
**Background:** Relapse of leukemia after pediatric hematopoietic cell transplantation (HCT) is a frequent cause of treatment failure. Immune reconstitution (IR) early after HCT is pivotal to generate a potent graft-versus-leukemia effect. We studied the association between IR of various lymphocyte subsets and outcomes in children receiving a cord blood HCT for hematological malignancies.

**Methods:** All consecutive patients with a hematological malignancy receiving a cord blood HCT between 2004-2014 at Great Ormond Street Hospital London and at the UMC Utrecht were included. Patients received a myeloablative regimen ± Thymoglobulin. Primary endpoint was relapse; secondary endpoints were overall survival, non-relapse mortality (NRM), acute GvHD (grade 2-4) and chronic GvHD. Lymphocyte-subsets (CD3+, CD4+, CD8+, NK and B-cells) were monitored every other week after engraftment. Various definitions of IR were analyzed including one in line with a reported association: CD4+ T-cell count \( > 50/\mu\text{L} \) consecutive measurements within 100 days post-HCT (Bar telink et al, BBMT 2013). Cox proportional hazard models and logistic regression models were used.

**Results:** 89 patients were included, with a median age of 7.1 years (range 0.7-18): 36 ALL (19 CR1, 14 CR2, 3 CR3), 49 AML (14 refractory, 35 CR) and 4 other malignancies. 36 patients received Thymoglobulin (Utrecht only). CD4-IR (count >50, twice <100 days) was the best predictor for endpoints; in multivariate (MV) analyses, CD4-IR was a predictor for lower probability of relapse in AML patients (MV: HR 0.29, 95% CI 0.03-0.98, \( p=0.04 \); figure 1), but not in ALL (\( p=0.14 \)). CD4-IR (count >50, twice <100 days) was the best predictor for endpoints; in multivariate (MV) analyses, CD4-IR was a predictor for lower probability of relapse in AML patients (MV: HR 0.29, 95% CI 0.03-0.98, \( p=0.04 \); figure 1), but not in ALL (\( p=0.14 \)). CD4-IR was also a predictor for NRM (MV: HR 0.13, 95% CI 0.03-0.52, \( p=0.004 \); figure 2). CD4-IR predicted OS in AML (MV: HR 0.17, 95% CI 0.06-0.53, \( p=0.002 \)), but not in ALL. However, CD4-IR did not have an impact on acute grade 2-4 (\( p=0.41 \)) or chronic GvHD (\( p=0.12 \)). Successful CD4-IR was less frequent in patients receiving Thymoglobulin (MV: OR 0.04, 95% CI 0.002-0.27, \( p=0.005 \)). Associations with the endpoints for the other lymphocyte-subsets were less predictive.

**Conclusion:** Early CD4-IR post cord blood HCT predicts the probability of relapse in AML as well as NRM in all patients. Thymoglobulin negatively impacts CD4-IR post cord blood HCT, hence the use and/or the dosing of Thymoglobulin should be carefully re-considered.

Higher Incidence of Grade III and IV Toxicities in Adolescents Undergoing Allogeneic Hematopoietic Cell Transplantation and Its Impact on Mortality at One Year Post-Transplant: A Retrospective Cohort Study of Pediatric Patients Undergoing Allogeneic Stem

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Background: Grade III-IV toxicities in the 30 days post allogeneic hematopoietic cell transplantation (alloHCT) is correlated with higher transplant-related mortality (TRM) at 1 year in adults. Despite extensive literature in the field there remains a paucity of data on the incidence of grade III-IV toxicities in children and adolescents undergoing alloHCT.

Methods: Retrospective cohort study of 166 patients (0.1-22y) who underwent alloHCT from January 2000 and December 2013 for malignant and non-malignant disease. Patients were conditioned on 1 of 3 Busulfan (Bu)-based conditioning regimens: reduced intensity (RIC): Bu(6.4-8mg/kg)+ Fludarabine (Flu) [150mg/m2], reduced toxicity (RTC): Bu(12.8-16mg/kg)+ Flu (180mg/m2) and myeloablative (MAC): Bu(12.8-16mg/kg)+ cyclophosphamide (120-200mg/kg) or melphalan (135mg/m2). Toxicities were scored using the CTCAE grading system in the 30 days post-alloHCT.

Results: Median age at alloHCT was 8.5y (0.1-22y), malignant n=102, non-malignant n=64. Median number of grade III-IV toxicities in all groups was 3 (0-17). On univariate analysis, age >12 (p=0.002) was the single risk factor associated with an increased incidence of grade III-IV toxicities in the 30 days post-transplant. Incidence of toxicities was not significantly different in malignant v. non-malignant groups, RIC v. RTC v. MAC regimens, donor, HLA, primary disease or hematopoietic co-morbidity index. 1yr TRM in patients with number of grade III-IV toxicities below median (<3) was 2.6% and 1yr TRM in those with above median (≥3) toxicities was 15.6% (p=0.007). A total of 59 pediatric patients received MAC regimens, n=37 <12y and n=22 ≥12. Of this cohort, 43% of patients <12y and 72.7% of patients ≥12 had above median number of grade III-IV toxicities (p=0.034). 1 year TRM was 10.8% for <12y and 22.7% for ≥12y (p=0.272). RIC and RTC regimens were not associated with more than median toxicities in patients ≥12 yrs. Detailed information provided below.

Conclusion: Despite recent advances in alloHCT, toxicity and organ impairment remain a significant cause of morbidity and mortality during the first year following alloHCT. Our preliminary results suggest that higher incidence of grade III-IV toxicities in the 30 days post-alloHCT correlates with higher risk of TRM at 1yr. Age ≥12y was significantly correlated with incidence of grade III-IV toxicities in the 30d post-transplant. Prospective studies to validate our finding and methods to decrease serious toxicities in adolescents are warranted.

Health-Related Quality of Life and Perception of Care of Mucopolysaccharidosis Type I - Hurler Syndrome Patients after Successful Hematopoietic Cell Transplantation: A Parents’ Perspective

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Background: Mucopolysaccharidosis type I-Hurler syndrome (MPS IH) is a lysosomal storage disease characterized by multi-system morbidity and death in early childhood. Hematopoietic cell transplantation (HCT) results in long-term survival, although with significant residual disease burden. The effect of this disease burden on the health-related quality of life of MPS IH patients after HCT is however still unknown. Furthermore, little is known about the perception of care of transplanted MPS IH patients.

Methods: 63 alive and engrafted MPS IH patients, transplanted at one of the seven participating centers within Europe were included in the study. The functional and psychosocial health were evaluated using two validated questionnaires: the Child Health Questionnaire (CHQ) and Pediatric Outcomes Data Collection Instrument (PODCI). Subscale and summary scores were compared to normative samples to derive z-scores and standard deviations (SD). The influence of various patient, donor, transplantation as well as disease-specific predictors was evaluated using univariate and multivariate linear regression analysis. Correlation analysis between the functional and psychosocial scores of the CHQ and PODCI was performed using Spearman’s rank correlation. The perception of care was evaluated by a third validated questionnaire: the Measure of Processes of Care (MPOC) questionnaire.

Results: The functional health of transplanted MPS IH patients was significantly diminished compared with normative data; mean physical summary z-score -2.5 (SD 1.5), mean global functioning z-score -3.6 (SD 2.5) (figure 1 and 2). The psychosocial health appeared to be comparable or only slightly reduced compared to normative data; mean psychosocial summary z-score -0.1 (SD 1.3) (figure 1). A higher obtained IDUA enzyme level after HCT predicted for superior functional health, supporting the use of only...