Results: Disease status (relapse/refractory, CR2, or CR3) did not have a significant effect on disease-free survival (p = 0.75). Clonal evolution, however, did have a significant negative impact on disease-free survival (p = 0.03). Day 100 disease free survival was 50% versus 100% for patients with and without clonal evolution, respectively. Similarly, one year disease-free survival was 20% and 83% for patients with and without clonal evolution. Among the patients with clonal evolution, there was no significant difference in disease-free survival between patients with only one new cytogenetic abnormality and those with more than one new cytogenetic abnormality (p = 0.19).

Conclusion: Clonal evolution appears to identify a very high-risk group of patients who may benefit from novel transplant strategies and post-HSCT interventions. Future studies should seek to validate these findings in a multi-institutional setting.

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HYPERTENSION IN PEDIATRIC ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

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Allogeneic haematopoietic stem cell transplant (AlloHSCT) in children is associated with serious complications. Hypertension (HT) is reported to occur in 21-63% of adult HSCT patients. Data on the incidence of HT in children undergoing HSCT are limited.

Objectives: To establish the incidence of and identify the risk factors associated with the development of HT in pediatric AlloHSCT patients and to determine the duration and impact of HT on cardiac function at one year and overall survival (OS).

Methods: We conducted a retrospective study of all children who underwent AlloHSCT at The Hospital for Sick Children from 2004 to 2007 and were followed in Toronto or Halifax. Demographic information, underlying diagnosis, conditioning regimen, GvHD prophylaxis, blood pressure, GvHD, survival, medication history and echocardiography results were collected in the first year post HSCT.

Results: 172 children (59% male; mean age = 8.46 years; range 0.25-18 years) underwent AlloHSCT during the study period. 67% had an underlying malignant disease; 83% received myeloablative conditioning and 45% received total body irradiation. 93% received cyclosporine for GVHD prophylaxis, most commonly in combination with methotrexate (78%). Stem cell donors were: living related donor (LRD) in 51%; living unrelated donor (LURD) in 33% and unrelated cord in 16%.

111/172 (65%) developed HT in the first 100 days after AlloHSCT. Children with malignant disease were less likely to develop HT compared to children without a malignancy (p < 0.008). Children who had a non-cord HSCT and developed GVHD were more likely to develop HT (p = 0.045). Gender, age and conditioning regimen were not associated with HT. 36/149 (24%) evaluable children were hypertensive at D+90, 16/138 (12%) at D+180 and 5/126 (4%) at one year. No child had ventricular dysfunction (measured by echo) at one year. A total of 46 patients had died by one year post transplant. HT did not influence OS at one year after AlloHSCT (p = 0.37).

Conclusions: HT occurs commonly post AlloHSCT in children but usually resolves by one year post transplant. HT did not lead to cardiac impairment or influence OS at one year.

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SIGNATURE PROFILES OF CMV-SPECIFIC T-CELLS IN PEDIATRIC PATIENTS WITH CMV REACTIVATION AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Depletion of cellular immunity as a consequence of conditioning before allogeneic hematopoietic stem cell transplantation frequently results in CMV reactivation, which may in turn lead to life-threatening infections and require timely antiviral treatment. We have investigated the functional signatures of CMV-specific CD4+ and CD8+ T-cells in 191 samples from 118 individuals. We included patients with either high or undetectable viral loads, and those who controlled or did not control their CMV reactivations. All patient subsets were compared to healthy donors. Polychromatic flow cytometric measurements of CD154 (CD40L), intracellular cytokines (IFNγ, IL2), and a degranulation marker (CD107a) revealed the functional status of various T-cells simultaneously. We found that dual IFNγ/IL2 producing CD8+ T-cells were significantly decreased in patients non-controlling their CMV reactivations compared to controllers. In contrast, CD8+ T-cells that produced IFNγ only were the most abundant subtype but they were present in a substantial number of non-controllers. Hierarchical clustering of distinct functional signatures revealed that polyfunctional CD8+ T-cells were acting in concert with other subsets, whereas the isolated production of IFNγ by CD8+ T cells heralds insufficient collaboration with others. In conclusion, our study revealed functional signatures that may be useful for immune monitoring, and they may change the interpretation of previous studies that assessed only IFNγ.

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MOLECULAR DETECTION OF ADENOVIRUS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background: Adenoviral (AdV) infections are a major cause of morbidity and mortality in hematopoietic stem cell transplant (HSCT) patients (pts). Quantitative molecular detection of AdV using polymerase chain reaction (PCR) has recently become more widely available in the clinical setting for early detection and monitoring of AdV infection, although challenges regarding interpretation of results and implications for treatment remain.

Methods: We performed a retrospective cohort study of all pediatric HSCT pts who underwent AdV PCR testing from May 2008 through April 2010. Clinical characteristics of AdV-positive (POS) pts were compared to AdV-negative (NEG) pts.

Results: Of 48 pts with AdV testing, 43 had complete transplant records and were included in the analysis. Seven (16.3%) pts were AdV-POS. Overall pt characteristics were comparable between the two groups. The following medication exposures were identified as risk factors influencing AdV status: preparatory regimens utilizing fludarabine (Relative Risk [RR] 8.73, 95% Confidence Interval [CI]: 1.18-64.27, p 0.006), melphelan (RR 3.47, 95% CI 0.76-15.94, p 0.08), and/or cyclophosphamide (RR 0.18, 95% CI 0.02-1.4, p 0.05), and GVHD prophylaxis with methylprednisone (RR 3.73, 95% CI 1.01-13.9, p 0.04). AdV-POS pts had higher GVHD grades with higher rates of GVHD of the gastrointestinal tract (RR 4, 95% CI 1.18-13.5, p 0.03) compared to AdV-NEG pts. Amongst seven AdV-POS pts, 57.1% had concomitant clinical manifestations of disease including: pneumonia, diarrhea, and/or disseminated disease. Clinical outcomes in four symptomatic pts included resolution of disease (2) and death (2), although one pt had concomitant bacterial sepsis. An additional AdV–POS pt had prolonged marrow suppression as a probable clinical manifestation of AdV disease and recovered. All AdV-POS pts received antiviral therapy, including one pt with severe disseminated disease that resolved following administration of liposomal cidofovir.

Conclusion: Our study at a large pediatric HSCT transplant center confirms previously identified risk factors for AdV infection in previous small studies in adults and children. This study provides important preliminary data for the design of a prospective trial which aims to identify specific HCST patient populations who