedic surgery patients.[7] There is evidence that adequate nutritional support can prevent postoperative complications. Therefore, the patient's nutritional status should be closely monitored and evaluated in terms of nutritional risk.[8] Although serological tests, anthropometric measurements, and screening tools are used for this, there has yet to be a method that has been reported as the gold standard.[9] Studies have shown that the Prognostic Nutrition Index (PNI) is also a comprehensive marker for evaluating the nutritional status of patients undergoing surgery.[10] PNI can be used to assess the nutritional and immunological situation of patients who have had surgery. (PNI: 10 x serum albumin (ALB, g/dl) + 0.005 total lymphocyte count (LYM, per mm^3)) Studies have reported that PNI is an essential predictor of poor postoperative outcomes and increased mortality in various malignancies.[11] However, PNI studies focusing on postoperative survival outcomes of patients operated on for femoral fractures are scarce. Therefore, we aimed to identify independent factors for adverse postoperative effects in patients with femoral fractures and to evaluate the association of PNI with 6-month survival in these patients.

MATERIAL AND METHOD

The study was carried out with the permission of Kastamonu University Clinical Researches Ethics Committee (Date: 19.10.2022, Decision No: 2022-KAEK-105). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Data Source

The data of this retrospective observational study were obtained from the Hospital Electronic Medical Record Information System (sisoft) and operating room patient records.

Patients

A retrospective evaluation was made using the hospitalization data obtained from the database of 210 patients who were operated only for femur fracture in Kastamonu Training and Research Hospital between January 2021 and November 2022. It was determined that the patients were not given any nutrition education during their hospitalization. Albumin (ALB) replacement therapy was used as conventional treatments only when the ALB concentration was < 30 g/l. The exclusion criteria were as follows:

- Missing data (n=7)
- Systemic slimming diseases (malignancy, tbc, hyperthyroidism) (n=11)
- Those who had major surgery in the last 6 months (n=4)
- Those who use drugs that can cause bone marrow depression (n=2)
- Patients under 65 years of age (n=47)
- Patients with chronic renal failure and severe liver dysfunction (n=23)

After applying all exclusion criteria, a total of 116 patients were identified; of these, 105 (90.5%) had proximal, 5 (4.3%) trunk fractures, and 6 (5.2%) had distal fractures.

Variables

Various potential factors that may affect mortality were investigated: age, gender, comorbidities, fracture sites, American Society of Anesthesiologists (ASA), type of anesthesia used in operation, duration of operation, need and amount of blood transfusion in operation, need for intensive care unit and length of stay, postoperative hospital stay, and preoperative laboratory values such as leukocyte, hemoglobin, platelet, neutrophil, lymphocyte, neutrophil-lymphocyte ratio, C-reactive protein (CRP), albumin, CRP/albumin ratio, prealbumin and PNI.

Statistical Analysis

The normality assumption was evaluated using the Kolmogorov-Smirnov test. Continuous data are presented as standard deviation according to statistical distribution, Categorical parameters, frequencies, and associated percentages. Student's t-test was used to analyze normally distributed continuous variables, and the Mann-Whitney U test was used to examine non-normally distributed continuous variables and ordinal variables. Chi-square or

Fisher's exact test was used to analyze categorical variables. The optimal cut-off value for PNI was determined using ROC curve analysis. In the analyzes, variables with an unadjusted p-value < 0.50 were identified as confounding factors and included in multivariate regression analyzes to identify independent predictors of adverse postoperative outcomes. Results were expressed as OR and 95% CI. Then, Kaplan Meier analysis was applied for survival processes according to the determined parameters. Log Rank (Mantel-Cox) statistics were used in the Kaplan-Meier survival analysis. All statistical analyzes were performed using the Statistical Package for Social Sciences version 26.0 (SPSS Statistics for Windows, Chicago, USA), and p<0.05 was considered significant.

RESULTS

Twenty-six (22.4%) of 116 patients who were operated for femoral fracture resulted in 6-month mortality. Demographic characteristics and laboratory values of the patients are given in **Table 1**.

Table 1. Demographic, clinical and laboratory characteristics.

N=157(ortalama±SS or percent)		
Age		80.73±8.06
Gender	Female	82(70.6%)
	Male	34(29.4%)
Additional Desease	No	71(61.2%)
	Diabetes Mellitus	8(6.8%)
	Hypertension	11(9.4%)
	Cardiac Disease	13(11.2%)
	Respiratory Disease	14(12.0%)
	Neurological Disease	7(6.0%)
Femur fracture	Proximal	105(90.5%)
	Saft	5(4.3%)
	Distal	6(5.2%)
Anesthesia Type	General Anesthesia	6(5.1%)
	Spinal Anesthesia	110(94.9%)
ASA	II	8(6.8%)
	III	61(52.5%)
	IV	47(40.5%)
Operation Time (min)		58.34±23.914
Blood Trasfusion Need	No	52(44.8%)
	Yes	64(55.2%)
Intensive Care Need	No	38 (32.7%)
	Yes	78 (67.3%)
Blood Transfusion Amount (Unit)		0.95±1.12
Hospitalization Time		6.83±4.88
Leukocyte		10.45±3.86
Hemoglobin		11.19±1.58
Platelet		222.02±73.24
Neutrophil		8.16±3.25
Lymphocyte		1.37±0.99
Neutrophil/Lymphocyte		8.07±6.65
Preoperative C Reactive Protein		30.26±44.96
Albumin		3.21±0.51
Prealbumin		13.32±4.85
C Reactive Protein / Albumin		10.39±16.52
Prognostic Nutrition İndex		32.17±5.16
Mortality	No	90 (77.6%)
	Yes	26 (22.4%)

ASA; American Society of Anesthesiologists

There was no difference in the demographic characteristics of the patients when they were compared according to their 6-month mortality status. Preoperative c-reactive protein (CRP), albumin, prealbumin, crp/albumin ratio and PNI values were found to be statistically significant among the groups according to mortality (p<0.05, **Table 2**).

Table 2. Demographic, clinical and laboratory characteristics of patients with and without mortality

		non-survived patients N=26 (22.4%) (mean±SD or percent)	Surviving patients N=90 (77.6%) (mean±SD or percent)	p
Age		83.19±7.07	80.02±8.22	0.071
Gender	Female	16 (61.5%)	66 (73.3 %)	.358
	Male	10 (38.5%)	24 (26.7 %)	
Additional Desease	No	15 (57.6%)	56 (62.2%)	0.426
	Diabetes mellitus	2 (7.6 %)	2 (2.2%)	
	Hypertension	2 (7.6%)	6 (6.6%)	
	Cardiac disease	3 (11.5%)	9 (10.0 %)	
	Respiratory disease	3 (11.5 %)	11 (12.2 %)	
	Neurological disease	1 (3.8 %)	6 (6.6%)	
Femur fracture	Proximal	24 (92.4 %)	80 (89.0%)	0.926
	Saft	1 (3.8%)	4 (4.4%)	
	Distal	1 (3.8%)	6 (%6.6%)	
Anesthesia Type	General anesthesia	3 (11.6 %)	3 (3.4%)	0.125
	Spinal anesthesia	23 (88.4%)	87 (96.6 %)	
ASA	II	1 (3.8%)	7 (7.7%)	0.127
	III	10 (38.4%)	52 (57.7%)	
	IV	15 (57.8 %)	31 (34.6%)	
Operation Time (min)		58.50±29.93	58.30±22.07	0.759
Blood Trasfusion Need	No	10 (38.4%)	42 (46.6%)	0.605
	Yes	16 (61.6%)	48 (53.4%)	
Intensive Care Need	No	4 (15.3%)	34 (37.7%)	0.057
	Yes	22 (84.7%)	56 (62.3%)	
Blood Transfusion Amount (Unit)		1.08±1.16	0.91±1.11	0.446
Hospitalization Time		7.77±7.21	6.56±3.98	0.965
Leukocyte		11.98±5.65	10.00±3.07	0.211
Hemoglobin		10.92±1.53	11.27±1.59	0.308
Platelet		218.04±69.35	223.17±74.66	0.650
Neutrophil		9.21±4.19	7.86±2.88	0.226
Lymphocyte		1.75±1.69	1.26±0.63	0.731
Neutrophil/Lymphocyte		9.30±11.16	7.71±4.65	0.837
Preoperative C Reactive Protein		42.71±47.81	26.67±43.72	0.014
Albumin		2.76±0.50	3.34±0.44	<0.001
Prealbumin		11.52±4.20	13.84±4.92	0.041
C Reactive Protein / Albumin		16.29±19.34	8.69±15.31	0.003
Prognostic Nutrition İndex		27.67±5.07	33.47±4.42	<0.001

ASA; American Society of Anesthesiologists

The female population was higher in both groups. Respiratory tract diseases were the most common chronic disease in both groups. Proximal femoral fracture was the most common type of fracture in both groups.

The optimal cut-off value for PNI was determined as 29.0 using ROC curve analysis. When the patients were evaluated according to the PNI cut-off value, there was a statistically significant difference between the two groups in terms of age, preoperative crp, albumin, prealbumin, crp/alb and mortality. (**Table 3**).

Table 3. PNI ≤29.0 and >29.0 patient characteristics

		PNI≤29.0	PNI>29.0	P
Age		84,47±6,80	79,43±8,09	0.003
Gender	Female	22 (73.3 %)	60 (69.7%)	0.891
	Male	8 (26.7%)	26 (30.3%)	
Additional Desease	No	17 (56.7%)	54 (62.7%)	0.369
	Diabetes mellitus	2 (6.7%)	2 (2.3%)	
	Hypertension	2 (6.7%)	6 (7.0%)	
	Cardiac disease	1 (3.3%)	11 (12.8%)	
	Respiratory disease	4 (13.3%)	10 (11.6%)	
	Neurological disease	4 (13.3%)	3 (3.6%)	
Femur fracture	Proximal	28 (93.4%)	77 (89.5%)	0.846
	Saft	1 (3.3%)	4 (4.6%)	
	Distal	1 (3.3%)	5 (5.9%)	
Anesthesia Type	General anesthesia	3 (10.0%)	3 (3.5%)	0.178
	Spinal anesthesia	27 (90.0%)	83 (96.5%)	
ASA	II	1 (3.3%)	7 (8.1%)	0.218
	III	13 (43.3%)	48 (55.8%)	
	IV	16 (53.4%)	31 (36.1%)	
Operation Time (min)		59,00±28,51	58,12±22,27	0.947
Blood Trasfusion Need	No	13 (43.3%)	39 (45.3%)	0.849
	Yes	17 (56.7%)	47 (54.7%)	
Intensive Care Need	No	3 (10.0%)	35 (40.6%)	0.004
	Yes	27 (90%)	51 (59.4%)	
Blood Transfusion Amount (Unit)		1,00±1,17	0,93±1,15	0.814
Hospitalization Time		7,63±6,71	6,55±4,06	0.701
Leukocyte		11,47±5,41	10,09±3,11	0.420
Hemoglobin		10,86±1,68	11,30±1,53	0.075
Platelet		229,13±74,77	219,53±72,98	0.607
Neutrophil		8,57±4,02	8,02±2,95	0.781
Lymphocyte		1,66±1,60	1,26±0,64	1,000
Neutrophil/Lymphocyte		7,63±4,63	8,22±7,24	0.975
Preoperative C Reactive Protein		51,78±58,80	22,76±36,53	0.012
Albumin		2,53±0,24	3,45±0,34	<0.001
Prealbumin		11,01±4,19	14,13±4,82	0.001
C Reactive Protein / Albumin		20,47±23,30	6,87±11,64	0.001
Mortality	No	13 (43.3%)	77 (89.5%)	<0.001
	Yes	17 (56.7%)	9 (10.5%)	

ASA; American Society of Anesthesiologists

All confounding factors other than ALB concentrations (which correlated with PNI) were included in the multivariate regression analyzes to identify independent factors associated with adverse postoperative outcomes (**Table 4**). For postoperative 6-month mortality, a PNI value >29.0 at admission (odds ratio [OR]: 7.610, 95% confidence interval [CI]: 2.131–27,171, P = 0.002) was defined as an independent factor.

Table 4. Multivariate regression analyzes of confounding factors

Confounding factors	OR (95% CI)	P values
Admission CRP	0.967 (0.900-1.059)	0.567
Prealbumin	0.948 (0.838-1.073)	0.401
CRP/Albumin ratio	1.066 (0.858-1.324)	0.563
Age	1.017 (0.949-1.090)	0.640
PNI <29.0	7.610 (2.131-27.171)	0.002

CRP; C-reactive protein

Kaplan Meier survival analysis (Log Rank) statistic was used to investigate the relationship between PNI and survival. In the group with PNI>29.0, the survival rates at the end of the 1st, 3rd and 6th months were 94.2%, 89.5%, and 89.5%, respectively, while the survival rates at the end of the 1st, 3rd and 6th months were %, respectively, in the group with PNI ≤29.0. 73.3%, 56.7% and 43.3% (**Figure 1**).

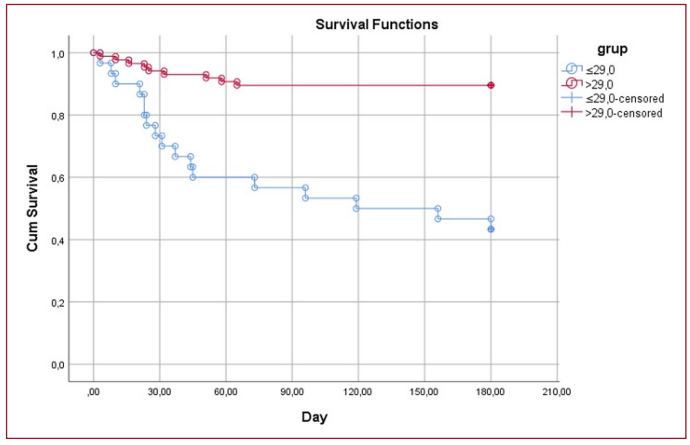

Figure 1. Kaplan Meier survival analysis

DICUSSION

In this study, we found that PNI, CRP, Albumin, CRP/Albumin ratio and Prealbumin at admission were independent factors for postoperative mortality in patients operated for femoral fracture, and PNI at admission was a good independent predictor. Our findings showed that in patients who will be operated for femoral fracture, nutritional evaluation is required at the time of admission and appropriate nutritional intervention should be considered for these patients.

In a study conducted by Li et al., they stated that albumin values decreased acutely, deeply and for a long time in the postoperative period in approximately 20-40% of patients who underwent surgical procedures.[12] In our study, mean albumin value was found to be low as 2.76±0.50 in patients with mortality in the postoperative 6-month period (p<0.001). This shows that there may be a risk of malnutrition that cannot be neglected in patients presenting with a femoral fracture. These patients received parenteral nutrition interventions as routine care when ALB concentration was < 3 g/dl.

Multivariate regression analysis showed that the nutritional status at admission of patients with femoral fracture was negatively associated with adverse outcomes in the

postoperative period. Albumin, prealbumin and PNI values at the time of admission were found to be statistically significantly lower in non-survival patients. The negative effects of malnutrition on the organism are quite high. Malnutrition significantly increases the risk of morbidity, mortality and hospitalization in surgical patients due to these adverse effects on the respiratory system, cardiovascular system, kidney functions, gastrointestinal system, immune system and wound healing.[13,14] Serological tests, anthropometric measurements and many nutritional scoring are used for malnutrition. The most commonly used definition for methods to identify malnutrition is ALB level <3.5 g/dL or LYM number <1500 cells (per mm^3).[15] The PNI value, which is calculated using albumin and lymphocyte values, may represent the general physiological functions and status of patients undergoing surgery, such as nutrition, immunity, and inflammation.[12,16] Therefore, PNI, which is used as a pre-treatment nutritional risk assessment tool, may be effective in predicting postoperative mortality. In a study including patients who underwent aortic valve replacement, it was reported that mortality was significantly higher in the patient group with a low PNI score.[17] Similarly, in our study, PNI was significantly lower in the mortality group ($p<0.001$). The 6-month survival rate was more than twice as high in the group with a high PNI score than in the group with a low score. Hypoalbuneemia is considered an indicator of global protein depletion.[18]

It has been reported that decreased albumin levels are associated with increased length of hospital stay, impaired wound healing, increased rates of wound infection, pneumonia and sepsis, increased incidence of postoperative complications, delayed physical rehabilitation, and decreased survival probability.[18-20] Koval et al. reported that albumin level was predictive for the length of hospital stay, in-hospital mortality and recovery of daily living activities after hip fracture.[19] Similarly, Pioli et al. showed that serum albumin level was a strong independent predictor of in-hospital and late mortality.[20] In our study, albumin levels were significantly lower in the mortal group. Based on the high correlation between nutrition and postoperative outcomes, this study suggested that patients with femur fracture should undergo nutritional assessment and nutritional intervention at presentation. Among the nutritional assessment parameters, there is also serum prealbumin, which is more sensitive to malnutrition that may occur due to its short serum half-life. According to Gianotti et al. showed a significant decrease in serum prealbumin values in the early postoperative period in the study conducted by him in which preoperative and early postoperative immunonutrition was applied.[21] In our research, prealbumin values were similarly lower than those with a mortal course ($p=0.041$).

Serum C-reactive protein (CRP), synthesized by the liver, is a positive acute phase reactant.[22] CRP is a non-specific systemic marker of inflammation.[23] Reports on the relationship between hip fracture and CRP levels are controversial in the literature. Belosesky et al. found no association between preoperative and postoperative CRP levels and 6-month mortality in geriatric patients undergoing hip fracture surgery.[24] Kim et al. showed that a high preoperative CRP level (>10.0 mg/dL) is associated with 1-year mortality after hip fracture surgery in the elderly. In our study, CRP values were approximately 1.5 times higher in patients who died within six months postoperatively ($p=0.014$). The CRP/ALB ratio (CAR), a new prognostic marker associated with inflammation, can be easily calculated by dividing the serum CRP level by the serum albumin level. CAR is mainly a marker of infection and malignancy.[25,26] However, few studies have focused on elderly patients undergoing orthopedic surgery.[27] On the other hand, Sercan et al. stated in their study that CAR is an essential marker in predicting 1-year mortality in the elderly after hip fracture.[28] Similarly, CAR was a predictor of mortality in our study ($p=0.003$).

This study has several limitations. First, this was a single-center study. Second, this study did not evaluate body mass index (BMI). BMI is an indicator for assessing nutritional status and is a good predictor of morbidity and mortality. Height values were not documented in this study, mainly because patients with femur fractures could not stand up to provide an accurate height measurement. Finally, we did not observe long-term complications and mortality.

CONCLUSION

This study showed that CRP, albumin, prealbumin, CRP/Albumin ratio and PNI values at presentation are independent risk factors for adverse postoperative outcomes in patients with femoral fractures. Our findings showed that all patients with femur fractures require nutritional assessment and appropriate nutritional intervention at presentation. PNI at admission can be a good indicator of nutritional assessment. A low prognostic nutritional index may predict mortality in patients with femoral fractures.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kastamonu University Clinical Researches Ethics Committee (Date: 19.10.2022, Decision No: 2022-KAEK-105).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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