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Prognostic value of the controlling nutritional status (CONUT) score in patients with diffuse large B-cell lymphoma: a meta-analysis

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Abstract

Background The significance of the controlling nutritional status (CONUT) score in predicting the prognostic outcomes of diffuse large B-cell lymphoma (DLBCL) has been widely explored, with conflicting results. Therefore, the present meta-analysis aimed to identify the prognostic significance of the CONUT in DLBCL by aggregating current evidence.

Methods The Web of Science, PubMed, Embase, CNKI and Cochrane Library databases were searched for articles from inception to October 15, 2024. The prognostic value of CONUT for DLBCL was analyzed by determining the pooled hazard ratios (HRs) with 95% confidence intervals (CIs). The Newcastle–Ottawa Scale (NOS) was used to analyze study quality.

Results Eight studies including 2687 cases were included in this work. The NOS scores of these studies were 7–9 (median, 8), demonstrating high quality. Our analyses revealed that an elevated CONUT score significantly predicted poor overall survival (OS) (HR = 1.63, 95%CI = 1.29–2.05, $p < 0.001$) and inferior progression-free survival (PFS) (HR=1.22, 95%CI = 1.12–1.33, $p < 0.001$) in patients with DLBCL. Further, the elevated CONUT score showed a significant correlation with the following clinicopathological factors in DLBCL: Ann Arbor stage III-IV, Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 2–4, presence of extranodal disease, ≥high intermediate National Comprehensive Cancer Network International Prognostic Index (NCCN IPI), presence of B symptoms, elevated lactose dehydrogenase (LDH) levels, and presence of bone marrow infiltration.

Conclusions An increased CONUT score was dramatically associated with poor OS and PFS in patients with DLBCL, as well as with clinicopathological characteristics representing DLBCL tumor development.

Keywords Diffuse large B-cell lymphoma, Prognosis, Meta-analysis, Blood-derived parameter, Survival, Controlling nutritional status (CONUT) score

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Introduction

Diffuse large B-cell lymphoma (DLBCL) is a form of non-Hodgkin lymphoma (NHL) with high aggressiveness and heterogeneity [1]. In 2022, there were 85,200 new cases and 41,600 deaths caused by lymphoma in China [2]. DLBCL accounts for approximately 30% of NHL cases diagnosed annually and over 1/4 of lymphomas across the USA [3]. The most common symptoms of DLBCL are rapidly progressive lymphadenopathy, B-symptoms, and higher lactate dehydrogenase (LDH) levels [4]. Approximately 60% of DLBCL patients are managed with the rituximab, cyclophosphamide, adriamycin, vincristine, and prednisone (R-CHOP) regimen [5]. Most patients with DLBCL respond well to first-line treatment; however, 30–40% fail to achieve remission or relapse [6, 7]. Therefore, effective prognostic marker for DLBCL must be urgently identified to enhance survival outcomes.

Prior studies have shown that inflammation and nutritional status can influence the prognosis of patients with cancer [8]. Previous studies have further indicated that a series of nutrition-related indexes, including the albumin-to-globulin ratio [9], prognostic nutritional index (PNI) [10], geriatric nutritional risk index (GNRI) [11], fibrinogen-to-albumin ratio [12], and skeletal muscle index (SMI) [13] are significant prognostic biomarkers of different tumors [14–18]. The controlling nutritional status (CONUT) score is a new nutritional parameter which was first proposed in 2005 [19]. CONUT assesses serum albumin, total lymphocyte quantity, and total cholesterol, to yield a total score of 0–12 (Table 1). Higher CONUT scores have been widely suggested to be associated with poor tumor prognosis in many malignancies, including non-small cell lung cancer [20], multiple myeloma [21], prostate cancer [22], cervical cancer [23], and renal cell carcinoma [24]. The value of CONUT in predicting DLBCL prognosis has been previously assess; however, the results remain inconsistent [25–32]. In certain studies, a high CONUT score was identified as a significant prognostic factor of DLBCL [25, 28, 32]; however, others failed to identify any such correlation [26]. Consequently, we performed a meta-analysis to analyze the utility of the CONUT score in predicting DLBCL patient prognosis.

Table 1 The CONUT scoring system

Variables	Degree of undernutrition			
	Normal	Light	Moderate	Severe
Serum albumin (g/dL)	≥ 3.5	3.0-3.4	2.5–2.9	< 2.5
Score	0	2	4	6
Total lymphocyte count (mm^3)	≥ 1600	1200–1599	800–1199	< 800
Score	0	1	2	3
Total cholesterol (mg/dL)	≥ 180	140–179	100–139	< 100
Score	0	1	2	3
CONUT score (total)	0–1	2–4	5–8	9–12

CONUT, controlling nutritional status

Materials and methods

Study guideline

This work was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [33]. The PRISMA checklist is provided in Supplementary file 1. This meta-analysis was registered in INPLASY under the number INPLASY2024120090 (The DOI number is https://doi.org/10.37766/inplasy2024.12.0090).

Search strategy

The PubMed, Web of Science, Embase, Cochrane Library, and China National Knowledge Infrastructure (CNKI) databases were searched from inception to October 15, 2024 using the following search strategy: (controlling nutritional status score OR controlling nutritional status OR CONUT) AND (lymphoma large B-cell OR diffuse large B-cell lymphoma OR lymphoma OR DLBCL). This search was conducted by combining keywords with free words. No limitation was placed on the language of publication. The detailed search strategies for each database are provided in Supplementary file 2. To identify other relevant studies, the reference lists of studies selected by electronic searches were also searched manually.

Eligibility standards

The eligibility criteria for studies were as follows: (1) pathological diagnosis of DLBCL; (2) studies investigating the relationship between the CONUT score and DLBCL prognosis; (3) studies with hazard ratios (HRs) with 95% confidence intervals (CIs) could be obtained or Kaplan–Meier survival curves; (4) a CONUT cut-off value was used to stratify patients with low/high CONUT.

The exclusion criteria were as follows: (1) reviews, meeting abstracts, comments, and case reports; (2) those having duplicate cases; and (3) animal studies.

Information acquisition and quality analysis

Two reviewers (JZ and YW) reviewed and obtained data from the qualified articles. Any dispute was settled through negotiation until a consensus was reached. Data on author, year, age, sex, sample size, study period, study design, study center, Ann Arbor stage, treatment, threshold, threshold determination, follow-up, survival analysis types, survival outcomes, and HRs with 95%CIs were acquired. Overall survival (OS) and progression-free survival (PFS) were the primary and secondary outcomes, respectively. OS was defined as the time from diagnosis to death from any causes or the last follow-up. PFS was defined as the time from the date of diagnosis until the last follow-up, documented progression, relapse, or death from any cause. HRs for OS and PFS were derived from the HR for high vs. low CONUT in the included

studies. Higher lactose dehydrogenase (LDH) levels were defined as ≥2U/L [27]. The definitions of each stage on the "Ann Arbor", "National Comprehensive Cancer Network International Prognostic Index (NCCN IPI)", and "Eastern Cooperative Oncology Group Performance Status (ECOG PS)" criteria are standard concepts which can be found at: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1480. The Newcastle–Ottawa Scale (NOS) was applied to analyze the study quality [34]; this scale evaluates the study design in three ways: comparability, population selection, and outcome. NOS scores range from 0 to 9, with a score ≥6 points indicating high-quality.

Statistical analysis

Pooled HRs with 95%CIs were analyzed to assess the prognostic value of CONUT for DLBCL. The between-study heterogeneity was assessed using the I^2 statistics as well as Cochran's Q-test. $I^2 > 50\%$ or a p-value < 0.10 (Q-test) indicates obvious heterogeneity, in which case a random-effects model was utilized; otherwise, the fixed-effects model was selected. Subgroup analyses were performed to investigate the prognostic value of CONUT in different DLBCL population groups. The relation of CONUT with patient clinicopathological factors was assessed through pooled odds ratios (ORs) with 95%CIs. Sensitivity analysis was performed by eliminating one article and calculating new HRs to assess their robustness and stability. We further adopted Funnel plot, Begg's and Egger's tests to evaluate publication bias in the enrolled articles. Further, we employed Stata version 12.0 software (Stata Corp, College Station, Texas, USA) in statistical analysis. Statistical significance was set at $P < 0.05$.

Results

Literature search process

The primary literature search identified 163 studies, of which 118 were retained after duplicate removal (Fig. 1). An additional 106 articles were excluded after title- and abstract-screening due to irrelevance or animal studies. Subsequently, the full-texts of 12 articles were analyzed, among which four were discarded due to lacking survival data ($n = 2$), irrelevant to DLBCL ($n = 1$), or not investigating CONUT ($n = 1$). Eventually, eight studies comprising

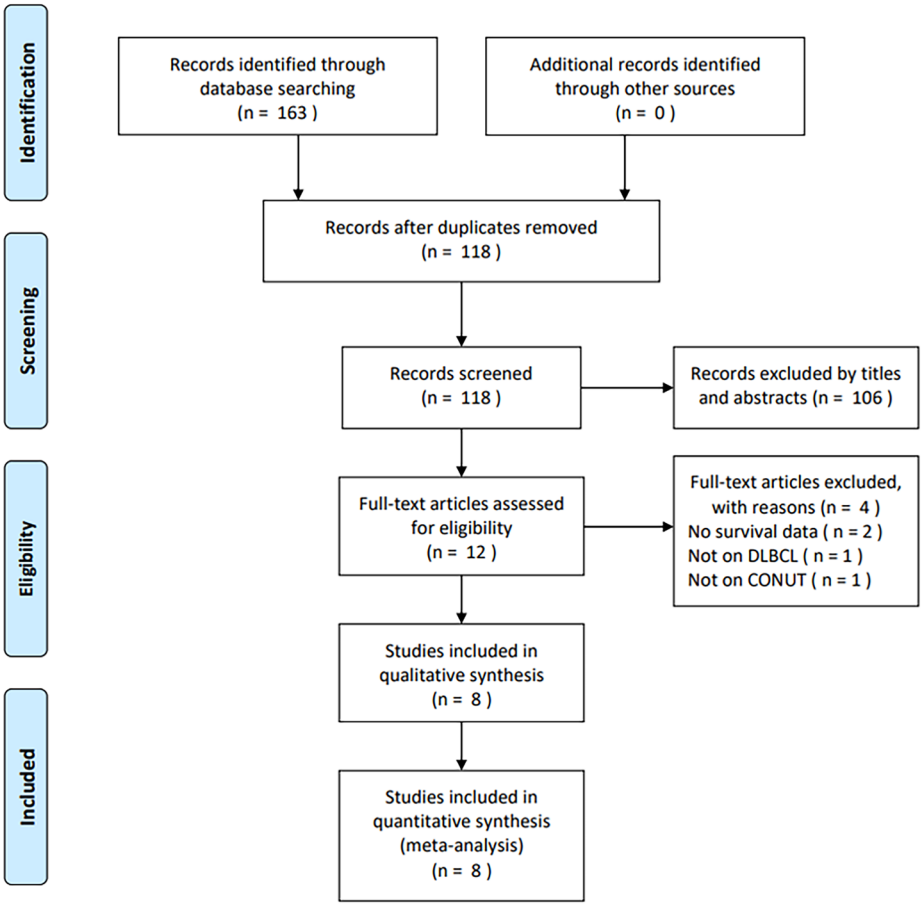

Fig. 1 Study selection flow diagram according to PRISMA guideline

2687 cases [25–32] were included in the present study (Fig. 1).

Included study characteristics

Table 2 presents the baseline study characteristics of the enrolled participants. All studies were published in 2020–2024, including three performed in Japan [25, 26, 31], two in China [29, 32], two in Turkey [27, 28], and one in Korea [30]. There were six English-language [25–28, 30, 31] and two Chinese-language [29, 32] articles, with sample sizes of 81–654 (median, 285.5). The enrolled articles had a retrospective design. There were six single center articles [26–31] and two multicenter studies [25, 32]. Seven studies included DLBCL cases of Ann Arbor stage I-IV [25–31], while one enrolled only stage III-IV cases [32]. Six articles managed patients using R-CHOP regimen [25, 27–30, 32], and two studies used the R-CHOP/ rituximab, cyclophosphamide, tetrahydropyranyl-adriamycin, vincristine, and prednisone (R-THP-COP) protocol [26, 31]. Three studies used a cut-off value of ≥ 5 [25, 28, 30], and one each applied ≥ 2 [27], ≥ 3 [31], ≥ 4 [26], ≥ 6 [29], and ≥ 7 [32], respectively. Six articles utilized receiver operating characteristic (ROC) curve to determine cut-off values [25–28, 31, 32], while two referred to the literature [29, 30]. Seven [25–28, 30–32] and four [26, 27, 29, 30] studies reported the relationship between CONUT and OS and PFS in patients with DLBCL, respectively. Six articles obtained HRs with 95%CIs through multivariate regression [26–31], while two studies used univariate analysis [25, 32]. The NOS scores of enrolled studies were 7–9 (median, 8), demonstrating high quality (Table 2).

CONUT and OS

Seven studies involving 2600 patients [25–28, 30–32] reported the utility of CONUT in predicting the OS of DLBCL. We further used the random-effects model giving obvious heterogeneity ($I^2 = 87.6\%$, $p < 0.001$). Based on the combined results, an elevated CONUT score was found to markedly predict poorer OS of DLBCL (HR = 1.63, 95%CI = 1.29–2.05, $p < 0.001$; Fig. 2; Table 3). As demonstrated in the subgroup analyses, the significant prognostic function of CONUT for OS was not influenced by study center, Ann Arbor stage, threshold, threshold measurement, or survival analysis (Table 3). Moreover, subgroup analyses also indicated that CONUT apparently forecast the OS in subgroups of Chinese and Korean studies, sample size ≥ 300, and R-CHOP treatment (all $p < 0.05$; Table 3).

CONUT and PFS

Four studies comprising 1134 patients [26, 27, 29, 30] showed an association between CONUT and PFS in DLBCL. Due to a lack of any obvious heterogeneity ($I^2 = 0$, $p = 0.548$), a fixed-effects model was applied

Table 2 Basic characteristics of included studies in this meta-analysis

Study	Year	Country	Sample size	Gender (M/F)	Age (years) Median(range)	Study period	Study center	Ann Arbor stage	Treatment regimens	Cut-off value	Cut-off determination	Follow-up (months) Median(range)	Survival outcomes	Survival analysis	NOS score
Matsukawa, T.	2020	Japan	615	337/278	69(20–97)	2008–2018	Multicenter	I-IV	R-CHOP	≥ 5	ROC curve	1–60	OS	Univariate	9
Nagata, A.	2020	Japan	476	261/215	68.5(27–97)	2004–2017	Single center	I-IV	R-CHOP/ R-THP-COP	≥ 4	ROC curve	45(1-177)	OS, PFS	Multivariate	8
Akgün Çağlıyan, G.	2021	Turkey	266	135/131	64(23–91)	2012–2020	Single center	I-IV	R-CHOP	≥ 2	ROC curve	51(1-190)	OS, PFS	Multivariate	8
Baysal, M.	2021	Turkey	81	42/39	63.5(25–93)	2015–2019	Single center	I-IV	R-CHOP	≥ 5	ROC curve	1–50	OS	Multivariate	7
Yao, J.	2021	China	87	49/38	52(21–77)	2012–2019	Single center	I-IV	R-CHOP	≥ 6	Literature	1-100	PFS	Multivariate	8
Go, S. I.	2023	Korea	305	175/130	63	2004–2022	Single center	I-IV	R-CHOP	≥ 5	Literature	106(1-192)	OS, PFS	Multivariate	8
Kaneda, Y.	2024	Japan	203	120/83	74(65–93)	2004–2019	Single center	I-IV	R-CHOP/ R-THP-COP	≥ 3	ROC curve	48(1-180)	OS	Multivariate	8
Shan, H.	2024	China	654	368/286	63	2009–2022	Multicenter	III-IV	R-CHOP	≥ 7	ROC curve	38.1(1-150)	OS	Univariate	9

M, male; F, female; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R-THP-COP, rituximab, cyclophosphamide, tetrahydropyranyl-adriamycin, vincristine, and prednisone; ROC, receiver operating characteristic; OS, overall survival; PFS, progression-free survival; NOS, Newcastle-Ottawa Scale

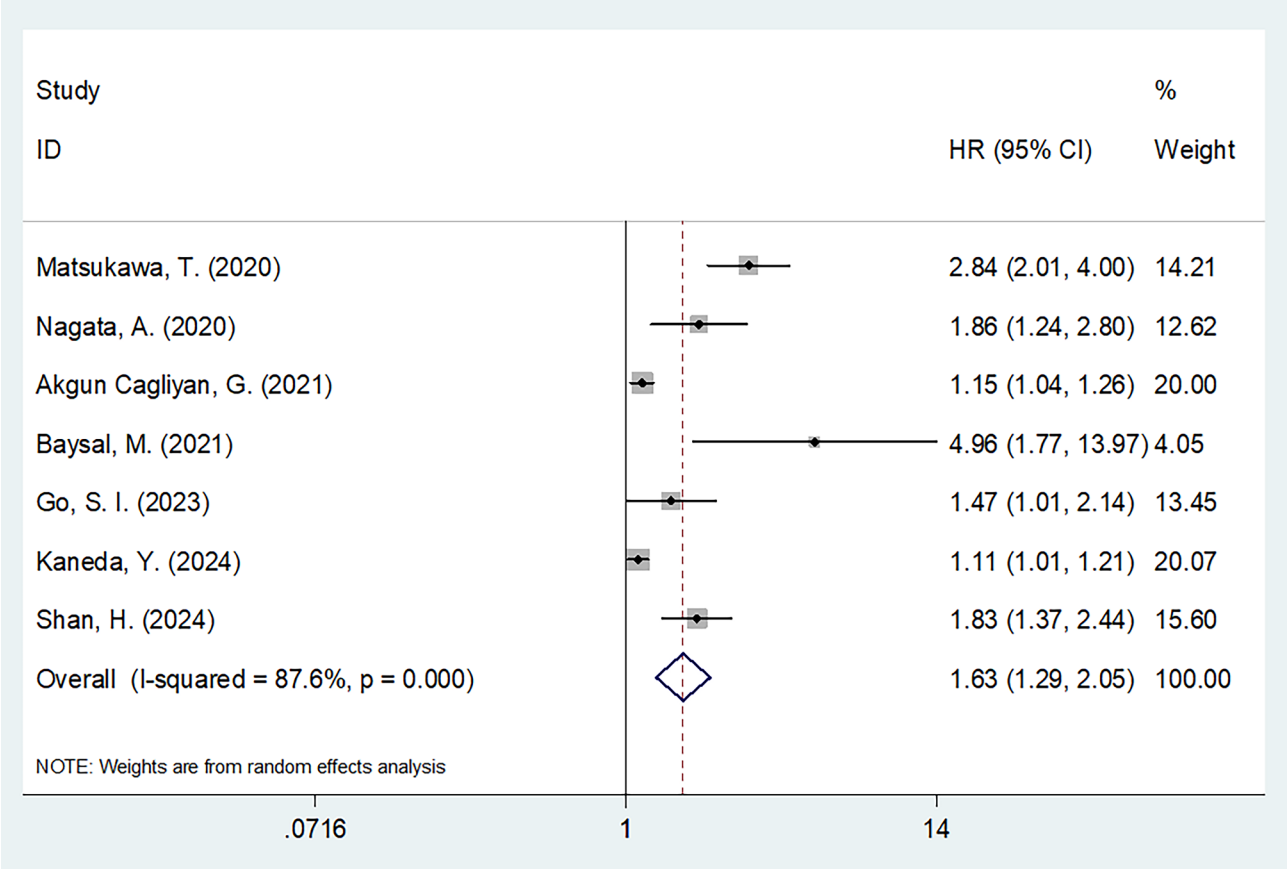

Fig. 2 Meta-analyses of association between CONUT score and OS in DLBCL

(Fig. 3). Based on the pooled results, a higher CONUT was found to significantly predict poor PFS (HR = 1.22, 95%CI = 1.12–1.33, $p < 0.001$) in DLBCL (Fig. 3; Table 4). Subgroup analyses further showed that an elevated CONUT still significantly predicted inferior PFS, despite differences in sample size, threshold, or threshold determination (Table 4). Furthermore, a high CONUT was still markedly correlated with poor PFS in patients with DLBCL receiving R-CHOP therapy ($p < 0.05$; Table 4).

Relation between CONUT and clinicopathological features

Five articles including 1749 cases [25–27, 29, 30] reported on the association of CONUT with patient clinicopathological characteristics. From the combined data, the greater CONUT score was evidently correlated with the following clinicopathological factors in DLBCL: Ann Arbor stage III-IV (OR = 4.07, 95%CI = 3.21–5.15, $p < 0.001$), ECOG PS of 2–4 (OR = 3.67, 95%CI = 2.31–5.84, $p < 0.001$), presence of extranodal disease (OR = 2.99, 95%CI = 2.15–4.17, $p < 0.001$), ≥high intermediate National Comprehensive Cancer Network International Prognostic Index (NCCN IPI) (OR = 7.36, 95%CI = 5.66–9.57, $p < 0.001$), B symptoms (OR = 4.65, 95%CI = 3.35–6.45, $p < 0.001$), higher lactose dehydrogenase (LDH) levels (OR = 3.73, 95%CI = 2.80–4.98, $p < 0.001$), and bone marrow infiltration (OR = 3.84, 95%CI = 1.91–7.75, $p < 0.001$) (Figs. 4 and 5, and Table 5). However, the CONUT score did not show any marked correlation with sex (OR = 1.10, 95%CI = 0.76–1.59, $p = 0.623$; Fig. 4; Table 5).

Sensitivity analysis

We later conducted sensitivity analysis by sequentially removing individual studies to assess whether our combined results were stable. Neither the OS nor PFS results changed significantly after excluding any individual article, verifying that our meta-analysis findings were robust and reliable (Fig. 6).

Publication bias

We utilized Funnel plots, Begg's, and Egger's tests to analyze possible publication bias. Symmetrical Funnel plots with p values > 0.05 indicated the absence of publication bias. Overall, neither OS ($p = 0.230$, $p = 0.118$ by Begg's and Egger's tests) or PFS ($p = 1.000$, $p = 0.227$ by Begg's and Egger's tests) showed any obvious publication bias (Fig. 7).

Table 3 Subgroup analysis of prognostic value of CONUT score for OS in patients with DLBCL

Subgroups	No. of studies	No. of patients	Effects model	HR (95%CI)	*p*	Heterogeneity I^2(%) Ph	
Total	7	2600	Random	1.63(1.29–2.05)	< 0.001	87.6	< 0.001
Country							
China	1	654	-	1.83(1.36–2.44)	< 0.001	-	-
Japan	3	1294	Random	1.77(0.94–3.34)	0.075	93.6	< 0.001
Turkey	2	347	Random	2.17(0.53-9.00)	0.284	86.9	0.006
Korea	1	305	-	1.47(1.01–2.14)	0.043	-	-
Sample size							
< 300	3	550	Random	1.18(0.99–1.40)	0.067	75.4	0.017
≥ 300	4	2050	Random	1.95(1.49–2.55)	< 0.001	57.3	0.071
Study center							
Single center	5	1331	Random	1.30(1.09–1.56)	0.004	73.8	0.004
Multicenter	2	1269	Random	2.25(1.46–3.47)	< 0.001	72.9	0.055
Ann Arbor stage							
I-IV	6	1946	Random	1.58(1.24–2.02)	< 0.001	87.7	< 0.001
III-IV	1	654	-	1.83(1.36–2.44)	< 0.001	-	-
Treatment							
R-CHOP	5	1921	Random	1.89(1.24–2.88)	0.003	89.5	< 0.001
R-CHOP/R-THP-COP	2	679	Random	1.38(0.84–2.28)	0.206	83.0	0.015
Cut-off value							
< 5	3	945	Random	1.18(1.03–1.35)	0.015	66.2	0.052
≥ 5	4	1655	Random	2.16(1.48–3.15)	< 0.001	69.7	0.019
Cut-off determination							
ROC curve	6	2295	Random	1.66(1.29–2.14)	< 0.001	89.4	< 0.001
Literature	1	305	-	1.47(1.01–2.14)	0.043	-	-
Survival analysis							
Univariate	2	1269	Random	2.25(1.46–3.47)	< 0.001	72.9	0.055
Multivariate	5	1331`	Random	1.30(1.09–1.56)	0.004	73.8	0.004

R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R-THP-COP, rituximab, cyclophosphamide, tetrahydropyranyl-adriamycin, vincristine, and prednisone; ROC, receiver operating characteristic; OS, overall survival; CONUT, controlling nutritional status; DLBCL, diffuse large B-cell lymphoma

Discussion

Gene expression analysis has identified two separate molecular DLBCL subtypes: the germinal center B-cell–like (GCB) and the activated B-cell–like (ABC) subtypes, with 10 to 15% of cases remaining unclassifiable [1]. The ABC subtype of DLBCL involves continuous B-cell receptor signaling and nuclear factor κB activation, whereas the GCB subtype is characterized by the expression of genes typical of germinal center B cells, such as BCL6 and EZH2 [35, 36]. This phenotypic difference is important, as targeted treatments may be more effective in one subtype.

The role of CONUT in predicting DLBCL prognosis has been previously analyzed; however, conclusions remain inconsistent. In this meta-analysis, we aggregated the data of 8 articles with 2687 patients [25–32], finding that a higher CONUT score evidently forecast poor OS and inferior PFS in patients with DLBCL. Additionally, an elevated CONUT score was remarkable correlated with advanced stage, extranodal disease, high NCCN IPI, presence of B symptoms, high LDH levels and bone marrow infiltration in DLBCL. Collectively, the CONUT score clearly predicted poor long- and short-term survival outcomes of DLBCL. This meta-analysis provides the first investigation of the prognostic significance of the CONUT score in patients with DLBCL.

CONUT assesses three factors: albumin, cholesterol, and lymphocyte count [19], with higher CONUT scores resulting from low contents of the three components. The exact mechanisms related to the prognostic value of CONUT for DLBCL remain to be further explored, but can be interpreted as follows. First, in the plasma, albumin is the most abundant protein and represents both the nutritional status of the human body and the systemic inflammation [37]. Cancer patients with hypoalbuminemia may suffer from immune deficiency, resulting in a reduced therapeutic effect and a consequent increased mortality [38]. Studies in the literature have indicated that patient malnutrition correlates with tumor progression and invasion, indicating that nutrition-related factors may affect malignancy prognosis [39]. Second, lymphocytes show anticancer activity and stimulate anticancer responses by diffusing in tumor-infiltrating lymphocytes [40]. Lymphocytes are the most important

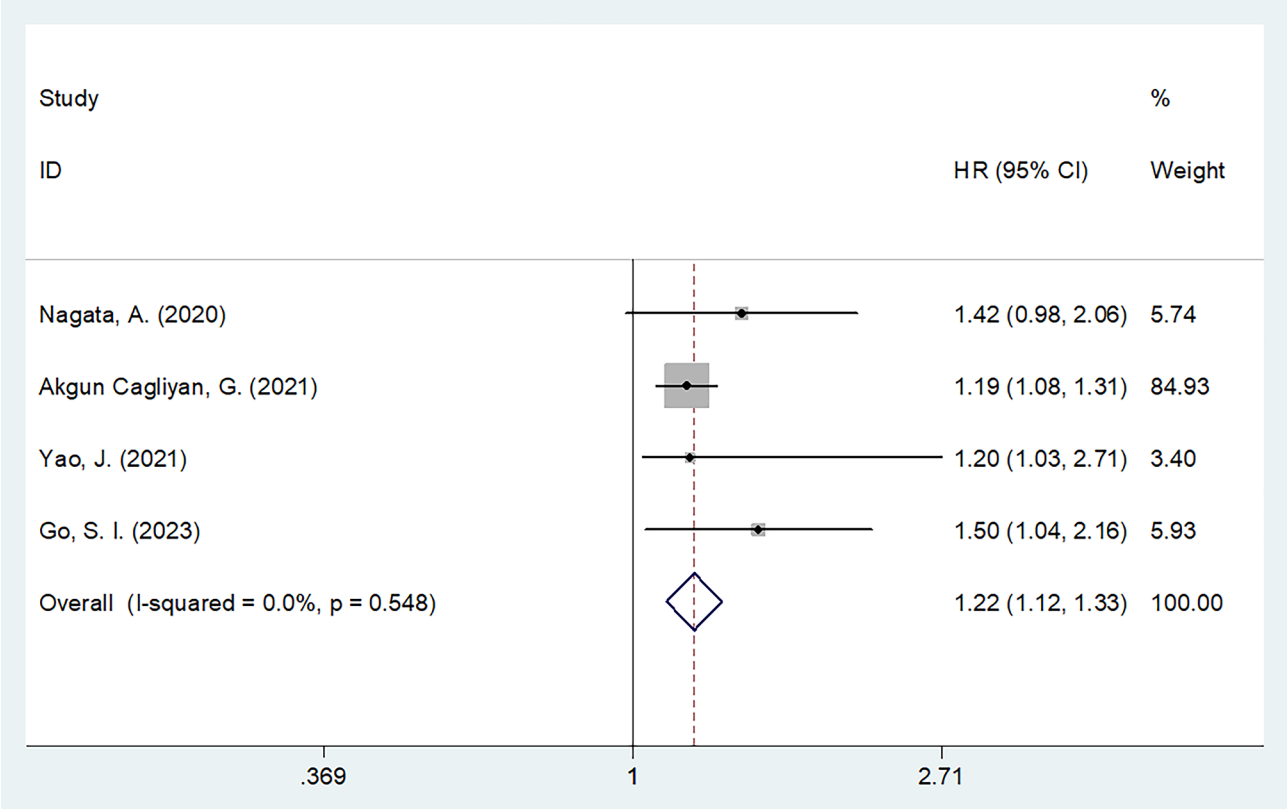

Fig. 3 Meta-analyses of association between CONUT score and PFS in DLBCL

Table 4 Subgroup analysis of prognostic value of CONUT score for PFS in patients with DLBCL

Subgroups	No. of studies	No. of patients	Effects model	HR (95%CI)	*p*	Heterogeneity I^2(%)	Ph
Total	4	1134	Fixed	1.22(1.12–1.33)	< 0.001	0	0.548
Country							
China	1	87	-	1.20(0.74–1.95)	0.453	-	-
Japan	1	476	-	1.42(0.98–2.06)	0.064	-	-
Turkey	1	266	-	1.19(1.08–1.31)	< 0.001	-	-
Korea	1	305		1.50(1.04–2.16)	0.030	-	-
Sample size							
< 300	2	353	Fixed	1.19(1.08–1.31)	< 0.001	0	0.965
≥ 300	2	781	Fixed	1.46(1.12–1.89)	0.004	0	0.839
Treatment							
R-CHOP	3	658	Fixed	1.21(1.10–1.32)	< 0.001	0	0.488
R-CHOP/R-THP-COP	1	476	-	1.42(0.98–2.06)	0.064	-	-
Cut-off value							
< 5	2	742	Fixed	1.20(1.10–1.32)	< 0.001	0	0.367
≥ 5	2	392	Fixed	1.38(1.03–1.85)	0.029	0	0.476
Cut-off determination							
ROC curve	2	742	Fixed	1.20(1.10–1.32)	< 0.001	0	0.367
Literature	2	392	Fixed	1.38(1.03–1.85)	0.029	0	0.476

R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R-THP-COP, rituximab, cyclophosphamide, tetrahydropyranyl-adriamycin, vincristine, and prednisone; ROC, receiver operating characteristic; PFS, progression-free survival; CONUT, controlling nutritional status; DLBCL, diffuse large B-cell lymphoma

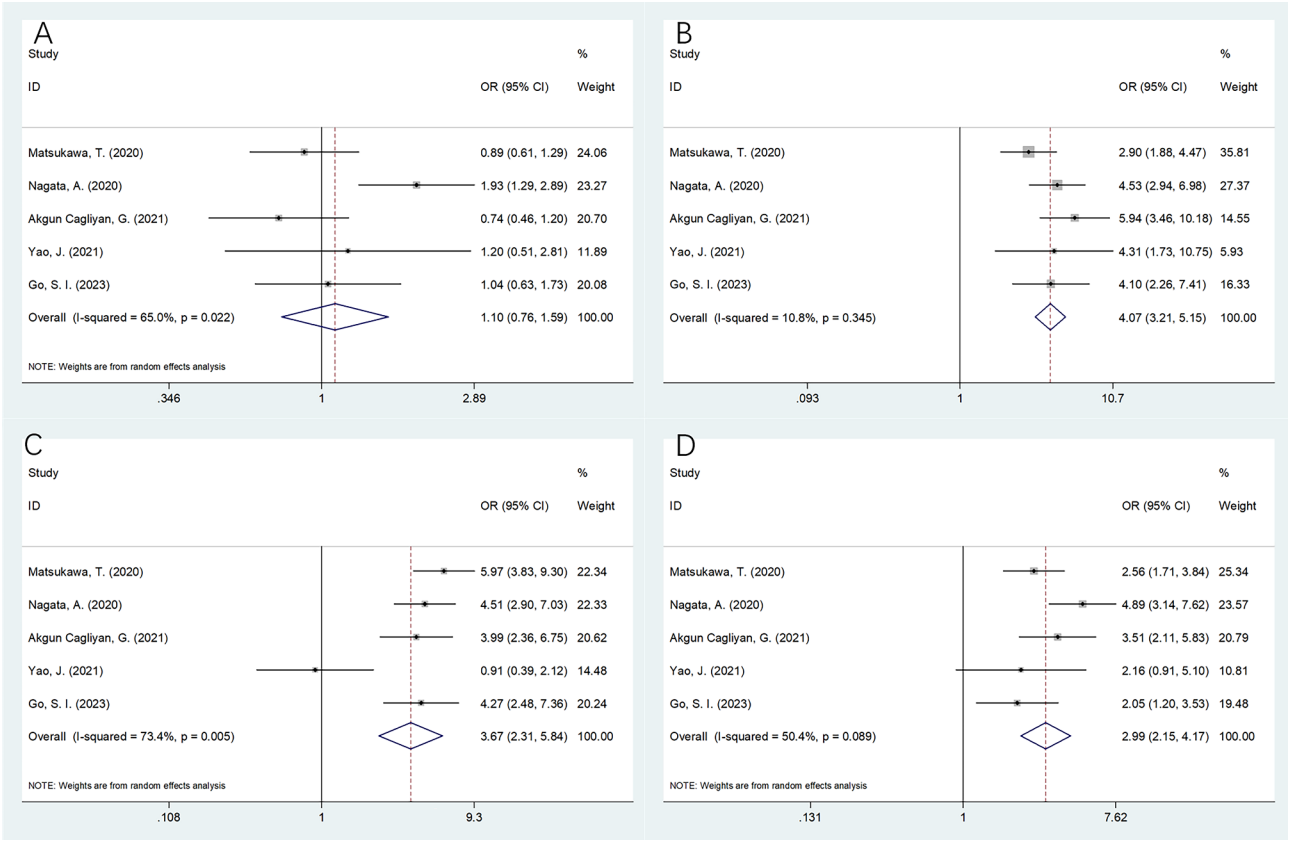

Fig. 4 The correlation between CONUT score and clinicopathological features of DLBCL. (**A**) Gender (male vs. female); (**B**) Ann Arbor stage (III-IV vs. I-II); (**C**) ECOG PS (2–4 vs. 0–1); and (**D**) Extranodal disease (yes vs. no)

antigen-responding immune cells, initiating specific immune responses following stimulation, thereby inhibiting tumor growth and improving tumor prognosis [41]. Intra-tumoral CD8 + T lymphocytes are associated with better OS, which can independently predict prognosis [42]. Third, cholesterol is predominantly synthesized in the liver, but also circulates in blood as low-density lipoprotein (LDL). LDL receptors (LDLRs) are distributed in either normal cell or tumor cell surface. The function of cell membranes, which aid in the transmission of signals, is dependent upon cholesterol [43]. A decrease in cholesterol levels can influence the antitumor activity of immune-competent cells. Further, previous studies have indicated an association between high LDL levels and low tumor survival [44]. Consequently, CONUT is considered a reliable prognostic marker of cancer prognosis.

The CONUT score has been demonstrated to have a prognostic value in various cancers through prior meta-analyses [45–49]. As shown by Peng et al., a higher CONUT score is associated with dismal OS in breast cancer in one meta-analysis involving 9 studies [45]. In one meta-analysis with 3783 patients, Lv et al. further reported that a high pretreatment CONUT score predicted poor PFS and cancer-specific survival (CSS) in esophageal cancer [46]. In another meta-analysis of 1409 cases, a high CONUT score showed a strong correlation with worse OS and recurrence-free survival (RFS) in biliary tract cancer [47]. According to Niu et al., one meta-analysis enrolling 3562 patients found that higher CONUT scores are associated with dismal survival in urological cancer patients [48]. Further, Takagi et al., showed that a higher CONUT score predicted dismal OS, CSS, and RFS in colorectal cancer surgical patients in a meta-analysis comprising 9 studies [49].

This work has some limitations. Firstly, most enrolled articles were from Asian countries. Consequently, the findings are more applicable to Asian DLBCL cases. Secondly, all of the included studies had a retrospective design. Consequently, inherent heterogeneity may exist. Thirdly, the thresholds of a high CONUT score remain non-uniform among eligible articles. Fourth, only one of the studies accounts for 84% of the weight in the PFS analysis, meaning that the combined results largely mirror the outcomes of this single study (Fig. 3). Therefore, large-scale multi-regional prospective studies are warranted to validate our meta-analysis findings. Moreover, the accurate mechanisms for the prognostic value of CONUT in DLBCL should be further investigated in future studies.

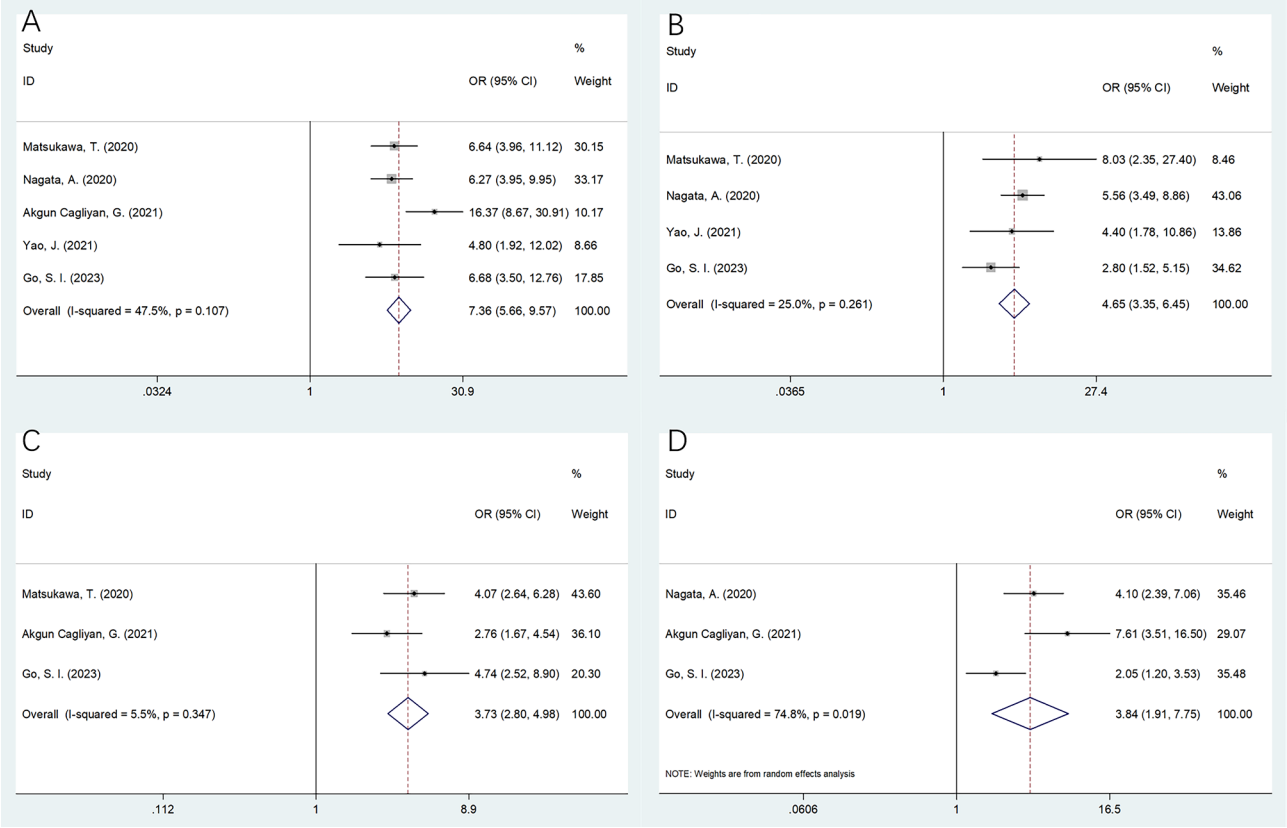

Fig. 5 The correlation between CONUT score and clinicopathological features of DLBCL. (**A**) NCCN IPI (≥ high intermediate vs. < high intermediate); (**B**) Presence of B symptoms (yes vs. no); (**C**) LDH (elevated vs. normal); and (**D**) Bone marrow infiltration (yes vs. no)

Table 5 The association between CONUT score and clinicopathological features in patients with DLBCL

Clinicopathological factors	No. of studies	No. of patients	Effects model	OR (95%CI)	*p*	Heterogeneity I^2(%)	Ph
Gender (male vs. female)	5	1749	Random	1.10(0.76–1.59)	0.623	65.0	0.022
Ann Arbor stage (III-IV vs. I-II)	5	1749	Fixed	4.07(3.21–5.15)	< 0.001	10.8	0.345
ECOG PS (2–4 vs. 0–1)	5	1749	Random	3.67(2.31–5.84)	< 0.001	73.4	0.005
Extranodal disease (yes vs. no)	5	1749	Random	2.99(2.15–4.17)	< 0.001	50.4	0.089
NCCN IPI (≥ high intermediate vs. < high intermediate)	5	1749	Fixed	7.36(5.66–9.57)	< 0.001	47.5	0.107
Presence of B symptoms (yes vs. no)	4	1483	Fixed	4.65(3.35–6.45)	< 0.001	25.0	0.261
LDH (elevated vs. normal)	3	1186	Fixed	3.73(2.80–4.98)	< 0.001	5.5	0.347
Bone marrow infiltration (yes vs. no)	3	1047	Random	3.84(1.91–7.75)	< 0.001	74.8	0.019

ECOG PS, Eastern Cooperative Oncology Group performance status; NCCN IPI, National Comprehensive Cancer Network International Prognostic Index; LDH, lactose dehydrogenase

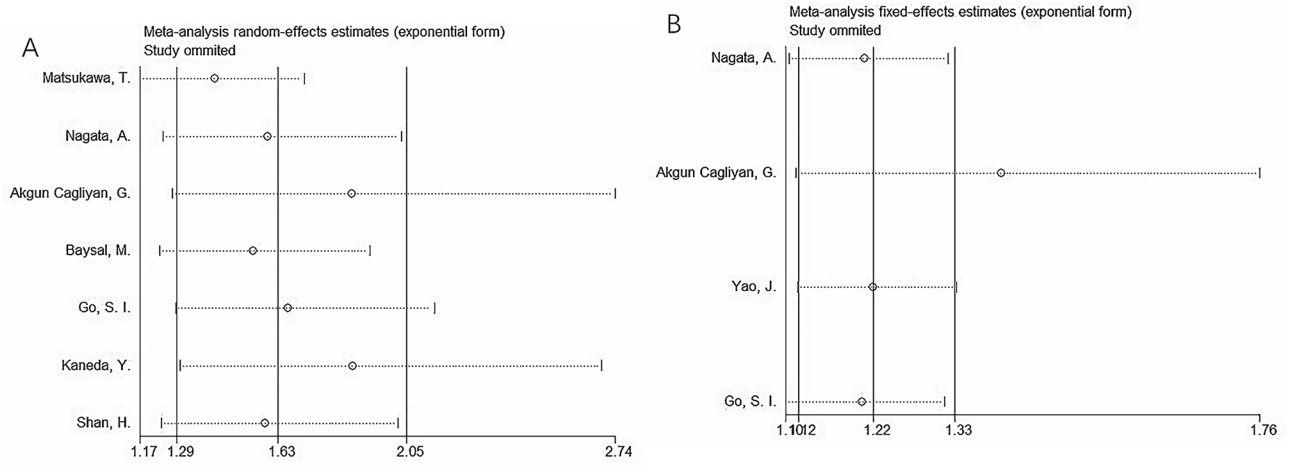

Fig. 6 Sensitivity analysis. (**A**) OS and (**B**) PFS

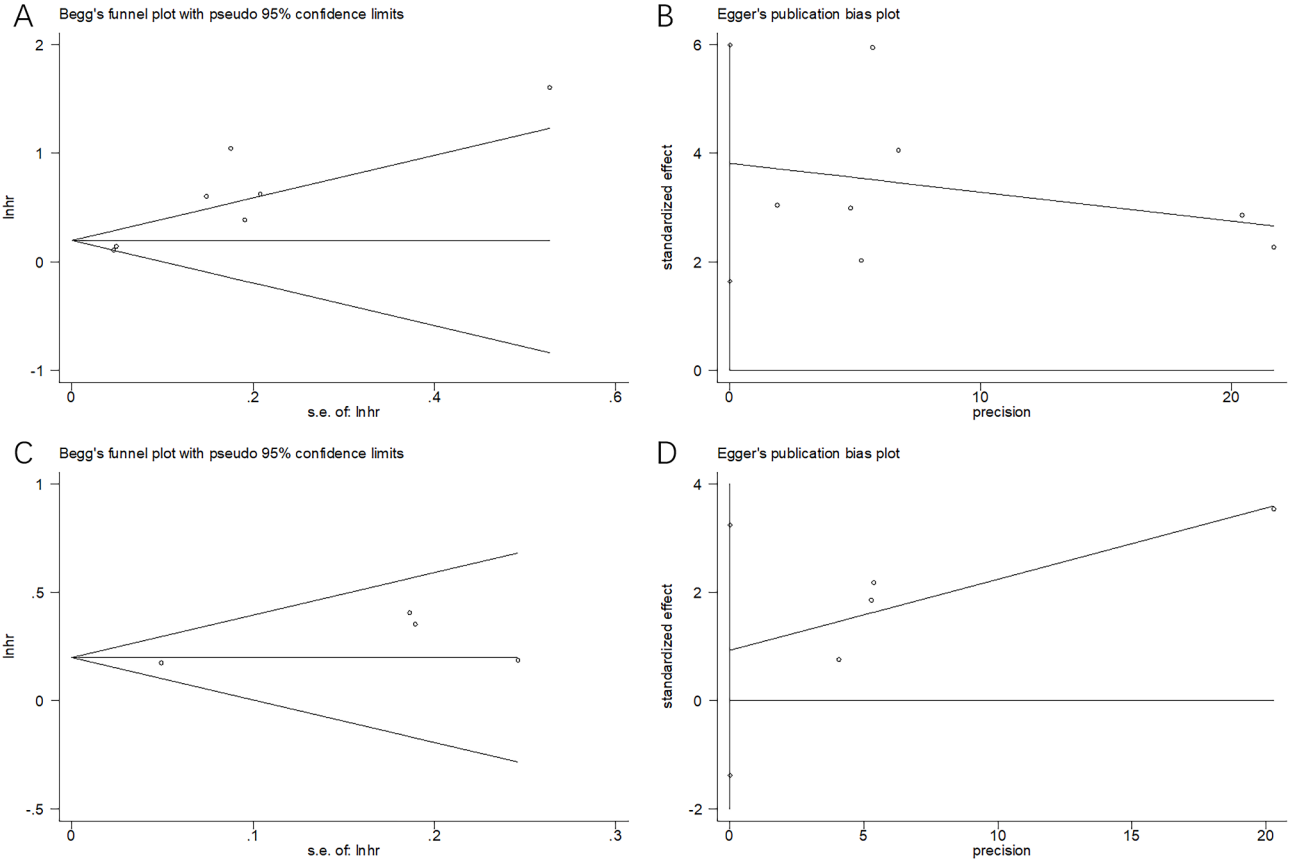

Fig. 7 Publication bias test. (**A**) Begg's test for OS, $p=0.230$; (**B**) Egger's test for OS, $p=0.118$; (**C**) Begg's test for PFS, $p=1.000$; and (**D**) Egger's test for PFS, $p=0.227$

Conclusions

In summary, this meta-analysis revealed a significant correlation between an elevated CONUT score and poor OS and in of patients with DLBCL. Moreover, a high CONUT score was significantly correlated with the clinicopathological features representing DLBCL development.

Abbreviations

CONUT	Controlling nutritional status
DLBCL	Diffuse large B-cell lymphoma
HR	Hazard ratio

CI	Confidence interval
OS	Overall survival
PFS	Progression-free survival
LDH	Lactose dehydrogenase
R-CHOP	Rituximab, cyclophosphamide, adriamycin, vincristine, and prednisone
PNI	Prognostic nutritional index
GNRI	Geriatric nutritional risk index
SMI	Skeletal muscle index
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
NOS	Newcastle–Ottawa Scale
OR	Odds ratio
ROC	Receiver operating characteristic
CSS	Cancer-specific survival
ECOG PS	Eastern Cooperative Oncology Group Performance Status
NCCN IPI	National Comprehensive Cancer Network International Prognostic Index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-025-03663-y.

Supplementary Material 1: The CONUT scoring system

Supplementary Material 2: The detailed search strategies for each database

Supplementary Material 3: The language editing certificate from Editage (www.editage.com)

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Author contributions
JZ and YW contributed to conception and design of the study, and reviewed and revised the article. JZ and YW performed the literature search and data extraction. JZ performed statistical analysis and prepared Figures and Tables. YW drafted the article. All authors have approved the final version of the manuscript.

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
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Competing interests
The authors declare no competing interests.

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