

Early Changes in Donor Fraction Cell-free DNA in Newly Transplanted Pediatric Heart Transplant Patients

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Abstract

Purpose: Heart transplantation is an accepted therapy for children with end-stage heart disease with average survival of 15-20 years. The highest risk for graft loss remains in the first 60 days post transplantation despite several advances in the care of these patients. Measurement of percent donor fraction (DF) cell-free DNA (cfDNA) allows for extremely sensitive monitoring of graft injury and may be useful early after heart transplant to detect patients at risk for graft failure or death.

Methods: This single center study reviewed early post-transplant DF cfDNA levels in children who received heart transplantation. The outcome measure was 60 day survival. Data reviewed included demographics of donor and recipient, key operative characteristics including ischemic time and bypass time were reviewed, and recipient and graft outcomes were analyzed. Declination curves were created for each patient based on these DF cfDNA data using an estimation modeling approach.

Results: 17 patients had at least one DF cfDNA level drawn in the peri-operative period. In general, each day was associated with a significant decrease in DF ($p < 0.001$), with a leveling off by day 8. This included 10 patients with samples on post-transplant day 0, 4 and 8 which made up the study cohort. Median (IQR) % DF cfDNA levels were 3.2% (1.81 - 5.80), 0.38% (0.22 - 1.00), and 0.22% (0.38 - 0.48) at day 0, 4, and 8 respectively. 7 patients had a decline in their DF cfDNA from day 4 to day 8 whereas 3 had an increase from day 4 to day 8. All three patients with an increase in % DF cfDNA from day 4 to day 8 died within 60 days of transplant and none of the 7 with a decline over this time period died in this period. Cause of death in those three patients included complications of hyper-acute rejection, primary graft dysfunction, and infection. One patient had an increase from day 0 to day 4 which clinically corresponded to a short ischemic time (115 minutes) and an episode of acute hypotension on post-transplant day #3. This patient had a decline in DF cfDNA by day 8 and a negative biopsy on day 9.

Conclusion: DF cfDNA is associated to peri-transplant graft survival and serial monitoring in the perioperative period may be helpful in early monitoring of graft function. DF cfDNA appears to significantly decline by 8 days post-transplant.