Prognostic value of the CONUT score in newly diagnosed diffuse large B-cell lymphoma

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Abstract. Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma and clinical outcomes remain heterogeneous despite standard R-CHOP therapy. The Controlling Nutritional Status (CONUT) score, an immunonutritional index based on serum albumin, total cholesterol and lymphocyte count, has emerged as a potential prognostic marker in this setting. In this retrospective observational study, the prognostic value of the pre-treatment CONUT score was evaluated in 110 adult patients with newly diagnosed DLBCL treated with standard R-CHOP at a tertiary center between October 2022 and September 2025. Patients were categorized into two groups according to their CONUT scores (<5 vs. ≥5), and baseline clinical characteristics, laboratory parameters and prognostic indices [International Prognostic Index (IPI) and National Comprehensive Cancer Network IPI (NCCN-IPI)] were compared. Overall survival (OS) and progression-free survival (PFS) were analyzed using the Kaplan-Meier method, and independent prognostic factors for OS were identified by Cox regression analysis. A CONUT score ≥5 was significantly associated with adverse clinical features, including advanced-stage disease (P=0.021), elevated lactate dehydrogenase (P=0.002), ECOG performance status ≥2 (P=0.021), higher IPI (P=0.015) and higher NCCN-IPI scores (P=0.032). Patients with CONUT ≥5 had significantly inferior OS (log-rank P=0.001) and PFS (log-rank P=0.003) compared with those with CONUT <5. Similar findings were observed in the low/low-intermediate IPI subgroup. In the multivariate analysis, advanced-stage disease (P=0.036) and a CONUT score ≥5 (P=0.042) remained independent predictors of OS. These findings indicate that a high pre-treatment CONUT score is associated with adverse baseline characteristics and predicts inferior survival outcomes in patients with DLBCL. Given its simplicity, low cost and availability in routine clinical practice, the CONUT score may serve as a useful adjunct to established prognostic indices, although prospective validation is warranted.

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Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL), accounting for 30-40% of all newly diagnosed adult cases (1,2). It is a biologically heterogeneous and clinically aggressive disease characterized by diverse pathological features, variable clinical behavior and complex underlying genetic alterations (3). Clinically, DLBCL commonly presents with rapidly enlarging lymphadenopathy, B symptoms and elevated lactate dehydrogenase (LDH) levels. Rituximab combined with cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) remains the foundation of first-line therapy; however, up to half of the patients develop relapsed or refractory disease, particularly those with adverse prognostic factors (4). These limitations underscore the need for additional prognostic markers that complement established clinical indices, including the International Prognostic Index (IPI) and its revised versions (5).

In recent years, host-related factors, especially nutritional and inflammatory statuses, have gained attention as clinically relevant predictors of outcomes in hematologic malignancies (6). Among the various nutritional tools, the Controlling Nutritional Status (CONUT) score, introduced in 2005, is a simple, objective and cost-effective index that incorporates serum albumin, total cholesterol and lymphocyte count (7).

High CONUT scores have been associated with inferior survival in several hematological malignancies, including multiple myeloma, DLBCL, peripheral T-cell lymphoma, adult T-cell leukemia, myelodysplastic syndrome and acute myeloid leukemia with myelodysplasia-related changes (8-11).

Despite these findings, data on the clinical utility of the CONUT score in real-world DLBCL populations remain limited, and variability in CONUT cutoff values across studies creates uncertainty regarding its optimal application in routine practice.

Given these gaps, the present study aimed to evaluate the prognostic significance of the pre-treatment CONUT score in patients with newly diagnosed DLBCL treated at a single tertiary center and to determine whether the CONUT score provides additional discriminatory value beyond that of conventional prognostic indices.

Materials and methods

Study design and setting. This retrospective observational chart review was conducted at the Hematology Department of Etlik City Hospital (Ankara, Türkiye). The study period extended from October 2022 to September 2025. The study protocol was approved by the Ethics Committee of Etlik City Hospital (approval no: AEŞH-BADEK1-2025-522). Informed consent was waived because of the retrospective nature of the study and the use of de-identified data.

Participants. All consecutive adult patients (aged ≥18 years) who were newly diagnosed with DLBCL at the Hematology Department during the study period and received standard first-line R-CHOP chemotherapy at our center were included.

Patients with double- or triple-hit lymphoma, primary central nervous system DLBCL and concomitant active malignancies were excluded. Patients with incomplete baseline clinical or laboratory data, missing follow-up information or pathological suspicion of transformation from indolent lymphoma were also excluded. This inclusive approach ensured the comprehensive capture of all eligible patients within the specified timeframe, minimizing potential selection bias and reflecting real-world clinical practice.

All patients received standard full-dose R-CHOP chemotherapy administered every 21 days, consisting of rituximab (375 mg/m^2 on day 1), cyclophosphamide (750 mg/m^2 on day 1), doxorubicin (50 mg/m^2 on day 1), vincristine [1.4 m/g/m^2 (maximum 2 mg) on day 1] and prednisone (100 mg/day on days 1-5). Primary granulocyte colony-stimulating factor (G-CSF) prophylaxis was routinely provided to patients aged ≥65 years, beginning on day 5 of each treatment cycle and continued for 3 consecutive days. For patients younger than 65 years, G-CSF was administered as secondary prophylaxis from the second cycle onward if neutropenia developed during the first cycle. Only patients who received full-dose R-CHOP were included in the study cohort.

Data collection and variables. Baseline demographic characteristics (age and sex), clinical features [B symptoms, bulky disease, extranodal involvement and Eastern Cooperative Oncology Group performance status (ECOG PS)] (12), and laboratory parameters (serum LDH, albumin, total cholesterol and absolute lymphocyte count) were extracted from electronic medical records prior to any lymphoma-directed therapy.

Additional disease-related variables, including the Ann Arbor stage (13) and Hans classification (14) for cell of origin, were also recorded. Prognostic indices, including the International Prognostic Index (IPI) (15) and National Comprehensive Cancer Network IPI (NCCN-IPI) (16) were also calculated. Clinical data related to the CONUT score (7) were collected, and treatment regimens and response assessments were documented.

Operational definitions. The CONUT score was calculated using baseline serum albumin, total cholesterol and lymphocyte count, as originally described by Ignacio de Ulíbarri *et al* (7). The most recent laboratory results obtained within seven days before initiating therapy were used.

The score was derived from three parameters representing protein reserves, immune status and lipid metabolism, as follows: i) Serum albumin (g/dl): ≥3.5=0 points; 3.0-3.49=2 points; 2.5-2.99=4 points; <2.5=6 points; ii) lymphocyte count (/mm^3): >1,600=0 points; 1,200-1,599=1 point; 800-1,199=2 points; <800=3 points; iii) total cholesterol (mg/dl): >180=0 points; 140-180=1 point; 100-139=2 points; <100=3 points. The total CONUT score was calculated by summing the scores of these components, with higher scores indicating more severe malnutrition.

In this study, patients were stratified using a cutoff value of 5, consistent with prior hematologic studies (17-19). Patients with a CONUT score <5 were categorized as having normal-to-mild malnutrition, whereas those with a CONUT score ≥5 were classified as having moderate-to-severe malnutrition.

Overall survival (OS) was defined as the time from diagnosis to death from any cause or until the last follow-up. Progression-free survival (PFS) was defined as the time from diagnosis to disease progression, relapse, death from any cause, or until the last follow-up. Treatment response was evaluated using the Lugano 2014 criteria for lymphoma response assessment (13).

Data sources and measurements. A total of two independent reviewers retrieved all data from the hospital's electronic medical record system to ensure their accuracy. Laboratory analyses were performed in the institution's accredited central laboratory using standardized methods. Serum albumin and total cholesterol levels were measured using automated biochemical analyzers, and lymphocyte counts were obtained from complete blood count tests.

Bias and quality control. Selection bias was minimized by including all consecutive eligible patients diagnosed within the study period. To reduce information bias, the clinical and laboratory data were cross-checked by two independent reviewers. Patients with incomplete baseline data or missing follow-up information were excluded, and no patients included in the final cohort were lost to follow-up. Nonetheless, a certain degree of bias inherent in the retrospective design may be present.

Study size. No formal sample size calculation was performed. Instead, all eligible patients who met the inclusion criteria within the study period were included, yielding a final cohort of 110 subjects.

Statistical analysis. All data were entered and analyzed using SPSS Statistics version 23 (IBM Corp.). Descriptive statistics for categorical variables were presented as counts and percentages. Comparisons between categorical variables were performed using Pearson's χ^2 test. The normality of numerical variables was assessed using the Kolmogorov-Smirnov or Shapiro-Wilk tests.

Patients were divided into two groups according to a CONUT score cutoff value of 5, and their clinical characteristics were compared. The CONUT parameters and their scoring distributions were summarized in a separate table as counts and percentages.

OS and PFS were analyzed using the Kaplan-Meier method and differences between groups were assessed using the log-rank test. Kaplan-Meier survival curves were generated for the entire cohort as well as for subgroups stratified according to IPI risk classification (low/low-intermediate vs. high-intermediate/high-risk).

Univariate and multivariate Cox proportional hazards regression analyses were performed to identify independent prognostic factors for OS. Statistical significance was defined as $P<0.05$, and $P<0.001$ was considered highly significant.

Results

Baseline characteristics. The clinical and demographic characteristics of the study cohort are shown in Table I. Among the 110 patients included in the study, 53 (48.2%) were female and the mean age was 60.8±13 years (median, 64; range, 19-86 years). At diagnosis, half of the patients (50%) presented with Ann-Arbor stage IV disease. Bulky disease was observed in 31.8% of cases and extranodal involvement of more than one site was found in 20.9% of cases. According to the cell of origin classification, 30% of patients were classified as the germinal center B-cell (GCB) subtype, whereas 70% were classified as the non-GCB (NGCB) subtype.

Regarding prognostic indices, 34.5% of patients were classified as high-risk according to the IPI, while 30.9% were considered high-risk according to the NCCN-IPI. Elevated LDH levels were observed in 71.8% of patients and 41.8% had an ECOG PS of ≥2.

At the completion of first-line therapy, 77.3% of patients achieved complete remission and 1.8% achieved partial remission. Refractory or progressive disease was observed in 9.1% of patients and 11.8% of patients died during treatment.

Distribution of CONUT parameters. The distribution of the CONUT parameters is presented in Table II. When patients were evaluated according to serum albumin, lymphocyte count and total cholesterol levels, 25.5% had a normal nutritional status, 39.1% were mildly malnourished, 25.5% were moderately malnourished and 10% were severely malnourished.

Comparison of clinical characteristics according to CONUT groups. Patients were categorized into two groups according to the CONUT score (<5 vs. ≥5), and their clinical characteristics are summarized in Table III. No statistically significant differences were observed in terms of sex, age distribution (≤60 vs. >60 years), extranodal involvement or GCB/NGCB subtype ($P>0.05$).

In contrast, several disease-related features showed clear separation. Advanced-stage disease (stage III-IV) was significantly more common in patients with CONUT ≥5 than in those with lower scores (82.1 vs. 60.6%, $P=0.021$). Elevated LDH levels were also observed at a substantially higher frequency in the CONUT ≥5 group (89.7 vs. 62.0%, $P=0.002$).

Table I. Clinical and demographic characteristics of the study cohort (n=110).

Characteristic	Value
Sex	
Female	53 (48.2)
Male	57 (51.8)
Median age (range)	64 (19-86)
Ann-Arbor Stage	
Stage I	18 (16.4)
Stage II	17 (15.5)
Stage III	20 (18.2)
Stage IV	55 (50.0)
Bulky disease	
Yes	35 (31.8)
No	75 (68.2)
GCB subtype	
Yes	33 (30.0)
No	77 (70.0)
IPI score	
Low risk	29 (26.4)
Low-intermediate	22 (20.0)
High-intermediate	21 (19.1)
High risk	38 (34.5)
NCCN-IPI score	
Low risk	10 (9.1)
Low-intermediate	33 (30.0)
High-intermediate	33 (30.0)
High risk	34 (30.9)
Extranodal involvement	
0-1 site	87 (79.1)
>1 site	23 (20.9)
ECOG PS	
0	3 (2.7)
1	61 (55.5)
2	46 (41.8)
Elevated LDH	
Yes	79 (71.8)
No	31 (28.2)
Response to first-line treatment	
Partial response	2 (1.8)
Complete response	85 (77.3)
Refractory/progressive disease	10 (9.1)
Died during treatment	13 (11.8)
Median follow-up (range), months	11.1 (0.4-34.0)
Overall mortality	25 (22.7)

Values are expressed as n (%) unless otherwise indicated. GCB, germinal center B-cell subtype; IPI, International Prognostic Index; NCCN-IPI, National Comprehensive Cancer Network-IPI; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LDH, lactate dehydrogenase.

Similarly, patients with an ECOG PS of ≥2 were more prevalent in the CONUT ≥5 group (56.4 vs. 33.8%, $P=0.021$).

Table II. Clinical characteristics of patients according to CONUT parameters.

Parameter/nutritional status categories	n (%)
Serum albumin, g/l	
≥35	63 (57.3)
30-34.9	26 (23.6)
25-29.9	11 (10.0)
<25	10 (9.1)
Total lymphocyte count/mm^3	
≥1,600	51 (46.4)
1,200-1,599	13 (11.8)
800-1,199	17 (15.5)
<800	29 (26.4)
Total cholesterol, mg/dl	
≥180	36 (32.7)
140-179	31 (28.2)
100-139	29 (26.4)
<100	14 (12.7)
CONUT total score	
Normal (0-1)	28 (25.5)
Mild (2-4)	43 (39.1)
Moderate (5-8)	28 (25.5)
Severe (9-12)	11 (10.0)

CONUT, Controlling Nutritional Status.

Table III. Clinical characteristics of patients according to CONUT groups.

Characteristic	CONUT <5, n (%)	CONUT ≥5, n (%)	P-value
Age, years			0.225
≤60	34 (47.9)	14 (35.9)	
>60	37 (52.1)	25 (64.1)	
Sex			0.822
Female	33 (46.5)	19 (48.7)	
Male	38 (53.5)	20 (51.3)	
Ann-Arbor stage			0.021
I-II	28 (39.4)	7 (17.9)	
III-IV	43 (60.6)	32 (82.1)	
LDH			0.002
≤250	27 (38.0)	4 (10.3)	
>250	44 (62.0)	35 (89.7)	
Extranodal site			0.366
0-1	58 (81.7)	29 (74.4)	
>1	13 (18.3)	10 (25.6)	
ECOG PS			0.021
0-1	47 (66.2)	17 (43.6)	
≥2	24 (33.8)	22 (56.4)	
GCB subtype			0.240
GCB	24 (33.8)	9 (23.1)	
Non-GCB	47 (66.2)	30 (76.9)	
IPI score			0.015
0-2	39 (54.9)	12 (30.8)	
≥3	32 (45.1)	27 (69.2)	
NCCN-IPI score			0.032
0-3	33 (46.5)	10 (25.6)	
≥4	38 (53.5)	29 (74.4)	

Pearson's χ^2 test was used for statistical comparisons. CONUT, Controlling Nutritional Status; LDH, lactate dehydrogenase; ECOG PS, Eastern Cooperative Oncology Group Performance Status; GCB, germinal center B-cell; IPI, International Prognostic Index; NCCN-IPI, National Comprehensive Cancer Network-IPI.

In addition, higher IPI (≥3) and NCCN-IPI (≥4) scores were significantly associated with CONUT ≥5 (69.2 vs. 45.1%, P=0.015; and 74.4 vs. 53.5%, P=0.032, respectively).

OS analysis. The median follow-up duration for the entire cohort was 11.1 months (range, 0.4-34.0). During the follow-up period, 25 patients (22.7%) died.

Patients with a CONUT score ≥5 had significantly shorter mean OS time than those with lower scores (20.5±2.6 months, 95% CI 15.4-25.7 vs. 28.8±1.3 months, 95% CI 26.4-31.4; log-rank, P=0.001). The corresponding Kaplan-Meier survival curve is presented in Fig. 1.

When stratified by IPI subgroups, patients in the low-risk/low-intermediate category (n=51) with CONUT ≥5 experienced significantly poorer OS than those with CONUT <5 (19.7±3.5 months, 95% CI 12.9-26.6 vs. 32.5±0.7 months, 95% CI 31.2-33.9; log-rank P=0.002; Fig. 2).

In contrast, among patients in the high-intermediate/high-risk IPI subgroup (n=59), OS did not differ significantly between those with CONUT ≥5 and CONUT <5 (18.3±3.1 months, 95% CI 12.2-24.5 vs. 23.7±2.4 months, 95% CI 19.0-28.3; log-rank P=0.158; Fig. 3).

PFS analysis. Patients with a CONUT score ≥5 had significantly shorter PFS than those with CONUT <5 (18.3±1.9 months, 95% CI 14.5-22.2 vs. 29.7±1.2 months, 95% CI 27.3-32.2; log-rank P=0.003). The corresponding Kaplan-Meier survival curve is presented in Fig. 4.

When stratified by IPI subgroups, patients in the low-risk/low-intermediate category (n=51) with CONUT ≥5 experienced significantly poorer PFS than those with CONUT <5 (22.8±2.9 months, 95% CI 17.2-28.4 vs. 32.9±0.7 months, 95% CI 31.5-34.4; log-rank P=0.025; Fig. 5).

In contrast, among patients in the high-intermediate/high-risk IPI subgroup (n=59), PFS did not differ significantly between those with CONUT ≥5 and CONUT <5 (15.9±2.3 months, 95% CI 11.3-20.4 vs. 24.8±2.3 months, 95% CI 20.3-29.4; log-rank P=0.142; Fig. 6).

Cox regression analysis. The results of the univariate and multivariate Cox proportional hazards analyses for OS are presented in Table IV.

In the univariate analysis, several factors were significantly associated with poorer survival, including age >60 years

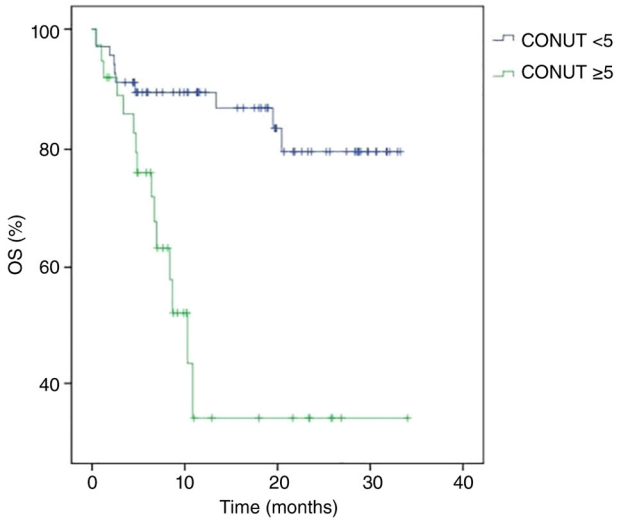

Figure 1. Kaplan-Meier survival curve according to the CONUT cutoff value of 5. Mean OS was 28.8±1.3 months (95% CI, 26.4-31.4) in the CONUT <5 group and 20.5±2.6 months (95% CI, 15.4-25.7) in the CONUT ≥5 group (log-rank P=0.001). OS, overall survival; CONUT, Controlling Nutritional Status.

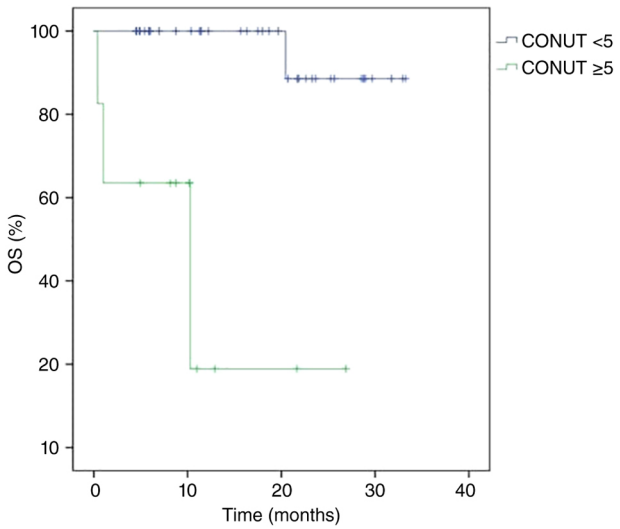

Figure 2. Kaplan-Meier survival curve according to the CONUT cutoff value of 5 in patients with low-risk and low-intermediate International Prognostic Index. Mean OS was 32.5±0.7 months (95% CI, 31.2-33.9) in the CONUT <5 group and 19.7±3.5 months (95% CI, 12.9-26.6) in the CONUT ≥5 group (log-rank P=0.002). OS, overall survival; CONUT, Controlling Nutritional Status.

[hazard ratio (HR) 3.639; 95% CI 1.364-9.708; P=0.010], advanced-stage disease (HR 12.873; 95% CI 1.741-95.179; P=0.012), elevated LDH (HR 5.353; 95% CI 1.261-22.730; P=0.023), ECOG PS ≥2 (HR 2.793; 95% CI 1.232-6.330; P=0.014) and CONUT score ≥5 (HR 3.547; 95% CI 1.578-7.972; P=0.002).

In the multivariate model, only advanced-stage disease and CONUT score ≥5 remained independent predictors of OS. Advanced-stage disease was associated with a 9.668-fold increased mortality risk (95% CI 1.159-80.646; P=0.036), whereas a CONUT score ≥5 conferred a 2.584-fold higher risk of death (95% CI 1.034-6.455; P=0.042).

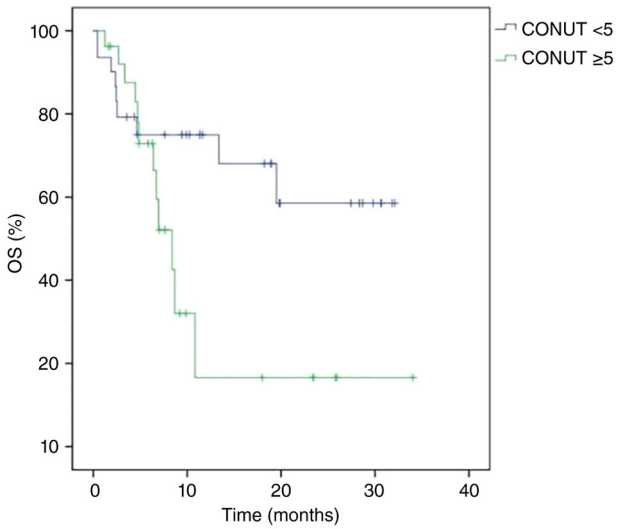

Figure 3. Kaplan-Meier survival curve according to the CONUT cutoff value of 5 in patients with high-intermediate and high-risk International Prognostic Index. Mean OS was 23.7±2.4 months (95% CI, 19.0-28.3) in the CONUT <5 group and 18.3±3.1 months (95% CI, 12.2-24.5) in the CONUT ≥5 group (log-rank P=0.158). OS, overall survival; CONUT, Controlling Nutritional Status.

Discussion

In the present single-center retrospective study, it was found that a high pre-treatment CONUT score (≥5) was significantly associated with adverse baseline features, including advanced Ann-Arbor stage, elevated LDH levels, poor performance status, and higher IPI and NCCN-IPI scores, in patients with newly diagnosed DLBCL. Furthermore, a CONUT score ≥5 emerged as an independent predictor of inferior OS and was associated with inferior PFS, underscoring the prognostic relevance of the host nutritional and immunological status in this disease. These associations suggest that the CONUT score reflects not only nutritional and immunological status but also disease burden and biological aggressiveness. Therefore, CONUT may provide complementary prognostic information beyond conventional survival prediction and help identify patients with more unfavorable baseline characteristics. These findings align with the growing recognition that patient-related factors, beyond tumor biology, meaningfully contribute to clinical outcomes in lymphoid malignancies.

The present results are consistent with those of previous studies evaluating the prognostic impact of CONUT in DLBCL. Baysal *et al* (10) demonstrated that high CONUT scores were independently associated with poor OS in a cohort of 81 patients. Similarly, Kaneda *et al* (11) confirmed the independent prognostic value of the CONUT score in patients with DLBCL. The selection of a CONUT cutoff value of 5 was based on previously published studies in DLBCL and other hematologic malignancies, in which this threshold demonstrated meaningful prognostic discrimination and identified patients with moderate-to-severe nutritional impairment. In particular, Go *et al* (19) and Wang *et al* (17) reported that a CONUT score ≥5 was associated with inferior clinical outcomes in patients with DLBCL, supporting the clinical relevance of this cutoff value. Although receiver operating characteristic-based

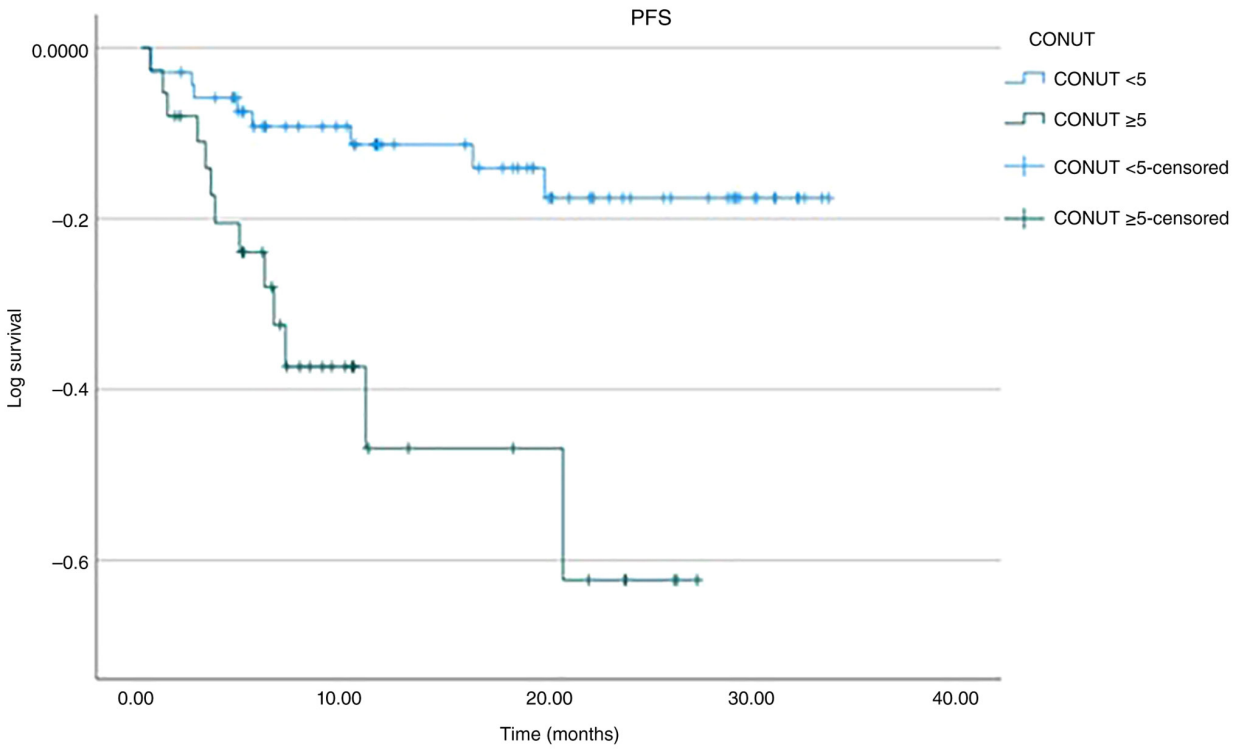

Figure 4. Kaplan-Meier PFS curves according to CONUT score (<5 vs. ≥5) in the entire study cohort. Mean PFS was 29.7±1.2 months (95% CI, 27.3-32.2) in the CONUT <5 group and 18.3±1.9 months (95% CI, 14.5-22.2) in the CONUT ≥5 group (log-rank P=0.003). PFS, progression-free survival; CONUT, Controlling Nutritional Status.

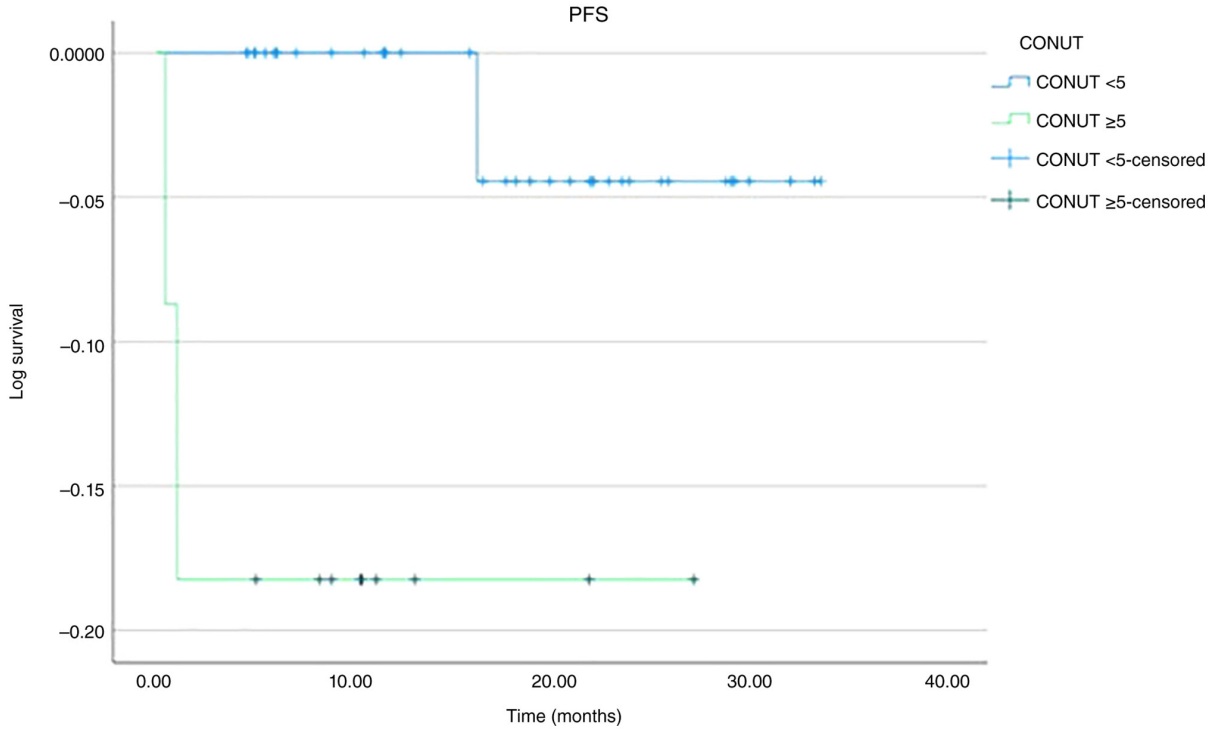

Figure 5. Kaplan-Meier PFS curves according to CONUT score (<5 vs. ≥5) in the low-risk/low-intermediate International Prognostic Index subgroup. Mean PFS was 32.9±0.7 months (95% CI, 31.5-34.4) in the CONUT <5 group and 22.8±2.9 months (95% CI, 17.2-28.4) in the CONUT ≥5 group (log-rank P=0.025). PFS, progression-free survival; CONUT, Controlling Nutritional Status.

optimization was not performed in the present study because of the retrospective design and limited number of events, the use of an established threshold facilitates comparison with previously published literature and enhances the external applicability of the present findings. Furthermore, two recent meta-analyses by Lu *et al* (8) and Zhang *et al* (9) reinforced the association

Table IV. Cox regression analysis of risk factors for overall survival.

	Univariate analysis			Multivariate analysis		
Variable	HR	95% CI	P-value	HR	95% CI	P-value
Age >60 years	3.639	1.364-9.708	0.010	2.979	0.999-8.882	0.050
Advanced stage (Ann-Arbor)	12.873	1.741-95.179	0.012	9.668	1.159-80.646	0.036
Elevated LDH	5.353	1.261-22.730	0.023	2.007	0.433-9.307	0.373
Extranodal >1	1.383	0.577-3.312	0.467	0.737	0.304-1.788	0.500
ECOG PS ≥2	2.793	1.232-6.330	0.014	0.692	0.250-1.918	0.479
CONUT ≥5	3.547	1.578-7.972	0.002	2.584	1.034-6.455	0.042

HR, hazard ratio; CI, confidence interval; LDH, lactate dehydrogenase; ECOG PS, Eastern Cooperative Oncology Group Performance Status; CONUT, Controlling Nutritional Status.

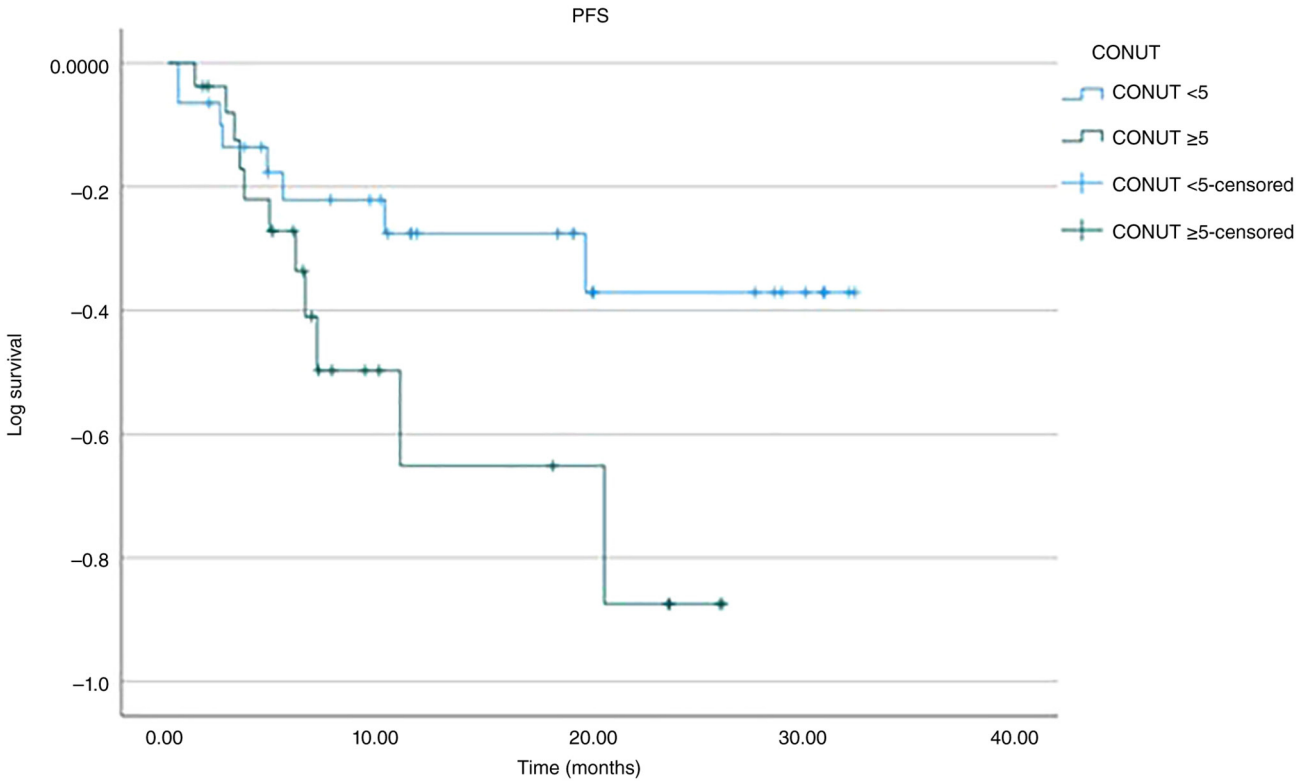

Figure 6. Kaplan-Meier PFS curves according to CONUT score (<5 vs. ≥5) in the high-intermediate/high-risk International Prognostic Index subgroup. Mean PFS was 24.8±2.3 months (95% CI, 20.3-29.4) in the CONUT <5 group and 15.9±2.3 months (95% CI, 11.3-20.4) in the CONUT ≥5 group (log-rank P=0.142). PFS, progression-free survival; CONUT, Controlling Nutritional Status.

between elevated CONUT scores and inferior survival in various hematologic malignancies. A 2025 meta-analysis focusing specifically on DLBCL further confirmed that high CONUT scores are consistently linked to poorer OS across diverse populations, supporting its robustness as a prognostic biomarker (20). Similarly, emerging evidence from other hematologic malignancies has shown that the prognostic value of the CONUT score extends beyond DLBCL, reinforcing the concept that immunonutritional status is a shared determinant of clinical outcomes across hematologic cancers (21). In parallel, recent literature highlights an increasing shift toward incorporating host-related inflammatory and immunonutritional markers, such as the systemic immune-inflammation index, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and lymphocyte-to-monocyte ratio, into prognostic assessments in DLBCL, as these indices have shown strong associations with survival and disease aggressiveness (22,23). Several contemporary studies suggest that combining tumor-derived markers with host fitness parameters significantly improves survival prediction compared with IPI or NCCN-IPI alone (22,23). The present findings align with this evolving paradigm, reinforcing the notion that the CONUT score may capture clinically meaningful vulnerabilities not reflected in standard clinical or pathological indices.

The biological rationale underlying the prognostic value of the CONUT score likely reflects the complex interplay between nutritional depletion, systemic inflammation and immune dysfunction in cancer patients (8,21). Serum albumin, one of the core components of CONUT, serves as a surrogate marker for both nutritional reserve and inflammatory burden, and hypoalbuminemia is widely recognized as a negative prognostic indicator in malignancies. The total lymphocyte count reflects the integrity of host immune competence, and lymphopenia indicates impaired cellular immunity and diminished antitumor surveillance. Low cholesterol levels, the third parameter of the CONUT score, may indicate metabolic exhaustion or cancer-related catabolism. Accumulating evidence suggests that cholesterol plays a critical role in lymphocyte activation, membrane signaling and proliferation (24-26). Taken together, a high CONUT score integrates immunonutritional deficits into a single objective index that reflects host vulnerability and may correspond to a more aggressive disease phenotype.

From a clinical perspective, the CONUT score has several strengths. It is inexpensive, reproducible and derived entirely from laboratory parameters routinely obtained at diagnosis, making it an accessible addition to established prognostic systems such as the IPI and NCCN-IPI. Despite optimal R-CHOP-based management, a substantial proportion of patients continue to experience relapse or refractory disease, emphasizing the need for complementary markers that can refine initial risk stratification. The subgroup analyses of the present study showed that the prognostic impact of CONUT was particularly pronounced in patients with low or low-intermediate IPI scores, suggesting that it can unmask a subset of biologically vulnerable patients who may otherwise be categorized as lower-risk using conventional indices alone. These observations underscore the potential of CONUT to guide individualized surveillance strategies, nutritional interventions and early supportive care planning. Furthermore, its ease of implementation positions the CONUT score as a practical risk assessment tool, even in centers with limited resources.

Given its simplicity, low cost and availability from routinely obtained laboratory parameters, the CONUT score may be considered as part of the baseline assessment of patients with newly diagnosed DLBCL. Patients with elevated CONUT scores may benefit from closer clinical monitoring, early nutritional evaluation and supportive care interventions. However, prospective studies are required before CONUT-guided therapeutic modifications can be recommended in routine clinical practice.

Furthermore, the fact that CONUT remained an independent predictor of OS despite adjustment for key prognostic markers, including stage, LDH and performance status, suggests that immunonutritional status contributes unique biological information beyond traditional tumor-related factors.

This finding raises the possibility that the CONUT score can be incorporated into multimodal prognostic algorithms or used as a screening tool to identify patients who may benefit from early nutritional optimization, metabolic interventions or closer clinical surveillance.

The present study had certain limitations. Its retrospective, single-center design carries an inherent risk of selection and information bias, despite careful efforts to ensure data completeness and accuracy. Although the sample size was comparable to that of previous CONUT studies on DLBCL, it limited the statistical power of subgroup analyses. Additionally, although a cutoff value of 5 was adopted in accordance with prior research [Go *et al* (19) and Wang *et al* (17)], variability in CONUT thresholds across studies complicates direct comparison. While most published studies in DLBCL have used a cutoff value of 5, Nagata *et al* (27) used a cutoff value of 4, whereas Akgün Çağlıyan *et al* (28) identified an optimal cutoff value of 1.5 by receiver operating characteristic analysis and classified patients using a threshold of ≥2, highlighting the lack of a universally accepted CONUT cutoff in patients with DLBCL. The median follow-up duration was relatively short, which may have limited the assessment of long-term survival outcomes and late relapses. Due to the relatively short follow-up period and the concentration of mortality events within the first 24 months, formal landmark analyses at 12 and 24 months were not performed. CONUT was assessed only at baseline, and dynamic changes during treatment, which may also have prognostic value, were not evaluated in this study. Larger prospective multicenter studies with longer follow-up are needed to validate the present findings, establish standardized cutoff values and determine whether targeted nutritional or immunological interventions can improve patient outcomes.

In conclusion, the current study demonstrated that a high pre-treatment CONUT score (≥5) is significantly associated with adverse clinical features and predicts inferior OS and PFS in patients with DLBCL. Given its simplicity, low cost and availability in routine clinical practice, the CONUT score may serve as a valuable adjunct to established prognostic systems. Integrating this tool into baseline assessment could enhance risk stratification and help identify patients who may benefit from early nutritional and supportive care. Future prospective studies are warranted to determine whether CONUT-guided nutritional or host-directed interventions can improve survival outcomes in DLBCL.

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Availability of data and materials

The data generated in the present study are not publicly available due to confidentiality restrictions but can be obtained from the corresponding author upon reasonable request and ethics approval.

Authors' contributions

SS, BAK and AD contributed to the study conception, data collection and drafting of the manuscript. SS and HBAÖ

performed the statistical analysis. SS and HBAÖ confirm the authenticity of all the raw data. SS, BAK, AD, HBAÖ, KA and AKG contributed to data interpretation and manuscript revision. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki (1964) and its later amendments. Ethical approval was obtained from the Etlik City Hospital Ethics Committee (approval no. AEŞH-BADEK1-2025-522). The requirement for informed consent was waived due to the retrospective design and the use of anonymized data.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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