

TROMBOEMBOLISMO VENOSO: ASPETTI CLINICI E
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NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A POTENTIAL PREDICTOR OF THROMBOSIS IN CLASSICAL HODGKIN LYMPHOMA: AN EXPLORATORY ANALYSIS

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Background and Aims. The neutrophil-to-lymphocyte ratio (NLR) is a simple inflammatory biomarker associated with prognosis and cancer-associated thrombosis (CAT). This study aimed to evaluate NLR as a predictor of CAT in patients with classic Hodgkin lymphoma (cHL)

Methods. We retrospectively evaluated adult patients (>18 years) diagnosed and treated for cHL between 2017 and 2020 at our institution and included in the "Thro-HL" multicenter study. Patients receiving anticoagulation for any indication were excluded. All suspected thrombotic events (TE) were confirmed by imaging. Thrombotic event-free survival (t-EFS) was defined as the time from diagnosis to the occurrence of thrombosis or last follow-up. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal NLR cut-off for predicting TE. Associations between dichotomized NLR, established clinical risk scores (Khorana, Throly, Thro-HL), and TE were assessed using Pearson's Chi-square test. Time-to-event analyses were performed using Cox proportional hazards regression. A multivariable backward stepwise Cox model was used to assess the independent predictive value of NLR beyond clinical scores. Statistical significance was set at $p < 0.05$.

Results. A total of 90 patients were included. Forty-eight patients (53.3%) were male and 42 (46.7%) female. Median age at diagnosis was 42 years (range 18-85). Disease stage was early favorable in 11.1%, early unfavorable in 38.9%, and advanced in 50%. Median NLR at diagnosis was 4 (range 0.4-21.2). Khorana score was intermediate in 82.2% and high in 15.6% (2.2% not assessable, NA). Throly score was low in 15.6%, intermediate in 62.2%, and high in 21.1% (1.1% NA). Thro-HL score was low in 44.4%, intermediate in 33.3%, and high in 21.1% (1.1% NA). Eighteen patients (20%) experienced venous TE (VTEs), no arterial events were reported. Median observed t-EFS was 22.2 months (range 0.1-49.2). Median follow up was 28.3 months (range 1.3-50.3). All patients were alive at last follow up. ROC analysis identified $NLR > 3.9$ as the optimal cut-off for predicting TE (AUC 0.633; sensitivity 72.2%; specificity 54.3%). In univariate analysis, elevated NLR ($p = 0.045$), Khorana score

($p = 0.046$), Throly score ($p = 0.01$), and Thro-HL score ($p = 0.008$) were all significantly associated with TE. In univariate Cox regression, the Khorana high-risk category was associated with increased risk compared with intermediate risk (HR 2.99, 95% CI 1.03-8.62, $p = 0.043$). The Throly score showed an overall significant association ($p = 0.015$), with a non-significant trend for high-risk patients (HR 6.96, 95% CI 0.87-55.69, $p = 0.067$). The Thro-HL score demonstrated a strong association with thrombosis ($p = 0.010$), with significantly higher risk in the high-risk group (HR 7.33, 95% CI 1.94-27.67, $p = 0.003$). $NLR > 3.9$ was associated with a trend toward increased risk (HR 2.62, 95% CI 0.93-7.35, $p = 0.067$). In multivariable analysis, only the Thro-HL score remained independently associated with thrombotic risk, while NLR and the other scores were not retained.

Conclusions. NLR showed a trend toward association with CAT in cHL, but it was not independently predictive after adjustment for established clinical risk models. Yet it should be assessed in larger cohorts to determine whether NLR may complement existing tools for thrombotic risk stratification in this population.

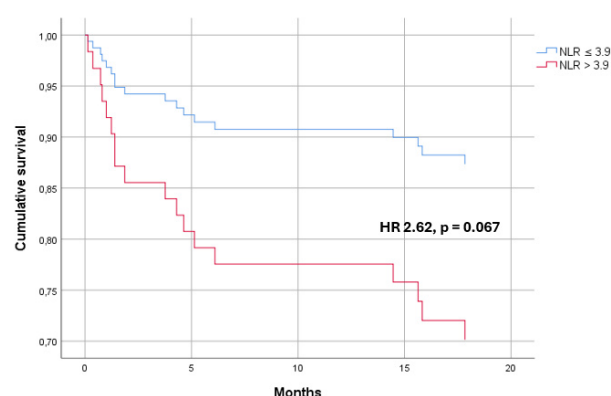


Figure 1. Kaplan-Meier curves for thrombotic events according to NLR categories (cut-off 3.9). Patients with $NLR > 3.9$ showed a higher incidence of thrombotic events compared to those with $NLR \leq 3.9$. In univariable Cox regression analysis, $NLR > 3.9$ was associated with a non-significant trend toward increased thrombotic risk (HR 2.62, 95% CI 0.93-7.35, $p = 0.067$).