Gene Expression Monitoring in Pediatric Heart Transplant recipients

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Background

AlloMap gene expression testing is a non-invasive screening tool approved for use in heart transplant recipients age 15 and older. Experience with AlloMap in pediatric heart transplant recipients is limited. We sought to describe the variations in AlloMap scores seen in pediatric heart transplant recipients.

Methods and findings

This is a retrospective study of all pediatric heart transplant recipients with AlloMap scoring at a single institution between 2013 and 2014. All possible scores were recorded. Other variables recorded at the time of each AlloMap score included immunosuppressive regimen, patient demographics and endomyocardial biopsy (EMB) results. Patients were excluded if they had undergone other solid or multi-solid organ transplantation. One hundred AlloMap scores were available from 42 patients, with a median age at transplantation of 4.3 years. The median AlloMap score for all patients was 32 (IQR, 30-35). Of the 100 AlloMap scores, 10% were collected in patients 12 years of age. There was little difference in the median score between age groups (p=0.143). Forty-five scores had a concomitant biopsy. Twenty-eight (62%) patients had ISHLT grade 0 and 16 (36%) had ISHLT grade 1 rejection. AlloMap scores were higher in patients with evidence of ISHLT grade 1 acute cellular rejection (ACR) on EMB (p=0.044). AlloMap scores were similar across all immunosuppression regimens (p=0.403), with TAC+MMF (n=43) and TAC+SIR (n=27) being the most commonly used regimens. In patients with multiple AlloMap readings, the median change in AlloMap score from baseline reading was 2 (IQR, 2-5) without significant change on biopsy findings.

Conclusions

In pediatric heart transplant recipients, AlloMap scores were higher in patients with ISHLT grade 1 rejection than in patients with ISHLT grade 0 rejection. AlloMap scores did not appear to be affected by patient age or immunosuppression regimen. Further studies should be performed to confirm the findings of this study and determine the place for AlloMap in post-transplant monitoring of pediatric patients.

Abbreviations

ACR: Acute Cellular Rejection; AMR: Antibody Mediated Rejection; AZA: Azathioprine; EMB: Endomyocardial biopsy; ISHLT: International Society for Heart and Lung Transplantation; MMF: Mycophenolate mofetil; MUSC- Medical University of South Carolina; PRED: Prednisone; TAC: Tacrolimus; SIR: Sirolimus.

Introduction

Rejection is a leading cause of morbidity in pediatric heart transplant recipients, often through progression to graft failure and death. In the most recent era, 15% of patients experienced treated rejection within the first year post-transplant, with rates of rejection being highest in patients greater than 1 year of age. Frequent monitoring with cardiac catheterization and endomyocardial biopsy (EMB) has been utilized to monitor patients in the post-transplant period for evidence of rejection. However, EMB has been associated with risks such as tricuspid valve damage and regurgitation, conduction system abnormalities, and cardiac perforation. Endomyocardial biopsy is subject to sampling error and inter-observer variability, and can only detect acute cellular rejection (ACR) once cellular infiltration and damage has occurred. Major complications have also been reported with cardiac catheterization including arrhythmias, hemodynamic compromise, perforation, and death. During these procedures, patients are exposed to high doses of ionizing radiation which may increase the child's risk of cancer development during their lifetime. Additionally, patients require hospitalization for monitoring after this invasive procedure, incurring an average hospital cost of $1200-$5600 per biopsy. AlloMap Molecular Expression Testing (CareDx, Brisbane, CA) is an innovative, non-invasive method for determining the risk of rejection in adult and adolescent heart transplant recipients ages 15 years and older and at least 2 months post-transplant. However, experience in pediatric heart transplant recipients is limited. The primary aim of this project was to evaluate AlloMap scores and determine the correlation of these scores with EMB results in pediatric heart transplant patients. The secondary aims of this project are to determine what transplant-related factors, if any, alter the reliability of AlloMap scores in the pediatric heart transplant population and to describe the use of various immunosuppressive regimens at this institution and the relationship of these regimens and their effects on the patient's AlloMap score.

Conclusions

Our study suggests that AlloMap gene expression testing may be useful to detect the presence of ISHLT Grade 1 rejection in pediatric heart transplant recipients who are at least 6 months post-transplant. Additional experience with AlloMap scoring in pediatric patients is needed to confirm the results of this study characterize the role of AlloMap in pediatric patients, validate its use across all grades of rejection, and to determine its potential for replacement of endomyocardial biopsy in post-transplant rejection monitoring.