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Impact of anti-HLA antibodies on survival and the development of coronary artery vasculopathy in paediatric heart transplant recipients

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Introduction:
It is now well established that pre-transplant detection of donor-specific and non-donor-specific anti-HLA antibodies (DSAs / NDSAs) in heart transplant recipients is associated with a worse outcome. In adult patients, DSAs and NDSAs have been found to be associated with increased episodes of acute rejection, and more severe coronary artery vasculopathy (CAV), measured by intra-vascular ultrasound (IVUS). In paediatric recipients, DSAs have been associated with increased graft failure rates, but the link between DSAs and CAV in children has not previously been examined.

Methods:
Since mid-2007, all heart transplant recipients at Great Ormond Street Hospital have been routinely screened for anti-HLA antibodies using the Luminex testing platform. Routine screening for CAV using IVUS started in late 2004. Data on antibody status and IVUS measurements, along with further clinical and demographic information, were extracted from the relevant clinical databases and collated using Excel. Using the R statistical package, the maximum intimal thickness (as measured by IVUS) at various time-points post-transplant (2-4 months, 1 year, 3-4 years) was compared in those with and without pre-transplant DSAs and NDSAs (using a threshold of 1000 mean fluorescence intensity) using Welch's two-sample t-test. Differences in survival between groups was compared using Kaplan-Meier survival curves and the log rank test.

Results:
97 paediatric heart transplant recipients had pre-transplant antibody testing using the Luminex platform. Of these, 32 patients had at least one IVUS study post-transplant. The average maximal intimal thickness at the 1 year IVUS study in recipients with DSAs was 1.17mm versus 0.76mm in those without DSAs ($p=0.01$). Pre-transplant DSAs did not significantly affect survival, but the presence of NDSAs was associated with increased post-transplant mortality ($p=0.03$).

Discussion:
CAV is a leading cause of death and graft failure in paediatric heart transplant recipients. These results indicate that even very low levels of pre-transplant DSA may lead to more severe CAV compared to recipients without DSAs, and that pre-transplant NDSAs are associated with increased post-transplant mortality. Our sample size is currently small, and more advanced analyses examining the role of DSAs and NDSAs in post-transplant outcome will be possible as our cohort grows over time.