conducted a retrospective cohort study to describe the risk factors and natural history of post-transplant DM and HTN. Consecutive allogeneic HCT recipients from 2003–2005 were included in this study if they had survived >1 year post-transplant and had not received a previous HCT. DM and HTN were defined by published adult and pediatric guidelines. The final cohort consisted of 180 patients (adult [≥18 years] 106, pediatric [<18 years] 74); the median age was 27 (range 0.2–69) years. Before HCT, 13% had DM, 9% had HTN, 18% smoked and 19% were obese. Pediatric patients were less likely to have pre-transplant DM, HTN, smoking history or high-risk disease and more likely to receive myeloablative (MA) conditioning. MA conditioning (Cy + 1320 cGy TBI ± Flu) was given to 66% recipients, remainder received non-MA conditioning (Cy + Flu + 200 cGy TBI). All patients are followed until at least 2 years post-HCT at our center; among these 1 year survivors, 156 (87%) were alive at 2 years. Acute or chronic graft-versus-host disease occurred in 118 (66%) patients; of these, 34% received cyclosporine (CSA) for >12 months and 47% received prednisone for >12 months. Within 2-years after HCT, 54 (30%) had DM while 126 (70%) had HTN. Rates were similar for adult (DM 30%, HTN 68%) and pediatric (DM 30%, HTN 73%) recipients. At 2 years post-HCT, 12% had persistent DM while 39% had persistent HTN. Increasing cumulative dose of corticosteroids increased the likelihood of having persistent DM at 2 years post-transplant (no steroids 7%, ≤ 0.25 mg/kg/d 13%, >0.25 mg/kg/d 27%, p = 0.02); such an association was not observed for HTN. On multivariate analyses, risk factors for DM included history of DM pre-HCT (relative risk [RR] 5.0 [95% CI, 2.8–8.9]) and prednisone exposure (RR 2.4 [1.3–4.5]), while no predictive factors for resolution of post-HCT DM were identified. CSA exposure was the only risk factor for post-HCT HTN (RR 1.6 [1.1–2.5]), while history of HTN pre-HCT was predictive for persistent HTN beyond 2 years (RR 3.07 [1.1–8.3]). DM and HTN are frequent among survivors of adult and pediatric allogeneic HCT and can persist for an extended period of time after transplantation. Continued monitoring and treatment of DM and HTN is necessary in HCT survivors, especially if survivors have been exposed to corticosteroids.

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MORTALITY OF HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS ADMITTED TO A MEDICAL INTENSIVE CARE UNIT (MICU) AS PREDICTED BY THE HEMATOPOIETIC CELL TRANSPLANTATION COMORBIDITY INDEX (HCTCI)

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Introduction: Severity of illness scores validated in the critical care setting are known to underestimate mortality in cancer patients. We evaluated the Hematopoietic Cell Transplantation Comorbidity Index (HCTCI) score (Sorror et al) as a predictor of mortality in HCT recipients requiring intensive care.

Methods: A retrospective review of HCT recipients transplanted between January 1, 1997, and March 1, 2007 was preformed. The HCTCI score was calculated for each patient at the time of admission to the MICU. The primary endpoint was defined as survival for seven days from the time of discharge from the MICU. Covariates analyzed included age, sex, conditioning regimen, need for mechanical ventilation, use of vasopressors, time from transplant to MICU admission, HCT type, and absolute neutrophil count (ANC) at the time of MICU admission.

Results: Seventy-four of 892 patients (8.3%) required MICU care. Forty-two (57%) were males, 32 (43%) females and the median age was 47 (range: 22–71). Twenty-three (31%) patients received autologous, 26 (35%) matched related donor (MRD) and 25 (34%) matched unrelated donor (MUD) HCT. Overall mortality was 72%. Using the Wilcoxon signed-rank test, the HCTCI score was found to be highly predictive of mortality (p<0.0001). None of the patients with an HCTCI score of ≥10 survived. Univariate analysis identified transplant type [mortality: autologous 52%, MRD 73%, MUD 88%; p = 0.02], conditioning [mortality: myeloablative 91% versus non-myeloablative 57%; p = 0.002], mechanical ventilation (MV): [mortality: MV n = 43, 79% versus no MV n = 31, 61%; p = 0.0003], and ANC [mortality: < 500 /μL 88%, ANC ≥ 500 /μL 60%; p = 0.01] as correlating with mortality. In multivariate analysis only the HCTCI score remained significantly correlated with mortality (p = 0.001) with a point estimate of the odds ratio of 2.8 (95% C.I. 1.5–5.3).

Conclusion: This retrospective study demonstrates the predictive value of the HCTCI for mortality when calculated on admission to the MICU at our institution. The HCTCI score is easily calculated and readily applicable in the clinical setting. Prospective study of the HCTCI is needed for validation of this tool as a predictor of mortality on MICU admission.

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UTILITY OF THE PSYCHOSOCIAL ASSESSMENT OF CANDIDATES FOR TRANSPLANTATION (PACT) SCALE IN ALLOGENEIC BMT

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The Psychosocial Assessment of Candidates for Transplantation (PACT) scale was completed on 120 allogeneic BMT patients pre-transplant, from 11/2003 to 6/2007. The PACT has 8 items, each rated on a 5-point scale, and an initial and final rating independently based on the rater's overall impressions of the candidate's acceptability for transplant. This study assessed utility of the PACT scale for psychosocial screening in allogeneic BMT. Examined were associations of the eight PACT subscales and the final rating with medical outcomes, post-transplant. Significant relationships (P ≤ 0.05) between PACT subscales and medical outcomes are as follows: better scores on compliance with medications and medical advice associates with lower in-hospital mortality, shorter length of stay and readmission duration, and faster neutrophil and platelet engraftment; better scores on drug/alcohol use associates with faster platelet engraftment; better scores on family/support system availability and on relevant knowledge and receptiveness to education associates with decreased risk of mortality. The final rating score and medical outcomes are not significantly related; however, study findings underscore the prognostic value of the PACT subscales and, thus, utility for screening of BMT candidates.

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ETHICAL REASONING ABOUT PATIENT ELIGIBILITY IN ALLOGENEIC BMT BASED ON PSYCHOSOCIAL CRITERIA

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Chairpersons of hospital ethics committees (HEC) and BMT clinicians were compared regarding willingness to proceed with allogeneic BMT given select psychosocial risk factors. A self- administered questionnaire was sent to 62 HEC chairpersons at hospitals with an accredited BMT Program; response rate was 37%. Items included background information, followed by six case vignettes from a 2006 national survey on which BMT physicians, nurses, and social workers agreed not to proceed with allogeneic BMT based on the following risk factors: suicidal ideation; use of addictive, illicit drugs; history of non-compliance; has no caregiver; is alcoholic; and has mild dementia. Opinions regarding transplant differed on one case only, patient with mild dementia; 27% of HEC chairpersons recommended not proceeding with BMT, which was significantly lower than nurses (68%, p < 0.001), physicians (63.5%, p < 0.001), and social workers (51.9%, P = 0.05). That HEC chairpersons disagreed with BMT clinicians in the case of mild dementia may suggest that they view dementia patients as more deserving of consideration for BMT than patients who have some element of choice in the psychosocial risk factor. In general, qualitative data reveal patterns of informal ethical reasoning that suggest transplant decisions may be linked to patient responsibility for the psychosocial risk factor as well as medical benefit/outcome.

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AVASCULAR NECROSIS (AVN) IN SURVIVORS OF HEMATOPOIETIC-CELL TRANSPLANTATION (HCT): A LARGE SINGLE INSTITUTION STUDY

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AVN is a debilitating complication of HCT. We describe a contemporary cohort of patients with AVN after HCT to describe its

presentation, treatment and risk-factors. AVN was defined as the presence of joint symptoms with confirmatory radiological findings on X-ray, CT or MRI at any time after HCT. Among 3527 HCT recipients from 1990–2007, 73 (2.1%) cases of post-HCT AVN were identified; of these, 8 (0.7%) occurred after autologous and 65 (2.7%) after allogeneic HCT (sibling 33, unrelated 19, umbilical cord blood 13). Median age at HCT for cases was 29 (range, 4–60) years and included 23% pediatric recipients (<18 years). Median followup was 7 (range, 1–16) years. Myeloablative conditioning was used in 74% and 77% received total body irradiation (TBI). Acute and chronic graft-versus-host disease (GVHD) occurred in 69% and 65%, respectively. Use of prednisone (or equivalent) was very prevalent; 8% had received no prednisone, 23% had received a cumulative dose of ≤0.5 mg/kg/day, and 69% had received >0.5 mg/kg/day prior to diagnosis of AVN. AVN affected 155 joints in these 73 patients (median number of joints involved 2 [range, 1–6]) and was diagnosed at a median of 18 months (interquartile range 11–33 months) post-HCT. Proximal femur (54%) and distal femur (36%) were the most common sites. Association Research Circulation Osseous stage, which classifies progressively worsening radiological abnormalities and amount of bone involvement from stage 0–4, could be assigned for 52 cases; of these, stage 3 or 4 (that requires surgical intervention) was present in 60%. Thirty-five (48%) received surgical treatment for AVN, among which joint replacement was performed in 31 patients. Risk factor analysis was performed using a randomly selected cohort of 148 HCT recipients frequency matched by age, gender and year of HCT and with no joint symptoms. Risk of AVN was higher in allogeneic HCT recipients (odds ratio (OR) 2.7 (95% CI, 1.2–6.2), P = 0.01) and with exposure to corticosteroids (OR 15.9 (6.5–39.1), p < 0.01); diagnosis, conditioning intensity and use of TBI did not increase its risk. In conclusion, AVN is a relatively rare complication of HCT, typically occurs within the first 3 years after HCT, presents with advanced stages and frequently requires surgical management. Allogeneic HCT recipients, especially those exposed to corticosteroids, are at highest risk and may benefit from screening for early detection and treatment to avoid joint replacement surgery.

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DIAGNOSIS OF MENTAL HEALTH DISORDER DOES NOT EFFECT OUTCOME IN ALLOGENEIC BONE MARROW TRANSPLANT

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Background: Psychiatric disturbance before allogeneic stem cell transplant (allo-SCT) has been associated with worse survival and quality of life and is used in predictive indices for transplant outcome.

Methods: We report a retrospective study that analyzed 142 patients who underwent fully ablative allo-SCT between January 2005 and June 2008. Patients with mental health disorder (MHDx) were identified from pre-transplant psychosocial assessment and physician evaluation before transplant. Patients were assigned MHDx if they were taking psychotropic medication or specific MHDx was documented. Wilcoxon rank sum and Chi-square tests were used to compare patients with MHDx to patients without MHDx. Outcomes between these groups were estimated using the Kaplan-Meier method via the log rank test.

Results: We identified 41 patients with MHDx and 101 patients without. The Wilcoxon rank sum test analysis showed that patients with MHDx had a significantly longer period from diagnosis to transplant (P = 0.001). Patients with MHDx had an increased incidence of acute graft versus host disease (AGVHD) (P = 0.003), but not chronic graft versus host disease (CGVHD) (P = 0.30). Kaplan-Meier analysis showed no significant statistical difference in Relapse Mortality (RM) (0.31), Non-Relapse Mortality (NRM) (P = 0.41) or Overall Survival (OS) (P = 0.99). (See table below.) One and two-year survival for patients with MHDx (56.2% and 47.2% respectively) and without MHDx (57.2% and 44.2% respectively) were not statistically significant.

Conclusion: Identifying comorbidities that have an impact on post-transplant survival is crucial to improving transplant outcome. While this study shows no statistical association between MHDx and OS, RM or NRM it demonstrates a significant association of MHDx on time period from diagnosis to transplant and incidence of AGVHD. Identifying patients with MHDx early in pre-transplant staging and initiating appropriate treatment might reduce time to transplant and AGVHD. Providing targeted psychosocial services could lead to an overall improved quality of life. This study did not indicate that MHdx leads to worse outcome. Further investigation into pre-transplant MHdx and its role in pre-transplant care as well as in transplant is warranted.

	No MHD	MHDx	P-value
Months from Diagnosis to Transplant (mean +SD)	9.9 + 14.6	19.1 + 23.0	0.001
AGVHD	59 / 101 (58.4%)	33 / 41 (80.5%)	0.003
CGVHD	33 / 101 (32.7%)	9 / 41 (22.0%)	0.30
Non-Relapse Mortality	28 / 101 (27.7%)	14 / 41 (34.1%)	0.41
Relapse Mortality	22 / 101 (21.8%)	5 / 41 (12.2%)	0.31
Overall Survival	51 / 101 (51.5%)	22 / 41 (53.7%)	0.99

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ALLELIC VARIATION IN TP53 AND MDM2 DNA REPAIR GENES CONSTITUTE GENETIC RISK FACTORS FOR LONG-TERM SURVIVAL IN ALLOGENEIC STEM CELL TRANSPLANTATION

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The p53 tumor suppressor pathway plays a major role in tumor development and cell survival. Germline single nucleotide polymorphisms (SNP)s in codon 72 of TP53 (Arg72Pro; rs1042522) and in the promoter region of the ubiquitin ligase MDM2 (-309; rs2279744) influence apoptotic activity in response to cellular stress. In vitro studies have demonstrated that cells homozygous for Arg72 in p53 have significantly increased apoptotic activity in response to cellular stress, while cells homozygous for Pro72 have increase in cell cycle arrest and DNA repair. We recently investigated the impact of these two SNPs on survival after transplantation from HLA 10/10 matched unrelated donors. In brief, analysis of samples and clinical outcome data contributed by the National Marrow Donor Program Research Sample Repository and by the Center for International Blood and Marrow Transplant Research, respectively, demonstrated that patients with two p53 72Pro alleles and at least one copy of the MDM2-309 G allele had an increase in mortality risk compared to patients with 2 p53 72Pro alleles and zero G alleles at -309 (HR = 1.41). We now report the results of a second independent cohort of donor-recipient pairs tested for the same p53 and MDM2 SNPs. All patients were treated at the Fred Hutchinson Cancer Research Center and represented 731 related and 669 unrelated pairs including HLA matched and mismatched cases. We find that patients with two p53 72Pro alleles and at least one copy of the MDM2-309 G allele had a significant increase in mortality risk compared to patients with 2 p53 72Pro alleles and zero G alleles at -309 (HR = 1.35). These results are consistent with our hypothesis that the combination of recipient genotypes for p53 Arg72/Pro and SNP -309 MDM2 affects post transplantation survival. Detailed analysis of other clinical outcome data are currently in progress.

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TASTE DISORDERS AND ORAL CLINIC EVALUATION IN PATIENTS SUBMITTED TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Graft versus host disease can affect the oral cavity leading to mucosal salivary gland damages and causing change in taste perception.