Machine Learning Program Enhances Transplant Risk Assessment in Myelofibrosis Patients Better Than Current Models

The open-access model shows that 25% of patients have 40% chance of dying within one year after transplant

(WASHINGTON—March 27, 2025) — A machine learning model generated by a team from the European Society for Blood and Marrow Transplantation (EBMT) outperformed standard statistical models in identifying and stratifying transplant risk for patients with myelofibrosis, according to new research published today in *Blood*, the American Society of Hematology's flagship journal.

"Although there are many models available to identify patients with high-risk myelofibrosis, we are still lacking tools to determine the risk of transplant for these patients," said one of the study's lead authors, Juan Carlos Hernández Boluda, MD, PhD, a hematologist at the Hospital Clínico of Valencia and lead of the myeloproliferative neoplasms committee within the EBMT Chronic Malignancies Working Party. "Our prognostic tool comprehensively and effectively identifies high-risk patients with myelofibrosis at high risk for mortality after transplantation, enabling better strategic planning and potentially improving outcomes."

Myelofibrosis is a rare blood cancer in which the bone marrow stem cells acquire a genetic defect, causing excessive production of blood cells along with a large number of inflammatory factors. This leads to the formation of scar tissue within the bones, resulting in anemia and migration of stem cells to other organs, primarily the spleen and liver. Although there are several therapies available to treat myelofibrosis, the only curative option remains allogeneic-hematopoietic cell transplantation (allo-HCT), when healthy stem cells from a donor are transplanted into a patient to replace the abnormal cells.

"The decision to perform a transplant in a patient with myelofibrosis is frequently very complex. Only about 10% of patients with myelofibrosis ultimately receive one," said Dr. Hernández Boluda. "Unfortunately, given the lack of risk assessment tools, providers typically have to rely on personal experience, rather than well-defined criteria, to help make this challenging decision."

The researchers sought to improve risk assessment for patients seeking allo-HCT, with a focus on predicting overall survival. They identified 5,183 adult patients from 288 EBMT registered centers, reporting to the EBMT registry, who had undergone first allo-HCT between 2005 and 2020. Of those records, 3,887 were used to train the algorithm, while 1,296 were used to assess and validate the new model. The median follow-up and overall survival for the training cohort was 58.2 months and 79.4 months, respectively; for the test cohort, median follow-up was 60.0 months and median overall survival was 73.7 months.

The EBMT research team estimated overall survival and progression-free survival through the Kaplan-Meier method. Non-relapse mortality was defined as the time from

the date of transplantation to the date of death (uncensored) or to the date of disease relapse (censored). Independent statisticians used separate methodologies (Cox regression methods or machine learning techniques) to evaluate the factors influencing overall survival within the same dataset, aiming to develop prognostic models to stratify patients into different risk groups of post-transplant mortality.

The resulting risk classifications were compared and contextualized to assess their clinical relevance. The researchers developed a prognostic model using random survival forests, a type of machine learning algorithm typically used for survival. The RSF model achieved higher concordance indices for predicting both overall survival and non-relapse mortality compared three alternative machine learning methods and was therefore selected as the primary approach for subsequent analyses. The machine learning model produced more reproducible results than comparison models. Additionally, it outperformed standard models in accuracy and identified a subset of high-risk patients with a 40% chance of dying within a year after transplant – 25% of patients with myelofibrosis. This data is helpful to contrast with disease-related risk factors, making it important for patients deciding whether or not to undergo transplant.

The research team translated their RSF model into an open-access, web-based calculator for providers to reference. The final tool predicts overall survival for patients after transplant based on 10 key patient characteristics, including patient age, performance status, comorbidity index, hematologic parameters, donor type, conditioning intensity, and type of graft-versus-host disease prophylaxis.

“Clinicians can use this calculator to enhance shared decision making with their patients,” said study author Donal McLornan, MRCP, PhD, FRCPath, a consultant in hematology and stem cell transplantation at the University College London Hospitals NHS Foundation Trust, EBMT Scientific Council co-chair and Chronic Malignancies Working Party chair. “This is a practical, easy-to-use tool that takes into account data any transplant clinician will already have on hand.”

“From a machine learning perspective, this model truly meets what I call the ‘three A’s’ for effectively integrating artificial intelligence into medicine,” added Adrián Mosquera, MD, PhD, a hematologist and machine learning expert also leading the research from the University Hospital of Santiago de Compostela. “First, it is broadly applicable: the variables that make up the model are easily obtainable regardless of the health care system. Second, it is highly accessible, thanks to a simple computational tool freely available on the web. Finally, it is clinically actionable: this tool supports multidisciplinary teams in deciding whether to pursue cell therapy or to evaluate other medical options and supports both clinicians and patients in making more informed decisions.”

The team cautioned that the study has some limitations, mainly its reliance on a patient registry, which lacked data for some variables, including the degree of bone marrow fibrosis and the presence of additional somatic mutations at the time of transplant. Moving forward, they hope to collate real-world data entered into the application and incorporate other specific disease factors to refine applicability of the model.

The web-based calculator is available at gemfin.click/ebmt/.

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The American Society of Hematology (ASH) (hematology.org) is the world's largest professional society of hematologists dedicated to furthering the understanding, diagnosis, treatment, and prevention of disorders affecting the blood. Since 1958, the Society has led the development of hematology as a discipline by promoting research, patient care, education, training, and advocacy in hematology.

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Claire Whetzel, 202-629-5085
cwhetzel@hematology.org