Original Article

The Utility of CONUT Score in Indolent Lymphoma Patients

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Abstract

Background and Aim: Similar to the uncertainties in the treatment criteria for indolent non-Hodgkin lymphoma (iNHL), the prognostic criteria have not been fully clarified. The Controlled Nutritional Status (CONUT) score is not only used as a predictor of malnutrition but also indicates prognosis in many chronic or malignant diseases. The aim of this study is to investigate the predictive and prognostic significance of the CONUT score in patients with iNHL. **Patients and Methods:** A retrospective evaluation was made of 109 patients with iNHL. The CONUT scores of the patients were compared between those with an indication for treatment and those followed without treatment. The same analysis was performed between patients who developed relapse after treatment. Survival analysis was performed on all patients, and associations between survival and the CONUT score were examined. **Results:** The median CONUT score was found to be higher in those who had treatment indications compared to those who did not (2 vs 1; P = 0.014). In the regression model, a CONUT absolute value above 5 was found as an independent risk factor predicting relapse. In the whole study population, a CONUT absolute value >2 predicted the risk of mortality with 53.9% sensitivity and 68.7% specificity (AUC ± SE = 0.639 ± 0.07; +PV = 35%; -PV = 82.6%; P = 0.034). **Conclusion:** CONUT score is a predictive and prognostic factor for patients with iNHL. The development of simple, low-budget prognostic and predictive biomarkers is critical not only for determining the course of the disease but also for follow-up and treatment management.

Keywords: *CONUT score, indolent lymphomas, prognosis, survival*

Introduction

Indolent non-Hodgkin lymphoma (iNHL) can be defined as "lymphoma that grows slowly, has a weak tendency to spread and has mild symptoms" and which are more common than one-third of all lymphomas.[1] Although most patients with iNHL do not need long-term treatment, some patients progress rapidly or transform into aggressive lymphomas.[2,3] Similar to the uncertainties in the treatment criteria, the prognostic criteria have not yet been fully clarified. Therefore, the development of simple, low-cost, practical, easy-to-calculate prognostic biomarkers has been a critical issue.[4]

The Controlled Nutritional Status (CONUT) score is a practical indicator used as a predictor of malnutrition, which is also used as a prognostic marker. A high CONUT score has been shown to have an impact on prognosis in patients with breast cancer, cardiovascular disease, hypertension, end-stage renal disease, and diffuse large B-cell lymphoma (DLBCL).[5] The aim of this study was to investigate the predictive and prognostic significance of the CONUT score in patients with iNHL.

Materials and Methods

This retrospective study was conducted on patients diagnosed with iNHL in the Hematology Department of Diskapi Yildirim Beyazit Training and Research Hospital between 2010 and 2021. Demographic information,

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specific diagnosis, date of diagnosis, comorbidities, Charlson Comorbidity Index (CCI), Eastern Cooperative Oncology Group (ECOG) score, treatment regimens (the criteria of the d'Etude des Lymphomes Folliculaires (GELF) had been used to determine the treatment indication of the patients), treatment response and follow-up periods were recorded for all patients.

At the time of diagnosis, complete blood count (CBC) and hematological parameters including hemoglobin (Hb) levels, hematocrit (Hct) levels, platelet count, white blood cell count (WBC), total lymphocyte count, albumin concentrations, total cholesterol levels, lactate dehydrogenase (LDH) levels, ferritin, erythrocyte sedimentation rate (ESR) and B12 vitamin levels were examined. Using these data, demographic and clinical characteristics, response assessment, and survival rates were analyzed. The impact of the parameters on survival was analyzed. Progression-free survival (PFS) and overall survival (OS) were examined. Patients receiving lipid-lowering therapy and patients diagnosed with diseases causing malabsorption, chronic liver disease, or urinary protein loss before the diagnosis of iNHL were excluded from the study.

The CONUT score was calculated retrospectively according to the serum albumin value, lymphocyte count, and total cholesterol levels. Serum albumin concentration ≥3.50 g/dL was scored as 0 points, 3.00–3.49 g/dL as 2 points, 2.50–2.99 g/dL as 4 points, and <2.50 g/dL as 6 points. Total lymphocyte counts ≥1600 mm^3 was scored as 0 points, 1200–1599 mm^3 as 1 point, 800–1199 mm^3 as 2 points, and <800 mm^3 as 3 points. Total cholesterol levels ≥180 mg/dL were scored as 0 points, 140–179 mg/dL as 1 point, 100-139 mg/dL as 2 points, and <100 mg/dL as 3 points. All 3 parameters were scored according to their value and classified as Normal (0-1 point), Mild (2-4 points), Moderate (5-8 points), and Severe (9-12 points).[6]

Statistical analysis

Data obtained in the study were analyzed statistically using SPSS for Windows vn. 20.0 software (IBM Corp., Armonk, NY, USA). The Conformity of the data to normal distribution was evaluated with the Kolmogorov-Smirnov test. Numerical variables were expressed as mean ± standard deviation or median (min-max) values and categorical data as number (n) and percentage (%). The Chi-square and Fisher's Exact tests were used to compare categorical data, and the Student's t-test or the Mann-Whitney U-test to compare numerical variables between two groups. Comparisons of three or more groups of data were made using the ANOVA test (post-hoc: Bonferroni test) or the Kruskall Wallis H test (post-hoc: Dunn's test). Stepwise multivariable logistic regression analysis and Cox regression analysis were used to identify independent predictors. The diagnostic performance of the independent predictors was tested with ROC Curve analysis and the predictive values were determined according to the Youden index method. Survival plots were tested with Kaplan-Meier analysis. A value of bidirectional $P < 0.05$ was considered statistically significant in all analyses.

Ethical approval and informed consent

Approval for the study was granted by the Institutional Ethics Review Board of Ankara Diskapi Yildirim Beyazit Research and Training Hospital (date: 23.05.2022, no: 138/02). All procedures performed in studies involving human participants 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. As a standard of care/action of Ankara Diskapi Yildirim Beyazit Research and Training Hospital, the patient records confirmed that all the study patients gave informed consent at the time of hospitalization and before the administration of chemotherapy and other relevant diagnostic/therapeutic standards of care.

Results

The study population consisted of 109 patients, including 49 marginal zone lymphoma (MZL), 28 follicular lymphomas (FL), 13 hairy cell leukemia (HCL), and 19 other iNHLs. Among the patients who needed treatment, the highest rate was in patients diagnosed with HCL. (MZL: 44.9% vs FL: 60.7% vs HCL: 92.3% vs other iNHLs: 73.7%; $P = 0.007$). Development of relapse and response rates did not differ significantly between the diagnostic groups. The median PFS level was higher in the FL group compared to the other diagnoses (MZL: 77.8 months vs FL: 104.4 months vs other iNHLs: 70.0 months; $P = 0.002$). Median OS was 65.8 months in MZL, 91.9 months in FL, 48.1 months in HCL, and 93 months in other iNHL. There was no statistically significant difference between diagnoses in terms of OS (p = 0.366). The demographic and clinical characteristics of the patients are shown in Table 1.

Evaluation of patients with indications for treatment and received treatment

Patients with indication for treatment and without treatment (watch and wait) were compared and the male gender (58.5% vs. 31.8%; $P = 0.011$), FL diagnosis group (18.5% vs. 2.3%; $P = 0.008$), DM (18.5% vs. 4.5%; $P = 0.042$), absolute CONUT value (2 vs 1; $P = 0.014$), and stage IV disease (72% vs. 27.3%); $P < 0.001$) were found to be parameters related to treatment indications.

Table 1: The clinical and dermographic characteristics of patients

	MZL (*n*=49)	FL (*n*=28)	HCL (*n*=13)	Other iNHLs (*n*=19)	All (*n*=109)	*P*[a]
Age of diagnosis (mean±SD)	63.8±10.1	55.5±13.8	60.7±13.4	61.2±16.8	61.6±12.8	0.204
Gender *n*, (%)						
Male	15 (30.6)	17 (60.7)	11 (84.6)	9 (47.7)	52 (47.7)	0.002
Female	34 (69.4)	11 (39.3)	2 (15.4)	10 (52.6)	57 (52.3)	
Comorbidty *n*, (%)						
Yes	31 (63.3)	18 (64.3)	5 (38.5)	12 (63.2)	66 (60.6)	0.405
No	18 (36.7)	10 (35.7)	8 (61.5)	7 (36.8)	43 (39.4)	
CONUT score median (IQR)	2 (3)	2 (3)	1 (2)	3 (4)	2 (3)	0.109
CONUT score *n*, (%)						
Normal	24 (49.0)	16 (57.1)	6 (46.2)	6 (31.6)	52 (47.7)	0.363
Mild	20 (40.8)	11 (39.3)	5 (38.5)	8 (42.1)	44 (40.4)	
Moderete	5 (10.2)	1 (3.6)	2 (15.4)	5 (26.3)	13 (11.9)	
Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Stage *n*, (%)						
I	13 (26.5)	8 (28.6)	1 (7.7)	3 (15.8)	25 (22.9)	0.092
II	6 (12.2)	5 (17.9)	0 (0)	1 (5.3)	12 (11.0)	
III	7 (14.3)	5 (17.9)	0 (0)	1 (5.3)	13 (11.9)	
IV	23 (46.9)	10 (35.7)	12 (92.3)	14 (73.7)	59 (54.1)	
Treatment indication *n*, (%)						
Yes	22 (44.9)	17 (60.7)	12 (92.3)	14 (73.7)	65 (59.4)	0.007
No	27 (55.1)	11 (39.3)	1 (7.7)	5 (26.3)	44 (40.4)	
Hb (gr/dL) [mean±SD]	11.8±2.7	13.2±2.5	9.8±3.5	12.3±2.7	12±2.9	0.004
Plt (x10^6/L) Median (IQR)	203 (203)	231 (81)	73 (64)	207 (124)	197 (163)	<0.001
Wbc (x10^6/L) Median (IQR)	7.6 (7)	6.4 (4)	3.6 (12)	6.7 (3)	6.6 (6)	0.542
LDH (U/L) Median (IQR)	228 (93)	199 (102)	191 (51)	196 (71)	214 (75)	0.012
ESR (mm/h) Median (IQR)	22 (27)	12 (29)	22 (22)	14 (37)	20 (26)	0.298
Ferritin (ng/mL) Median (IQR)	72 (97)	75 (99)	118 (149)	49 (184)	79 (104)	0.799
Vitamin B12 (pmol/L) Median (IQR)	251 (174)	262 (79)	130 (182)	255 (182)	247 (156)	0.125
PFS, months Median [Min-Max]	77.8 (68.3-87.4)	104.4 (89-119.6)	-	70 (29-110.9)	105 (93-117.3)	0.048*
OS, months Median [Min-Max]	65.8 (54.2-77.4)	91.9 (73-110.9)	48.1 (32.6-63.6)	93 (67.10-118.9)	89.7 (77-102.4)	0.366*
Final status *n*, (%)						0.048
Survivor	36 (73.5)	23 (82.1)	10 (76.9)	14 (73.7)	83 (76.1)	
Exitus	13 (26.5)	5 (17.9)	3 (23.1)	5 (26.3)	26 (23.9)	

CONUT: Controlled Nutritional Status, ESR: Erythrocyte sedimentation rate, FL: Follicular lymphoma, Hb: Hemoglobin, HCL: Hairy cell leukemia, MZ: Marginal zone lymphoma, Plt: Platelet, PFS: Progression free survival, OS: Overall survival, WBC: White blood cell count, LDH: Lactate dehydrogenase. [a]: P<0.05 indicates statistical significance. *: PFS and OS were calculated by the Kaplan Meier method

In terms of laboratory findings, the mean hemoglobin level, median neutrophil level, median platelet level, and mean total cholesterol levels were lower in those who received treatment, and the median ferritin level was higher in those who followed without treatment. In the multivariate regression model, in which the potential risk factors associated with the need for treatment were included, male gender (OR: 4.62; P = 0.005), stage IV disease (OR = 19.18; P < 0.001), and low hemoglobin levels (OR = 0.83; P = 0.046) were found to be independent predictors of the treatment indication. When the CONUT score was categorized according to the current scoring, it was seen that the patients with a moderate CONUT score were also associated with the treatment indication. The univariate and multivariate regression analyses performed with the parameters found to be significantly different in the comparison of the patients who received and did not receive treatment are shown in Table 2.

In the entire study population, a CONUT score >1 (absolute value) predicted the need for treatment with 63.1% sensitivity and 63.6% specificity (AUC ± SE = 0.637 ± 0.06; PPV = 71.9%; NPV = 53%; P = 0.013).

Table 2: Risk factors associated with indication for treatment

Variables	Univariable regression			Multivariable regression		
	OR	95% CI	*P*	OR	95% CI	*P*
Gender						
• Female	ref			ref		
• Male	3.02	1.35-6.74	0.007*	4.62	1.58-13.44	0.005*
Diagnosis						
• MZL	ref			ref		
• HCL	1.9	0.74-4.88	0.184	1.18	0.86-5.35	0.892
• FL	14.73	1.77-122.23	0.013*	15.89	1.58-101.4	0.009*
• Other iNHLs	3.44	1.07-11.03	0.038*	4.22	1.17-12.33	0.020*
Comorbidity						
• No	ref			ref		
• Yes	0.41	0.18-0.94	0.034*	0.52	0.17-0.98	0.038*
CONUT Score	1.25	1.01-1.54	0.045*	1.10	0.55-2.2	0.892
CONUT Score						
• Normal	ref	2.15-7.12	0.911	ref	2.42-7.11	0.281
• Mild	2.71	0.81-1.14	0.042*	3.85	0.91-2.09	0.041*
• Moderete	1.83			1.23		
Stage						
• I	ref			ref		
• II	3.17	0.74-13.59	0.121	4.89	0.95-32.83	0.097
• III	2.71	0.65-11.29	0.170	3.19	0.63-16.23	0.162
• IV	12.41	4.07-37.84	<0.001*	19.75	5.14-71.52	<0.001*
Hemoglobin (g/dL)	0.81	0.70-0.95	0.008*	0.83	0.67-0.98	0.046*
Neutrophil ($\times 10^3/mm^3$)	0.15	0.04-1.12	0.040*	0.90	0.80-1.02	0.118
Platelet ($\times 10^3/mm^3$)	1.00	0.99-1.00	0.010*	0.99	0.99-1.00	0.780
Ferritin (ng/mL)	1.01	1.00-1.01	0.039*	1.00	0.00-1.04	0.150
Total cholesterol (mg/dl)	1.89	1.02-2.23	0.048*	0.99	0.98-1.00	0.054
					Nagelkerke R^2=0,601; *P*<0,001	

CONUT: Controlled Nutritional Status, FL: follicular lymphoma, HCL: hairy cell leukemia, MZL: marginal zone lymphoma, NHL: non-hodgkin lymphoma. **P*<0.05 indicates statistical significance

Table 3: Risk factors associated with relapse and refractory disease

Variables	Univariate			Multivariate		
	HR	95% CI	*P*	HR	95% CI	*P*
Age of diagnosis	0.99	0.95-1.04	0.707	0.99	0.94-1.04	0.696
Gender						
• Female	ref					
• Male	0.55	0.17-1.82	0.328	1.88	0.50-7.02	0.347
Diagnosis						
• Mzl	ref			ref		
• Hcl	0.82	0.16-4.22	0.808	1.12	0.22-4.14	0.921
• Fl	0.06	0.01-185.9	0.999	0.17	0.16-179.7	1.221
• Other inhls	3.47	1.01-12.12	0.045*	4.21	1.32-11.00	0.632
Comorbidity						
• No	ref					
• Yes	0.67	0.22-2.10	0.494	0.52	0.12-2.17	0.377
• Conut score (absolute value)	1.36	1.02-1.81	0.034*	0.75	0.32-1.77	0.021*
Conut score categories						
• Normal	ref			ref		
• Mild	1.82	0.49-6.79	0.372	1.98	0.419-8.02	0.334
• Moderate	5.69	1.25-25.82	0.024*	7.73	1.44-42.57	0.017*

CONUT: Controlled Nutritional Status, FL: follicular lymphoma , HCL: hairy cell leukemia, MZL: marginal zone lymphoma, NHL: non-hodgkin lymphoma. **P*<0.05 indicates statistical significance

Table 4: Risk factors associated with overall survival of the patients

Variables	Univariate			Multivariate		
	OR	95% CI	*P*	OR	95% CI	*P*
Age of diagnosis	1.06	1.02-1.10	0.001*	1.10	1.04-1.17	0.001*
Gender *n* (%)						
• Female	ref			ref		
• Male	0.93	0.43-2.04	0.865	0.72	0.22-2.35	0.593
Diagnosis. *n* (%)						
• MZL	ref			ref		
• HCL	0.65	0.23-1.83	0.415	0.89	0.11-2.34	0.512
• FL	0.99	0.28-3.48	0.987	1.54	0.87-7.27	1.112
• Other iNHLs	0.96	0.34-2.72	0.946	1.43	0.97-3.45	0.817
Comorbidity						
No	ref			ref		
Yes	2.87	1.08-7.64	0.034*	3.12	1.11-8.23	0.067
CONUT Score (absolute value)	1.33	1.13-1.57	<0.001*	1.3	1.10-1.53	0.002*
CONUT Score Categories						
• Normal	ref			ref		
• Mild	1.45	0.58-3.58	0.421	2.03	1.23-4.53	0.843
• Moderate	4.20	1.56-11.31	0.005*	4.11	2.19-17.98	0.041*
Hemoglobin (g/dL)	0.82	0.73-0.93	0.003*	0.82	0.65-1.04	0.107
WBC ($\times 10^3/mm^3$)	1.00	0.97-1.03	0.989	1.00	0.95-1.06	0.745
Platelet ($\times 10^3/mm^3$)	1.00	0.99-1.01	0.840	1.00	0.99-1.00	0.338
ESR (mm/h)	1.02	1.01-1.03	0.046*	1.01	0.98-1.03	0.429-
Vitamin B12 (pmol/L)	1.00	0.99-1.01	0.396	0.99	0.99-1.00	0.162
Ferritin (ng/mL)	1.02	1.01-1.03	0.006*	1.00	0.99-1.00	0.260
LDH (/l)	1.02	1.01-1.03	0.001*	1.00	0.99-1.01	0.087

CONUT: Controlled Nutritional Status, ESR: Erythrocyte sedimentation rate, FL: follicular lymphoma, HCL: hairy cell leukemia, MZL: marginal zone lymphoma, NHL: non-hodgkin lymphoma. **P*<0.05 indicates statistical significance

Evaluation of patients with relapse

When the current clinical and demographic parameters of the patients followed up with remission and the patients who developed relapse were compared, it was observed that the patients who developed relapse were mostly in the other iNHL diagnosis group, and the CONUT score was found to be higher in these patients.

In the regression model in which these potential risk factors were included, a moderate CONUT score (HR: 7.73; $P = 0.017$) was determined as an independent risk factor predicting relapse. The univariate and multivariate regression analyses performed with the parameters found to be significantly different in the comparison of the relapsed patients and patients followed in remission are shown in Table 3.

Evaluation of survivals

When dead and alive patients were compared in terms of the current clinical and demographic parameters, it was seen that a significant difference was found regarding, CONUT score (5-8 points), age at diagnosis, presence of comorbidity, hemoglobin, ESR, ferritin and LDH levels. According to univariate analysis; moderate CONUT score**,** increased age at diagnosis, decreased hemoglobin levels, increased ESR level, increased ferritin levels, and increased LDH levels were found to be associated with mortality.

In the regression model in which these potential risk factors were included, an increased CONUT score (HR: 1.3; $P = 0.002$) was determined to be an independent risk factor predicting mortality. The univariate and multivariate regression analyses performed with the parameters were found to be significantly different in the comparison of the dead and alive patients which is shown in Table 4. In the whole study population, a CONUT score >2 predicted the risk of mortality with 53.9% sensitivity and 68.7% specificity (AUC ± SE = 0.639 ± 0.07; PPV = 35%; NPV = 82.6%; $P = 0.034$). According to ROC analysis, an absolute CONUT score greater than 2 was found to predict mortality risk with 61.9% sensitivity and 71.8% specificity (AUC ± SE = 0.695 ± 0.07; +PV = 59.1%); -PV = 74.2%, $P = 0.011$).

Discussion

The management of iNHL presents a dilemma to both the patient and the physician, as the treatment of all

patients immediately after the diagnosis has no effect on survival, and some patients are followed up with a watch-wait method, sometimes for years without treatment. When evaluating treatment initiation conditions in iNHL, it can be said that in general terms cases are investigated when symptoms occur in the presence of a high tumor burden and organ damage. The criteria of the d'Etude des Lymphomes Folliculaires (GELF) and British National Lymphoma Survey (BNLI) are treatment initiation guidelines that relatively contain the aforementioned parameters. Some physicians start treatment when macroscopic involvement of the bone, kidneys, and liver are seen, and the rapid clinical progression compared to the previous 3 months is accepted as an "aggressive disease".[2,3,7] The Gene Expression Profile (GEP), International Prognostic Index (IPI), and other indices are useful in predicting prognosis for diffuse large B-cell lymphoma (DLBCL), whereas indices with such precise limits are not available for iNHLs. The existing criteria cannot be applied easily in daily clinical practice and cannot determine prognosis effectively. In light of all these conditions, it has been clearly stated that not only the uncertainties in the treatment criteria but also the prognostic criteria are not clear in iNHL patients. Therefore, parameters or a scoring system that can predict both prognosis and survival, which can be applied at the time of diagnosis during the outpatient clinic examination, is a primary need of iNHL patients.[4] Patients with iNHL in need of treatment are less sensitive to chemotherapy because they have tumors with a lower proliferation rate, so a more difficult treatment process can be expected.[1] It is known that malnutrition, anorexia, and cachexia increase chemotherapy unresponsiveness and toxicity secondary to chemotherapy, and are poor prognostic markers in several cancers. However, although the prognostic value of nutritional status is known, it still cannot be evaluated routinely.[5,8,9] Some studies have shown that the albumin value at diagnosis can be used to predict prognosis in DLBCL patients. Low serum albumin has been identified as a poor prognostic factor that can be used in DLBCL.[10] In a study covering all lymphomas, it was stated that hypoalbuminemia mechanisms can be summarized as an abnormal distribution of albumin in the intravascular and extravascular sections, protein synthesis deficiency due to malnutrition and decreased albumin, and aggressive tumor behavior secondary to inflammation.[11]

Lymphopenia is associated with overall survival and progression-free survival in NHL patients. It also correlates with performance status and specific prognostic factors. Lymphopenia in lymphoma patients can be perceived not only as a survival parameter but also as a biological mechanism that stimulates tumor progression. In addition to the increased risk of death due to treatment toxicity, the poor outcome observed in lymphopenic patients may also be due to loss of immune response. Physiologically, lymphocyte homeostasis depends on the presence and function of dendritic cells. The differentiation of dendritic cells is impaired by the overproduction of many cytokines, such as interleukin (IL)-6, PGE2, IL-10, and transforming growth factors, which are produced especially in lymphoma and other solid tumors. Thus, poor prognosis criteria in lymphoma may emerge.[12,13] There are studies showing that low cholesterol levels negatively affect the prognosis in lymphoma and many solid tumor patients. In a study that analyzed patients with the transformation from iNHL to DLBCL, there was seen to be a very poor prognosis and still no clear criteria for the predictability. A high-density lipoprotein cholesterol (HDL-C) value associated with total cholesterol was considered a negative and independent prognostic factor for overall survival (OS).[14] The mechanism can be briefly explained as its role in hypercytokinemia and acute phase reaction, which occurs in lymphoma cells and may affect lipid metabolism, just as in lymphopenia and hypoalbuminemia.[14-16]

The CONUT score, which includes albumin, lymphocyte, and cholesterol values, and evaluates the immune system and nutrition, provides information about the mortality and prognosis of hematological malignancies, solid tumors, and many chronic diseases.[5] While studies have been conducted on the effects of the CONUT score in both chronic diseases such as hypertension and in solid tumors such as breast cancer, there are also studies that are significantly decisive on the prognostic importance of the CONUT score in patients with multiple myeloma, T-cell leukemia/lymphoma and DLBCL, which have been conducted within the framework of hematological malignancies.[17-21] To the best of our knowledge, there has been no previous analysis of the CONUT score in iNHL patients. Therefore in the current study, the CONUT score was evaluated in this group of patients who lack a practical approach in terms of diagnosis, treatment, and prognosis, and still have an unmet need in this regard. The study results demonstrated that the median CONUT score (CONUT score ≥2) was higher in those who needed treatment than in those who did not. It was also determined that moderate and high (>5) CONUT scores were independent risk factors predicting relapse. When the whole study population of iNHL patients was evaluated, the CONUT score was determined to predict the risk of mortality. The results of this study revealed that the CONUT score can be a prognostic marker in determining the need for treatment and predicting the risk of recurrence and mortality in iNHL patients. It was

seen that as the CONUT score increases, the need for treatment, recurrence, and mortality increases.

This study had some limitations. As the patient data were obtained from a single center, this may limit the generalizability of results to the general disease population. The retrospective design can be considered another limitation. In addition, the nutritional status of the patients and other related records (calorie intake, body mass index, and other nutritional determining parameters) were not recorded at the time of diagnosis.

In summary, prognostic scoring systems such as the International Prognostic Index (IPI), the revised IPI (R-IPI), and the National Comprehensive Cancer Network IPI (NCCN-IPI) are widely used to predict the prognosis of NHL patients and to reveal treatment strategies. However, IPI, R-IPI, and NCCN-IPI are lacking in assessing nutritional status. The GELF and BNLI scores used in iNHL patients also suffered from the same deficit. Emerging evidence suggested that the CONUT score as a nutritional index plays an important role in the prognosis of NHL patients.

In conclusion, the results of this study demonstrated that the CONUT score is a decisive prognostic factor for patients with iNHL and a high CONUT score may be associated with a poor prognosis. In addition, the CONUT score has shown how important it is in the proper assessment and management of nutritional status from the moment of diagnosis.[22]

It can be considered that the CONUT score, which is practical, inexpensive, rapidly detectable in the outpatient setting, and contains vital information for the evaluation of patients, will shed light on the management of iNHL patients after more extensive studies. However, more randomized controlled, multicenter, and prospective studies are needed for CONUT scoring to replace existing prognostic scoring.

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Conflicts of interest

There are no conflicts of interest.

References

1. Mugnaini EN, Ghosh N. Lymphoma. Prim Care 2016;43:661-75.
2. de Leval L, Jaffe ES. Lymphoma classification. Cancer J 2020;26:176-85.
3. Gribben JG. How I treat indolent lymphoma. Blood 2007;109:4617-26.
4. Luan C, Wang F, Wei N, Chen B. Prognostic nutritional index and the prognosis of diffuse large b-cell lymphoma: A meta-analysis. Cancer Cell Int 2020;20:1-8.
5. Çağliyan GA, Hacioğlu S, Koluman BÜ, Ilkkilic K, Nar R, Başer MN, *et al*. Is CONUT score a prognostic index in patients with diffuse large cell lymphoma? Turk J Med Sci 2021;51:2112-9.
6. De Ulíbarri JI, González-Madroño A, de Villar NG, González P, González B, Mancha A, *et al*. CONUT: A tool for controlling nutritional status. First validation in a hospital population. Nutr Hosp 2005;20:38-45.
7. Lumish M, Falchi L, Imber BS, Scordo M, von Keudell G, Joffe E. How we treat mature B-cell neoplasms (indolent B-cell lymphomas). J Hematol Oncol 2021;14:1-19.
8. Yamamoto M, Saito H, Uejima C, Tanio A, Tada Y, Matsunaga T, *et al*. Prognostic value of combined tumor marker and controlling nutritional status (CONUT) score in colorectal cancer patients. Yonago Acta Med 2019;62:124-30.
9. Kanemasa Y, Shimoyama T, Sasaki Y, Hishima T, Omuro Y. Geriatric nutritional risk index as a prognostic factor in patients with diffuse large B cell lymphoma. Ann Hematol 2018;97:999-1007.
10. Bairey O, Shacham-Abulafia A, Shpilberg O, Gurion R. Serum albumin level at diagnosis of diffuse large B-cell lymphoma: An important simple prognostic factor. Hematol Oncol 2016;34:184-92.
11. Waldmann T, Trier J, Fallon H. Albumin metabolism in patients with lymphoma. J Clin Investig 1963;42:171-8.
12. Ray-Coquard I, Cropet C, Van Glabbeke M, Sebban C, Le Cesne A, Judson I, *et al*. Lymphopenia as a prognostic factor for overall survival in advanced carcinomas, sarcomas, and lymphomas. Cancer Res 2009;69:5383-91.
13. Goldrath AW, Bevan MJ. Selecting and maintaining a diverse T-cell repertoire. Nature 1999;402:255-62.
14. Xu J, Wei Z, Zhang Y, Chen C, Li J, Liu P. A novel scoring system based on the level of HDL-C for predicting the prognosis of t-DLBCL patients: A single retrospective study. Biomed Res Int 2018;2018. Available form: https://doi.org/10.1155/2018/2891093. [Last accessed on 2018 Oct 29].
15. Spiegel RJ, Schaefer EJ, Magrath IT, Edwards BK. Plasma lipid alterations in leukemia and lymphoma. Am J Med 1982;72:775-82.
16. Hiatt RA, Fireman BH. Serum cholesterol and the incidence of cancer in a large cohort. J Chronic Dis 1986;39:861-70.
17. Sun X, Luo L, Zhao X, Ye P. Controlling Nutritional Status (CONUT) score as a predictor of all-cause mortality in elderly hypertensive patients: A prospective follow-up study. BMJ Open 2017;7:e015649.
18. Li W, Li M, Wang T, Ma G, Deng Y, Pu D, *et al*. Controlling Nutritional Status (CONUT) score is a prognostic factor in patients with resected breast cancer. Sci Rep 2020;10:1-10.
19. Okamoto S, Ureshino H, Kidoguchi K, Kusaba K, Kizuka-Sano H, Sano H, *et al*. Clinical impact of the CONUT score in patients with multiple myeloma. Ann Hematol 2020;99:113-9.
20. Ureshino H, Kusaba K, Kidoguchi K, Sano H, Nishioka A, Itamura H, *et al*. Clinical impact of the CONUT score and mogamulizumab in adult T cell leukemia/lymphoma. Ann Hematol 2019;98:465-71.
21. Matsukawa T, Suto K, Kanaya M, Izumiyama K, Minauchi K, Yoshida S, *et al*. Validation and comparison of prognostic values of GNRI, PNI, and CONUT in newly diagnosed diffuse large B cell lymphoma. Ann Hematol 2020;99:2859-68.
22. Kaneda Y, Kanemura N, Nakamura N, Ikoma Y, Yamaguchi K, Matsumoto T, *et al*. The pretreatment controlling nutritional status (CONUT) score is an independent prognostic factor in elderly patients with diffuse large B-cell lymphoma. Blood 2018;132:4210.