



## Prognostic nutritional index predicts perioperative adverse events in patients undergoing hemiarthroplasty after a hip fracture

Cem Yalın KILIÇ<sup>1,\*</sup>, Onur GÜRSAN<sup>2</sup>, Ahmet Emrah AÇAN<sup>3</sup>, Emre GÜLTAÇ<sup>1</sup>

<sup>1</sup>Department of Orthopedic Surgery, Faculty of Medicine, Muğla Sıtkı Koçman University, Muğla, Turkey

<sup>2</sup>Department of Orthopedic Surgery, Faculty of Medicine, Dokuz Eylül University, İzmir, Turkey

<sup>3</sup>Department of Orthopedic Surgery, Faculty of Medicine, Balıkesir University, Balıkesir, Turkey

Received: 27.04.2021

Accepted/Published Online: 31.05.2021

Final Version: 01.01.2022

### Abstract

The relation of the prognostic nutritional index (PNI) with perioperative adverse events (PE) has never been described in hip fracture surgery patients. Therefore, this study aimed to evaluate the impact of preoperative PNI on the outcome of patients undergoing hemiarthroplasty after a hip fracture. A total of 154 adult patients aged  $\geq 65$  years undergoing hemiarthroplasty after a hip fracture were included in this retrospective study. The outcomes of interest were the length of stay in hospital and PE during hospitalization, defined as death, surgical site infection, major bleeding, cardiopulmonary complications, acute renal failure, pneumonia, cerebrovascular accidents, and sepsis. PNI was calculated from the following formula:  $10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{total lymphocyte count (per mm}^3\text{)}$ . Patients' information, including demographic data, routine preoperative laboratory tests, and PNI, was collected to assess the association between these factors and the PE. Perioperative adverse events occurred in 21 (13.6%) of the patients. Older patients and those with more comorbid conditions such as heart failure, coronary artery disease, diabetes mellitus, cerebrovascular diseases, and chronic obstructive pulmonary diseases were tended to have a higher rate of PE. Patients with PE had lower PNI ( $45.2 \pm 4.2$  vs.  $51.6 \pm 5.4$ ;  $p < 0.001$ ) on admission. Multivariate analysis showed that age (OR: 2.23, 95% CI 1.15-4.45,  $p=0.042$ ), presence of diabetes (OR: 2.34; 95% CI: 1.74-6.89;  $p=0.005$ ) and PNI  $< 47.2$  (OR 2.54, 95% CI 1.32-5.72,  $p = 0.004$ ) were significant and independent predictors of PE. This study is the first to demonstrate that the lower preoperative PNI is associated with PE in patients undergoing hip fracture surgery.

**Keywords:** prognostic nutritional index, hip fracture, surgery, prognosis, complication

### 1. Introduction

Hip fracture surgery is not only associated with a high rate of perioperative adverse events (PE), morbidity and mortality but also associated with increased costs (1). The combination of improvements in surgical techniques, extending surgical indications and an aging society with increasing medical comorbidities makes preoperative risk assessment increasingly important to guide patients in the preoperative decision for hip fracture surgery (2, 3). Previous studies have reported that prolonged operative time, older age, duration between injury and surgery, timing of rehabilitation, surgical technique, and presence of significant comorbidities are associated with a higher incidence of complications in hip fracture surgery, such as surgical site infection, delayed wound healing, and cardiovascular adverse events (4-9). These studies showed that the preoperative health condition is an extremely important consideration when deciding whether it is safe to proceed with hip fracture surgery especially in elderly patients.

Nutritional status is also an important preoperative risk factor for PE in patients undergoing surgery for hip fracture

(10, 11). While several tools for assessing nutritional status have been evaluated in patients undergoing various surgeries, most of these are difficult to use in daily clinical practice due to their complexity (12). In contrast, the prognostic nutritional index (PNI) can be easily calculated with parameters which are routinely evaluated in laboratory tests during preoperative diagnostic workup and are easy to repeat (13). The PNI, which is based on serum albumin concentration and total peripheral lymphocyte count, was originally proposed to assess the perioperative immunological status and surgical risk in patients undergoing gastrointestinal surgery (14). In recent years, the PNI has been shown to be a prognostic marker in patients with various solid tumors (15, 16), in patients with acute heart failure (17), pulmonary embolism (18) and in patients undergoing cancer surgery (19). However, there is only one study in the literature evaluating the significance of C-reactive protein/PNI ratio for predicting outcomes in hip fracture surgery which revealed that the PNI was not an independent prognostic factor for adverse events in these patients (20). Therefore, the aim of our study was to

\* Correspondence: cykilinc@gmail.com

assess the value of preoperative PNI as a predictor of PE in patients undergoing hip fracture surgery.

## 2. Materials and Methods

### 2.1. Study design and selection of patients

This is a retrospective and observational study which was approved by the regional ethics committee. The medical records of all patients, aged  $\geq 65$  years undergoing hemiarthroplasty after a hip fracture from July 2017 to May 2019 in Muğla Sıtkı Koçman University Hospital were retrospectively analyzed. Patient demographic characteristics, comorbid conditions, and medical history were obtained for all patients from patient medical records. Complete blood count and routine biochemical analyses were measured at admission and before the surgery. Exclusion criteria were as follows: patients with incomplete records, patients with chronic, or infectious diseases or taking immunosuppressive drugs which may influence the status of albumin and lymphocyte counts, patients with high energy trauma, patients with previous same side hip surgery and patients with pathological fracture due to malignancy or metabolic disease.

PNI was calculated using the following formula:  $10 \times$  serum albumin value (g/dl) +  $0.005 \times$  total lymphocyte count in the peripheral blood (per  $\text{mm}^3$ ).

### 2.2. Study endpoints

The outcomes of the study were length of stay and PE during hospitalization, which was included death, deep wound infection, major bleeding requiring transfusion, cardiopulmonary complications, thromboembolic events, pulmonary embolism, acute renal failure, pneumonia, cerebrovascular accidents, sepsis.

### 2.3. Statistical analysis

Statistical Package for Social Sciences (SPSS) for Windows-version 20.0 (SPSS, Chicago, IL, USA) software was used for statistical analyses. The continuous variables are expressed as means (minimum-maximum values), and we compared these variables between patients with and without PE using a 2-tailed Student *t* test. Nonparametric tests (Mann–Whitney *U* test) were performed when appropriate. Fisher exact and  $\chi^2$  tests were used to compare categorical variables. Multivariate logistic regression analyses were applied to determine crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the relationship between preoperative variables including PNI and PE. For all analyses,  $P < 0.05$  was considered statistically significant.

## 3. Results

A total of 180 patients aged  $\geq 65$  years underwent hemiarthroplasty in our institution during the study period. Twelve patients were excluded due to incomplete data, 6 patients were excluded due to have a chronic, or infectious disease or due to were taking immunosuppressive drugs, 3 patients were excluded due to pathological fracture, and 5 patients were excluded due to high energy trauma mechanism. After implementation of exclusion criteria, the

final study population consisted of 154 patients (mean age  $71.2 \pm 9.5$  years, and 48% male). Hypertension was the most frequent comorbidity (51.9 %), followed by coronary artery disease (26 %), and diabetes mellitus (20.8 %). Median length of stay was 9 days.

### 3.1. Perioperative adverse events

PE occurred in 21 (13.6%) patients. Comparison of baseline characteristics, laboratory parameters, length of hospital stay and PNI in patients with and without PE are shown in Table 1. Patients who had PE were older ( $76.1 \pm 7.6$  vs  $69.5 \pm 6.1$  years;  $p < 0.001$ ) and were more likely to have underlying comorbid diseases such as coronary artery disease (52.4 vs 21.8%;  $p = 0.003$ ), diabetes mellitus (47.6% vs 16.5%;  $p < 0.001$ ), heart failure (19% vs 5.3%;  $p = 0.045$ ), cerebrovascular disease (23.8% vs 8.3%;  $p = 0.046$ ) and chronic obstructive pulmonary disease (38.1% vs 9.8%;  $p < 0.001$ ).

**Table 1.** Baseline characteristics and length of stay of patients with and without perioperative adverse events undergoing hip fracture surgery

	No Adverse Event (n=133)	Adverse Event (n=21)	P Value
<b>Male</b>	63 (47.4)	11 (52.4)	0.526
<b>Age (years)</b>	$69.6 \pm 6.1$	$76.1 \pm 7.6$	<0.001
<b>Systolic blood pressure (mmHg)</b>	$125.4 \pm 15.3$	$126.4 \pm 13.4$	0.785
<b>Diastolic blood pressure (mmHg)</b>	$78.1 \pm 8.8$	$78.1 \pm 8.3$	0.423
<b>Medical History</b>			
Atrial fibrillation	6 (4.5)	3 (14.3)	0.107
Smoking	31 (23.3)	4 (19)	0.785
Diabetes mellitus	22 (16.5)	10 (47.6)	<0.001
Hypertension	66 (49.6)	14 (66.7)	0.146
Coronary artery disease	29 (21.8)	11 (52.4)	0.003
Cerebrovascular disease	11 (8.3)	5 (23.8)	0.046
Heart failure	7 (5.3)	4 (19.0)	0.045
Chronic obstructive pulmonary disease	13 (9.8)	8 (38.1)	<0.001
<b>Laboratory Results</b>			
White blood count ( $\times 10^3$ cells/mL)	$8.7 \pm 3.5$	$8.40 \pm 3.2$	0.442
Hemoglobin (g/dL)	$12.2 \pm 1.9$	$12.03 \pm 1.6$	0.228
Albumin (g/dL)	$3.91 \pm 0.57$	$3.52 \pm 0.33$	0.075
Creatinine (mg/dL), median (IQR)	1.0 (0.7-1)	1.0 (0.9-1.2)	0.324
Glucose (mg/dL)	$106.8 \pm 39.5$	$111.1 \pm 47.3$	0.153
<b>Length of stay (median, days)</b>	5.0 (4.0-9.0)	15.0 (10.0-25.0)	<0.001
<b>Prognostic nutritional index</b>	$51.6 \pm 5.4$	$45.2 \pm 4.2$	<0.001

Values are given as mean  $\pm$  SD or number (%) unless otherwise indicated

Although the difference did not reach statistical significance, patients who had PE had lower preoperative albumin levels compared to patients without PE ( $3.52 \pm 0.33$  vs  $3.91 \pm 0.57$  g/dL respectively;  $p=0.075$ ). Patients with PE had lower preoperative PNI levels than those with uncomplicated in-hospital course ( $45.2$  ( $41-49.4$ ) vs  $51.6$  ( $46.2-57$ );  $p<0.001$ ). Patients with perioperative complications had longer length of stay ( $15$  vs  $5$  days, median, respectively;  $p < 0.001$ ) compared with uncomplicated patients.

### 3.2. Predictors of perioperative adverse events

Univariate analysis showed that the following variables were associated with PE: heart failure, coronary artery disease, diabetes mellitus, cerebrovascular diseases, chronic obstructive pulmonary diseases, preoperative PNI levels. The parameters that proved to be significant on the univariate analysis were subsequently tested with the multivariate model (Table 2). Multivariate analysis showed that only age (OR: 2.23, 95% CI 1.15-4.45,  $p=0.042$ ), presence of diabetes (OR: 2.34; 95% CI: 1.74–6.89;  $p=0.005$ ) and PNI  $< 47.2$  (OR 2.54, 95% CI 1.32-5.72,  $p = 0.004$ ) were significant and independent predictors of PE.

**Table 2.** Multivariate analysis for the prediction of perioperative adverse events

	OR	95% CI	P
Age (per 1 y)	2.231	1.152-4.451	0.042
Diabetes mellitus (presence vs absent)	2.341	0.865-4.476	0.005
Coronary artery disease (presence vs absent)	0.788	0.410-0.936	0.236
Prognostic nutritional index $< 47.2$	2.542	1.321-5.721	0.004
COPD (presence vs absent)	1.125	0.955-3-214	0.065

### 4. Discussion

Our study investigated the incidence of PE after hip fracture surgery and identified risk factors for these complications. In this single-center, retrospective, and observational study of 154 patients, over the age of 65, the incidence of PE was 13.6%. The results of this study showed that older age, presence of diabetes and lower preoperative PNI were independent prognostic factors for PE. To the best of our knowledge, this is the first study to demonstrate an association between preoperative PNI and PE in hip fracture surgery patients.

Although several clinical and laboratory variables have been established as the predictors of perioperative complications in patients undergoing hip surgery, preoperative nutritional status have not been comprehensively evaluated in these studies (21). Aldebeyan and colleagues analyzed the data of 10,117 patients with hip fractures and showed that hypoalbuminaemia was an independent predictor of postoperative complications and patients with

hypoalbuminaemia had a longer hospital length of stay. In a recently published retrospective and observational cohort study, Wilson et al. examined the relationship of nutrition parameters with the modified frailty index and postoperative complications in hip fracture patients (22). Of the 377 patients, 2.6% and 17.5% of patients were malnourished as defined by total lymphocyte count of  $<1500$  cells/  $\text{mm}^3$  and albumin of  $<3.5$  g/dL, respectively. The authors showed that both total lymphocyte count and albumin weakly correlated with frailty but combining malnutrition and frailty revealed an increased predictive synergy for postoperative complications (22).

Malnutrition can be identified using a variety of anthropomorphic measurements, laboratory values, and screening tools. Although, malnutrition is most identified using serum albumin levels, PNI is not only a marker of nutritional status but also reflective immunologic status. To date, several studies showed that the prediction of surgical risk is possible by evaluating preoperative immunonutritional status with PNI in various types of surgeries such as gastrointestinal surgery (23), neurosurgery (24) and lung surgery (25).

However, the prognostic impact of PNI in patients undergoing hip surgery is remained unexplored. In a recent study, Ren and colleagues, prospectively evaluated the significance of C-reactive protein/PNI ratio for predicting the prognosis in eighty patients undergoing hip fracture surgery (20). The results of this study showed that PNI was not an independent prognostic factor but low C-reactive protein /PNI ratio was significantly associated with low one-year mortality rate after hip fracture surgery (20). Nevertheless, our findings showed that preoperative PNI may predict perioperative adverse events in patients undergoing surgery for hip fracture.

This study has several limitations. First, this study included only patients aged  $\geq 65$  years undergoing hemiarthroplasty after a hip fracture. Our hospital is a referral hospital, to which patients are referred from peripheral hospitals, which may affect our results. Therefore, caution should be taken in extrapolating these results to other surgical populations. Another important limitation of the current study is the fact that it was a retrospective analysis. Due to its retrospective nature, the study is prone to various forms of bias, such as selection bias and recall bias.

Preoperative PNI measurement can help identify patients at high risk for of PE after hip fracture surgery. The estimation of the PNI is inexpensive and easily available from laboratory data in daily clinical practice. Therefore, we suggest that the PNI should be calculated routinely before surgery, and it could be a useful indicator for pretreatment nutritional management in adult patients undergoing hip fracture surgery.

**Conflict of interest**

None to declare.

**Acknowledgments**

None to declare.

**References**

- Oliver D, Griffiths R, Roche J, Sahota O. Hip fracture. *BMJ Clin Evid.* 2007 Oct 10; 2007. pii: 1110.
- Dharmarajan TS, BanikP, Hip fracture. Risk factors, preoperative assessment, and postoperative management. *Postgrad Med.* 2006 Jun-Jul;119(1):31-8.
- Marufu TC, Mannings A, Moppett IK. Risk scoring models for predicting peri-operative morbidity and mortality in people with fragility hip fractures: Qualitative systematic review. *Injury.* 2015 Dec;46(12):2325-34.
- Smith EB, Parvizi J, Purtill JJ. Delayed surgery for patients with femur and hip fractures-risk of deep venous thrombosis. *J Trauma.* 2011;70(6): E113-6.
- Siu AL, Penrod JD, Boockvar KS, Koval K, Strauss E, Morrison RS. Early ambulation after hip fracture: effects on function and mortality. *Arch Intern Med.* 2006;166(7):766-71.
- Cheng T, Zhang GY, Liu T, Zhang XL. A meta-analysis of percutaneous compression plate versus sliding hip screw for the management of intertrochanteric fractures of the hip. *J Trauma Acute Care Surg.* 2012;72(5):1435-43.
- Jamal Sepah Y, Umer M, Khan A, Ullah Khan Niazi A. Functional outcome, mortality, and in-hospital complications of operative treatment in elderly patients with hip fractures in the developing world. *Int Orthop.* 2010;34(3):431-5.
- Franzo A, Francescutti C, Simon G. Risk factors correlated with post-operative mortality for hip fracture surgery in the elderly: a population-based approach. *Eur J Epidemiol.* 2005;20(12):985-91.
- Karres J, Heesakkers NA, Ultee JM, Vrouwenraets BC. Predicting 30-day mortality following hip fracture surgery: evaluation of six risk prediction models. *Injury* 2014; 46:371-7.
- Mazzola P, Ward L, Zazzetta S, et al. Association Between Preoperative Malnutrition and Postoperative Delirium After Hip Fracture Surgery in Older Adults. *J Am Geriatr Soc.* 2017 Jun;65(6):1222-1228.
- van Wissen J, van Stijn MF, Doodeman HJ, Houdijk AP. Mini Nutritional Assessment and Mortality after Hip Fracture Surgery in the Elderly. *J Nutr Health Aging.* 2016;20(9):964-968.
- Jones JM. The methodology of nutritional screening and assessment tools. *J Hum Nutr Diet.* 2002 Feb;15(1):59-71; quiz 73-5.
- T. Nozoe, M. Kohno, T. Iguchi, et al. The prognostic nutritional index can be a prognostic indicator in colorectal carcinoma, *Surg. Today* 42 (2012) 532-535.
- Tokunaga R, Sakamoto Y, Nakagawa S, Miyamoto Y, Yoshida N, Oki E, Watanabe M, Baba H. Prognostic Nutritional Index Predicts Severe Complications, Recurrence, and Poor Prognosis in Patients with Colorectal Cancer Undergoing Primary Tumor Resection. *Dis Colon Rectum.* 2015 Nov;58(11):1048-5.7
- Yang Z, Zhang B, Hou L, Xie Y, Cao X. Pre-operative prognostic nutritional index predicts the outcomes for triple-negative breast cancer, *Tumour Biol.* 35(2014) 12165-12171.
- Hong S, Zhou T, Fang W, Xue C, Hu Z, Qin T, Tang Y, Chen Y, Ma Y, Yang Y, Hou X, Huang Y, Zhao H, Zhao Y, Zhang L. The prognostic nutritional index (PNI) predicts overall survival of small-cell lung cancer patients. 2014 Dec;35(12):12165-71.
- Cheng YL, Sung SH, Cheng HM, Hsu PF, Guo CY, Yu WC, Chen CH. Prognostic Nutritional Index and the Risk of Mortality in Patients with Acute Heart Failure. *J Am Heart Assoc.* 2017 Jun 25;6(6).
- Hayiroğlu Mİ, Keskin M, Keskin T, Uzun AO, Altay S, Kaya A, Öz A, Çinier G, Güvenç TS, Kozan Ö. A Novel Independent Survival Predictor in Pulmonary Embolism: Prognostic Nutritional Index. *Clin Appl Thromb Hemost.* 2018 May;24(4):633-639.
- Okada S, Shimada J, Teramukai S, Kato D, Tsunozuka H, Miyata N, Ishihara S, Furuya T, Nakazono C, Ishikawa N, Inoue M. Risk Stratification According to the Prognostic Nutritional Index for Predicting Postoperative Complications After Lung Cancer Surgery. *Ann Surg Oncol.* 2018 May;25(5):1254-1261.
- Ren H, Wu L, Hu W, Ye X, Yu B. Prognostic value of the c-reactive protein/prognostic nutritional index ratio after hip fracture surgery in the elderly population. *Oncotarget.* 2017 May 24;8(37):61365-61372.
- Christopher P. Miller, Rafael A. Buerba, Michael P. Leslie. Preoperative Factors and Early Complications Associated with Hemiarthroplasty and Total Hip Arthroplasty for Displaced Femoral Neck Fractures. *Geriatr Orthop Surg Rehabil.* 2014 Jun; 5(2): 73-81.
- Aldebeyan S, Nooh A, Aoude A, Weber MH, Harvey EJ. Hypoalbuminaemia-a marker of malnutrition and predictor of postoperative complications and mortality after hip fractures. *Injury.* 2017 Feb;48(2):436-440.
- Lee JY, Kim HI, Kim YN, Hong JH, Alshomimi S, An JY, Cheong JH, Hyung WJ, Noh SH, Kim CB. Clinical Significance of the Prognostic Nutritional Index for Predicting Short- and Long-Term Surgical Outcomes After Gastrectomy: A Retrospective Analysis of 7781 Gastric Cancer Patients. *Medicine (Baltimore).* 2016 May;95(18): e3539.
- Oe S, Togawa D, Yamato Y, Hasegawa T, Yoshida G, Kobayashi S, Yasuda T, Banno T, Arima H, Mihara Y, Ushirozako H, Yamada T, Matsuyama Y. Preoperative age and prognostic nutritional index are useful factors for evaluating postoperative delirium among patients with adult spinal deformity. *Spine (Phila Pa 1976).* 2019 Apr 1;44(7):472-478.
- Mori S, Usami N, Fukumoto K, Mizuno T, Kuroda H, Sakakura N, Yokoi K, Sakao Y. The Significance of the Prognostic Nutritional Index in Patients with Completely Resected Non-Small Cell Lung Cancer. *PLoS One.* 2015 Sep 10;10(9): e0136897.