Age Is Just a Number

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SHL Frost

Patients with blood cancers are often treated with hematopoietic cell transplantation (HCT), a therapy regimen that is used to restore the blood system after wiping out both diseased and normal blood cells with radiation and/or chemotherapy. Depending on the nature of the transplant a range of serious complications can follow, influenced by numerous factors. Yet, for many years age alone has been the prime determinant for decisions regarding whether or not a patient should receive HCT, and what kind of pretreatment it should be combined with. Transplant protocols are generally divided between intense and less intense ("mini") transplants and applied to patients based on age, with an arbitrary cutoff or around 55–60 years. Younger people have typically been believed to tolerate more intense treatment regimens, but the truth is much more complex; age in years is a rather poor stand-alone measurement for predicting tolerance to therapy.

In 2005, Dr. Mohamed Sorror and colleagues at Fred Hutch and University of Washington developed a tool for objective and reliable assessment of health status before HCT to aid in the decision-making: the HCT-comorbidity index (HCT-CI). Comorbidities include compromised organ functions that affect the treatment planning and outcome after therapy, and the investigators demonstrated that a weighted scoring system that included those factors could predict patient survival after transplant (Sorror et al. 2005). The index included definitions for dysfunctions of multiple organs such as liver, lung, heart or kidney, in addition to diseases like diabetes, obesity, infection and psychiatric disturbances. The severity of the pre-transplant comorbidities was thought to interact with the HCT regimens, thereby increasing the risk of treatment-related toxicities and mortality.

Despite this and other advances in HCT outcomes research, many transplant protocols have remained dependent on subjective age-based rationales, and the importance of integrating both age and comorbidities into the selection process needed to be evaluated. For example, does age have any significance at all in treatment decision-making? This question was answered in a recent study published in *Journal of Clinical Oncology* by Drs. Mohamed Sorror and Barry Storer, along with colleagues from the Clinical Research Division and external collaborators. They concluded that age by itself is an inadequate prognostic marker and that treatment decisions based solely on this measurement could lead to significant loss of life and resources. A modest prognostic impact was seen for ages of 40 years and above, but there was no increase in risks after HCT among patients

older than 60 years of age compared with those 40–60 years old. Interestingly, high-dose pretreatment was better tolerated among patients older than 60 years if they were otherwise medically healthy, compared with much younger patients suffering from significant comorbidities.

A new index comprising both comorbidities and age was developed using retrospective pre-transplant medical histories and post-transplant outcomes for 3,033 patients provided by five medical institutions, enabling classification of patients before HCT according to their biologic age rather than their chronologic age. Four distinct risk groups were identified using the comorbidity/age index, based on risks of death from reasons other than relapse as well as overall survival. "The result of these studies will significantly advance our knowledge about how to tailor treatments so that we recommend transplants based on the overall health of patients not based on merely age," said Dr. Sorror. Despite the clear superiority of the composite index, its adoption in clinics for selection of the most beneficial transplantation strategies might be hampered by its complexity compared to the simplicity of using chronological age data. A validated web-based application (www.hctci.org) was thus developed to minimize the burden on physicians to calculate the biologic age scores.

Dr. Sorror explains that there is an uncertainty among oncology providers regarding relative benefits of HCT and conventional chemotherapy for treatment of patients older than 60 years of age. "They are often forced to estimate the risks and benefits of treatments on their own, because no systematic risk-assessment strategy or real-time information is available to decide treatment options." The investigators have therefore established a large multi-center consortium study, funded by the American Cancer Society and the Patient-Centered Outcomes Research Institute. Information will be collected prospectively starting at the onset of a specific blood cancer (acute myeloid leukemia), and extensive evaluation of patients will be performed at enrollment and continuously thereafter to determine what factors have the greatest impact on HCT outcomes. Hopefully, seeing beyond age will soon be a clinical reality.

Sorror ML, Storb RF, Sandmaier BM, Maziarz RT, Pulsipher MA, Maris M.B, Bhatia S, Ostronoff F, Deeg HJ, Syrjala KL, Estey E, Maloney DG, Appelbaum FR, Martin PJ, Storer BE. 2014. Comorbidity-age index: A clinical measure of biologic age before allogeneic hematopoietic cell transplantation. *J Clin Oncol*. 32(29):3249-56.

See also: Sorror ML, Maris MB, Storb R, Baron F, Sandmaier BM, Maloney DG, Storer B. 2005. Hematopoietic cell transplantation (HCT)-specific comorbidity index: a new tool for risk assessment before allogeneic HCT. *Blood* 106(8):2912 -2919.

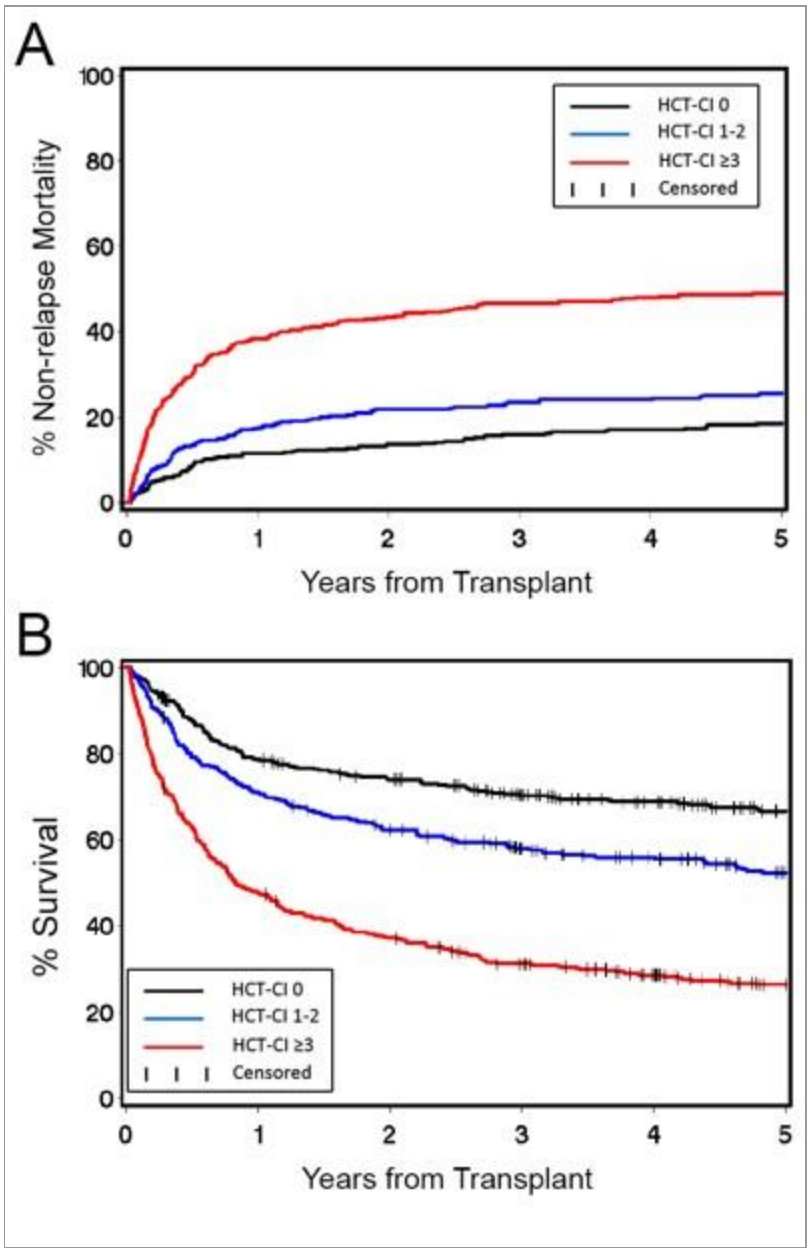

Image provided by Dr. Mohamed Sorror.

Comparisons of outcomes related to the composite hematopoietic cell transplantation-comorbidity/age index (HCT-CI/age). Panel A shows cumulative incidences of non-relapse mortality; panel B shows Kaplan-Meier survival curves of the validation set (n=1,180).