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## The Relationship Between Preoperative Prognostic Nutritional Index and Postoperative Mortality in Patients with Hip Fracture

### İleri Yaş Kalça Kırığı Hastalarında Preoperatif Prognostik Beslenme İndeksinin Postoperatif Mortaliteyle İlişkisi

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**ABSTRACT Objective:** Hip fractures are an important health problem in geriatric patients. Preoperative estimation of mortality risk can be done by assessing malnutrition, establishing a perioperative treatment plan, determining the prognosis, and reducing morbidity and mortality. The prognostic nutritional index (PNI) is a simple, cost-effective, and easily applicable indicator of nutritional status in patients. This study aimed to determine the relationship between preoperative PNI and postoperative mortality in patients with hip fracture.

**Materials and Methods:** This prospective observational study included 183 patients aged 65-95 years who had I-IV American Society of Anesthesiologists physical status and were operated within the first 48 h after hip fracture. Patients were divided into two groups according to the 37.25 cutoff value of PNI. In total, 172 patients completed the study, of which 53 were in the low PNI group and 119 in the high PNI group.

**Results:** The length of hospital stay, postoperative delirium, and 3-month mortality were significantly higher in the low PNI group than in the high PNI group ( $p=0.035$ ,  $p=0.001$ ,  $p=0.0001$ , respectively).

**Conclusion:** Using PNI for diagnosing malnutrition in patients with hip fractures can help create an optimized treatment plan and reduce mortality. PNI is an easily calculated, objective, and inexpensive biomarker that can be used in routine screening.

**Keywords:** Prognostic nutritional index, hip fracture, mortality, delirium, malnutrition

**ÖZ Amaç:** Kalça kırıkları geriatric hasta grubunda önemli bir sağlık sorunudur. Malnütrisyonun saptanması, perioperatif tedavi planının oluşturulması, prognozun belirlenmesi ve böylece morbidite ve mortalitenin azaltılması açısından önemlidir. Prognostik beslenme indeksi (Prognostic nutritional index, PNI), hastaların beslenme durumunun bir göstergesi olan basit, uygun maliyetli ve kolay uygulanabilir bir parametredir. Bu çalışmanın amacı, postoperatif kalça kırığı hastalarında preoperatif PNI ile mortalite arasındaki ilişkiyi incelemektir.

**Gereç ve Yöntem:** Bu prospektif gözlemsel çalışmaya, kalça kırığı sonrası ilk 48 saat içinde ameliyat edilen, ASA skoru I-IV arası olan, 65-95 yaş arası 183 hasta dahil edildi. Hastalar PNI'nin 37.25 eşik değerine göre 2 gruba ayrıldı. Toplamda 172 hasta çalışmayı tamamladı: 53'ü Grup Düşük PNI'de ve 119'u Grup Yüksek PNI'de sınıflandı.

**Bulgular:** Hastanede kalış süresi Grup Düşük PNI'de anlamlı olarak daha yüksekti ( $p=0.035$ ). Postoperatif deliryum Grup Düşük PNI'de anlamlı olarak daha yüksek bulundu ( $p=0,001$ ). 3 aylık mortalite Grup Düşük PNI'de anlamlı olarak daha yüksekti ( $p=0.0001$ ).

**Sonuç:** Rutin taramalarda kullanılabilecek kolay hesaplanabilen, objektif ve ucuz bir biyobelirteç olan PNI ile kalça kırıklarında malnütrisyon tanısı konarak optimize bir tedavi planı oluşturmak ve mortaliteyi azaltmak mümkün olabilir.

**Anahtar Kelimeler:** Prognostik beslenme indeksi, kalça kırığı, mortalite, deliryum, malnütrisyon

## Introduction

The risk of osteoporosis increases with the decrease in bone mineral density with advancing age, and hip fractures occur as a result of low energy trauma [1]. The incidence of hip fractures is an important health problem in the world with an aging population [2]. Hip fractures with a 1-year mortality of 20-30% in the geriatric patient group fractures cause long intensive care unit and hospital stays [3]. While the treatment and care process of hip fracture negatively affects the patient physically, psychologically and socially, it also creates a serious economic burden for the health system [4]. Therefore malnutrition increases the postoperative complications shown in studies [5-7].

Nutrition of the patient is important as it is a modifiable risk factor [8]. Preoperative estimation of mortality risk by detecting malnutrition in hip fractures, establishing a perioperative treatment plan, determining the prognosis and reduce morbidity and mortality. The prognostic nutritional index (PNI) is calculated by serum albumin concentration and peripheral blood lymphocyte count. Its formula is  $10 \times \text{serum albumin (g/dL)} + 0.05 \times \text{total lymphocyte count (/mm}^3\text{)}$  [9]. The albumin concentration is an indicator of nutritional status associated with postoperative complications. Lymphocyte values may decrease with malnutrition, viral infections, autoimmune and inflammatory system activations. PNI is a simple, cost-effective and easily applicable parameter that has been frequently used in mortality, morbidity and prognosis studies in recent years to evaluate the immunological and nutritional status of patients in cancer surgery [9-12]. To our knowledge, there are very few studies investigating the relationship of PNI in hip fracture patients [13,14]. Therefore, the primary aim of this study was the relationship between preoperative PNI and 3-month mortality in postoperative hip fracture patients. Secondary aim of this study was the association of preoperative PNI and delirium.

## Materials and Methods

This prospective observational study was conducted between January-March 2021, approved by the Institutional Board of our University Hospital, Department of Orthopedics and Traumatology, with the number 21/01/2021-8. Patients were informed about the surgery, anesthesia, intensive care procedures, their participation to the study and the publication of the study, and their written consent was obtained. The study is reported according to the

Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [15].

The study included hip fracture patients aged 65-95 years, with American Society of Anesthesiologists (ASA) physical status I-IV, operated within the first 48 hours after the fracture, without delirium and neurological disease in the preoperative period. Patients with hematological disease, liver pathologies, chronic kidney disease, patients who underwent general anesthesia, had insufficient follow-up data, and refused to participate in the study were excluded from the study.

When the patients came to the operating room, routine monitoring (ECG, SPO<sub>2</sub>, non-invasive blood pressure) was followed by radial artery cannulation so arterial blood pressure monitoring was performed. After mild/moderate sedation with 1.5 mcg/kg IV fentanyl under 4 lt/min mask O<sub>2</sub>, hemispinal anesthesia was administered with 10 mg of hyperbaric bupivacaine through the L3-4 spinal space in the lateral position. The following variables were recorded on admission: demographic findings (age, gender, body mass index (BMI)), additional diseases before surgery; hypertension (HT), diabetes mellitus (DM), pulmonary pathologies (COPD, asthma, interstitial pulmonary disease, atelectasis, OSAS), cardiac pathologies (CAD, CHF, PHT, previous MI/stent, AF, pacemaker/ICD).

All patients were admitted and followed in the intensive care unit after surgery. No vasopressor/inotrope was used perioperatively. Postoperative mechanical ventilation or renal replacement therapy support was not required. Operation times, the amount of fluid given during the operation and blood transfusion, intensive care and hospital stays were recorded. Patients were followed up for 3-month mortality. The mental status of the patients at the preoperative and postoperative 48th hour was evaluated with the Confusion Assessment Method (CAM) [16]. The CAM method was validated in our country [17].

Lymphocyte count and albumin values were recorded from the 1st day preoperative blood results and PNI was calculated with the formula  $10 \times \text{serum albumin (g/dL)} + 0.05 \times \text{total lymphocyte count (/mm}^3\text{)}$  [9]. Patients were divided into 2 groups according to the 37.25 cut-off value of PNI. CRP (C reactive protein) and Pro-BNP (B-type natriuretic peptide) values were recorded.

## Statistical Analysis

Statistical analyses were performed with SPSS 21.0 (SPSS Inc, Chicago, IL, USA). All demographic data were

analyzed using descriptive statistical methods (mean, standard deviation, frequency). Comparisons between groups were performed using Student’s t-test and ve Chi-square test for normally distributed data and the Mann-Whitney U test for non-parametric data. A p value of < 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was executed to assess the predictive value of PNI for mortality, and the cutoff values were analyzed by Youden index.

If the true difference in the mean response of matched pairs is 3,94, a sample size of 164 patients achieved a power of 0,80 which allowed for the detection of a 10 % PNI difference by using the Power Analysis Program (G-Power, P.S. version 3.1.2). Prior data indicate that the difference in the response of matched pairs is normally distributed with standard deviation 10.2. The Type I error probability associated with this test of this null hypothesis is 0.05 [14].

## Results

183 patients with hip fractures who were operated under spinal anesthesia were eligible for the study and were divided into 2 groups, Group Low PNI and Group High PNI, according to the PNI cut-off value. In total, 172 patients completed the study: 53 in Group Low PNI and 119 in Group High PNI (Fig. 1).

The mean PNI calculated from albumin and lymphocyte values was 40.12±6.32 and is shown in Table 1. as the demographic findings of the patients.

There was no significant difference between the two groups in terms of age and gender (p > 0.05). BMI was significantly lower in Group Low PNI (p=0.025). ASA scores were significantly higher in Group Low PNI (p=0.005). (Table 2) When the additional diseases of the patients are evaluated, there was no significant difference between the two groups in terms of preoperative HT, DM, pulmonary and cardiac pathologies (p > 0.05).

From the preoperative laboratory results, lymphocyte and albumin levels were significantly lower and CRP values were significantly higher in Group Low PNI (p=0.0001). PRoBNP was significantly higher in Group Low PNI (p=0.029). (Table 2)

There was no significant difference between the two groups in terms of operation times (p > 0.05). The amount of fluid and blood transfusion given intraoperatively was similar in both groups (p > 0.05). While there was no significant

difference between the two groups in terms of intensive care unit length of stay (p > 0.05), the length of hospital stay was significantly higher in Group Low PNI (p=0.035). (Table 2)

Postoperative delirium was found to be significantly higher in Group Low PNI (p=0.001). 3-month mortality was significantly higher in Group Low PNI (p=0.0001). (Table 2)

According to the ROC curve analysis, preoperative PNI level was a predictor for mortality with an area under the

		<b>n=172</b>
Age (years)		80.18±8.24
<b>Sex</b>	Male	55 (32.0%)
	Female	117 (68.0%)
BMI		26.02±4.97
<b>ASA</b>	1	5 (2.9%)
	2	62 (36.0%)
	3	88 (51.2%)
	4	17 (9.9%)
	5	0 (0%)
<b>Preoperative hypertension</b>	Yes	129 (75%)
	No	43 (25.0%)
<b>Preoperative diabetes mellitus</b>	Yes	117 (68.0%)
	No	55 (32.0%)
<b>Preoperative pulmonary pathology</b>	Yes	141 (82.0%)
	No	31 (18.0%)
<b>Preoperative cardiac pathology</b>	Yes	109 (63.4%)
	No	63 (36.6%)
CRP (C-reactive protein)		64.88±59.53
PRoBNP (B-type natriuretic peptid)		3385.12±6433.01
Lymphocyte (/mm <sup>3</sup> )		1157.61±549.41
Albumin (gr/dL)		3.40±0.66
Prognostic Nutritional index		40.12±6.32
Perioperative fluid (mL)		1957.26±890.81
Perioperative blood transfusion (units)		0.2733±0.61
Operation time (hours)		1.83±0.64
<b>Postoperative delirium</b>	Yes	16 (9.3%)
	No	156 (90.7%)
Length of hospital stay (days)		13.41±5.34
Length of ICU stay (days)		2.33±1.36
<b>3 months mortality</b>	Yes	38 (22.1%)
	No	134 (77.9%)
BMI: Body mass index, ASA: American Society of Anesthesiologists		

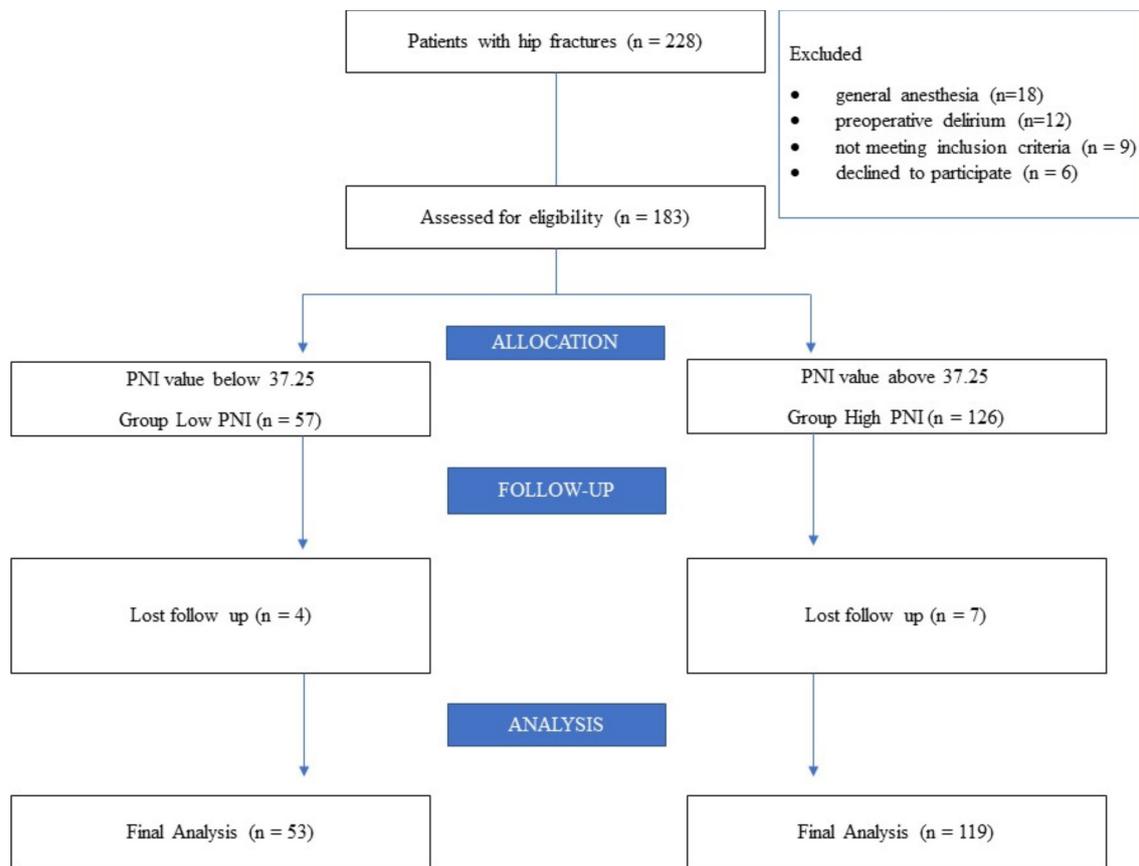


Figure 1. Flowchart of the hip fracture patients

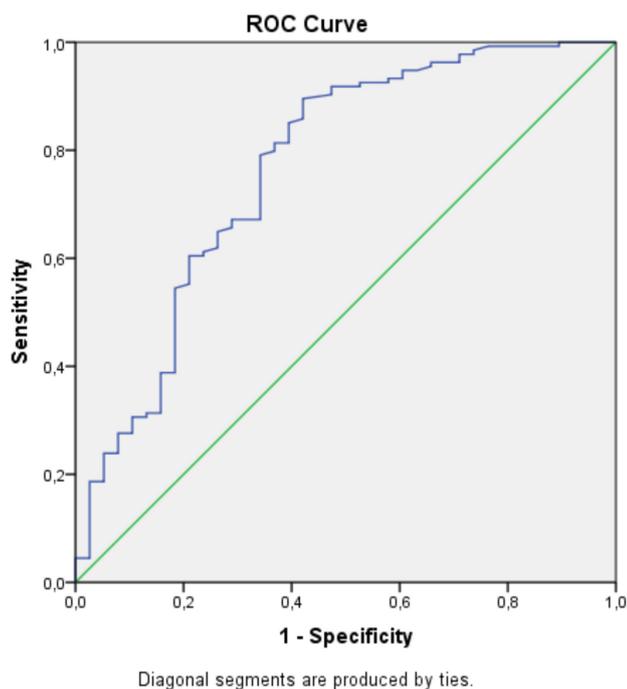


Figure 2. The ROC curve analysis

curve (AUC) of 0.767 (95% CI: 0.673-0.861,  $p=0.0001$ ) (Fig. 2) The sensitivity and specificity were 0.791 and 0.342 respectively with the cut-off value of 37.25.

## Discussion

In this prospective observational study, it was found that low PNI values calculated from preoperative laboratory results highly increased hospital stay length ( $p=0.035$ ), postoperative delirium ( $p=0.001$ ) and 3-month mortality ( $p=0.0001$ ) in hip fracture patients operated under spinal anesthesia.

The incidence of 3-month mortality ranges from 5-24% in hip fractures [18]. This high mortality is related to the preoperative functional status and accompanying comorbidities of the patients as well as the trauma and surgical process [19]. In this study, 3-month mortality was found to be 22.1% in all patient groups, consistent with the literature, but the Low PNI group mortality was found to be as high as 47.2% ( $p=0.0001$ ). Wilson et al. by evaluating albumin

		<b>Group Low PNI n=53 (30,81%)</b>	<b>Group High PNI n=119 (69,28%)</b>	<b>p-value</b>
Age (years)		81.67±8.81	79.51±7.92	0.112
<b>Sex</b>	Male	18 (34.0%)	37 (31.1%)	0.709
	Female	35 (66.0%)	82 (68.9%)	
BMI		24.74±6.25	26.59±4.19	0.025*
<b>ASA</b>	1	0 (%)	5 (4.2%)	0.005*
	2	11 (20.8%)	51 (42.9%)	
	3	33 (62.3%)	55 (46.2%)	
	4	9 (17.0%)	8 (9.9%)	
<b>Preoperative hypertension</b>	Yes	13 (24.5%)	30 (25.2%)	0.924
	No	40 (75.5%)	89 (74.8%)	
<b>Preoperative diabetes mellitus</b>	Yes	39 (73.6%)	78 (65.5%)	0.297
	No	14 (26.4%)	41 (34.5%)	
<b>Preoperative pulmonary pathology</b>	Yes	41 (77.4%)	100 (84.0%)	0.301
	No	12 (22.6%)	19 (16.0%)	
<b>Preoperative cardiac pathology</b>	Yes	37 (69.8%)	72 (60.5%)	0.242
	No	16 (30.2%)	47 (39.5%)	
CRP (C-reactive protein)		92.48±59.86	52.95±55.52	0.0001*
ProBNP (B-type natriuretic peptid)		5126.13±9087.01	2570.18±4547.35	0.029*
Lymphocyte (/mm <sup>3</sup> )		859.62±363.65	1290.33±567.01	0.0001*
Albumin (gr/dL)		2.74±0.64	3.69±0.42	0.0001*
Perioperative fluid (mL)		1879.24±864.54	1992.01±903.68	0.445
Perioperative blood transfusion (units)		0.37 ±0.68	0.22±0.55	0.164
Operation time (hours)		1.88±59.60	1.80±50.66	0.0453
<b>Postoperative delirium</b>	Yes	11 (20.8%)	5 (4.2%)	0.001*
	No	42 (79.2%)	114 (95.8%)	
Length of hospital stay (days)		13.99±5.31	12.13±5.23	0.035*
Length of ICU stay (days)		2.15±1.06	2.41±1.48	0.393
<b>3 months mortality</b>	Yes	25 (47.2%)	13 (10.9%)	0.0001*
	No	28 (52.8%)	106 (89.1%)	

BMI: Body mass index, ASA: American Society of Anesthesiologists, ICU: Intensive Care Unit, \*p<0.05 is defined as statistically significant

and total lymphocyte counts separately, found that mortality in hip fractures with malnutrition was approximately 25% [20]. PNI calculated with the albumin lymphocyte formula reflects the balance between inflammation and nutrition. In this study, we concluded that PNI is more sensitive marker and can detect mortality more effectively than separately assessed albumin and total lymphocyte counts.

Lu et al. retrospectively demonstrated that low albumin and lymphocyte levels are prognostic factors in determining 1-year mortality in hip fractures with advanced age [21].

Hypoalbuminemia may occur in synthesis disorders such as hepatocellular dysfunction and protein malnutrition, renal losses such as nephrotic syndrome, gastrointestinal losses such as protein-losing enteropathy, and increased catabolism such as sepsis [22]. Lymphopenia can be seen in viral infections, autoimmune and inflammatory system activations and some types of gastrointestinal cancer, malnutrition and suppression of immunity. Although the exact mechanism is not understood, increased serum cortisol levels may cause a decrease in lymphocyte count [23]. PNI biomarker, which

we think can be used in routine screening of malnutrition in patients with hip fracture, has been shown to be an independent prognostic marker in various malignant tumors [9-12]. In this paper, it was expected that BMIs would be low and ASA scores would be high in Group Low PNI as it indicated malnutrition ( $p=0.025$ ,  $p=0.005$ , respectively). In accordance with the literature, albumin and lymphocytes were low, and CRP and PProBNP were found to be significantly higher in Group Low PNI ( $p=0.0001$ ,  $p=0.0001$ ,  $p=0.0001$ ,  $p=0.029$ , respectively) [24]. Preoperative comorbidities, operation times, the amount of fluid and blood transfusion given intraoperatively was similar in both groups. Postoperative delirium and hospital stay length were also increased in Group Low PNI, that shown before in the study of Xing H. et al. ( $p=0.001$ ,  $p=0.035$ , respectively) [14]. The increase in post-fracture complications such as delirium, the deterioration of the general condition of the patients, prolongs the duration of care and increases the hospitalization period.

The main limitation of this study is that it is based on data from a single center; therefore, prospective randomized controlled trials are required. The second limitation of our study is the small number of our sample group. Different results can be obtained in studies with larger patient groups.

#### Conclusion

In conclusion, malnutrition is an important factor increasing postoperative mortality in hip fractures. We think that it is possible to create an optimized treatment plan and reduce mortality by making the diagnosis of malnutrition in hip fractures with PNI, an easily calculated, objective and inexpensive biomarker that can be used in routine screening.

#### Ethics

**Ethics Committee Approval:** The study was approved by the Institutional Board of our University Hospital, Department of Orthopedics and Traumatology, with the number 21/01/2021-8.

**Informed Consent:** Patients were informed about the surgery, anesthesia, intensive care procedures, their participation to the study and the publication of the study, and their written consent was obtained.

**Peer-review:** Externally peer-reviewed.

#### Authorship Contributions

Surgical and Medical Practices: İ.S., Y.S., H.D., Concept: N.C., D.B., D.A., M.I.B., Design: N.C., M.I.B., Data Collection or Processing: D.B., İ.S., Analysis or Interpretation: N.C., Y.S., D.A., M.I.B., Literature Search: N.C., D.B., İ.S., D.A., H.D., Writing: N.C., D.B., İ.S., Y.S., D.A., H.D., M.I.B.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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