

## Research Article

# The Relationship Between the Prognostic Nutritional Index and Overall Survival in Elderly Patients with Epithelial Ovarian Cancer

 Atakan Demir,<sup>1</sup>  Ozkan Alan,<sup>2</sup>  Sinan Koca,<sup>3</sup>  Heves Surmeli<sup>4</sup>

<sup>1</sup>Department of Medical Oncology, Acibadem University Faculty of Medicine, Acibadem Maslak Hospital, Istanbul, Turkey

<sup>2</sup>Department of Medical Oncology, Tekirdag State Hospital, Tekirdag, Turkey

<sup>3</sup>Department of Medical Oncology, Medeniyet University Goztepe Training and Research Hospital, Istanbul, Turkey

<sup>4</sup>Department of Medical Oncology, Kartal Dr Lutfi Kirdar Training and Research Hospital, Istanbul, Turkey

### Abstract

**Objectives:** Ovarian neoplasm is the most common cause of mortality in gynecologic malignancies. In this study, we aimed to investigate the prognostic role of pretreatment prognostic nutritional index (PNI) in geriatric Turkish female patients with advanced epithelial over cancer.

**Methods:** We retrospectively collected the data of 116 elderly ovarian cancer patients who treated between 2008 and 2019. The PNI was calculated as following:  $[(10 \times \text{serum albumin (g/dL)}) + (0.005 \times \text{total lymphocyte count})]$ .

**Results:** The median PNI was 44.8. Median OS was 45 months (95% CI: 31.6–58.3) in patients with  $\text{PNI} \leq 44.8$ , 79 months (95% CI: 77.6–80.3) in patients with  $\text{PNI} > 44.8$  ( $p=0.002$ ). In cox regression analysis, PNI was found to be an independent prognostic factor as affecting overall survival.

**Conclusion:** From this point of view, it may be considered that nutritional status should be evaluated more prominently for predicting prognosis in geriatric population.

**Keywords:** Ovarian cancer; overall survival; prognosis; prognostic nutritional index

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Ovarian neoplasm is the most common cause of mortality in gynecologic malignancies.<sup>[1]</sup> The ninety-five percent of ovarian malignancies develop from epithelial cells; the other types arise from other ovarian cell types such as germ cell tumors, sex cord-stromal tumors.<sup>[2]</sup> The more than half of the patients have the advanced-stage disease at diagnosis due to lack of symptoms in early stage. Several prognostic factors such as clinical stage, histology, tumor grade, presence of maximal debulking surgery or platinum resistance have been shown in patients with epithelial

ovarian cancer.<sup>[3–5]</sup> The prognostic nutritional index (PNI) was described in 1984 by Onodera T. et al. They defined the prognostic role of PNI in malnourished cancer patients who underwent gastrointestinal surgery.<sup>[6]</sup> Then, PNI has been reported as a prognostic marker in patients with various solid tumors in literature.<sup>[7–9]</sup> Miao et al. showed that PNI was associated with progression and overall survival in patients with ovarian cancer for the first time in literature.<sup>[10]</sup> Beside this, two retrospective studies were reported that pretreatment PNI was an independent prognostic marker

**Address for correspondence:** Atakan Demir, MD. Acibadem Üniversitesi Tıp Fakültesi, Acibadem Maslak Hastanesi, Tıbbi Onkoloji Anabilim Dalı, Istanbul, Turkey

**Phone:** +90 212 304 44 44 **E-mail:** atakandemir85@gmail.com

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in patients with advanced epithelial over cancer (EOC).<sup>[11, 12]</sup> But geriatric patients have been not evaluated as a different group in these studies (age cut-off value was 50 years). Therefore, the prognostic role of PNI in elderly patients with EOC remains unclear.

In this study, we aimed to investigate the prognostic role of pretreatment PNI in geriatric Turkish female patients with EOC.

## Method

### Patients

We retrospectively evaluated the data of epithelial ovarian cancer patients aged sixty-five and over. Four different medical oncology centers in Turkey were involved. Patients who had confounding factors affecting lymphocyte counts and albumine level such as chronic liver disease, nephrotic syndrome and active infection were excluded.

We obtained the demographic, clinicopathologic features, and laboratory results from the medical oncology clinic database retrospectively. Baseline hemoglobin (Hb), neutrophil, lymphocyte, platelet (PLT) counts, albumin level, clinicopathologic findings, and date of death or last follow-up were the variables recorded in the SPSS database. The PNI was calculated as follows:  $[(10 \times \text{serum albumin (g/dL)}) + (0.005 \times \text{total lymphocyte count})]$ .

### Statistical Analysis

Overall survival were calculated using the Kaplan-Meier method from operation date. Prognostic factors were compared using the log-rank test in univariate analysis. Hazard ratios (HR) with 95% confidence intervals (CI) were also calculated. All p values were two-sided in the tests and p values of 0.05 were considered as statistically significant. Multivariate analysis was carried out using the Cox proportional hazards model to assess the effect of prognostic factors on survival. SPSS 22.0 program was used for statistical analysis.

### Results

One hundred and thirty patients with adequate data were analyzed. The median age was seventy-two years (range 65–91 years). The most common pathologic subtype was serous carcinoma (87%). The data for demographic and clinicopathologic findings are showed in Table 1. The median value of the PNI was 44.8 (min 24.1–max 58.5).

The median follow-up time was 38 months (min 1 month–max 165 months). During the follow-up period, fifty-five percent of patients died. Median overall survival (OS) was 61 months (95% CI: 48.3–73.6). Two-year OS rate was 80% and five-year OS rate was 49%. The median OS was 45

**Table 1.** Baseline demographic and clinicopathological findings

	n	%
Median Age (years) (min.–max.)	72	(65–91)
ECOG performance score		
0	30	26
1–2	106	74
Stage (FIGO)		
1	6	5
2	21	18
3	89	77
Pathology		
Serous	101	87
Clear cell	6	5
Endometrioid	9	8
Optimal surgery		
Yes	106	91
No	10	9
Adjuvant treatment		
Yes	108	93
No	8	7
Neutrophile (μ/L) (min.–max.)	5520	(500–15200)
Hemoglobulin level (g/dL) (min.–max.)	11.8	(9–14.0)
Lymphocyte (μ/L) (min.–max.)	1460	(500–3550)
Platelet (μ/L) (min.–max.)	328	(97–730)
Albumin (g/dl) (min.–max.)	3.8	(2.7–4.6)
Prognostic nutritional index (PNI) (median) (min.–max.)	44.8	(24.1–58.5)
Neutrophil-lymphocyte ratio (NLR) (median) (min.–max.)	3.7	(0.42–17.5)
Platelet-lymphocyte ratio (PLR) (median) (min.–max.)	21.2	(4.6–78.4)

ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Min.: Minimum; Max.: Maximum.

months (95% CI: 31.6–58.3) in the cohort with PNI  $\leq$ 44.8, while the median OS of the cohort with PNI  $>$ 44.8 was 79 months (95% CI: 77.6–80.3), (p=0.002; Fig. 1).

Univariate Cox regression analysis showed that Age, Stage, and PNI had statistically significant associations with overall survival. In multivariate analysis demonstrated that Stage (HR: 2.5) and PNI (HR: 0.5) were the significant independent prognostic parameters for OS, The univariate and multivariate analysis results related to overall survival were shown in Table 2.

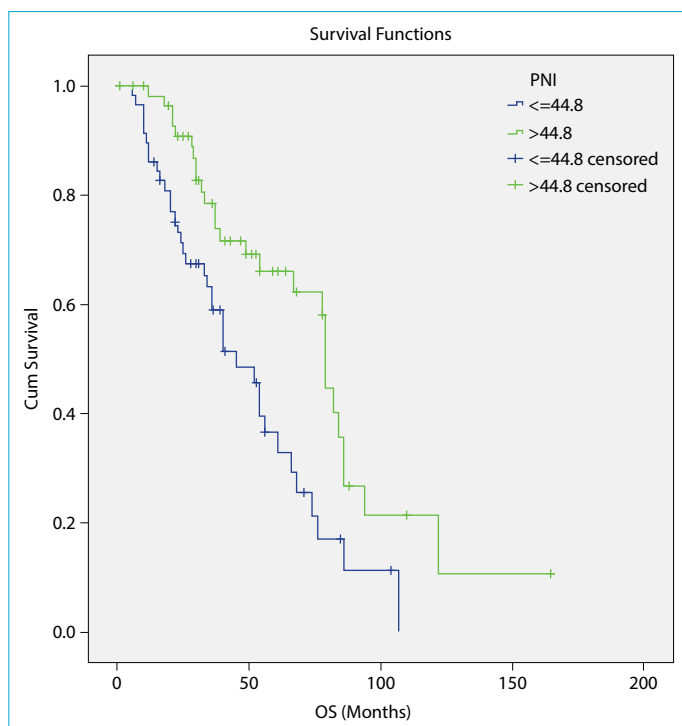
### Discussion

Identification of immunological and nutritional status of patients is helpful in determining the inflammatory process and the prognosis of disease due to malignancies. Increase of proinflammatory cytokines such as IL-1, IL-6 and TNF results in decrease of albumin levels in malignancies. Low serum albumin levels in pretreatment pe-

**Table 2.** Cox-regression model of overall survival

	MedianOS (months)	Univariate analysis 95% CI				Multivariate analysis 95% CI			
		HR	Lower	Upper	p	HR	Lower	Upper	p
Age									
<75	67	1.7	1.08	2.9	<b>0.02</b>				
≥75	40								
ECOG PS									
0	61	0.8	0.4	1.5	0.6				
1–2	66								
Stage									
1–2	79	2.3	1.2	4.5	<b>0.009</b>	2.4	1.3	4.6	<b>0.01</b>
3	64								
NLR									
≤3.7	52	0.8	0.4	1.33	0.8				
>3.7	68								
PLR									
≤21.2	74	1.2	0.7	2.0	0.4				
>21.2	56								
PNI									
≤44.8	45	0.4	0.2	0.7	<b>0.003</b>	0.5	0.3	0.8	<b>0.003</b>
>44.8	79								

OS: Overall survival; CI: Confidence interval; HR: Hazard ratio; ECOG: Eastern Cooperative Oncology Group; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; PNI: Prognostic nutritional index.

**Figure 1.** Overall survival graphic according to PNI by Kaplan Meier.

riod were predictive for cancer-related mortality.<sup>[13]</sup> Total lymphocyte count is also considered as an indicator of immune response although it is not cancer-specific. Low PNI with low serum albumin content and low lympho-

cyte count indicate failure of immune response and/or malnutrition. Therefore, prognostic nutritional index that firstly developed by Onadero et al. for perioperative risk assessment in gastrointestinal cancers, has gained value as a parameter showing prognosis in cancer patients with many studies later.<sup>[6]</sup> In a large colorectal cancer cohort study with 1321 patients; PNI was found to be an independent factor on prognosis.<sup>[14]</sup> In another study with esophageal squamous cell carcinoma patients, the prognostic effect of PNI on long-term cancer-specific survival was identified.<sup>[15]</sup> Similarly, cervical cancer patients with low PNI score had a shorter overall survival than patients with high PNI score.<sup>[16]</sup>

Approximately 50% of patients diagnosed with ovarian cancer are in geriatric population. (>65 years).<sup>[17]</sup> Overall survival of ovarian cancer patients decreases with age. In an analysis, the age-standardized one-year overall survival in 65–69 age range was 57%, while this rate was 45% in the 70–74 and 33% in the 80–84 age range. Various theories have been put forward to explain this age-related decrease in survival. The occurrence of aggressive cancers in older age, higher grade and more advanced stage; individual patient factors such as excessive comorbidities, cognitive impairment and malnutrition, prejudices of healthcare providers resulting in inadequate surgery for the elderly and suboptimal chemotherapy are some of the factors involved in this situation.<sup>[18–20]</sup>

PNI is generally a cheap and easily applicable parameter since it can be calculated from routine biochemical and blood count methods. Especially in geriatric patient population, prognostic factors such as PNI support the process of making treatment decisions that prevent over-treatment or under-treatment, will avert unnecessary costs and morbidity. Therefore, the relationship between survival and PNI in patients with ovarian cancer over 65 years of age is the aim of this study.

In this study, the cut-off value of PNI which is effective on overall survival, was considered as 44.8 by using median PNI value. This value complies with the value 45 proposed in the original operation of PNI.<sup>[6]</sup> When the PNI cut-off value is taken as 44.8; there is a statistically significant difference in survival of patients. This significance on overall survival was obtained both univariate and multivariate analyses. Therefore; when assigning treatment decisions in geriatric population; PNI is reasonable and independent risk factor which indicates patients' both immune and nutritional status.

Having a retrospective design, small number of patients and including no data on patient treatment modalities are limitations of this study. Especially in patients with geriatric age, predictive value on treatment and prognosis of PNI and nutritional status, should be investigated in more comprehensive clinical studies. In this way, more accurate and reliable survival predictions in the light of the information obtained by this means will guide health care providers in determining the most appropriate treatment to be applied to patients or determining the time to switch to supportive treatment instead of cancer-oriented treatment.

#### Disclosures

**Ethics Committee Approval:** All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethics/institutional review board approval of research Faculty of Medicine, Acibadem University, Istanbul, Turkey (Number: 2019-14/16, Date: 12.09.2019).

**Informed consent:** Written informed consent was obtained from the patients for participation of this study and for publication of this original research. A copy of the written consent is available for review by the Editor-in-Chief of this journal."

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