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RESEARCH ARTICLE / ARAŞTIRMA MAKALESİ

Are Prognostic Nutrition Index Levels Associated with Prognosis in Adolescents with Anorexia Nervosa?

Anoreksiya Nervosa Hastalığı Olan Ergenlerde Prognostik Nutrisyonel Endeks Düzeyleri Prognoz ile İlişkili midir?

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Abstract:

The aim of this study was to investigate the relationship between prognostic nutritional index (PNI) levels and sociodemographic data, disease characteristics, comorbidity, and prognosis in children and adolescents diagnosed with anorexia nervosa (AN). The study included 45 patients diagnosed with AN and 42 healthy controls. The researcher administered the Sociodemographic Data Form, the Affective Disorders and Schizophrenia Interview Schedule for School-Age Children-Present and Lifetime Version (K-SADS), the General Assessment Scale for Children (CGAS) to both groups, and the Clinical Global Impression-Severity Scale (CGI-SS) to the patient group. Eating Attitude Test (EAT), Eating Disorder Examination Questionnaire (EDE-Q), Self-Reflection and Insight Scale, The Revised Child Anxiety Depression Scale–Child Version (RCADS-CV), Leyton Obsession Inventory-Child Version (LOE-CV), Parental Autonomy Support Scale (PASS), and Shortened Level of Expressed Emotion Scale (SLEES) were completed by participants. In the patient group, PNI levels were significantly lower than in the control group ($p<0.05$). A negative correlation was found between symptom severity scores and PNI levels ($p < 0.05$). A positive correlation was found between body mass index (BMI) and PNI levels ($p=0.05$). PNI levels were significantly lower in those with Major Depressive Disorder (MDD), non-suicidal self-injury (NSSI), and suicide attempts compared to those without ($p< 0.05$). In children and adolescents diagnosed with AN, PNI levels were not associated with exiting the diagnostic criteria but may be associated with disease severity, BMI, comorbid MDD, NSSI, and suicide attempt. Therefore, it was thought that PNI levels may be an indirect prognostic factor for AN in children and adolescents.

Keywords: Prognostic nutritional index, Anorexia nervosa, Non-suicidal self-injury, Suicide attempt**.**

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Öz:

Bu çalışmada, anoreksiya nervoza (AN) tanısı alan çocuk ve ergenlerde prognostik nutrisyonel endeks (PNI) düzeyleri ile sosyodemografik veriler, hastalık özellikleri, komorbidite ve prognoz arasındaki ilişkinin incelenmesi amaçlanmıştır. Çalışmada AN tanısı alan 45 hasta ve 42 sağlıklı kontrol denek dahil edilmiştir. Araştırmacı, her iki gruba Sosyodemografik Veri Formu, Okul Çağı Çocukları için Duygusal Bozukluklar ve Şizofreni Görüşme Programı - Mevcut ve Yaşam Boyu Versiyonu (K-SADS), Çocuklar için Genel Değerlendirme Ölçeği (CGAS) ve hasta grubuna Klinik Global İzlenim-Şiddet Ölçeği (CGI-SS) uygulamıştır. Yeme Tutumu Testi (EAT), Yeme Bozukluğu Muayene Anketi (EDE-Q), Öz Yansıtma ve İçgörü Ölçeği, Revize Edilmiş Çocuk Anksiyete Depresyon Ölçeği-Çocuk Versiyonu (RCADS-CV), Leyton Obsesyon Envanteri-Çocuk Versiyonu (LOE-CV), Ebeveyn Özerklik Desteği Ölçeği (PASS) ve Kısaltılmış Duygu İfade Düzeyi Ölçeği (SLEES) katılımcılar tarafından doldurulmuştur. Hasta grubunda PNI düzeylerinin kontrol grubuna göre anlamlı olarak daha düşük olduğu saptanmıştır ($p<0,05$). Semptom şiddeti puanı ile PNI düzeyleri arasında negatif korelasyon saptanmıştır ($p < 0,05$). Vücut kitle indeksi (BMI) ile PNI düzeyleri arasında pozitif korelasyon bulundu ($p=0,05$). Majör Depresif Bozukluk (MDB), intihar girişimi olmayan ve intihar girişimi olanlarda PNI düzeyleri, MDB, intihar girişimi olmayanlara göre anlamlı olarak daha düşüktü ($p < 0,05$). AN tanısı alan çocuk ve ergenlerde PNI düzeyleri tanı kriterlerinden çıkma ile ilişkili bulunmamakla birlikte, hastalık şiddeti, BMI, komorbid MDD, NSSI ve intihar girişimi ile ilişkili olabilir. Bu nedenle, PNI düzeylerinin çocuk ve ergenlerde AN için dolaylı bir prognostik faktör olabileceği düşünülmüştür.

Anahtar Kelimeler: Prognostik nutrisyonel endeks, Anoreksiya nervoza, İntihar dışı kendine zarar verme, İntihar girişimi.

Introduction

Anorexia nervosa (AN) is an eating disorder (ED) characterized by fear of gaining weight or becoming overweight, engaging in behaviors to prevent weight gain, and distorted body image perception (Regier et al., n.d.). It is a serious psychiatric disorder marked by a high risk of death from starvation, malnourishment, medical complications, a high prevalence of comorbid mental illnesses, treatment resistance, and suicide. (Mitchell & Peterson, 2020). This disorder peaks during adolescence and has the highest mortality rate among all psychiatric disorders (Neale & Hudson, 2020). In a prospective study of adolescents and adults requiring hospitalization, the 12-year standardized mortality rate was 8.85%. Self-induced vomiting, laxative usage, the bulimic subtype of AN, comorbid depression, lower body weight, chronic symptom patterns, and obsessive-compulsive features were all linked to a worse prognosis (Morris & Twaddle, 2007; Jagielska & Kacperska, 2017). To improve outcomes, it is crucial to evaluate poor prognostic criteria in the course of the disease and better identify the underlying factors.

The prognostic nutritional index (PNI) value is calculated using the formula: lymphocyte count per $mm^3 \times 5$ + albumin. Subsequent studies have shown that PNI has prognostic value in a variety of clinical conditions, including malignancy, infection, cardiovascular disease, and psychiatric comorbidities (Kayhan et al., 2022; Sertdemir et al., 2021; Yildirim et al., 2021).

Although serum albumin level appears to be a logical indicator of general nutritional status and disease severity, it is not associated with the severity of AN and should not be used to guide treatment decisions (Mehler & Koutsavlis, 2021). Albumin has a long half-life and is not sensitive to detecting acute changes in nutritional status. Therefore, it should not be used as a stand-alone indicator of nutritional assessment (Zhang et al., 2019). Poor nutritional condition, reduced liver function, increased renal loss, and, most importantly, the body's reaction to systemic inflammation can all contribute to hypoalbuminemia in critically ill individuals (Vincent et al., 2014). In a study evaluating leukopenia and infection incidence to determine whether patients with anorexia have an increased risk of infection, it was found that total leukocyte count and absolute neutrophil, lymphocyte, and monocyte counts were significantly lower in AN patients than in the control group (T K Bowers, 1978). Low lymphocyte count has previously been shown to predict increased mortality in various chronic diseases. Total blood lymphocyte count is considered a nutritional status biomarker and a prognostic factor across multiple clinical settings (Walsh et al., 2020). Thus, PNI using these two parameters may be suitable for rapid assessment of immunonutritional status in AN patients.

PNI is a combined score derived from serum albumin and lymphocyte levels that reflects an individual's immunological, inflammatory, and nutritional status and serves as a simple assessment tool. To the best of current knowledge, no study in the literature has evaluated PNI levels in patients with AN. This study aimed to examine the relationship between PNI levels and sociodemographic variables, disease characteristics, comorbidities, and prognosis in children and adolescents diagnosed with AN.

Methods

Participants

The study sample comprised 45 female volunteers diagnosed with AN according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria who were followed up between January 1, 2019, and December 30, 2023, at Uludağ University Faculty of Medicine, Child and Adolescent Mental Health and Diseases Clinic, and Outpatient Clinic. The control group comprised 42 healthy female volunteers who visited the Uludağ University Faculty of Medicine, Child Health and Diseases Well-Child Clinic during the same period. The inclusion criteria for the patient group were as follows: female gender, aged between 12 and 18 years, and having obtained written informed consent from both the patient and their legal guardian via an informed consent form. The following were the requirements for the healthy control group's inclusion: female, between the ages of 12 and 18, and not diagnosed with AN based on DSM-V

criteria, BMI between 18.5 and 24.9, no diagnosis of any acute or chronic medical illness at the time of albumin and hemogram testing, absence of any psychiatric complaints or diagnoses and having obtained informed consent from both the patient and their legal guardian via an informed consent form.

Measure

The sociodemographic details of the participants and their parents, including age, educational attainment, occupation, and socioeconomic position, were documented using the Sociodemographic Data Form. The Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) was used for diagnostic purposes in children and adolescents and validated in Turkish (Ünal et al., 2019). The Children's Global Assessment Scale (CGAS) was used to assess psychosocial functioning (Shaffer et al., 1983). There are publications in the literature on its use in children and adolescents in Turkey (Demir et al., 2011; Karakuş et al., 2022). The Clinical Global Impressions-Severity Scale (CGI-SS) was created by Guy (William Guy, 1976) to evaluate clinical study participants and track treatment-induced changes over time. This scale was only applied to the patient group. The Eating Disorder Examination Questionnaire (EDE-Q) was adapted as a self-report measure based on the ED assessment interview (C. G. Fairburn, 1994) and was validated for Turkish (Yucel et al., 2011). The Eating Attitudes Test (EAT-40) is a self-report scale developed to measure AN symptoms (Garner & Garfinkel, 1979) and validated for Turkish (Savaşır I, 1989). The Self-Reflection and Insight Scale (SRIS) was developed (Grant et al., 2002) and validated for Turkish (Emine Lamiser Atik, 2013). The Revised Child and Adolescent Anxiety and Depression Scale-Child Version (RCADS-CV) is a screening tool for clinical symptoms of depression and anxiety disorders (Chorpita et al., 2000) and validated for Turkish (Gormez et al., 2017). The Leyton Obsessional Inventory-Child Version (LOI-CV) revised the Leyton Obsessive Compulsive Inventory, which was developed for adults, and adapted it for adolescents and younger children (BERG et al., 1988), and was validated for Turkish (Boysan et al., 2016). The Parental Autonomy Support Scale (PASS) was developed to measure the levels of autonomy support received from parents (Soenens et al., 2007) and was validated for Turkish (Ipek H. & Gozukara O.). The Shortened Level of Expressed Emotion Scale for Adolescents (S-LEES) was developed to measure perceived emotional expression (Nelis et al., 2006) and was validated in Turkish (Vural et al., 2013).

Procedure

In the first stage, the routinely performed scales, tests, and clinical findings of the patients who met the inclusion criteria and agreed to participate in the study were reviewed. Height, weight, BMI, BMI percentile, BMI standard deviation score (SDS), albumin, lymphocytes, and differential diagnosis data were also obtained to assess medical complications associated with the study. For the control group, data were obtained similarly from volunteers who presented to the Child Health and Diseases Well-Child Clinic at our hospital, met the inclusion criteria, and consented to participate in the study. In the second stage, participants were invited, along with their legal guardians, and the study's interviews and scales were administered by the investigator, a child and adolescent psychiatrist. The relationship between sociodemographic data, the study's interviews and scales, and PNI levels was statistically analyzed in the patient and control groups. Additionally, in the patient group, the relationship between poor prognostic factors of AN and PNI levels was analyzed. Furthermore, participants were divided into three groups based on their diagnostic status at the time of assessment: those who still met the AN diagnostic criterion, those who did not, and a control group. PNI levels among these groups were statistically compared.

Statistical analysis

The normality of variable distribution was assessed with the Shapiro–Wilk test. Variables with normal distribution were presented as mean±standard deviation, and comparisons between two independent groups were made using the independent sample t-test. Variables not normally distributed were presented as median (minimum–maximum) values, and comparisons between two independent groups were performed using the Mann-Whitney U test. Categorical variables were presented as frequencies and percentages (n (%)), and comparisons were made using the Pearson chi-square, Fisher's exact chi-square, and Fisher–Freeman–Halton tests. Pearson and Spearman correlation coefficients were used to examine correlations between variables. The diagnostic performance of variables was evaluated using receiver operating characteristic (ROC) curve analysis. The optimal cut-off values in ROC analysis were determined according to the Youden J index. Statistical analyses were performed using IBM SPSS Statistics 28.0 and MedCalc 22.009 programs. A p-value of <0.05 was considered statistically significant. For comparisons among more than two independent groups, the Kruskal–Wallis test was used, and when significant differences were detected, pairwise comparisons were conducted with the Mann–Whitney U test. G-Power (version 3.1.9.7) was used to determine the minimum sample size. Accordingly, t tests, means: difference between two independent means (matched pairs), post hoc: compute achieved sample size, given a power, and effect size were selected. Accordingly, when α err prob=0.05 and effect size=0.54, it was determined that at least 87 participants should be included in each group (actual power=80%).

Ethical Approval

Approval of this study has been granted by the Bursa Uludağ University Clinical Research Ethics Committee *(Ethic Acceptance No: 2023-11/14 Number:2011-KAEK-26/339).*

Results

The study included 87 participants: 45 patients (51.7%) and 42 controls (48.3%), with a median age of 17 years (range, 12–18). In the patient group, compared to the control group, the ages of both parents, family income level, maternal education level, and the prevalence of bad habits were statistically significantly higher, while the number of siblings and school attendance rate were lower ($p < 0.05$ for each) (Table 1).

Table 1. *Comparison of sociodemographic characteristics between the patient and control groups*

Variables		Patient	Control	p-value
Age (years)*		17 (12–18)	17 (12–18)	0.468
Age of mother (years) *		45 (39–60)	42 (35–54)	0.013
Age of father (years) *		49 (40–65)	46 (40–57)	0.034
Birth order*		1 (1–4)	2 (1–6)	0.170
Number of siblings*		2 (1–5)	3 (1–7)	0.008
Monthly income (×1000 TL) *		30 (12–65)	25 (15–65)	0.040
School attendance#	1	33 (73.33)	42 (100.00)	<0.001
	2	10 (22.22)	0 (0.00)	
	3	2 (4.44)	0 (0.00)	
People Living Together #	1	38 (84.44)	35 (83.33)	0.121
	2	1 (2.22)	5 (11.90)	
	3	6 (13.33)	2 (4.76)	
Maternal education level#	1	0 (0.00)	3 (7.14)	0.006
	2	2 (4.44)	2 (4.76)	
	3	18 (40.00)	10 (23.81)	
	4	4 (8.89)	12 (28.57)	
	5	6 (13.33)	10 (23.81)	
	6	15 (33.33)	5 (11.90)	
Paternal education level#	1	0 (0.00)	0 (0.00)	0.128
	2	0 (0.00)	1 (2.38)	
	3	9 (20.93)	12 (28.57)	
	4	8 (18.60)	13 (30.95)	
	5	7 (16.28)	8 (19.05)	
	6	19 (44.19)	8 (19.05)	
Bad habits	1	37 (82.22)	42 (100)	0.016
	2	7 (15.56)	0 (0.00)	
	3	1 (2.22)	0 (0.00)	

*Data are presented as *median (minimum–maximum) or #n (%). School attendance: 1 = currently attending school, 2 = graduated, 3 = dropped out. People living together: 1 = nuclear family, 2 = extended family, 3 = divorced parents, 4 = institutional care. Maternal and paternal education level: 1 = no formal education, 2 = literate, 3 = primary school graduate, 4 = middle school graduate, 5 = high school graduate, 6 = university graduate. Bad habits: 1 = regular smoking, 2 = regular alcohol use, 3 = regular substance use.*

The scale scores of the EDE-Q ($p < 0.001$), LOI-CV ($p = 0.002$), EAT-40 ($p = 0.004$), and SAD (RCADS) ($p = 0.007$) were statistically higher in the patient group than in the control group. The BMI, BMI percentile, and age-adjusted BMI-SDS values at initial presentation during the illness period in the patient group were statistically significantly lower than those of the control group. When albumin, lymphocyte, and PNI levels were compared between the patient and control groups, all three were significantly lower in the patient group ($p < 0.001$ for each). The mean PNI level was 52.32±6.24 in the patient group and 60.32±3.51 in the control group (Table 2).

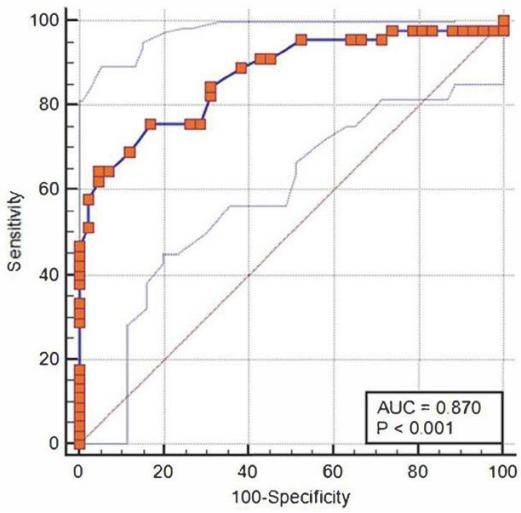
Table 2. *Comparison of total scale and subscale scores, albumin, lymphocyte, and PNI levels, BMI percentile, and BMI-SDS values between the patient and control group*

Scale score	Groups		p-value
	Patient	Control	
EDE-Q*	41.00 (0.00–208.00)	8.50 (0.00–114.00)	<0.001
LOI-CV*	18.00 (0.00–54.00)	10.00 (0.00–39.00)	0.002
EAT-40*	18.00 (3.00–87.00)	11.50 (3.00–50.00)	0.004
SAD#	13.78 ± 5.58	10.31 ± 6.02	0.007
BMI (Initial presentation during illness)	14.40 (10.20–17.80)	21.40 (17.50–24.90)	<0.001
BMI (Time of assessment)	18.95 (13.20–33.00)	21.40 (17.50–24.90)	<0.001
BMI-SDS	−3.93 ± 1.73	0.04 ± 0.93	<0.001
BMI Percentile	0.02 (0.02–11.70)	50 (1.80–98.90)	<0.001
Albumin	43.38 ± 4.84	46.62 ± 2.44	<0.001
Lymphocyte	1.79 ± 0.56	2.73 ± 0.66	<0.001
PNI	52.32 ± 6.24	60.32 ± 3.51	<0.001

*Data are presented as *median (minimum–maximum) or #mean ± standard deviation values. EDE-Q: Eating Disorder Examination Questionnaire, LOI-CV: Leyton Obsessional Inventory-Child Version, EAT-40 Eating Attitudes Test, SAD: Social Anxiety Disorder (RCADS), PNI: Prognostic Nutritional Index, BMI: Body Mass Index, BMI-SDS: Body Mass Index-Standard Deviation Score*

The performance of PNI levels in distinguishing between the patient and control groups was evaluated using ROC analysis. The area under the curve (AUC) was statistically significant (AUC = 0.870; p < 0.001).

According to the Youden-J index, the optimal cut-off value was 55 (55.25), with corresponding sensitivity and specificity values of 0.644 (95% confidence interval [CI]: 48.8–78.1) and 0.952 (95% CI: 83.8–99.4), respectively (Figure 1).



In the analysis of PNI levels in the patient group, when comparing psychiatric and medical comorbidities and complications at the time of initial presentation, PNI levels were significantly lower in those with MDD comorbidity (p = 0.006). When comparing PNI levels based on various disease features, PNI levels were significantly lower in individuals with non-suicidal self-injury compared to those without (p = 0.030) and in those with suicide attempts compared to those without (p = 0.047) (Table 3).

Table 3. *Comparison of PNI levels in the patient group in terms of psychiatric comorbidity and various patient characteristics at the time of diagnosis*

Variable		n	Descriptive statistics	p-value
MDD*	No	31	53.74 ± 6.63	0.006
	Yes	14	49.18 ± 3.87	
NSSI*	No	33	53.53 ± 6.31	0.030
	Yes	12	49.00 ± 4.84	
Suicide attempt#	No	37	53.00 (38.00–68.00)	0.047
	Yes	8	48.75 (42.50–56.00)	

*MDD: Major Depressive Disorder, NSSI: Non-suicidal Self-Injury. Data are presented as *mean ± standard deviation or #median (minimum–maximum) values.*

When the correlation between PNI levels and CGI-S scores and BMI parameters was examined in the patient group, a significant negative correlation was found with disease severity at initial presentation (r = −0.503, p < 0.001), and a significant positive correlation with the disease severity difference score (r = 0.360, p = 0.015), while no other significant correlations were observed (Table 4).

Table 4. *Correlation analysis results between PNI levels and the CGI-S scale scores, BMI, BMI-Percentile, and BMI-SDS of the participants in the patient group*

Disease severity (at the time of evaluation)	r	0.088
	p-value	0.564
Degree of improvement (at the time of evaluation)	r	−0.050
	p-value	0.744
Severity of side effects (at the time of evaluation)	r	0.013
	p-value	0.931
Disease Severity (initial presentation)	r	**−0.503**
	p-value	**<0.001**
Degree of Improvement (initial presentation)	r	−0.032
	p-value	0.835
Severity of side effects (initial presentation)	r	-
	p-value	-
Disease severity difference score	r	**0.360**
	p-value	**0.015**
Degree of improvement: difference score	r	−0.048
	p-value	0.757
Severity of side effects difference score	r	0.013

	p-value	0.931
BMI (initial presentation)	r	**0.294**
	p-value	**0.050**
BMI (at the time of evaluation)	r	0.150
	p-value	0.325
BMI percent change	r	−0.030
	p-value	0.847
BMI-Percentile	r	0.203
	p-value	0.181
BMI-SDS	r	0.262
	p-value	0.083

Percent change = (final value − initial value) / initial value, Difference score = (final value − initial value), CGI-S: Clinical Global Impressions-Severity, PNI: Prognostic Nutritional Index, BMI: Body Mass Index, BMI-SDS: Body Mass Index-Standard Deviation Score

When the participants were divided into three groups—those who continued to meet the diagnostic criteria, those who no longer met the criteria, and the control group—and PNI levels across these groups were compared, a statistically significant difference was observed ($p < 0.001$). Upon comparing the groups in pairs, no significant difference was found between those who continued to meet the diagnostic criteria and those who no longer met the criteria ($p = 0.213$), while significant differences in PNI levels were found between those who continued to meet the diagnostic criteria and the controls ($p < 0.001$), and between those who no longer met the diagnostic criteria and the controls ($p < 0.001$) (Table 5).

Table 5. *Comparison of PNI levels between those who continued to meet the diagnostic criteria for AN and ED, those who did not, and control groups*

Diagnostic Criterion	Groups	Descriptive Statistics	p-value			
			General	Control – No longer meeting criteria	Control – Continuing to meet criteria	No longer – Continuing to meet criteria
AN Criteria	Control (n = 42)	60.00 (52.50–67.00)	<0.001	<0.001	<0.001	0.213
	No longer meeting AN diagnostic criteria (n = 34)	53.25 (38.00–68.00)				
	Continuing to meet AN diagnostic criteria (n =11)	50.0 (42.50–58.00)				
ED Criteria	Control (n = 42)	60.00 (52.50–67.00)	<0.001	<0.001	<0.001	0.492
	Did not meet the diagnostic criteria (n = 31)	52.62 (38.00–68.00)				
	Continued to meet the diagnostic criteria for eating disorders (n = 14)	51.64 (42.50–58.00)				

AN: Anorexia Nervosa; ED: Eating Disorder. Values are presented as median (IQR). p-values are from non-parametric pairwise comparisons.

Discussion

The study's primary conclusions, which investigated the association between PNI levels and prognosis, comorbidities, clinical features, and sociodemographic factors in children and adolescents with AN, are as follows: PNI levels were significantly lower in the patient group than in the control group. A positive correlation was found between BMI and PNI levels. Negative correlation was found between the disease severity score and PNI levels. The patients with comorbid depression had PNI levels that were significantly lower than those without depression. Patients who had a history of NSSİ had considerably lower PNI levels than those who did not. Patients who had a history of suicide attempts had considerably lower PNI levels than those who did not. In the study, three groups—those continuing to meet an AN diagnostic criterion, those no longer meeting these criteria, and the control group—were compared. At the time of the evaluation, PNI levels were significantly lower in both groups, which continued to meet AN diagnostic criteria, while the group no longer met the criteria compared to the control group.

PNI was originally developed to predict mortality and perioperative complications in malnourished gastrointestinal cancer patients. In subsequent studies, PNI has been accepted as a parameter reflecting the immune-nutritional status in various diseases. It has been associated with mortality in adults with acute decompensated heart failure, acute myocardial infarction, and intensive care unit treatment for any reason, and with prognosis in children

with advanced chronic kidney disease (Candeloro et al., 2020; Kayhan et al., 2022; Zhang et al., 2019). Considering research findings showing PNI as a predictor of long-term prognosis, including all-cause mortality, across various diseases and clinical conditions (Candeloro et al., 2020), the PNI score, based on albumin and lymphocyte values, appears to be a suitable tool for rapidly assessing immunonutritional status in patients with AN.

In this study, the performance of PNI levels in distinguishing between patient and control groups was evaluated using ROC analysis, and the AUC was statistically significant (cut-off value of 55.25). In a 2020 study that staged AN in adult patients at the time of diagnosis, recovery rates were evaluated 1 year after disease onset (Ambwani et al., 2020). In this study, the time between the date PNI levels were first measured at the patient's admission to the units and the cross-sectional dates on which they were evaluated was reassessed as either under or over 1 year. When the performance of PNI levels measured within 1 year for distinguishing between patient and control groups was evaluated using ROC analysis, the AUC was 0.855, indicating significance. For PNI levels measured within the 1-year timeframe, a new cut-off value of 56.75 was established. These results suggest that re-evaluating PNI levels after 1 year could be valuable for prognosis determination and may be recommended for follow-up.

BMI values were significantly lower in the patient group than in the control group, consistent with the characteristics of AN. Statistical analysis further revealed a borderline positive correlation between PNI and BMI measured at the initial assessment during the disease period. For children and adolescents, BMI thresholds must be adjusted for growth (Hammer et al., 1991; Zipfel et al., 2000) and compared with their measured BMI levels with national reference data (Beaumont, P. He, 1988). In the present study, data for the patient and control groups were calculated using the percentile charts prepared by Neyzi et al. (Bundak et al., 2006). The BMI percentiles and SDS values of the patient and control groups at the initial evaluation of the disease phase were compared. It was discovered that the patient group's BMI percentiles and BMI-SDS values were substantially lower than those of the control group. In a study involving 404 children and adolescent patients with AN, compared to patients with significantly low BMI (BMI percentile ≥ 0.3), those with dangerously low BMI (BMI percentile < 0.3) had an average treatment duration that was 2 weeks longer, a BMI 0.46 kg/m² lower, and a BMI-SDS 0.44 lower at discharge (Engelhardt et al., 2021). In this respect, when the correlation of PNI levels, whose prognostic value was examined, with BMI percentile and BMI-SDS values was examined, no significant correlation was found between PNI levels and either metric. It was considered that this evaluation, conducted on a relatively small sample, could be reassessed with a sufficiently large sample.

In this study, which examined the correlation between PNI levels and various patient characteristics, we found a negative correlation between disease severity scores on the CGI-S scale—administered at the initial presentation during the disease period—and PNI among the 45 patients studied. Consistent with the hypothesis, PNI decreases with increasing disease severity. The hypothesis and results align with a study suggesting that symptom severity may help predict poorer treatment outcomes (Arcelus et al., 2011). A positive correlation was found between the disease severity difference score and PNI. In other words, as the difference between disease severity scores at the time of the evaluation and initial presentation increases, PNI also increases. This can be interpreted as follows: patients who initially had high disease severity scores at the initial presentation but later showed significant improvement also had higher PNI levels at their initial evaluation. No previous studies were found in the literature examining differences in disease severity scores, but this finding may support the idea that PNI could predict AN prognosis, consistent with the hypothesis.

Among the 45 AN patients included in the present study, 14 had MDD as a comorbidity at the initial diagnostic assessment. PNI levels were significantly lower in individuals with MDD. In line with the present study, the literature identifies MDD as the most common comorbidity in AN (Crone et al., 2023; Harmancı et al., 2021). Additionally, existing research links clinical depression with poorer AN outcome (Löwe et al., 2001), higher rates of suicide attempts, and increased mortality due to suicide (Favaro et al., 2006). In a study examining albumin in the pathophysiology of depression, higher serum albumin levels were associated with increased positive emotions, while negative emotions correlated negatively with serum albumin levels. It was argued that serum albumin in depressive patients could play a significant role in depressive symptoms and suicidal ideation (Harris & Barraclough, 1998). In this study, which examined PNI levels—a parameter derived from serum albumin values—we suggested that lower PNI levels in AN may be associated with MDD comorbidity.

PNI levels were found to be significantly lower in patients with NSSI and in those with suicide attempts compared to those without these characteristics. In a review of adolescents with EDs, it was found that 40.8% of the patients reported NSSI. It was reported that the prevalence of NSSI was higher in patients with BN (26%–55.2%) or the binge-eating/purging subtype AN (27.8%–68.1%) compared to the restrictive subtype AN (13.6%–42.1%) (Chesney et al., 2014; Franko et al., 2013). Suicidal ideation in AN patients has been reported at rates of 20%–43% in different studies. Compared to women aged 15–34 years in the general population, women with AN are about 5.2 times more likely to die early and 18 times more likely to die by suicide (Steinhausen, 2002). A study examining albumin in the pathophysiology of depression found that decreased serum albumin levels were negatively associated with severe depressive symptoms only in depressive patients with suicidal ideation. A higher level of suicidal ideation was observed in cases of low albumin levels (Madge et al., 2008). In this study, which examined PNI levels—a parameter based on serum albumin values—the results that show lower PNI levels are correlated with NSSI and suicide attempts in AN appear consistent with these findings. When the literature on NSSI and suicide attempts—significant risk factors for prognosis and mortality in AN—was reviewed, the findings obtained in the present study suggest that low PNI levels in AN may be associated with NSSI and suicide attempts during the course of the disorder.

In the study, when comparing PNI levels among groups with ongoing AN or ED diagnoses, those who no longer met the diagnostic criteria, and a control group, PNI levels were lower in both those who continued to meet AN or ED

criteria and those who did not, compared to the control group. However, no significant difference existed between individuals who continued to meet the diagnostic criteria and those who did not. While studies differ in their criteria, there is a general consensus that a favorable outcome means improvement in all core clinical symptoms of AN, a moderate outcome represents an improvement with some residual symptoms (Steinhausen, 2002), and a poor outcome is synonymous with the chronic persistence of the disorder. The findings from the present study suggest that although PNI levels are somewhat higher among those not meeting the criteria for ED or AN, they may not be associated with either continuing to meet the criteria or no longer meeting them.

Conclusion

The association of PNI with significant prognostic parameters for AN, including disease severity, BMI, MDD comorbidity, NSSI, and suicide attempts, but not with continuing to meet the diagnostic criteria for AN and ED, suggests that PNI levels may be considered an indirect prognostic parameter for AN in children and adolescents and that closer follow-up of AN patients with low PNI levels may be recommended However, there is a need for further multicenter studies with larger samples.

Limitations

Firstly, because AN predominantly involves women, only female participants were included in the study. Studies including both genders are needed to generalize the study results. The PNI levels measured at the time of the patients' initial presentation to our center during the course of AN were used. For some patients, this corresponded to the period of their initial AN diagnosis without prior treatment, while for others, it corresponded to the time when they were referred to us after insufficient remission in external centers. Additionally, PNI levels were measured only once, and some information was collected retrospectively. To ensure standardization, prospective studies are needed in which PNI levels are measured at the time of initial AN diagnosis and during follow-up. İn this study, K-SADS was administered only once to both patient and control groups, and past psychiatric symptoms were also inquired about. The retrospective nature of some of this information is one of the study's limitations.

Declarations

Ethics Committee Approval
Approval of this study has been granted by the Bursa Uludağ University Clinical Research Ethics Committee *(Ethic Acceptance No: 2023-11/14 Number:2011-KAEK-26/339).*

Consent for Publication
Not applicable

Availability of Data and Materials
Not applicable

Competing Interests
The author declares that no competing interests exist in this manuscript.

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Authors' Contributions
ÖAD proposed the main idea of the research, while CM, ST, and ŞEÇ were involved in reviewing and discussing the literature. ÖAD and ZGEÖ contributed to drafting the article and revising its content. All authors have reviewed and approved the final version of the article.

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