

Turkish Journal of Cerebrovascular Diseases 2025; 31(1): 38-44 doi: 10.5505/tjcvd.2025.58855

# Low Prognostic Nutritional Index and Mortality Risk in Patients with Spontaneous Intracerebral Hemorrhage

Spontan İntraserebral Hemorajili Hastalarda Düşük Prognostik Beslenme İndeksi ve Mortalite Riski

🕩 Fatma Ebru Algül, 🕩 Yüksel Kaplan

Department of Neurology, İnönü University Faculty of Medicine, Malatya, Türkiye

#### **ABSTRACT**

**Background:** Spontaneous intracerebral hemorrhage (ICH) is associated with a high risk of mortality and poor prognosis. ICH prognosis is closely related to nutritional status. The prognostic nutritional index (PNI) is a novel and useful marker calculated from the serum albumin concentration and lymphocyte count, which reflect inflammatory, immune, and nutritional status. We investigated the relationship between PNI and mortality in patients with supratentorial spontaneous ICH.

**Methods:** This retrospective study included patients diagnosed with supratentorial spontaneous ICH between January 2012 and June 2024. The sample was divided into survivors discharged from the hospital (n=65) and those who died in hospital (n=52). A PNI cut-off value, determined by receiver-operating characteristic curve analysis, was used to divide the sample further into high and low PNI groups for subsequent analysis.

**Results:** The low PNI group (<48.02) had significantly higher National Institutes of Health Stroke Scale scores, hematoma volumes, and lymphocyte and neutrophil counts, but lower hospital stay durations and albumin levels (P<.05) than the high PNI group. Univariate logistic regression analysis showed that the 28-day mortality rate was 2.391 times higher in the low PNI group than in the high PNI group (P<.005). Multivariate logistic regression analysis adjusted for confounding variables revealed that the 28-day mortality rate was 2.463 times higher in the low PNI group than in the high PNI group. The age subgroup analysis showed that the accuracy of the PNI cut-off value was higher in patients less than 70 years old (65.4%) than in those aged 70 years and older (58%).

**Conclusion:** Lower PNI values were associated with a worse prognosis in patients with supratentorial spontaneous ICH. Further studies in larger populations are needed to validate our findings.

**Keywords:** Intracerebral hemorrhage, prognostic nutritional index, prognosis, nutrition.

### ÖZ

**Amaç:** Spontan intraserebral hemoraji (İSH) yüksek mortalite riski ve kötü prognoz ile ilişkilidir. Beslenme durumu da prognoz ile yakından ilişkilidir. Prognostik nutrisyonel indeksi (PNİ), formülünde albümin ve lenfositleri içeren, bağışıklık yanıtını ve beslenme durumunu değerlendiren yeni ve yararlı bir belirteçtir. Biz de supratentoryal spontan intraserebral hemoraji hastalarında PNİ ile mortalite arasındaki ilişkiyi araştırmayı amaçladık.

**Yöntemler:** Bu retrospektif çalışmaya, Ocak 2012 ile Haziran 2024 arasında takip edilen supratentoryal spontan İSH tanılı hastalar dahil edildi. Çalışma popülasyonu taburcu edilenler (n=65) ve hastanede ölenler (n=52) olarak iki gruba ayrıldı. PNİ için ROC analizi ile bir kesme değeri belirlendi ve bu kesme değerine göre örneklem, sonraki analizler için yüksek ve düşük PNİ gruplarına ayrıldı.

**Bulgular:** Düşük PNİ'ye sahip hastaların (PNİ<48.02) Ulusal Sağlık İnme Ölçeği Enstitüleri (NIHSS) skorları, hematom hacimleri, lenfosit ve nötrofil sayımları anlamlı olarak yüksek, hastanede kalış süreleri ve albumin seviyeleri ise anlamlı olarak düşük tespit edilmiştir (P<.05). Univaryant lojistik regresyon analizinde 28 günlük mortalite oranı; düşük PNİ grubundaki hastalarda yüksek PNİ grubundaki hastalara göre 2.391 kat fazla bulunmuştur (P<.005). Değişkenlere göre ayarlama yapılmış multivaryant lojistik regresyon analiz modelinde de 28 günlük mortalite oranının; düşük PNİ değerine sahip hasta grubunda diğer hasta grubuna göre 2.463 kat fazla olduğu tespit edilmiştir. Yaşa göre yapılan subgrup analizinde 70 yaş altı olan grupta PNI cut off değerinin doğruluk ölçütünün (%65.4), 70 yaş üstüne göre (%58) daha yüksek olduğu tespit edilmiştir.

**Sonuç:** Supratentoryal spontan İSH hastalarında düşük PNİ değerlerinin kötü prognoz ile ilişkili olduğu bulunmuştur. Bulgularımızın doğrulanması için daha geniş popülasyonlar üzerinde yapılacak çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: İntraserebral hemoraji, prognostik beslenme indeksi, prognoz, beslenme.

Cite this article as: Algül FE, Kaplan Y. Low prognostic nutritional index and mortality risk in patients with spontaneous intracerebral hemorrhage. *Turk J Cerebrovasc Dis.* 2025;31(1):38-44.

Corresponding Author: Fatma Ebru Algül, ebruycl86@yahoo.com

Received: November 11, 2024 Accepted: February 2, 2025 Publishing Date: April 30, 2025



#### INTRODUCTION

Spontaneous intracerebral hemorrhage (ICH) accounts for about 15% of all strokes and has a high mortality rate <sup>1</sup>. ICH is associated with a poor prognosis, with a 30-day case fatality rate of 19.8% and a 1-year case fatality rate of 29.6%.<sup>2</sup>

The prognosis of patients with ICH is affected by multiple factors including age, hematoma size and location, peri-hemorrhagic edema, intracranial pressure, neurological deficits, inflammatory response, and nutritional status.<sup>3,4</sup>

It is not easy to evaluate the nutritional status of the patients. Despite advancements, reliable and effective predictors of risk and nutritional status remain lacking. Therefore, it is crucial to explore novel, fast, and effective biomarkers to predict the prognosis of patients with ICH. The prognostic nutritional index (PNI), first proposed by Mullen and colleagues in 1980, was designed to evaluate the prognosis of patients undergoing gastrointestinal surgery. Fafter optimization, the PNI formula was expressed as PNI=  $10 \times \text{serum}$  albumin (g/dL) + 0.005  $\times$  total lymphocyte count (mm³). This index, which reflects both inflammatory immune response and nutritional status, is essential for predicting the prognosis of patients with various diseases, including cancer, lymphoma, infectious diseases, postoperative complications and cardiac diseases.

Investigations of PNI in various neurological diseases found that low PNI is associated with poor prognosis in acute ischemic stroke, ischemic stroke patients receiving thrombolytic therapy, young stroke patients, subarachnoid hemorrhage, and patients with ICH.<sup>12-15</sup> Moreover, low PNI is a risk factor for hospital-acquired infections in patients with ischemic and hemorrhagic stroke. However, little is known about the relationship between PNI and mortality in ICH patients. Therefore, we investigated the association between PNI and in-hospital mortality in patients with supratentorial ICH.

#### **MATERIAL AND METHODS**

### **Study Population**

This retrospective study included patients admitted to the neurology intensive care unit or neurology inpatient service between January 2012 and June 2024, diagnosed with spontaneous ICH. The study was approved by the Clinical Research Ethics Committee of Inonu University Faculty of Medicine (approval number: 2024/6195). The study was performed in accordance with the Declaration of Helsinki.

## **MAIN POINTS**

- The Prognostic Nutritional Index (PNI) is an independent predictor of in-hospital mortality in patients with supratentorial spontaneous intracerebral hemorrhage.
- Lower PNI levels are significantly associated with increased stroke severity and larger hematoma volumes.
- Given its basis on routine and readily available laboratory parameters, PNI may be considered a practical, accessible, and cost-effective prognostic tool in patients with supratentorial spontaneous intracerebral hemorrhage.

The inclusion criteria included age >18 years, diagnosis of supratentorial spontaneous ICH on admission, and available clinical laboratory data on admission (platelet, absolute neutrophil, absolute lymphocyte and absolute monocyte counts, albumin, hemoglobin, and hematocrit).

Patients were excluded if the ICH was secondary to other etiologies (e.g., vascular malformation, anticoagulation use, tumor or hemorrhagic infarction), developed during hospitalization, or if there was a history of infectious disease, cancer, rheumatic disease, blood system disease, or other diseases that affected peripheral blood cells. Because outcomes are typically worse in patients with infratentorial ICH, we excluded patients with brainstem or cerebellar hematoma.

#### **Data Collection**

Clinical variables were obtained from the electronic medical record system, including demographic information (age of onset, sex, and discharge status); clinical history (hypertension, diabetes mellitus, smoking, alcohol abuse); neurological deficits and consciousness status (assessed by the National Institutes of Health Stroke Scale (NIHSS)), and duration from onset to hospitalization; ICH imaging characteristics (hematoma volume, intraventricular extension of the hematoma); and surgical interventions (decompressive surgery and external ventricular drainage).

The parenchymal hematoma volume was calculated on the admission computed tomography (CT) scans using the ABC/2 method.<sup>16</sup>

The PNI was calculated as  $10 \times$  serum albumin (g/dL) +  $0.005 \times$  total lymphocyte count (per mm3).

The patients were divided into two groups: survivors discharged from the hospital and those who died in hospital.

The cut-off value for PNI was determined by receiver-operating characteristic (ROC) curve analysis between the survival and death groups. The PNI cut-off value of 48.02 was used to divide the patients into low PNI (<48.02) and high PNI (≥48.02) groups.

#### **Subgroup Analysis**

To investigate the association between PNI and early mortality, the PNI value was compared in patients who died in hospital before and after 28 days in hospital.

Additionally, the sample was divided according to age: less than 70 years old vs. 70 years and older, and the accuracy of the PNI cut-off point was assessed in the age subgroups.

#### **Statistical Analysis**

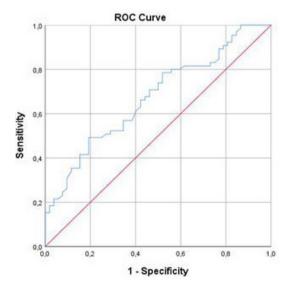
Statistical analysis were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). All statistical tests were two-tailed and P-values <.05 were deemed to indicate statistical significance. In the first step, time-dependent ROC analysis was used to determine the optimal PNI cut-off value to predict all-cause mortality (Figure 1). The optimal PNI cut-off of 48.02 was used to divide the patients into low PNI (<48.02) and high PNI ( $\geq$ 48.02) groups. In the second step, baseline characteristics were compared between groups. The normality of continuous

variables was verified using the Shapiro-Wilk (n<50) and Kolmogorov–Smirnov (n≥50) tests. Differences between the low and high PNI groups were assessed using the Mann-Whitney U-test for independent non-normally distributed variables and independent t-tests for normally distributed variables. The association between PNI and 28day mortality was assessed using univariate and multivariate Cox's proportional hazard models. Multivariate regression analyses were adjusted for potential covariates. ROC curves were used to determine the optimal PNI cut-off value for predicting survival and death in ICH patients. Linear regression analysis was performed to determine the relationship between PNI and clinical parameters (age, surgical intervention, NIHSS score, hematoma volume, duration of hospitalization, and sex). Binary logistic regression analyses were performed to assess associations between PNI and mortality status, adjusting for age and surgical intervention. The findings are expressed as the unstandardized coefficient (B), standard error, odds ratio (Exp(B)), and P-value.

#### **RESULTS**

PNI was significantly lower in patients who died than in survivors (P=.001). ROC curve analysis and the Youden index were used to determine the optimal PNI cut-off, to distinguish between survival and death. The area under the ROC curve for PNI was 48.02 (95% confidence interval (CI), 0.576-0.769; Figure 1). ROC curve analysis for survival and death revealed an optimal PNI cut-off value of 48.02 with specificity, sensitivity, and accuracy values of 80.8%, 49.2%, and 60.6%, respectively (Table 1).

Baseline characteristics are shown according to PNI value in Table 2. The median patient age was 70.92±13.91 (min/max, 22–102) years and 53% were male. The low PNI group were significantly older than the high PNI group (P=.002). The sex distribution, vascular risk factors (hypertension, diabetes mellitus, smoking, and alcohol use), surgical intervention, intraventricular expansion of hematoma, and monocyte, leukocyte, platelet, hemoglobin, and hematocrit levels were similar between groups. The NIHSS score, hematoma volume, lymphocyte count, and neutrophil count were significantly higher in the low PNI group, whereas the duration of hospitalization and albumin levels were significantly lower, compared with the high PNI group.



**Figure 1.** Receiver operating characteristics curve (ROC) of the PNI for prediction of mortality.

**Table 1.** Receiver-operating characteristics (ROC) curve analysis of PNI in the Survival/Death groups

	PNI
Cut-off	48.02
Specificity	80.8%
Sensitivity	49.2%
Area Under the Curve (AUC)	67.3%
Accuracy	60.6%
Accuracy for Age ≤ 70	65.4%
Accuracy for Age > 70	58%
95% CI	0.576-0.769
P	.001*

<sup>\*</sup>Statistically significant (P<.05).

Linear regression analysis revealed a statistically significant correlation between PNI and age and surgical intervention. However, PNI was not significantly correlated with the NIHSS score, hematoma volume, duration of hospitalization, or sex (Table 3). Binary logistic regression analysis showed that PNI remained a significant predictor of survival status (Survival/Death) after adjusting for age and surgical intervention (Tables 4 and 5). Figure 2 shows PNI values according to survival status.

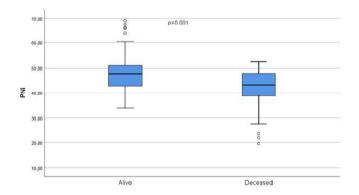


Figure 2. PNI values according to the Survival Status.

## **Subgroup Analysis**

Patients who died in hospital were further analyzed according to the PNI cut-off value. Of those who died before 28 days (n=41), 38 (97.4%) were in the low PNI group and 3 (2.6%) were in the high PNI group. Of those who died after 28 days (n=11), 1 (2.6%) was in the low PNI group and 10 (77%) were in the high PNI group (Table 2). Univariate logistic regression analysis showed that for patients with PNI <48.02, the crude hazard ratio (HR) for 28-day case fatality was 2.391 (95% CI: 1.264-4.521; P=.007) indicating that these patients had a higher risk of 28-day mortality than did those with PNI ≥48.02, which indicated that they served as the reference group. In multivariate analysis, after adjusting for potential confounding variables, the adjusted HR for patients with PNI <48.02 was 2.463 (95% CI: 1.067-5.688; P=.035), indicating that, after accounting for other factors, low PNI remained significantly associated with a higher risk of 28-day mortality (Table 6).

**Table 2.** Demographic and clinical characteristics according to the PNI cut-off value

	TOTAL	Low PNI <48.02 (n=72)	High PNI ≥48.02 (n=45)	P
Demographics				
Age*	70.92±13.91/22-102	73,1±11,8/52-91	66.33±17.87/33-80	.002**
≤ 70 year, n (%)	52 (44.5)	26 (36.2)	26 (57.8)	
> 70 year, n (%)	65 (55.5)	46 (63.8)	19 (42.2)	
Gender				.854
Male, n (%)	62 (53)	38 (52.8)	24 (53.3)	
Female, n (%)	54 (46.2)	34 (47.2)	21 (46.7)	
Survival/death, n (%)	65 (55)/52 (45)	33 (45.8)/39 (54.2)	32 (71.1)/13 (28.9)	
Mortality				
≤ 28day, n (%)	41 (78.8)	38 (97.4)	3 (23)	.013**
> 28 day, n (%)	11 (21.2)	1 (2.6)	10 (77)	.000**
NIHSS	12.87±7.81/1-27	21.17±5.27/12-27	20.55±6.13/8-27	
Duration of hospital	19.30±16.47/2-77	16.54±14.42/2-74	23.71±18.62/4-77	.260
Vascular Risk Factors				.063
HT, n (%)	80 (68.4)	52 (72.2)	28 (62.2)	.758
DM, n (%)	20 (17.1)	16 (22.2)	4 (8.9)	.974
Smoking, n (%)	27 (23.1)	16 (22.2)	11 (24.4)	
Alcohol use, n (%)	14 (12)	9 (12.5)	5 (11.1)	.049**
ICH Parameters				.363
Volume*	72.6±59.77/0.5-270	81.18±58.34/0.5-195	88.63±69.66/28.8-180	.089
Intraventricular expansion, n (%)	66 (56.4)	43 (59.7)	23 (51.1)	.427
Surgical Intervention	34 (29.1)	25 (34.7)	9 (20)	
Decompressive surgery, n (%)	15 (12.8)	10 (13.9)	5 (11.1)	
EV drainage, n (%)	19 (16.2)	15 (20.8)	4 (8.8)	.000**
Laboratory data				.049**
Absolute Lymphocyte Count*	1.57±0.79/0.2-4.82	1.25±0.5/0.2-2.85	1.56±0.33/1.26-2.2	.086
Absolute Neutrophil Count*	9.89±5.14/1.77-23.7	10.62±5.29/2.71-22.1	12.03±2.33/8.61-14.8	.656
Absolute Monocyte Count	0.74±0.61/0.1-3.5	0.7±0.57/0.1-3.5	1.31±1.12/0.68-3.5	.726
Leukocyte*	11.94±5.09/3.3-28.2	12.1±5.18/3.3-24.2	15.07±3.06/10.73-18.6	.127
Platelets	242.19±73.23/76-615	242.5±83.76/76-615	241.5±66.97/147-330	.115
Hemoglobin*	14.09±2.27/7.4-19.2	13.84±2.36/7.4-18	13.6±2.87/8.5-16.5	.000**
Hematocrit*	42.3±6.08/22.9-56.7	41.6±6.45/22.9-55.7	40.17±7.3/27.3-48.9	.000**
Albumin*	3.72±0.64/1.4-5.2	3.42±0.6/1.4-4.5	4.28±0.26/4.1-4.7	.049**
Absolute Monocyte Count	0.74±0.61/0.1-3.5	0.7±0.57/0.1-3.5	1.31±1.12/0.68-3.5	.086
Leukocyte*	11.94±5.09/3.3-28.2	12.1±5.18/3.3-24.2	15.07±3.06/10.73-18.6	.656
Platelets	242.19±73.23/76-615	242.5±83.76/76-615	241.5±66.97/147-330	.726
Hemoglobin*	14.09±2.27/7.4-19.2	13.84±2.36/7.4-18	13.6±2.87/8.5-16.5	.127
Hematocrit*	42.3±6.08/22.9-56.7	41.6±6.45/22.9-55.7	40.17±7.3/27.3-48.9	.115
Albumin*	3.72±0.64/1.4-5.2	3.42±0.6/1.4-4.5	4.28±0.26/4.1-4.7	.000**

<sup>\*</sup>The T test was used, and all other variables were analyzed using the Mann-Whitney U test \*\* Statistically significant (P<.05).

**Table 3.** Linear regression analysis between PNI and clinical parameters in patients with ICH

	Unstandardized Coefficients (B)	P	
Age (years)	-0.172	.002*	
Gender	1.689	.252	
NIHSS	-0.067	.602	
Hematoma volume	-0.005	.756	
Surgical Intervention	-4.136	.034*	
Duration of hospital	0.012	.788	

\*Statistically significant at the 0.05 level. A statistically significant correlation between PNI, age, and surgical Intervention was discovered in the linear regression analysis, while other clinical parameters (NIHSS score, hematoma volume, duration of hospital and gender) did not show a statistically significant correlation.

**Table 4.** Association between PNI and survival/death adjusted for age

	Unstandardized Coefficients (B)	Standard Error	Exp(B)	P
PNI	-0.082	0.030	0.922	.005*
Age	0.036	0.501	1.036	.031*

\*Statistically significant at the .05 level. Binary logistic regression is used. PNI remains a critical predictor of Alive/Deceased after adjusting for age.

**Table 5.** Association between PNI and survival/death adjusted for surgical intervention

	Unstandardized Coefficients (B)	Standard Error	Exp(B)	P
PNI	-0.079	0.030	0.924	.005*
Surgical Intervention	1.996	0.501	7.358	.000*

\*Statistically significant at the .05 level. Binary logistic regression is used. PNI remains a critical predictor of Alive/Deceased after adjusting for surgical intervention.

**Table 6.** Univariate and multivariate Cox proportional hazards regression analysis of PNI level affecting overall survival

	Univariate Analysis		Multivariate Analysis	
	Crude HR (95% CI)	Р	Adjusted HR (95% CI)	Р
	28-day case fatality			
PNI <48.02	1 (reference)		1 (reference)	
PNI ≥48.02	2.391 (1.264-4521)	.007	2.463 (1.067-5.688)	.035

A multivariate regression model; HR, hazard ratio; CI, confidence interval. All multivariate regression models were adjusted for variables: sex, age, platelet, neutrophil, monocyte, lymphocyte, albumin, hemoglobin, hematocrit.

The age subanalysis ( $\leq$ 70 years (n=52) vs.>70 years (n=65)) found that of those  $\leq$ 70 years old, 26 (36.2%) had a low PNI and 26 (57.8%) had a high PNI. In the >70 years old group, 46 (63.8%) had a low PNI while 19 (42.2%) had a high PNI (Table 2). Subgroup analysis performed to validate the PNI cut-off value revealed an accuracy of 65.4% for patients  $\leq$ 70 years old and 58% for those >70 years old (Table 1).

#### **DISCUSSION**

To our knowledge, our study is the first to investigate the relationship between PNI and in-hospital mortality in patients with supratentorial spontaneous ICH. Our findings suggest that patients with lower PNI on admission had a worse prognosis than those with higher PNI.

Nutrition is a critical issue for patients with stroke at all clinical stages. Furthermore, nutrition is an important determinant of post-stroke neurological recovery,<sup>17</sup> and current nutritional status has a significant impact on the effectiveness of rehabilitation treatment.<sup>18</sup>

Acute stroke is often accompanied by dysphagia, accounting for more than 50% of those affected.<sup>19</sup> Concomitant dysphagia is associated with reduced food and nutrient intake, decreased nutritional status, and increased incidence of malnutrition, which aggravates existing malnutrition, and affects quality of life.<sup>20-22</sup> Malnutrition is highly prevalent and often unrecognized in stroke patients, with a reported prevalence of 6.1–79%.<sup>17</sup> Furthermore, in patients with stroke, malnutrition is associated with mortality, length of hospitalization,<sup>23</sup> and a decline in functional status while in the hospital, resulting in decreased ability to perform activities of daily living in hospital and after discharge.<sup>24,25</sup> An appropriate increase in caloric intake through enteral nutrition during the early stages of ICH is associated with improved neurological outcomes at hospital discharge. Therefore, it is crucial to assess the severity of ICH on admission, make rational treatment decisions, and take appropriate measures to minimize the decline in patients' nutritional and immune status.<sup>26, 27</sup> Moreover, it is essential that patients adopt appropriate nutritional behaviors to facilitate neural plasticity and the neurological recovery processes.<sup>28</sup> Patients with ICH have increased metabolism, attributed to inflammation caused by the injury, leading to elevated resting energy expenditure. In this hypermetabolic state, increased energy requirements exacerbate the mismatch between food intake and energy expenditure, resulting in a negative energy balance and adverse clinical outcomes.<sup>29</sup>

Malnutrition plays a significant role in the prognosis of ICH. Malnour-ishment is associated with the development of complications and poor functional outcomes and is linked to compromised immune function, resulting in higher infection rates.<sup>30</sup> Furthermore, inflammatory factors inhibit albumin synthesis, while oxidative stress may result in albumin denaturation, contributing to a rapid decrease in serum albumin levels in patients in an inflammatory state.<sup>31,32</sup> Strong evidence indicates that low albumin levels increase in-hospital mortality from stroke and cardiovascular disease and that albumin therapy contributes to good neurological outcomes.<sup>33</sup> Thus, low serum albumin levels may be an independent predictor of poor prognosis and functional recovery in patients with ICH.<sup>27,34</sup>

Assessment of nutritional status in stroke patients is complex, but necessary in clinical practice.<sup>35,36</sup> Screening tools for the early detection of patients at risk of malnutrition allow clinicians to initiate timely and effective nutritional management programs to achieve better clinical outcomes. Therefore, early identification of malnutrition using appropriate nutritional parameters is crucial for improving functional status in patients diagnosed with hemorrhagic stroke.<sup>18,37</sup> The Mini Nutritional Assessment and its short form are among the most used screening tools for malnutrition;<sup>38</sup> that said, use of the controlling nutritional status (CONUT) score, developed by Ignacio et al.,<sup>39</sup> has increased recently. In contrast to these screening tools, the PNI is a biological marker that includes albumin and lymphocyte levels and allows rapid assessment using more readily accessible data. PNI indicates the patient's chronic inflammatory and nutritional status<sup>6</sup> and offers several advantages that make it suitable for routine

clinical practice. It is readily available, easily quantifiable, repeatable, and relatively cost-effective.<sup>40</sup> Moreover, PNI can help identify patients who may benefit from early nutritional therapy.<sup>41</sup> PNI is a dependable tool for the assessment and prediction of long-term outcomes in patients, with an emphasis on the importance of nutritional risk assessment.

Low PNI values suggest a reduction in serum albumin levels and an increase in lymphocyte count, which may stimulate the release of various proinflammatory cytokines, including interleukins, C-reactive proteins, and tumor necrosis factors.<sup>42</sup>

Previous studies have shown that PNI predicted poor prognosis in various diseases including cancer, chronic kidney disease, heart failure, hypertrophic cardiomyopathy, ischemic stroke, and aneurysmal subarachnoid hemorrhage.<sup>12-13,15,43-44</sup> One study found that PNI was an independent predictor of 30-day, 90-day, and 1-year mortality rates in patients with stroke.<sup>14</sup> A multivariate regression model showed that low PNI was independently associated with poor prognosis in patients with acute ischemic stroke who received IV thrombolytic therapy.<sup>12</sup> In a study of patients with acute ischemic stroke, Wang et al.,<sup>45</sup> found that low PNI (<48.43) was independently associated with post-stroke cognitive impairment. Furthermore, PNI scores were specifically correlated with global cognition and attention domain scores. Moreover, a decrease in the PNI score is significantly associated with the risk of post-stroke depression.<sup>46</sup>

A recent study of patients with ICH found that PNI <42.77 was associated with poor clinical profiles and increased risk of adverse outcomes, including in-hospital complications such as acute respiratory failure, stroke-associated pneumonia, urinary tract infection, seizures, and sepsis, and higher case fatality rates within 28 and 90 days<sup>47</sup> Li et al.,<sup>48</sup> reported that PNI was more effective in predicting in-hospital mortality in patients with hemorrhagic stroke than in those with ischemic stroke. Zhao et al. found that patients diagnosed with stroke-associated pneumonia following ICH had lower PNI values than those without pneumonia.<sup>25</sup>

Our findings, that low PNI (<48.02) was associated with in-hospital mortality and significantly increased the 28-day mortality rate, with a larger hematoma volume, and higher NIHSS scores, are consistent with reports in the literature.

Our study has several limitations. First, it was a retrospective, single-center study with a relatively small sample size, which limited our ability to establish causal relationships. Moreover, given the small sample size, our findings are not readily generalizable. Second, PNI was assessed at admission, and we did not consider dynamic changes over time. Third, our study included only patients with supratentorial ICH, the majority of whom are older adults.

Despite these limitations, our study has several strengths. Our main aim was to assess the relationship between PNI and in-hospital mortality in patients with supratentorial spontaneous ICH. We found that low PNI was associated with in-hospital mortality and significantly increased the risk of early mortality (<28 days). Finally, we found that the PNI cut-off of 48.2 was more accurate in patients less than 70 years of age than in those aged 70 years and older.

#### CONCLUSION

Early risk stratification at admission is essential for patients with ICH. The PNI reflects the nutritional, immune and inflammatory status of patients. Our findings suggest that lower PNI values may be a useful prognostic indicator for in-hospital mortality in patients with supratentorial ICH.

Larger prospective, multicenter, and longitudinal studies are needed to increase the generalizability of our findings and to determine whether potential dynamic changes in PNI values predict poor prognosis in patients with spontaneous ICH.

Because infratentorial ICH is associated with a higher likelihood of death or dependency,<sup>49</sup> we chose to focus on patients with supratentorial ICH, to minimize confounding factors and to evaluate more accurately the clinical impact of the PNI. Future studies should include different types of hemorrhage and a more diverse age range, to increase the demographic diversity of the findings.

**Ethics Committee Approval:** The study was approved by the Clinical Research Ethics Committee of İnönü University Faculty of Medicine (Date: September 11, 2024; Decision No: 2024/6195). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Informed Consent:** Written informed consent was not obtained from the patients due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

**Authorship Contributions:** Concept - F.E.A., Y.K.; Design - Y.K.; Supervision - Y.K.; Resources - F.E.A.; Materials - F.E.A., Y.K.; Data Collection and/or Processing - F.E.A.; Analysis and/or Interpretation - F.E.A., Y.K.; Literature Search - F.E.A., Y.K.; Writing Manuscript - F.E.A., Y.K.; Critical Review - Y.K.

**Declaration of Interest:** The authors have no conflicts of interest to declare. **Funding:** The authors declared that this study has received no financial support.

#### **REFERENCES**

- GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(5):439-458. [CrossRef]
- Chan CL, Ting HW, Huang HT. The incidence, hospital expenditure, and, 30 day and 1 year mortality rates of spontaneous intracerebral hemorrhage in Taiwan. J Clin Neurosci. 2014;21(1):91-94. [CrossRef]
- Ziai WC. Hematology and inflammatory signaling of intracerebral hemorrhage. Stroke. 2013;44(1):74-78. [CrossRef]
- Illanes S, Liesz A, Sun L, et al. Hematoma size as major modulator of the cellular immune system after experimental intracerebral hemorrhage. Neurosci. 2011;490(3):170-174. [CrossRef]
- Mullen JL, Buzby GP, Matthews DC, et al. Reduction of operative morbidity and mortality by combined preoperative and postoperative nutritional support. Ann Surg. 1980;192(5):604-613. [CrossRef]
- Jian-Hui C, Iskandar EA, Cai Sh I, et al. Significance of Onodera's prognostic nutritional index in patients with colorectal cancer: A large cohort study in a single chinese institution. *Tumour Biol.* 2016;37(3):3277-3283. [CrossRef]
- Zhang L, Ma W, Qiu Z, et al. Prognostic nutritional index as a prognostic biomarker for gastrointestinal cancer patients treated with immune checkpoint inhibitors. Front Immunol. 2023;14:1219929. [CrossRef]
- Luan C, Wang F, Wei N, et al. Prognostic nutritional index and the prognosis of diffuse large b-cell lymphoma: a meta-analysis. Cancer Cell Int. 2020;20:455. [CrossRef]
- 9. Hu X, Deng H, Wang Y, et al. Predictive value of the prognostic nutritional index for the severity of coronavirus disease 2019. *Nutrition*. 2021;84:111123. [CrossRef]

- Matsuda T, Umeda Y, Matsuda T, et al. Preoperative prognostic nutritional index predicts postoperative infectious complications and oncological outcomes after hepatectomy in intrahepatic cholangiocarcinoma. BMC Cancer. 2021;21(1):708. [CrossRef]
- Raposeiras Roubin S, Abu Assi E, Cespon Fernandez M, et al. Prevalence and prognostic significance of malnutrition in patients with Acute Coronary Syndrome. J Am Coll Cardiol. 2020;76(7):828-840. [CrossRef]
- Xiang W, Chen X, Ye W, et al. Prognostic nutritional index for predicting 3-month outcomes in ischemic stroke patients undergoing thrombolysis. Front Neurol. 2020; 11:599. [CrossRef]
- Qi H, Yang X, Hao C, et al. Clinical value of controlling nutritional status score in patients with aneurysmal subarachnoid hemorrhage. Word Neurosurgery. 2019;126:1352-1358. [CrossRef]
- Liu Y, Yang X, Kadasah S, et al. Clinical value of the prognostic nutrition index in the assessment of prognosis in critically ill patients with stroke: a retrospective analysis. Comput Math Methods Med. 2022;2022:4889920. [CrossRef]
- Wang X, Kang Z, Wang Y, et al. Application of prognostic nutritional index in the predicting of prognosis in young adults with acute ischemic stroke. World Neurosurg. 2023;178:292-299. [CrossRef]
- Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. Stroke. 1996;27(8):1304-1305. [CrossRef]
- Gomes F, Emery PW, Weekes CE. Risk of malnutrition is an independent predictor of mortality, length of hospital stay, and hospitalization costs in stroke patients. J Stroke Cerebrovasc Dis. 2016;25(4):799-806. [CrossRef]
- 18. Uchino, K, Billheimer D, Cramer SC. Entry criteria and baseline characteristics predict outcome in acute stroke trials. Stroke. 2001;32(4):909-916.
  [CrossRef]
- 19. Smithard DG, O'Neill PA, England RE, et al. The natural history of dysphagia following a stroke. *Dysphagia*. 1997;12(4):188-193. [CrossRef]
- Campbell SE, Avenell A, Walker AE. Assessment of nutritional status in hospital in-patients. QJM. 2002;95(2):83-87. [CrossRef]
- Sánchez-Kuhn A, Medina Y, García-Pérez M, et al. Transcranial direct current stimulation treatment in chronic after-stroke dysphagia: A clinical case. *Psicothema*. 2019;31(2):179-183. [CrossRef]
- Zhou H. The effect of comprehensive rehabilitation nursing on swallowing function and nutritional status of patients with dysphagia after stroke. J Chronic Dis. 2016;17(3):330-332.
- 23. Yoo SH, Kim JS, Kwon SU, et al. Undernutrition as a predictor of poor clinical outcomes in acute ischemic stroke patients. *Arch Neurol.* 2008;65(1):39-43. [CrossRef]
- Sato M, Ido Y, Yoshimura Y, et al. Relationship of malnutrition during hospitalization with functional recovery and postdischarge destination in elderly stroke patients. J Stroke Cerebrovasc Dis. 2019;28(7):1866-1872. [CrossRef]
- Zhao G, Chen Y, Gu Y, et al. The clinical value of nutritional and inflammatory indicators in predicting pneumonia among patients with intracerebral hemorrhage. Sci Rep. 2024;14(1):16171. [CrossRef]
- Becerril-Gaitan A, Ding D, Ironside N, et al. Association between body mass index and functional outcomes in patients with intracerebral hemorrhage. Neurology. 2024;102(2):e208014. [CrossRef]
- Liu R, Chen C, Zhao Y, et al. The Osaka prognostic score and Naples prognostic score: Novel biomarkersfor predicting short-term outcomes after spontaneous intracerebral hemorrhage. BMC Neurology. 2023;23(1):272. [CrossRef]
- 28. Dávalos A, Ricart W, Gonzalez-Huix F, et al. Effect of malnutrition after acute stroke on clinical outcome. Stroke. 1996;27(6):1028-1032. [Cross-Ref]
- Koukiasa P, Bitzani M, Papaioannou V, et al. Resting energy expenditure in critically ill patients with spontaneous intracranial hemorrhage. JPEN J Parenter Enteral Nutr. 2015;39(8):917-921. [CrossRef]

- Nii M, Maeda K, Wakabayashi H, et al. Nutritional improvement and energy intake are associated with functional recovery in patients after cerebrovascular disorders. J Stroke Cerebrovasc Dis. 2016;25(1):57-62. [CrossRef]
- Bito R, Hino S, Baba A, et al. Degradation of oxidative stress-induced denatured albumin in rat liver endothelial cells. Am J Physiol Cell Physiol. 2005;289(3):531-542. [CrossRef]
- 32. Coffelt SB, de Visser KE. Cancer: Inflammation lights the way to metastasis. *Nature*. 2014;507(7490):48-49. [CrossRef]
- Ginsberg MD, Hill YY, Palesch KJ, et al. The ALIAS Pilot Trial: A dose-escalation and safety study of albumin therapy for acute ischemic, Stroke-I: Physiol. Responses Saf. Results. Stroke. 2006;37(8):2100-2106. [CrossRef]
- 34. Tabernero A, Granda B, Medina A, et al. Albumin promotes neuronal survival by increasing the synthesis and release of glutamate. *J Neurochem*. 2002;81(4):881–891. [CrossRef]
- 35. Norman K, Matthews DE. Editorial: 'Old tools, new insights': assessment of nutritional and metabolic status. *Curr Opin Clin Nutr Metab Care*. 2017;20(5):311-313. [CrossRef]
- 36. Holmes C, Racette S. The utility of body composition assessment in nutrition and clinical practice: An overview of current methodology. *Nutrients*. 2021;13(8):2493. [CrossRef]
- 37. Wensveen FM, Valentic S, Šestan M, et al. Interactions between tissue and the immune system in health and malnutrition. *Semin Immunol*. 2015;27(5):322-333. [CrossRef]
- 38. Guigoz Y. The Mini Nutritional Assessment (MNA) review of the literature-What does it tell us?. *J Nutr Health Aging*. 2006;10(6):466-487.
- Ignacio de Ulíbarri J, González-Madroño A, de Villar NGP, et al. CONUT: a tool for controlling nutritional status. First validation in a hospital population. Nutr Hosp. 2005;20(1):38-45.
- Kang BW, Chau I. Current status and future potential of predictive biomarkers for immune checkpoint inhibitors in gastric cancer. ESMO Open. 2020;5(4):e000791. [CrossRef]
- 41. Ciancarelli I, Morone G, Iosa, M, et al. Influence of oxidative stress and inflammation on nutritional status and neural plasticity: New Perspectives on Post-Stroke Neurorehabilitative Outcome. *Nutrients*. 2023;15(1):108. [CrossRef]
- 42. Gupta D, Lis CG, Pretreatment serum albumin as a predictor of cancer survival: A systematic review of the epidemiological literature. *Nutr J*. 2010;9:69. [CrossRef]
- 43. Huang Y, Zhang Q, Li P, et al. The prognostic nutritional index predicts all-cause mortality in critically ill patients with acute myocardial infarction. BMC Cardiovascular Disorders. 2023;23(1):339. [CrossRef]
- 44. Nakatani M, Migita K, Matsumoto S, et al. Prognostic significance of the prognostic nutritional index in esophageal cancer patients undergoing neoadjuvant chemotherapy. *Dis Esoph.* 2017;30(8):1-7. [CrossRef]
- 45. Wang Y, Zhang G, Shen Y, et al. Relationship between prognostic nutritional index and post-stroke cognitive impairment. *Nutr Neurosci.* 2024;27(11):1330-1340. [CrossRef]
- Gu M, Wang J, Xiao X, et al. Malnutrition and poststroke depression in patients with ischemic stroke. J Affect Disord. 2023;334:113-120. [CrossRef]
- 47. Jhang SW, Liu YT, Kor CT, et al. Low prognostic nutritional index predicts in-hospital complications and case fatality in patients with spontaneous intracerebral hemorrhage: A retrospective study. *Nutrients*. 2024;16(12):1841. [CrossRef]
- Li L, Zhang H, Yang Q, et al. The effect of prognostic nutritional indices on stroke hospitalization outcomes. Clin Neurol Neurosurg. 2024;247:108642. [CrossRef]
- 49. Rost NS, Smith EE, Chang Y, et al. Prediction of functional outcome in patients with primary intracerebral hemorrhage: *The FUNC score*. Stroke. 2008;39(8):2304-2309. [CrossRef]