THE IMPACT OF BASELINE IMMUNE-INFLAMMATORY INDICES AND MICROENVIRONMENT IN RICHTER TRANSFORMATION: A CASE SERIES

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CLL-444

INTRODUCTION

Richter transformation (RT) is characterized by an aggressive clinical course and a complex tumor microenvironment. While systemic inflammation indices—SII, SIRI, and NLR—are established prognosticators in solid tumors, their utility in RT is confounded by the immune dysregulation and baseline lymphocytosis inherent to chronic lymphocytic leukemia (CLL).

AIM

To evaluate the prognostic significance of baseline inflammatory scores and identify disease-specific thresholds for predicting treatment response and overall survival (OS) in RT.

METHOD

Retrospective case series analysis of patients with RT (2017–2025). The analysis followed the principles of the Declaration of Helsinki; data were analyzed anonymously.

Single-center referral practice for hematologic malignancies at the Hematology Unit of Pisa.

Fourteen consecutive patients with biopsy-proven RT. Key features included a high prevalence of TP53 mutations and complex karyotypes. Patients were predominantly male, reflecting an older adult population. All had prior CLL, mostly heavily pretreated with BTK or BCL2 inhibitors.

Heterogeneous salvage strategies, including chemoimmunotherapy (R-CHOP, R-DHAOx, R-DA-EPOCH) or targeted therapies (BTK inhibitors, brentuximab, pembrolizumab, venetoclax). A subset underwent consolidation with autologous stem cell transplantation or CAR-T therapy.

OS and best clinical response (CR vs non-CR). SII, SIRI, and NLR were analyzed as proxies for microenvironment activity.

CONCLUSIONS

Systemic inflammation scores are potent biomarkers for the aggressive RT microenvironment. However, traditional cutoffs are inapplicable in this setting. RT-specific calibration via the Youden index is required to account for the unique hematologic landscape of transformed CLL. These findings highlight the need for early identification of high-inflammation phenotypes to guide intensified therapeutic strategies.

RESULTS

High baseline inflammation correlated with inferior outcomes, reflecting a protumor microenvironment. Patients who died exhibited a mean SII higher than survivors (433.7 vs 6.3). NLR was higher in nonresponders compared with patients achieving CR (1.89 vs 0.06). Standard oncologic cutoffs (eg, NLR >3) proved inaccurate because of the "dilution effect" of underlying CLL lymphocytosis. ROC curve analysis identified the Youden index as an essential tool for determining the optimal balance of sensitivity and specificity for OS. Current data suggest significantly lower thresholds (NLR >0.7; SII >150) than those used in conventional solid tumor models.

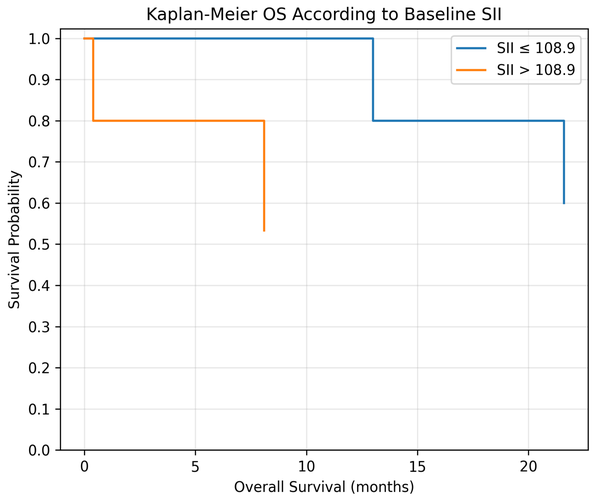

Figure 1: OS curve according to baseline SII (systemic immune-inflammation index)

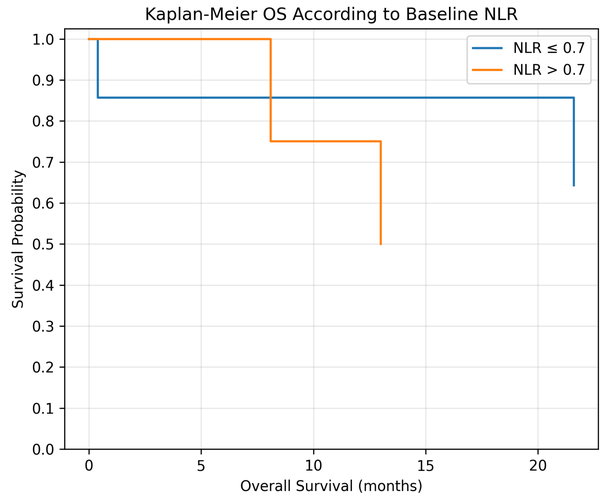

Figure 2: OS curve according to baseline NLR (neutrophil-to-lymphocyte ratio)

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