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Validation of the Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) in Single and Multiple Institutions: Limitations and Inferences

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Dear Editor

We would like to comment on two recent studies published in the September 2008 issue of *Biology of Blood and Marrow Transplantation*. Both studies focused on validating the discriminative capacity of the Hematopoietic Cell Transplantation specific-Comorbidity Index (HCT-CI) [1] for outcomes among recipients of allogeneic [2] and autologous [3] HCT.

The first study reviewed comorbidities among patients who were given HLA-matched related HCT (MRD, n=184) or HLA-matched or mismatched umbilical cord blood (UCB, n=189). Numerous conditioning regimens were used that were designated either as nonmyeloablative (NMA, n=223) or myeloablative (MA, n=150). While assessing overall outcomes, patients were also classified into four subgroups (MRD-NMA, n=96; MRD-MA, n=88; UCB-NMA, n=127; and UCB-MA, n=62). In the combined cohort, HCT-CI scores of 0, 1, 2, and ≥ 3 predicted both non-relapse mortalities (NRM, 10%, 20%, 24%, and 28%, p=.01) and overall survivals (OS, 72%, 67%, 51%, and 48%, p=.01) at 2 years. Further, in multivariate risk models, the HCT-CI was the only independent prognostic factor for NRM and OS, while age, donor source, disease-risk, and conditioning type were not. In addition, the distribution of comorbidity scores, as assigned by the HCT-CI, was similar among the four subgroups of patients, which validated its sensitivity to detect comorbidities.

While the overall results confirmed earlier findings by us[1] and others[4-10], including multi-institutional experiences[11,12], that the HCT-CI was a strong predictor of allogeneic HCT outcomes, the authors concluded, based on subgroup analyses, that the HCT-CI did not predict NRM and OS as robustly as had been suggested. While trends for NRM and OS were seen among three of the four subgroups, the analyses were limited by the relatively small numbers of patients per group. It is theoretically possible that the HCT-CI may be more discriminatory for some subgroups of patients than for others; however, the most likely explanation for the subgroup findings is random variation caused by small sample size, as well as the heterogeneity of the patient groups with respect to disease and other risk factors. The performance of other comorbidity indices in these patients might have been informative [13-15]. Uniform failure of

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all indices to discriminate outcomes consistently among the subgroups would confirm the notion that sample sizes were too small for validation studies.

In comparison, the concurrently published Ottawa study, despite a relatively small sample size (N=126), had the advantage of a homogeneous patient population. All patients had a single diagnosis, multiple myeloma, received autologous HCT, and were given a single conditioning regimen. Further, the authors compared the performance of the HCT-CI to another comorbidity index, described by Charlson, which strengthened their conclusion that indices specifically designed to assess comorbidities in the setting of HCT could provide accurate information about HCT-related toxicities and help decision making.

However, the finding that lung, liver, and renal comorbidities were equally well captured by HCT-CI and the CCI was surprising [1,4]. The HCT-CI was designed to be more sensitive in grading those comorbidities by including laboratory tests, while the CCI relied on clinical findings. Lack of information on laboratory data in many patients, for example 49% of patients did not have pulmonary function assessment, might have downgraded the sensitivity of the HCT-CI and, hence, masked the true distribution of comorbidities in the overall cohort.

We agree that validation of the HCT-CI in different institutions and across a broad range of transplant conditions is important. This validation must take into account appropriate sample sizes, adequate numbers of tested events, accurate scoring methodology, and the use of other comorbidity indices for comparison. Our ongoing efforts are focused on such validation, both retrospectively and prospectively, among large cohorts of patients from different institutions. Large sample sizes will allow for robust subset analyses and appropriate adjustment of confounding factors needed to confirm the validity and generalizability of the HCT-CI. In the meantime, we believe that comorbidity evaluation should be a vital part of pretransplant assessment and decision-making.

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References

1. Sorror ML, Maris MB, Storb R, et al. Hematopoietic cell transplantation (HCT)-specific comorbidity index: a new tool for risk assessment before allogeneic HCT. Blood 2005;106:2912–2919. [PubMed: 15994282]
2. Majhail NS, Brunstein CG, McAvoy S, et al. Does the hematopoietic cell transplantation specific comorbidity index predict transplant outcomes? A validation study in a large cohort of umbilical cord blood and matched related donor transplants. Biol Blood Marrow Transplant 2008;14:985–992. [PubMed: 18721761]
3. Labonté L, Iqbal T, Zaidi MA, et al. Utility of comorbidity assessment in predicting transplantation-related toxicity following autologous hematopoietic stem cell transplantation for multiple myeloma. Biol Blood Marrow Transplant 2008;14:1039–1044. [PubMed: 18721767]
4. Sorror ML, Giralt S, Sandmaier BM, et al. Hematopoietic cell transplantation-specific comorbidity index as an outcome predictor for patients with acute myeloid leukemia in first remission: Combined FHCRC and MDACC experiences. Blood 2007;110:4608–4613.
5. Lim ZY, Ho AY, Ingram W, et al. Outcomes of alemtuzumab-based reduced intensity conditioning stem cell transplantation using unrelated donors for myelodysplastic syndromes. Br J Haematol 2006;135:201–209. [PubMed: 16939494]
6. Maruyama D, Fukuda T, Kato R, et al. Comparable antileukemia/lymphoma effects in nonremission patients undergoing allogeneic hematopoietic cell transplantation with a conventional cytoreductive or reduced-intensity regimen. Biol Blood Marrow Transplant 2007;13:932–941. [PubMed: 17640597]

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7. Fujimaki K, Sakai R, Fujisawa S, et al. Usefulness of hematopoietic cell transplantation-specific comorbidity index after allogeneic hematopoietic stem cell transplantation [Japanese]. Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy] 2008;35:87–91.
8. Boehm A, Sperr WR, Leitner G, et al. Comorbidity predicts survival in myelodysplastic syndromes or secondary acute myeloid leukaemia after allogeneic stem cell transplantation. Eur J Clin Invest 2008;38:945–952. [PubMed: 19021720]
9. Barba P, Piñana JL, Amoroso A, et al. Validation of comorbidity indexes in reduced-intensity conditioning (RIC) allogeneic stem cell transplantation. The Hematopoietic Cell Transplantation Comorbidity index is the best predictor of NRM and survival. Blood 2008;112:1125.#3277[abstr.]
10. Lim S-N, Lee J-H, Lee J-H, et al. Pre-transplant comorbidity as an outcome predictor in hematopoietic cell transplantation for severe aplastic anemia. Blood 2008;112#4295[abstr.]
11. Mohty M, Labopin M, Cornelissen JJ, et al. Association between the haematopoietic cell transplantation-specific comorbidity index and non-relapse mortality after reduced-intensity conditioning allogeneic stem cell transplantation for AML in first complete remission: From the Acute Leukemia Working Party; European Group for Blood and Marrow Transplantation. Bone Marrow Transplant. 2009Abstract#183, (in press)
12. Farina L, Bruno B, Patriarca F, et al. The hematopoietic cell transplantation comorbidity index (HCT-CI) predicts clinical outcomes in lymphoma and myeloma patients after reduced-intensity or non-myeloablative allogeneic stem cell transplantation. Leukemia. 10.1038/leu.2009.1prepublished online 5 February 2009
13. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–383. [PubMed: 3558716]
14. Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL Jr. Prognostic importance of comorbidity in a hospital-based cancer registry. JAMA 2004;291:2441–2447. [PubMed: 15161894]
15. Kaplan MH, Feinstein AR. The importance of classifying initial co-morbidity in evaluating the outcome of diabetes mellitus. J Chronic Dis 1974;27:387–404. [PubMed: 4436428]