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CORRESPONDENCE

Letters to the Editor

Ethnic Diversity and Immunological Barriers in Heart Transplantation

With great interest we read the recent article by Morris et al. (1) reporting on panel reactive antibody (PRA)-associated ethnic disparities of sensitization status and post-heart transplant outcomes in a total of 19,704 patients listed for heart transplantation. African American heart transplant (HT) recipients experienced more graft failure than other ethnicities. Human leukocyte antigen (HLA) mismatch was related to graft failure, and ethnic subpopulations were more likely to have HLA mismatch than white HT recipients. By using Cox proportional regression to adjust for potential confounders, African American race, Hispanic ethnicity, and sensitization were reported to be independent predictors of higher incidences of graft failure (1).

We would greatly appreciate the authors' comments on whether an attempt was made to evaluate the influence of different induction therapies and immunosuppressive treatment regimens on outcomes. Maintenance levels of immunosuppressant drugs within therapeutic ranges are essential for successful preservation of graft function. Several studies were undertaken to investigate the relationships among genotype, pharmacokinetics, and therapy outcome. Ethnic disparities can be explained in part by genetically determined polymorphisms of xenobiotic-metabolizing enzymes, transport proteins, and drug targets (2,3). To improve outcomes in high-risk subpopulations, immunosuppressive therapies must be individualized accordingly. Strategies aimed at improving transplant outcomes might include the use of more aggressive induction therapies, higher immunosuppressive doses, different combinations of immunosuppressive agents, tighter post-transplant monitoring and control of concurrent disease states (4).

In sensitized patients, a final prospective lymphocyte crossmatch (CXM) is considered the sine qua non condition for transplantation. More than 10% and 25% of new listings on the pediatric and adult heart transplantation waiting list, respectively, in 2004 required prospective CXM according to the United Network of Organ Sharing (UNOS) (5). Standard complement dependent cytotoxicity (CDC) assays have been demonstrated to be rather insensitive in detecting circulating HLA antibodies compared to novel solid-phase or microsphere-based assays. It has been shown that standard CDC-based PRA testing failed to identify anti-HLA-antibodies in 25% of transplantation patients who possessed antibodies as detected by flow cytometry (6). Novel immunological assays facilitate the highly sensitive and quantitative detection of both class I and II alloantibodies. Virtual CXM based on high-resolution HLA and non-HLA alloantibody detection techniques providing full antibody specificity disclosure compared to conventional PRA assays allows prediction of compatible donor–recipient combinations (7). Other allogeneic non-HLA antigens that have been associated with poor allograft survival, such as MICA, are not expressed on peripheral blood lymphocytes, rendering the traditional CXM to donor lymphocytes unsuitable for detecting this class of clinically relevant alloantibodies (8). To this end, it is also possible to detect antibodies reactive to MICA and HLA-C antigens, completing the repertoire of potentially clinically relevant HLA antibodies. Especially in high-risk ethnic subpopulations, a virtual CXM might improve outcomes while minimizing the risk for post-transplant antibody-mediated rejection episodes.

The investigators should be commended because their study adds an important piece of evidence to the field and underscores the importance of individualized management of transplantation recipients. Individualized strategies accounting for interindividual genetic variability of donors and recipients will become increasingly important as globalization will further increase ethnic diversity.

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