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627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Prognostic Significance of the Neutrophil/Lymphocyte Ratio in Diffuse Large B-Cell Lymphoma: A Systematic Review and Meta-Analysis

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PROGNOSTIC SIGNIFICANCE OF THE NEUTROPHIL/LYMPHOCYTE RATIO IN DIFFUSE LARGE B-CELL LYMPHOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

BACKGROUND: The neutrophil-lymphocyte ratio (NLR) has stunned up as an easy to use prognostic biomarker in different cancers. Although the exact mechanism remains to be elucidated, reduced infiltration of intratumoral lymphocytes along with the development of neutrophil extracellular traps (i.e., NETosis) has been postulated as endogenous mechanisms for tissue damage and inflammation. We previously reported a NLR ≥4 as independently associated to inferior complete response rates to chemoimmunotherapy and worse survival in Latin American (LATAM) patients with diffuse large B-cell lymphoma (DLBCL; Beltran, Clin Lymphoma Myeloma Leuk, 2020). Here we present a systematic review and meta-analysis on the prognostic value of the NLR in DLBCL.

METHODS: A systematic search was conducted using PUBMED, EMBASE and SCOPUS databases up to the most recent date (October 2022). Prospective and retrospective cohorts were reviewed using the diagnosis of DLBCL according to the WHO criteria. The NLR was defined as the ratio between absolute neutrophil and lymphocyte counts in peripheral blood prior to initiating therapy. Two independent reviewers selected the studies and subsequently extracted the data. Clinical variables included gender, age, tumor stage, IPI, presence of B symptoms, serum LDH level, extranodal location, ECOG performance status, treatment regimen, NLR value, Hazard Ratio with its respective 95% confidence interval (CI). Once the quality of the extracted data was verified, a quantitative synthesis of the information was conducted through a meta-analysis-based approach. Additionally, a sensitivity analysis was performed using the leave-one-out method and a NLR cut-off of >4. A meta-regression model was applied to assess the influence of a sample size <200 (based on previous reviews) on the heterogeneity of the results. Primary endpoints were overall survival (OS) and progression-free survival (PFS) rates. Association was reported by Hazard Ratio (HR). Risk of bias was assessed using the Newcastle-Ottawa Scale adapted by Hassan-Murad et al. Data were analyzed using the R program version 4.2.3.

RESULTS: Fifteen studies were identified and 4,149 patients were included. Only 3 studies were from Latin America. The median NLR was 4.1 (range 1.5 to 5.54). Thirteen studies with 3,498 patients showed a significant association between NLR and OS (HR: 1.57 [95% CI: 1.3-1.9, I2: 46%; P=0.04]), and 11 studies with 2,660 patients found no association between NLR and PFS (HR: 1.32 [95%CI: 0.8-2.03, I2: 0%; P=0.72]).

When reanalyzing the data by region, the NLR was associated to worse OS in Latin American patients (HR: 1.94 [95%CI: 1.14-3.3, I2: 51%; P=0.15]), followed by Europe (HR: 1.79 [95%CI: 1.41-2.27, I2: 0%; P=0.74]) and finally Asia (HR: 1.26 [95% CI: 0.8-1.8,

I2: 62%; P=0.02]) Regarding the association between NLR and PFS according to region, Europe (HR: 5.08 [95%CI: 0.7-38, I2: 93%; P<0.001]) and Asia (HR: 1.28 [95CI %: 0.95-1.71, I2: 56%; P=0.03]) did not present an association. We could not perform analysis for Latin America due to only one study was available for analysis. Regarding the cut-off point for NLR, a cut-off of >4 was adversely associated with OS (HR: 1.63 [95%CI: 1.36-1.95, I2: 0%; P=0.46]), and a trend for worse PFS (HR: 1.70 [CI-95%: 1.24-2.33, I2: 51%; P=0.08]). In the sensitivity analysis, when we excluded the results of Jing Wang et al, the heterogeneity disappeared (I2=0%, p<0.01). However, the effect size of the association was not significantly increased (HR: 1.69 [95% CI: 1.46-1.96, I2: 0%; P<0.01]). In the sensitivity analysis for PFS, the results remained stable.
The absence of publication bias between studies was confirmed for OS (p= 0.42), but not for PFS (p< 0.0001). A sample size <200 did not influence heterogeneity.
DISCUSSION: Our study found the NLT as a relevant prognostic factor for OS in DLBCL patients. The main limitation was the inconsistency of the cut-off values for the NLR in the different studies included, suggesting the need to standardize this cut-off for future research studies. However, a cut-off point >4 could be a promising clinical biomarker for this patient population.

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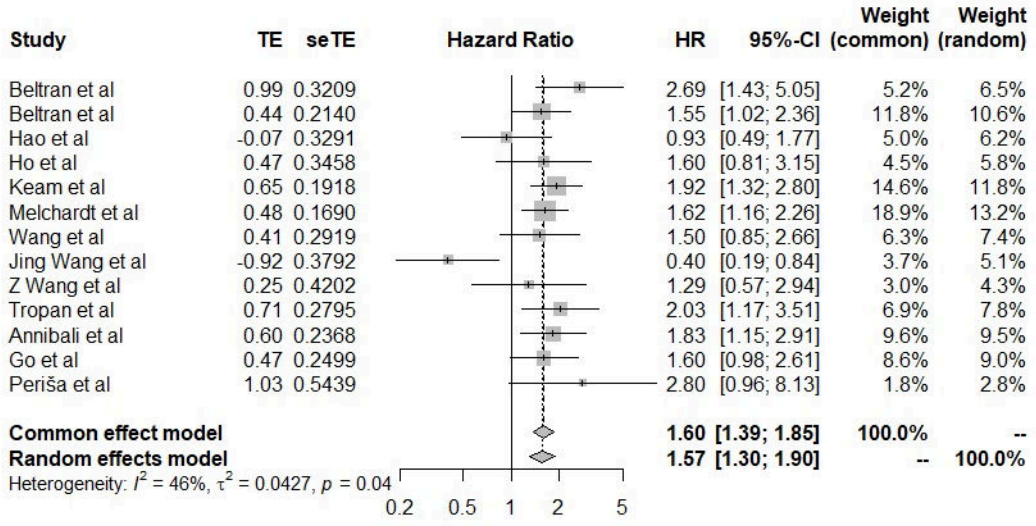

Figure 1. Meta-analysis for Neutrophil-Lymphocyte Ratio in Overall Survival.

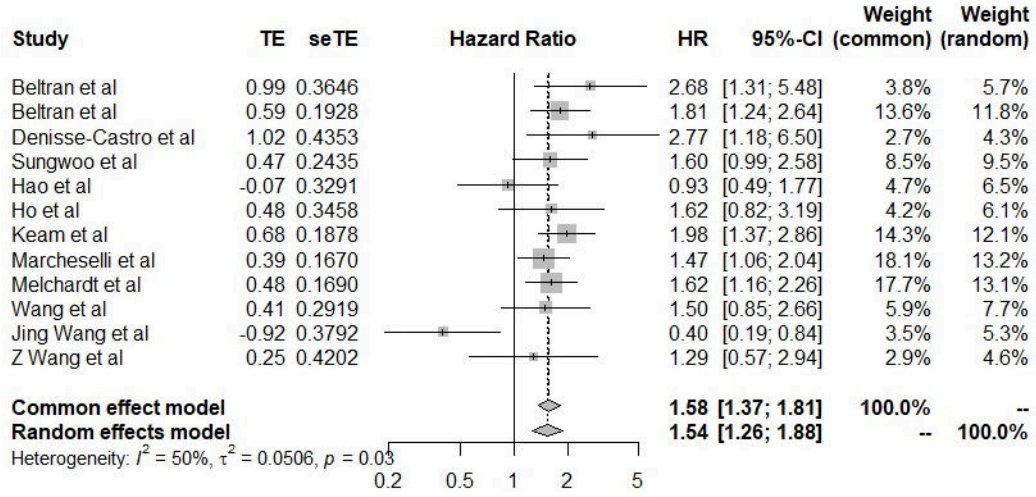

Figure 2. Meta-analysis for Neutrophil-Lymphocyte Ratio in Progression-Free Survival.

Figure 1

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