



May the prognostic nutritional index (PNI) play a role in predicting age-related macular degeneration?

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Abstract

Aim It is known that a healthy and balanced diet plays an important role in the etiopathogenesis of age-related macular degeneration (AMD). The aim of this study is to show the possible relationship between the prognostic nutritional index (PNI) and AMD.

Methods This observational longitudinal study included 50 patients who were diagnosed with AMD and 100 participants as control group in the Ophthalmology Polyclinic of Kırşehir Ahi Evran Training and Research Hospital between December 2022 and February 2023. The PNI scores of the patients were calculated with the formula $(10 \times \text{albumin (g/L)} + (0.005 \times \text{total lymphocyte count}))$, using routine hemogram and biochemical assays.

Results One hundred fifty participants were included in the study (average age: 73.7 ± 8.6 years, male: 53.3%). When adjusted for age, sex, and total comorbidity index score via multivariate logistic regression analysis, the association between AMD and PNI scores (OR=0.3; CI: 0.2–0.4; $p=0.01$) and

Charlson Comorbidity Index (CCI) scores (OR=6.8; CI: 2.8–16.6; $p=0.01$) was statistically significant.

Conclusion The use of PNI scores may be practical and useful in routine clinical practice for predicting AMD.

Keywords Prognostic nutritional index · Age-related macular degeneration · Diabetes mellitus · Hypertension

Introduction

Age-related macular degeneration (AMD) is a multifactorial disease and a common cause of severe vision loss [1]. Many studies on determining the possible causes and risk factors of AMD are found in the literature [2]. Although this disease has been considered an inevitable consequence of natural aging, in recent years numerous equally important risk factors have been identified in the etiology of this disease, including lifestyle-related factors such as smoking or food intake that can affect retinal health [3]. Hence, it is recommended that patients maintain a healthy diet, monitor other risk factors (such as hypertension (HT), obesity, and atherosclerosis), and take nutritional supplements (antioxidants) in order to prevent this disease [4].

The prognostic nutrition index (PNI) is a new prognostic scoring system that reflects both the inflammatory and nutritional status of the patient [5].

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PNI scores are calculated by multiplying the albumin and lymphocyte counts of patients. This indicator measures nutrition and immunological status. It can be easily calculated with peripheral blood serum albumin and lymphocyte counts and serves as an indicator of the nutritional status of patients [5]. Recently, various oncological studies have found that this index is a marker associated with and a predictor of colorectal cancer, gastric cancer, malignant pleural mesothelioma, hepatocellular carcinoma, and pancreatic cancer [6–10].

It is known that nutrition is an important factor in the etiopathogenesis of AMD, and that patients with this disease usually eat an unhealthy, carbohydrate- and fat-heavy diet that is dissimilar to the healthy Mediterranean diet [11]. In addition, these patients generally have multiple comorbidities [12]. Anthropometric measurements alone are not sufficient to determine the nutritional status of patients in these cases [13]. It is thought that PNI scores may be a marker that indicates nutritional status, especially in AMD patients who are elderly, have multiple comorbidities, and eat an unhealthy diet [14]. Our literature review revealed no studies that examined the relationship between PNI scores and AMD. Hence, it was aimed in the present study to determine the relationship between PNI scores and AMD, as well as to identify other possible risk factors.

Materials and methods

This retrospective cohort study included 150 participants between the ages of 55 and 90 in the Ophthalmology department of our tertiary hospital between December 2022 and February 2023. One hundred individuals without any systemic or chronic ocular diseases who presented for routine check-ups at the aforementioned center between the same dates were also included as a control group.

Ethical approval was provided by the local ethics committee (No: 2023–02/15) in accordance with the principles of the Declaration of Helsinki. Patients previously diagnosed by an ophthalmologist with an eye disease other than AMD, patients under 55 years of age, patients with end stage liver or kidney diseases, patients with a active infection, smokers or alcohol users, and patients with impaired cognitive function were excluded from the study.

Visual acuity and biomicroscopic findings of the anterior and posterior segments of the patients' eyes were examined on admission to the hospital. The results of hemograms (neutrophils, lymphocytes, platelets, and hemoglobin) and biochemical tests (glucose, bilirubin, total cholesterol, triglycerides, urea, creatinine, albumin) from the patients' electronic medical records were analyzed using the computer system. The PNI scores of the patients were calculated using the formula $(10 \times \text{albumin (g/L)} + (0.005 \times \text{total lymphocyte count}))$ via routine hemogram and biochemical assays (15).

Statistical analysis

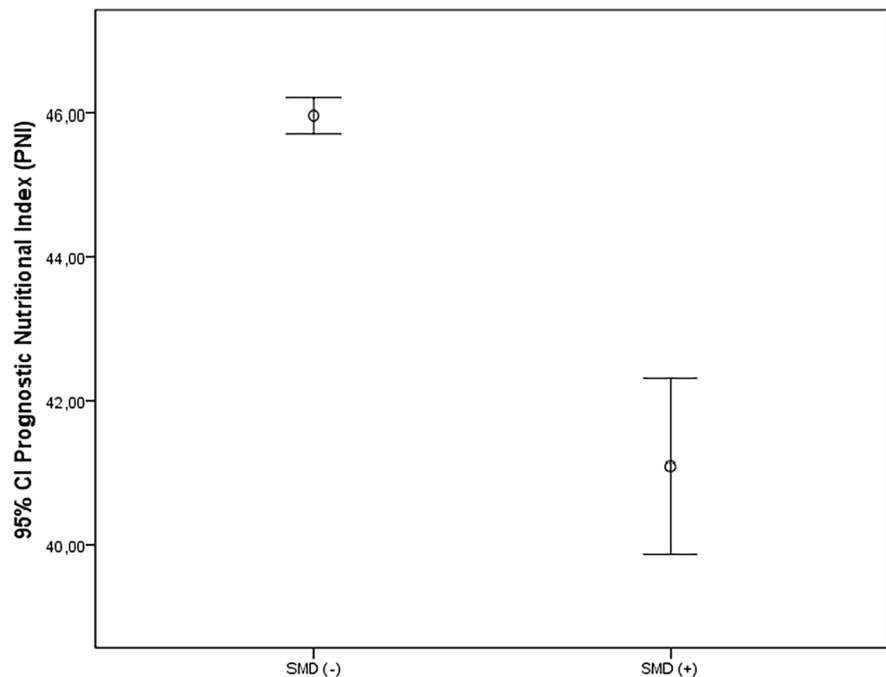
As this is a retrospective cohort study, only patients who were admitted to our hospital within a certain period of time were included in this study. We performed a post-hoc computational power analysis with G Power 3.1.9.7 and calculated a power (1- b err prob) of 0.99 with an effect size of 0.83 for the mentioned sample size (n:150).

The Kolmogorov–Smirnov test was used to determine the normality of the data distribution. Continuous variables with normal distribution are expressed as mean \pm standard deviation. Categorical variables are expressed in numbers and percentages. Continuous variables were compared using t-tests or the Mann–Whitney U test for independent samples. Categorical variables were compared using chi-square tests. Univariate and multivariate regression analyses were used to calculate odds ratios (OR) and 95% confidence intervals (CI) for the independent determinants of AMD. The independent association between AMD and PNI was examined using a model adjusted for age, sex, and concomitant diseases. Receiver operating characteristic curve (ROC) and area under the curve (AUC) analysis for PNI score was performed to determine the best discriminatory power for AMD. The Youden index method was used to find cutoff values for PNI scores to predict AMD. The cutoff value with the highest Youden index was accepted as the best cutoff value. A p-value of $p < 0.05$ was considered significant in the statistical analysis. All analyses were performed using SPSS (IBM SPSS Inc., Chicago, USA) version 24.

Table 1 Characteristics of the sample

Variables	Total (N=150)	AMD (+) (N=50)	AMD (-) (N=100)	<i>p</i> value
Demographics and laboratory parameters				
Age (years), mean \pm SD	73.7 \pm 8.6	73.8 \pm 8.1	73.7 \pm 8.9	0.09
Gender (male), n (%)	80 (53.3)	32 (64.0)	48 (48)	0.05
Hypertension, n (%)	117 (78)	46 (92.0)	71 (71)	0.01
Diabetes mellitus, n (%)	71 (47.3)	33 (66.0)	38 (38.0)	0.01
CCI	2.5 \pm 0.8	2.7 \pm 0.8	2.5 \pm 0.7	0.15
Lymphocyte, ($\times 10^9/L$)	1.9 \pm 0.7	1.9 \pm 0.8	2.0 \pm 0.6	0.25
Albumin, (g/dL)	4.4 \pm 0.3	4.1 \pm 0.4	4.5 \pm 1.3	0.01
PNI	44.3 \pm 3.5	41.1 \pm 4.3	45.9 \pm 1.3	0.01

CCI Charlson comorbidity index, PNI prognostic nutritional index. Categorical variables were indicated as numbers (%) and determined by the Chi-square test. Numerical variables with normally distributed were indicated as mean \pm standard deviation (SD) and determined by t-test. Values given in bold indicate statistically significant results ($p < 0.05$)

Fig. 1 Error bar of PNI score in AMD (+) and AMD (-) group

Results

A total of 150 individuals were included in the study (average age: 73.7 \pm 8.6 years, male: 53.3%). The demographic and laboratory parameters of the participants are presented in Table 1.

There was no statistically significant difference between the AMD group and the control group in terms of age ($p = 0.09$), sex ($p = 0.05$), or Charlson Comorbidity Index (CCI) score ($p = 0.15$). However, more patients in the AMD group were diagnosed with

diabetes mellitus (DM) ($p = 0.01$) or HT ($p = 0.01$). When the laboratory parameters of the patients were examined, it was seen that there was no significant difference between the two groups in terms of lymphocyte counts ($p > 0.05$). However, the PNI scores of the AMD group was significantly lower than those of the control group ($p = 0.01$) (Fig. 1).

Single-variable regression analysis showed that HT (OR = 4.7; CI: 1.6–14.2; $p = 0.01$), DM (OR = 3.2; CI: 1.6–6.4; $p = 0.01$), and PNI (OR = 0.4; CI: 0.3–0.6; $p = 0.01$) were associated with AMD. When adjusted

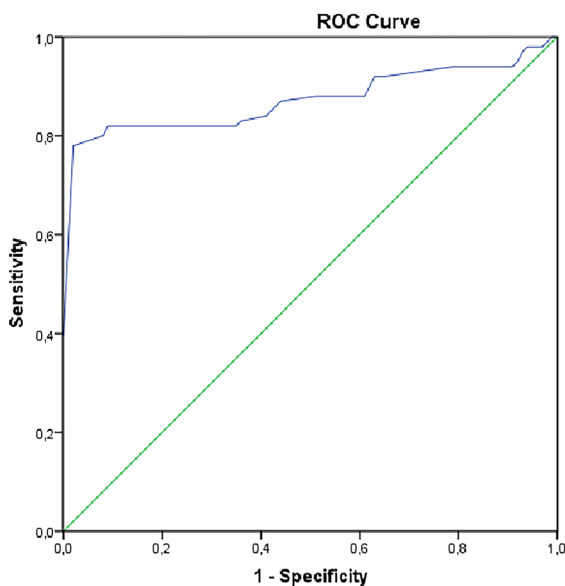
Table 2 Association of PNI and CCI with AMD

	Unadjusted analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Age	0.9 (0.9–1.01)	0.08	0.9 (0.9–1.05)	0.69
Gender (male)	2.1 (0.9–4.1)	0.05	1.9 (0.6–6.2)	0.28
Hypertension	4.7 (1.6–14.2)	0.01	–	–
Diabetes mellitus	3.2 (1.6–6.4)	0.01	–	–
CCI	1.4 (0.8–2.1)	0.15	6.8 (2.8–16.6)	0.01
PNI	0.4 (0.3–0.6)	0.01	0.3 (0.2–0.4)	0.01

CI Confidence interval, CCI Charlson comorbidity index, PNI prognostic nutritional index, OR Odds ratio. Values given in bold indicate statistically significant results ($p < 0.05$). Multivariate analysis was adjusted for variables, including age, gender, CCI, and PNI

for age, sex, and total comorbidity index score via multivariate logistic regression analysis, the association between AMD and PNI scores (OR=0.3; CI: 0.2–0.4; $p=0.01$) and CCI scores (OR=6.8; CI: 2.8–16.6; $p=0.01$) proved statistically significant (Table 2).

The ability of the PNI score to predict AMD was evaluated by ROC curve analysis. The AUC value obtained as a result of the analysis is presented in Fig. 2. PNI scores significantly predicted the presence of AMD. According to the Youden index results, the cut-off value of PNI scores for AMD was 45.01 (AUC=0.87, sensitivity 82%, specificity=81%) ($p=0.01$) (Fig. 2).

**Fig. 2** Roc curve analysis of PNI score in AMD (+) group

Discussion

In the present study, AMD patients obtained significantly lower scores from the recently developed PNI scoring system. These data appear to be an objective indicator of AMD, in the etiology of which nutrition and diet and in the treatment of which vitamin and mineral supplementation are known to have very important roles. It was also found that AMD is associated with other comorbidities such as DM and HT. In line with this findings, CCI scores were associated with AMD. According to our literature review, this is the first study on the PNI and CCI scores of AMD patients.

The role of dietary components, food groups, antioxidants, and vitamin or mineral supplements in the diagnosis and prognosis of AMD has been the subject of many studies in the literature [15, 16]. The Mediterranean diet is characterized by a high intake of vegetables, fruits, legumes, cereals, and nuts. In a recent study conducted by Merle et al., adherence to this diet was associated with a lower risk of AMD [16]. In another study, high intake of certain fats such as saturated fats, trans fats, and omega-6 fatty acids was associated with a two-fold increase in the prevalence of AMD, while high intake of monounsaturated fats was potentially protective against AMD [17].

PNI score is an easy to examine and quickly calculable parameter that provides valuable information about the nutritional status of patients [18]. Albumin is of importance in the diet due to its anti-inflammatory, antioxidant, and anticoagulant properties and its effects on osmotic pressure. Eating a low-protein diet is often associated with hypoalbuminemia [19]. Lymphocytes, another element of PNI, are an important peripheral blood cell type that indicate inflammation [20]. Patients with nutritional deficiencies have decreased lymphocyte cell counts due to the impact of poor nutrition on the immune system [21]. In the light of all information, a decrease in PNI scores is considered an important predictive factor of nutritional deterioration. The PNI scores of the patients with AMD being lower than those of the controls in the present study suggests that low PNI scores may be related to malnutrition in these patients.

Many prior studies indicate a possible link between AMD and DM. It is assumed that changes in the function and structure of the retinal pigment epithelium, Bruch's membrane, and choroidal circulation due to

DM increase the risk of AMD [22]. It was reported in the Blue Mountains Eye Study that DM is significantly associated with the prevalence of geographic atrophy [23]. In the Age-Related Eye Disease Study, the participants with unilateral neovascular AMD who had a history of DM had a higher prevalence of bilateral neovascular AMD than those without DM [24]. However, it has been reported in the cohort study by Jung et al., which included roughly 3.5 million participants, that there was no significant relationship between DM and AMD [25]. Although there are conflicting results in the literature on this subject, in the present study there was a significant relationship between AMD and DM.

There is a consensus among most epidemiological studies that essential HT is a risk factor for AMD [26] [27]. High blood pressure is associated with lower choroidal blood flow in patients with AMD and this may be a pathogenetic mechanism for the involvement of HT in the genesis of AMD. In addition, AMD and essential HT share common pathogenetic pathways. For example, oxidative stress, which is elevated in essential HT, contributes to the development of choroidal neovascularization [28, 29]. Similar to the literature, in the present study HT was associated with AMD.

In recent studies, it has been shown that various systemic diseases are associated with AMD [30]. Similarly, in the current study, the CCI score, which indicates the total cumulative effect of comorbidities, and AMD were correlated. In addition, it was shown for the first time that every 1 unit increase in CCI scores increased the risk of AMD more than six times. There are few studies on the relationship between CCI and other chronic eye diseases in the literature. In this context, these findings highlight the importance of multidisciplinary approaches to this disease and the importance of considering chronic diseases in the prognosis of patients diagnosed with AMD. In addition, prospective randomized controlled trials are needed to further clarify the relationship between CCI and AMD.

The present study has some limitations. To fill the gap created by the retrospective nature of the current study, prospective studies with a larger number of patients are needed. In addition, since the height and weight of the patients were not measured, their body mass indices could not be calculated and it was unclear which patients were obese. It is important

to note that despite efforts to account for potential demographic and clinical covariables, residual confounding may still exist in our analysis. Therefore, further prospective, large-scale studies are needed to clarify the exact relationship between PNI and AMD.

One of the strengths of the study was the finding that the significance of the relationship between PNI scores and AMD persisted after corrections for all complicating factors (age, sex, and comorbidities). The nutritional statuses of the patients were also evaluated with a scale shown in the literature to be valid.

Conclusions

In today's world where healthy and balanced nutrition is becoming increasingly important, nutritional factors were shown to be highly involved in the etiology of AMD. Identifying individuals with low PNI scores may allow healthcare providers to implement targeted interventions to support and strengthen their immune function, improve their nutritional status and address underlying inflammatory or oxidative stress conditions.

Author contribution All authors contributed to the study conception and design. Material preparation and data collection were performed by RNA. Analysis were performed by ZK. The first draft of the manuscript was written by ZK and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Conflict of interests The authors have no relevant financial or non-financial interests to disclose.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University B (No:2023–02/15).

Consent to participate Inform consent is waived according to do study desing.

Consent for publication None.

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