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Background: Nutritional parameters represent modifiable factors to improve outcomes after HSCT. Pediatric studies linking weight to survival are over 10 years old, and analyses of prealbumin (PAB) levels have not examined the impact on survival.
Methods: We conducted a retrospective chart review of all pediatric HSCT at our institution from 7/1/2007 to 6/30/2011 (N = 77). Wilcoxon rank-sum test was used to compare weight characteristics as well as PAB and albumin levels (admission, days 0, +7, +14,+28, and +90 for albumin alone) between the autologous (auto) and allogeneic (allo) groups. Survival analyses utilized the Kaplan-Meier method and the log-rank test to compare differences. Effects on survival were examined with a Cox proportional hazards model and analyses of non-relapse mortality (NRM) incorporated competing risks.
Results: Mean weights as % of ideal body weight at admission were above 100% and not significantly different between the auto and allo groups (p = 0.80). BMI at admission was not significantly different between the auto and allo groups (19.5 and 19.3 respectively, p = 0.97). At day +30, the auto group had greater % weight loss than the allo group with mean weight loss of 1.7% (p = 0.01). In the auto group, weight loss at day +30 was associated with significantly worse day +100 and 1 yr survival compared to those who had weight gain (p = 0.03). The lowest median PAB level was 13.8 mg/dL on day 0 for allo patients and 12.2 mg/dL on day +7 for auto patients. Similarly, the lowest median albumin level was 2.9 g/dL on day 0 for allo patients and 2.8 g/dL on day +7 for auto patients. Differences between groups at these time points were statistically significant (p<0.05). Univariate analyses identified PAB levels below 15 mg/dL at day +7 as significantly decreasing day +100 and 1 yr survival in the allo group (p = 0.0003). Additionally, allo patients with a PAB level below 12 mg/dL at any time between day 0 to +14 had worse day +100 and 1 yr survival (p = 0.023). Multivariate analysis of the combined groups demonstrated a significant impact of decreased PAB levels between day 0 to +14 on NRM, with a hazard ratio of 0.85 (95%CI 0.76-0.96, p = 0.006). Accordingly, this represents an increase in NRM risk of 120% per 5 mg/dL decrease in PAB.
Conclusion: Nutritional support should be maximized early in the transplant course. As PAB is decreased in the setting of inflammation, future studies should prospectively evaluate PAB in conjunction with inflammatory markers.

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MOYAMOYA SYNDROME TREATED WITH ENCEPHALODUROARTERIOSYNANGIOSIS FOLLOWED BY HEMATOPOIETIC CELL TRANSPLANTATION IN PATIENTS WITH SICKLE CELL DISEASE

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Background: Patients with sickle cell disease (SCD) have a high risk of intracranial large vessel vasculopathy, leading to a proliferation of microvasculature at the base of the brain known as moyamoya syndrome. This confers a high risk of intraventricular hemorrhage and permanent neurologic deficits. Moyamoya syndrome can be treated surgically with a revascularization procedure called encephaloduroarteriosynangiosis (EDAS), which has been shown to decrease but not eliminate the risk of stroke. Hematopoietic cell transplantation (HCT) from a compatible sibling is the most effective way of preventing central nervous system (CNS) complications in SCD patients at risk for CNS events. There have been several reports of patients with SCD and moyamoya syndrome undergoing EDAS successfully; however, there have been no reports of these patients undergoing EDAS followed by HCT.
Results: We report six pediatric cases of patients with SCD who developed moyamoya syndrome, all of whom underwent EDAS followed by HCT. All patients underwent EDAS procedure successfully. One patient experienced a stroke less than a month after EDAS. Another patient developed a foot-drop post-EDAS, though imaging did not show any new areas of infarct. All patients underwent HLA-matched sibling-donor HCT. The chronic transfusion therapy was successfully discontinued in the two patients who had been on it prior to treatment. Post-transplant, one patient developed seizures, with imaging consistent with possible infarct; the patient was placed on antiepileptics and has not had subsequent seizures. In all follow-up imaging, there has been no progression of the patients' moyamoya syndrome.
Conclusion: These are the first reported cases of EDAS successfully followed by HCT in patients with SCD and moyamoya syndrome. Five of the six patients had no further CNS events, and all remained neurologically stable, with no progression of their moyamoya syndrome. HCT is the standard of care in patients with SCD at risk for CNS complications, leading to excellent stroke-free survival rates. Patients with moyamoya syndrome and SCD are at high risk of developing CNS complications. Transplant-eligible SCD patients who develop moyamoya syndrome may benefit from EDAS prior to HCT in order to minimize CNS complications. Further investigation by way of an international, multicenter prospective study is needed to determine the long-term outcome and potential benefits of this therapeutic combination.

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COMPARISON OF SURVIVAL AND INCIDENCE OF GRAFT VERSUS HOST DISEASE IN FULLY MATCHED, SINGLE C MISMATCHED AND OTHER MISMATCHED UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTS IN A PEDIATRIC POPULATION

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It is well understood that undergoing hematopoietic stem cell transplant (HSCT) from an unrelated (URD) compared to a matched sibling donor (MSD) results in increased graft versus host disease (GVHD) and for the pediatric population this often but not always negatively impacts overall survival. In the current era of high resolution Class I / Class II typing there is a lack of clarity about the impact

Table 1. Supplemental Patient Data

Patient	Presenting Symptoms of Initial CNS Event	Age at Diagnosis of Moyamoya Syndrome	Age at EDAS Procedure	Age at HCT	Post-HCT Complications
1	Seizures	11 years 6 months	12 years 2 months	12 years 8 months	Seizure, Possible Left Middle Cerebral Artery Infarct
2	Visual changes	13 years 2 months	Two-Step Procedure: 13 years 4 months and 13 years 7 months	13 years 9 months	None
3	Seizures	2 years 6 months	4 years 6 months	5 years 6 months	None
4	Left-Sided Hemiparesis	3 years	6 years 6 months	8 years 6 months	None
5	Seizures, Personality Changes	7 years 6 months	Two-Step Procedure: 8 years 10 months and 8 years 11 months	13 years	None
6	Eye pain	6 years	11 years 9 months	13 years 6 months	None

of using donors that are not fully matched on both GVHD incidence and overall survival. Historically there is evidence that an isolated C mismatch may not affect these outcomes but this has been evaluated almost exclusively in adult patients with hematologic malignancies. We collected data on a 146 consecutive pediatric patients (median age 9 years) who received an unrelated donor transplant at Children's Hospital Boston from 1/2004 through 12/2010 for malignant and nonmalignant conditions. 97% received bone marrow as the stem cell source and 97% received fully myeloablative conditioning. 75% underwent HSCT for a hematologic malignancy (leukemia/lymphoma), 11% for immunodeficiency and the remainder for other indications, primarily bone marrow failure syndromes. 70% of patients had a donor fully matched at both A,B,C,DR, DQ loci on high resolution typing, 10% had a single C mismatch and the remaining 20% had a donor with 1 or 2 other mismatches excluding a single C mismatch (none had a DR mismatch and all were at least a 5/6 match on A, B, DR). 45% experienced GVHD: 13% acute only, 51% chronic only and 32% both. There was no statistically significant difference in the proportion of patients who had acute GVHD of any grade and/or limited or extensive chronic GVHD between those having a fully matched, single C mismatch or other mismatched donor ($p = 0.7$). There was also no significant difference in survival between the groups. 100 day and 1 year overall survival were 93%/77% with fully matched donors, 87%/60% for single C mismatched donors ($p = 0.2$) and 96%/76% for other mismatched donors. Thus it appears that in the era of high-resolution HLA typing and improved supportive care HLA mismatched donors can provide outcomes similar to those using fully matched donors in pediatric patients undergoing HSCT for malignant and nonmalignant conditions.

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EPIDEMIOLOGY OF BACTERIAL, FUNGAL AND VIRAL INFECTIONS IN CHILDREN AND ADOLESCENTS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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The epidemiology of bacterial, fungal and viral infections was retrospectively analyzed in a cohort of 759 children and adolescents who underwent allogeneic hematopoietic stem cell transplantation (HSCT) in a single institution, between 1990-2009, to study the impact of changes in transplantation methodology on the distribution of pathogens and mortality due to infections. There were 243 matched-related, 239 matched-unrelated (MUD) and 176 haploidentical donor transplants. Independent logistic regression was conducted at 0-30 days (A), 30-100 days (B) and >100 days (C) post-transplant. On multivariate analysis, total body irradiation ($p = 0.001$, A; 0.005, C), apheresis product ($p = 0.02$, A; 0.01, B), acute ($p = 0.002$, B) and chronic ($p = 0.03$, C) graft vs host disease (GVHD) were associated with higher risk for bacterial infections at the respective time periods. CMV serostatus ($p = 0.05$, B), presence of acute ($p = 0.001$, B), chronic GVHD ($p<0.001$, C) and age >10 yrs ($p = 0.02$, C) were associated with higher risk for fungal infections. CMV serostatus ($p = 0.0005$, A; 0.03 B; 0.002 C), acute ($p = 0.01$, A) and chronic GVHD ($p = 0.001$, C), were associated with higher risk for viral infections. MUD donor transplants were associated with a higher risk of viral infections ($p = 0.001$). Bacterial ($p = 0.002$) and fungal ($p = 0.0004$) infections in period A, decreased in the 2005-2009 era. There were 321 episodes of bacteremia in 231(30%) patients, of whom 168 episodes (52%) were in period C. *Staphylococcus epidermidis* (33%) and *Escherichia coli* (12%) were the most common causes of bacteremia. Candidemia, mostly *C.albicans*, was detected in 49 (6%) patients, 26 (54%) in period C. There were 45 patients with proven aspergillosis, 20 (44%) in period A. Non-aspergillus molds were detected in 16 (2%) patients. CMV and adenoviremia was detected in 146 (20%) and 68 (9%) patients respectively. Parainfluenza was the most common respiratory viral infection detected in 70 (9%) patients, 35(50%) in period C. This is the largest retrospective study providing a time line of infections in children and adolescents who have undergone allogeneic HSCT.

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CYCLOSPORINE AREA UNDER THE CURVE IN CHILDREN UNDERGOING HAEMATOPOIETIC STEM CELL TRANSPLANTATION: LIMITED SAMPLING STRATEGY AT STEADY-STATE

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Haematopoietic stem cell transplantation (HSCT) outcomes may be optimized by cyclosporine dose adjustment according to systemic exposure (measured by area under the curve (AUC)) rather than trough concentration. We have previously developed and validated a limited sampling strategy (LSS) for estimating cyclosporine AUC after the initial IV dose in children undergoing HSCT. In this study we aim to develop a LSS to estimate AUC at steady-state.

Children undergoing myeloablative HSCT and given cyclosporine q12h as a 2-hour infusion and methotrexate/methylprednisolone for acute graft-versus-host disease (GVHD) prophylaxis were eligible. Cyclosporine AUC was determined once weekly until engraftment using 9 concentration-time points. Steady state was defined as being reached after administration of 4 identical doses.

The association between cyclosporine AUC using all available data points (AUC-all) and the AUC values predicted by each LSS was described using the adjusted coefficient of determination (r^2); values > 0.9 were acceptable. Precision and mean bias < 15% were acceptable.

18 children (0.3-17 years) participated. Mean actual dose infusion time was 123± 4.4 min. Mean AUC-all at steady state was 4894±1386 h*mcg/L. Individual cyclosporine whole blood concentrations drawn at 2, 2.5, 3, and 4 hours after the start of the infusion correlated most highly with AUC-all (Spearman rho coefficient: 0.847, 0.926, 0.942, and 0.903, $p<0.0001$, respectively). Values of AUC predicted by the 3, 4 and 5-point LSS were strongly associated with AUC-all (spearman rho coefficient > 0.998; $p<0.0001$).The 3-point LSS (2, 3 and 4 hours) is likely the method of choice for determining cyclosporine AUC at steady state when given as 2 hour infusion to children undergoing HSCT. Validation of the LSS in a different sample is required before this LSS strategy can be implemented. The relationship between acute GVHD and cyclosporine AUC at different time periods after HSCT merits further study.

Table 1. Association between AUC-all and AUC generated by LSSs

Sample times (hours after start of infusion)	Adjusted r^2	Mean bias (%; range)	Precision (%)
2, 3 and 4	0.9962	0.05 (-5.3 to 4.6)	3.6
2, 3, 4 and 10	0.9981	0.03 (-2.0 to 2.0)	1.2
2, 2.5, 3, 4 and 10	0.9990	0.05 (-2.0 to 3.0)	0.9

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THROUGH THEIR EYES: THE EXPERIENCES OF THE MINOR AND YOUNG ADULT MATCHED SIBLING HEMATOPOIETIC CELL DONORS – A RETROSPECTIVE STUDY FROM A SINGLE REGIONAL INSTITUTION

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Matched sibling donor hematopoietic cell transplantation (HCT) is considered the standard of care for many disorders, yet the donor's emotional and physical needs may be overlooked and the donor viewed as a therapeutic modality in the process of saving the life of an ill sibling. In this IRB-approved study, we explored the meaning of the donor's experiences through his own words and recollections, and the contextual influences and critical events across the transplant trajectory. A semi-structured interview was conducted in private