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803.EMERGING TOOLS, TECHNIQUES, AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

Artificial Intelligence Models for Risk Stratification and Prognosis in AML-NOS

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Introduction

Despite recent therapeutic advances in acute myeloid leukemia (AML), the prognosis remains unfavorable, with mortality rates ranging from 50-80%. The current prognostic classification by the European Leukemia Net (ELN 2022) stratifies patients into favorable, intermediate, and adverse risk categories based on recurrent genetic abnormalities. However, there is a subset of patients with no identified AML-related mutations: AML defined by differentiation (World Health Organization [WHO] 2022) or AML not otherwise specified (NOS) (International Consensus Classification [ICC] 2022). These cases are classified as intermediate risk by default, but their prognosis remains an area for improvement due to clinical heterogeneity, variable treatment responses, and the lack of specifically designed studies to analyze prognostic factors in this group. Precise risk stratification and survival prognosis for AML-NOS patients are crucial for tailored treatment planning and improved outcomes. This study seeks to bridge this gap by assessing the effectiveness of supervised Artificial Intelligence (AI)-based models for prognosis in newly diagnosed AML-NOS patients.

Methods

Our methodology involves two settings at diagnostic time: initially using only mostly clinical/morphological data, and then adding the genetic information. We conducted a retrospective study on 286 newly diagnosed AML patients from three different Spanish hospitals, 234 were classified as non AML-NOS and the remaining 52 classified as AML-NOS. For each patient, a total of 40 initial demographic, clinical, hematological, biochemical, and morphological variables were available. AI models were trained using a Random Survival Forest (RSF) on the non-NOS patients and then tested on the independent AML-NOS cohort. Missing data was imputed using a random forest iterator and the 40 initial variables were reduced to 18, available at every healthcare complex, with a selection based on LASSO regularization for the first model, adding the additional genetic data for the second one (comprising a total of 15 relevant variables). A 3-fold cross-validation was performed on the training data (non-NOS) to optimize model hyperparameters and maximize the c-index. The RSF model was then retrained on the entire training dataset with these optimal parameters, and the model's performance was evaluated on the test data (AML-NOS cohort) with the c-index and Brier score, finally assessing variable importance with a permutation-based approach.

Results

The models achieved a c-index for Overall Survival (OS) of 0.775 and 0.773 for each model respectively (not including and including genetic variables), as well as a Brier score at 2 years of 0.388 and 0.298, respectively. The AI model was able to divide the AML-NOS cohort into three groups based on different prognosis using a 3-way risk stratification scheme. Both models (excluding and including genetic variables) successfully passed the pairwise log-rank test ($p<0.01$) for these three groups. The top 5 impactful variables related to a worse prognosis, selected by the AI model and included in both models, were ECOG>2, advanced age, chronic cardiopathy, and the presence of cardiovascular risk factors (such as arterial hypertension, diabetes mellitus, dyslipidemia, obesity, and smoking). In the first model, low glomerular filtration rate was also among the top five

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relevant variables, while the second model included TP53 mutation status as a significant factor impacting the prognosis of AML-NOS patients.

Conclusions

Our results demonstrate the efficacy of the proposed AI-based prognosis model using the RSF algorithm in providing robust ranking and risk stratification for AML-NOS patients. Importantly, the variables used for stratification are standard clinical measures available in any facility, underscoring the practical applicability. Moreover, when introducing genetic variables, the model gains greater generalization and predictive power. We found that TP53 was linked to worse prognosis in AML-NOS patients, consistent with previous findings. These results could be leveraged to guide more tailored therapeutics strategies for this patient cohort. Future studies should validate these models with larger datasets and explore new potential diagnostic subgroups.

Disclosures López-Caro: *Spotlab:* Current Employment. **Bermejo-Peláez:** *Spotlab:* Current Employment. **Díez Navarro:** *Spotlab:* Current Employment. **Brau Queralt:** *Spotlab:* Current Employment. **Postigo Camps:** *Spotlab:* Current Employment. **Ledesma-Carbayo:** *Spotlab SL:* Other: shareholder and member . **Luengo-Oroz:** *Spotlab:* Current Employment. **Martínez-López:** *Janssen:* Honoraria; *Pfizer:* Honoraria; *Altum Sequencing:* Current equity holder in private company.

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