

# DEVELOPMENT AND VALIDATION OF A RISK SCORE FOR PEDIATRIC PRECURSOR B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA BASED ON RECURRENCE FACTORS

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**Introduction:** Precursor B-cell acute lymphoblastic leukemia (B-ALL) primarily affects children and adolescents, it is a fast-growing disease that can be fatal if not treated in time. Even with the advances in treatment, an important number of patients still have recurrence and consequently a poor prognosis. **Objective:** The aim of this study was to develop a prognostic risk score based on transcriptomic and clinical data of pediatric B-ALL. **Methods:** We retrospectively collected RNA-seq and clinical information, including age, sex, white blood cell count at diagnosis, central nervous system (CNS) involvement, and minimal residual disease (MRD) on day 29 of treatment of 132 B-ALL patients from the Therapeutically Applicable Research to Generate Effective Treatments. First, we determined which genes were differentially expressed between patients who had a relapse versus those who did not. These genes were then subjected to univariate Cox and Lasso-Cox regression, an artificial intelligence algorithm that chose the most important genes and created our model. For this, 92 patients were used for training and 40 for validation. Subsequently, a prognostic score was generated according to the numerical expression value of eight genes, among which three genes (ALX4, CHRNA2, and FUT7) were related to better survival, and five were related to poorer survival (CHPF, FOXO6, PTCH1, SH3BP4, and TAF45). According to the median score, we classified our patients into high and low risk, then performed an analysis of differentially expressed functions between the groups. We used the area under the curve (AUC) to assess the prediction ability of the model. Subsequently, a multivariate Cox analysis was performed, incorporating our model with clinical information, using hazard ratios (HR) and 95% confidence intervals (CI). The following variables were used: male or female sex, age above or below 10 years, CNS involvement or not, white blood cell count above or below 30,000 cells/mm<sup>3</sup>, and MRD greater or lower than 0.01. **Results:** The AUC of the model was 0.72 for 5 years, showing a good predictive capacity. Multivariate Cox regression indicated that age over 10 years (HR 1.84; CI 1.08-3.12; p = 0.02), MRD > 0.01 (HR 1.86; CI 1.07-3.22; p = 0.03), and our risk score (HR 3.81; CI 2.74-5.30; p < 0.001) were significant prognostic factors. Functional analysis revealed that in the high-risk group, the most upregulated biological processes were cytoplasmic translation and aerobic respiration. The most impacted pathways included ribosome, thermogenesis, oxidative phosphorylation, and chemical carcinogenesis mediated by reactive oxygen species. **Discussion:** White blood cell

count, CNS involvement, age, and MRD are well-established prognostic factors for B-ALL. In our study, age over 10 years and MRD > 0.01 were confirmed as significant prognostic factors. Although white blood cell count and CNS involvement were relevant, they did not show statistical significance in our analysis. Thus, our risk score, which presented a good AUC and a high HR, proved to be an important prognostic factor, suggesting that it can improve risk stratification. **Conclusion:** We developed an effective risk score for B-ALL, demonstrating good predictive ability based on gene expression. We offer a useful tool for risk stratification and management of patients.

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## DESAFIOS NO DIAGNÓSTICO DE ANEMIA SEVERA EM UM HOSPITAL DO INTERIOR DE MINAS GERAIS – RELATO DE CASO

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**Introdução:** Anemia é definida como a diminuição da concentração de hemoglobina no sangue e raramente é uma doença por si só. As condições que levam à anemia incluem deficiência de eritropoiese, hemólise e perda sanguínea. Diagnosticar e tratar anemia severa em hospitais de pequeno porte representa um desafio significativo devido à limitação de recursos e à dificuldade de acesso a especialistas. Este relato descreve o caso de uma mulher com anemia severa, destacando os desafios no diagnóstico e tratamento em um ambiente com recursos limitados. Informações foram coletadas por meio de registros de prontuário e exames laboratoriais, respeitando os princípios éticos de pesquisa. **Relato do caso:** Uma mulher de 36 anos foi admitida em um hospital de pequeno porte no Leste de Minas Gerais com dispneia, dor abdominal e anemia grave. Inicialmente, o diagnóstico não foi definido, e a paciente apresentou um quadro arrastado. Recebeu várias hemotransfusões, tratamento para infecção urinária e toracocentese para derrame pleural, evoluindo para insuficiência respiratória e intubação orotraqueal. Após cerca de um mês, foi transferida para um hospital de média complexidade em Ipatinga. Na unidade de terapia intensiva, a paciente manteve anemia grave (hemoglobina de 4,3g/dL na admissão), derrame pleural, doença renal (creatinina 3,16mg/dL) e adenomegalias. As hipóteses diagnósticas incluíam síndrome hemofagocítica, microangiopatia, neoplasia hematológica e colagenose. Foram solicitados exames de imagem, laboratoriais e coleta de mielograma. A paciente foi acompanhada pelas equipes de terapia intensiva, infectologia, hematologia e nefrologia. **Exames realizados:** Tomografia de tórax: Derrame pleural bilateral, mais volumoso à direita, com atelectasia, derrame pericárdico e linfonodos mediastinais de dimensões limítrofes, adenomegalias axilares. Tomografia de abdome: Pequeno acúmulo de líquido na cavidade pélvica, linfonodos inguinais de dimensões limítrofes, fígado e baço em alterações. Mielograma: Hemodiluído. Sorologias: HIV, hepatite B e C, HTLV e