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624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Novel Risk Models and Promising Biomarkers for Prognostic Prediction in T-Cell Lymphoma with Pleural Effusion

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Introduction: T-cell lymphomas (TCLs), a cluster of lymphoproliferative diseases, display high heterogeneity of characteristics, and lack for accurate prognostic models and precision treatment at present. Pleural effusion (PE) is a relatively severe manifestation of lymphomas, which has been found to be associated with worse prognosis in tumor patients, posing more challenges for risk stratification in TCL patients.
Methods: Entire of 472 new diagnosed TCL patients were included from Shandong Provincial Hospital (2010-2022), and 130 among them with PE were retrospectively investigated to evaluate the prognostic value of clinical factors. The study was performed with the approval of the Medical Ethical Committee of Shandong Provincial Hospital, and all samples were collected with informed consents. RNA sequencing datasets GSE5584, GSE58445 and GSE6338 from GEO database were applied for the identification and function analysis of PE-related genes (PERGs). LASSO Cox regression analysis was utilized to reveal the prognostic role of PERGs in TCL patients. Immunohistochemistry (IHC) was applied to explore the expression and prognostic significance of HIF1A in TCLs.
Results: 130 TCL patients with PE were found to display worse prognosis compared to non-PE group ($P < 0.0001$). Three clinical variables were confirmed as independently prognostic factors in TCL patients with PE, including serum albumin concentration (ALB) < 40 g/L (HR = 0.346, P = 0.0452), PE volume (PEV) > 500ml (HR = 2.192, P = 0.0269) and serum procalcitonin concentration (PCT) > 0.05ng/ml (HR = 3.408, P = 0.0036). After addition of these three variables to NCCN IPI, we constructed NAPP prognostic model (NAPP score = 3 × NCCN IPI - ALB + 8 × PEV + 12 × PCT) in TCL patients with PE. With an Akaike information criterion (AIC) of 363.14 and concordance index (C-index) of 0.71, NAPP prognostic model obviously improved the prediction performance of NCCN IPI (AIC = 741.01 and C-index = 0.52). Then we used the "cutoff" package in R to choose optimum marginal value, patients with NAPP risk score < 41 were deemed as low risk while ≥ 41 were high risk. Kaplan-Meier survival curve clarified that there was significant discrepancy of OS between the two groups (Fig. 1A, $P < 0.0001$). The 1-, 3-, and 5-year AUC values of NAPP for OS were 0.70, 0.64 and 0.64. The point estimated value of AUC at each prediction time was above 0.60 (Fig. 1A), suggesting that NAPP score had obvious superiority in predictive ability than current NCCN IPI and prognostic index for PTCL-unspecified (PIT) risk models.
Subsequently, based on GSE55846, we found 50 miRNAs were differentially expressed ($|\log_2 FC| > 1.5$ and $P < 0.05$) between TCL patients with and without PE. Then, 239 predicted target genes of the 50 differentially expressed miRNAs were selected as PERGs based on miRTarBase and TargetScanHuman 8.0 databases. GO and KEGG analysis revealed the tight relationship between PERGs and tumor immunity. Besides, we constructed a signature including 4 PERGs (HIF1A, FERMT2, NFACT1 and COL1A1) in GSE58445. The 1-year AUC value for OS in the cohort was 0.78, indicating that PERGs signature had reliable predictive ability for OS in TCL patients. Moreover, the expression of hypoxia inducible factor-1 alpha (HIF1A) was verified to be decreased in TCL patients with PE through IHC. TCL patients with low expression of HIF1A suffered obviously inferior prognosis (Fig. 1B, $P < 0.0001$), especially in PE group. In non-PE group, there were no statistical differences of OS between the two groups based on HIF1A expression ($P = 0.48$). These results indicated that HIF1A might serve as a promising prognostic biomarker in TCL patients with PE.
Conclusions: A novel NAPP risk model was firstly constructed and demonstrated to achieve accurate risk stratification for TCL patients with PE. PERGs, especially HIF1A, were closely related to tumor immune, and could act as molecular predictors for prognosis in TCL patients. These findings have the promising potential to facilitate the identification of high-risk population and the establishment of individualized treatment in TCL patients with PE.

Disclosures No relevant conflicts of interest to declare.

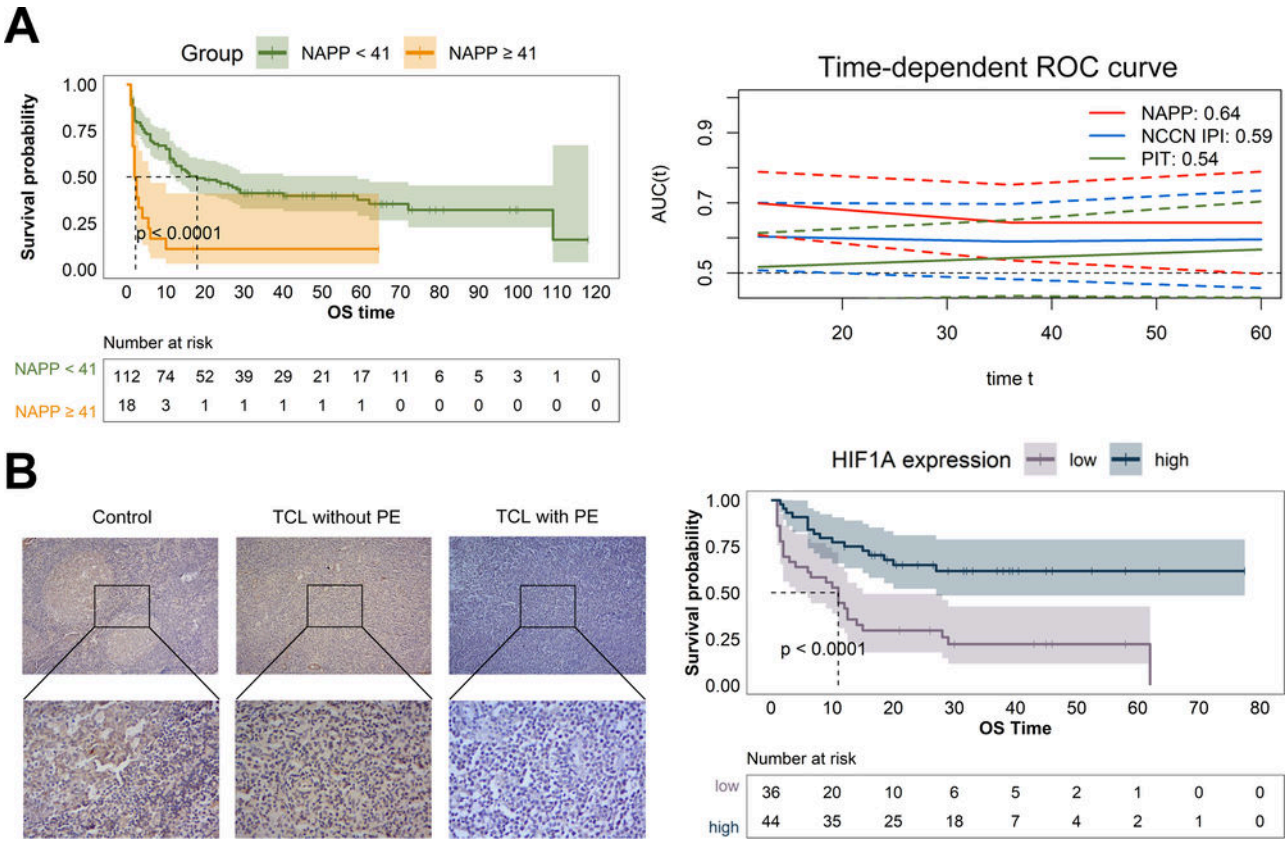

Figure 1

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