Introduction: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) is indicated for patients with intermediate or high risk primary Myelofibrosis (MF), and also in patients with Policitemia Vera or Essential Thrombocythemia who have progressed to high risk MF. The results for allogeneic HSCT with myeloablative conditioning seem to be better for patients younger than 45 years, determining lower relapse risk. However, Reduced Intensity Conditioning (RIC) for patients between 45 and 65 years-old has shown to be a promising strategy, with less mortality related to the procedure. This study aims describing a series of patients diagnosed with myelofibrosis, transplanted in the Hospital de Clínicas (HC) from the Federal University of Paraná and Hospital Nossa Senhora das Graças (HNSG) (Curitiba, Brazil).
Patients and Methods: From 1984 to 2011, fourteen patients with MF were submitted to HSCT, eleven from the HC and three from HNSG. The median of age was 42 years (10-51). There were ten males and four females. In average, five blood transfusions were done per patient (0-61). Five male patients received the graft from a female donor, and two patients received an unrelated HSCT. The median of duration of the disease was 20 months (2-150). According to Dupriez Classification, all the patients were of intermediate and high risk. Five patients had a myeloablative conditioning (Busulfan plus Cyclophosphamide: 4; Cyclophosphamide plus Total Body Irradiation:1) while nine had a RIC transplant (Fludarabine 150mg/m2 plus Melphalan 140mg/m2:6; Fludarabine plus Melphalan plus Antithymocyte Globulin:2; Fludarabine 180mg/m2 plus Bulsufan 10mg/m2 plus Antithymocyte globulin 5mg/kg:1).
Results: In the myeloablative conditioning group (n=5), all the patients presented marrow engraftment; one relapsed. Three patients presented grade II-IV acute graft versus host disease, and four developed severe chronic graft versus host disease. Four patients died, and the only survivor was 10 years-old. Median survival was 479 days. In RIC group (n=9), engraftment didn't occur in one patient (which had splenomegaly of 18 cm at the time of transplantation), and another three relapsed. The other seven patients remained alive and free of disease, with median survival of 750 days (34-1872; P= 0,000123).
Conclusion: In spite of the limited number of patients in this study, data suggest that RIC regimens improved survival in HSCT for myelofibrosis in our center, even with a slightly greater relapse risk. Except for very young patients, this strategy should be considered for further investigation.

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Assessment of the Hematopoietic Cell Transplantation Comorbidity Index in Patients Receiving Reduced-Intensity Allogeneic Hematopoietic Stem Cell Transplantation

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Allogeneic hematopoietic stem cell transplantation (HSCT) is an established therapy for malignant and nonmalignant hematologic disorders. Reduced-intensity conditioning (RIC) regimens have expanded the use of HSCT to the elderly patients and to patients that are otherwise ineligible for conventional transplants. However, RIC HSCT still remains associated with a significant morbidity and mortality and the careful assessment of risks and benefits before transplantation is essential. Major factors which influence non-relapse mortality (NRM) and overall survival (OS) after HSCT are diagnosis, type of transplant and the patient's risk profile, which includes age and presence of comorbidities. The use of the hematopoietic cell transplantation-specific comorbidity index (HSCT-CI) has been proposed to predict the probability of non-relapse mortality (NRM) and overall survival (OS) following HSCT. Since its development, HSCT-CI has been evaluated at different institutions for various hematologic diseases. We performed a single-center retrospective study to assess the prognostic value of HSCT-CI on transplant outcomes in a cohort of patients undergoing RIC HSCT. We analyze patients receiving a RIC HSCT between January 2005 and December 2010. The median patient age at the time of transplantation was 57 years (range: 19-75 years). The patient diagnoses included AML (32%), NHL (28%), MM (15%), MDS (10%), HD (5%), CLL (5%), ALL (3%), MPD (1%) and nonmalignant hematologic (1%). The median pre-transplantation HSCT-CI score was 2 (range: 0-9). Among 133 patients, OS at 2 years was 36%. The 2 yr OS is 34%, 33% and 41% in the low-, intermediate-, and high-risk HSCT-CI groups respectively ($P = .72$). The corresponding NRM at 2 years was 39%, 41% and 38% ($P = .85$). Further subgroup analysis (patient age, diagnosis, conditioning, remission status and prior stem cell transplant) disclosed no significant differences in the OS prediction by the HCT-CI score. In conclusion, we found no predictive value of HSCT-CI for the determination of 2-year OS or 2-year NRM in allogeneic HSCT receiving reduced-intensity condition.

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Risk Factors for Prolonged Length of Hospitalization in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation

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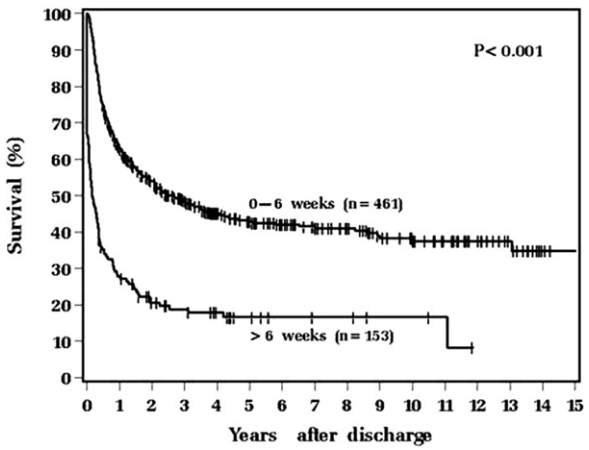
Prolonged hospitalization exposes patients (pts) undergoing allogeneic hematopoietic cell transplantation (HCT) to risks of iatrogenic complications and results in significant morbidity and mortality as well as expense, however, there are limited data on risk factors that contribute to length of stay (LOS) in HCT pts.

663 pts underwent HCT from 1/1997 to 12/2011. Among 663 pts, 49 died in the hospital within 6 weeks (wks) of transplant and were excluded, leaving 614 pts, median age 44 (range 18-71 years), for analysis. Pts underwent HCT for acute myeloid leukemia (n=258), acute lymphoblastic leukemia (n=98), myelodysplastic syndrome (n=87), chronic myeloid leukemia (n=78), non Hodgkin lymphoma (n=55), aplastic anemia (n=20), Hodgkin disease, myeloproliferative neoplasm, and plasma cell disorders (remaining n=18). The majority of pts underwent myeloablative transplant (n=599, 97.6%); 15 (2.4%) had a reduced-intensity transplant. 317 (51.6%) pts received a transplant from a related donor, 250 from an unrelated donor (40.7%) and 47 (7.7%) received cord blood.

153 pts (25%) were identified to have a prolonged LOS, defined as $\geq$6 wks. In univariable analyses, variables associated with LOS included: poor performance status (PS) (odds ratio [OR] 1.31 per 10 point decrease on Karnofsky scale, $P = .017$), unrelated donor transplant (OR 3.45, $P < .001$), cord blood transplant (OR 7.86, $P < .001$), HLA mismatch (OR 4.45, $P < .001$), and CD34+ cell dose (median

2.04x10^6/kg, range 0.01-26), (OR 1.43 per 1x10^6/kg decrease, $P < .001$). Prior chemotherapy, lymphoid malignancies, longer interval from diagnosis to HCT, and positive CMV status were also associated with LOS, with a trend towards significance ($P = .06$ for all). In multivariable, logistic regression analyses, poor PS (OR 1.31 per 10 point decrease,$P = .031$), unrelated donor (OR 3.14 $P < .001$), cord blood transplantation (OR 2.42, $P = .048$), CMV positivity of either donor or recipient (OR 1.91, $P = .018$), and CD34+ cell dose (OR 1.35 per 1x10^6/kg decrease, $P < .001$) were significantly associated with prolonged LOS. 5-year non-relapse mortality (NRM) for pts hospitalized ≥6 wks was significantly worse than for pts hospitalized <6 wks (60.2% vs. 31.8%, $P < .001$), as was overall survival (OS) at 5 years, (16.6% vs. 42.8%, $P < .001$). There were no differences in the incidence or degree of acute GVHD.

In conclusion, hospitalization ≥6 wks following HCT is associated with significantly worse NRM and OS. Poor PS, CMV positivity, decreased CD34+ cell dose, and unrelated and cord blood transplants have previously been identified as factors predictive of poor outcome and are also factors that contribute to prolonged LOS. Efforts should be made to optimize modifiable factors such as cell dose in HCT pts, especially those with other risk factors, such as having an unrelated or cord blood donor.



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Cytomegalovirus Viremia is a Risk Factor for Late-Onset Hemorrhagic Cystitis Following Allogeneic Hematopoietic Stem Cell Transplantation

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Purpose: Late-onset hemorrhagic cystitis (LOHC) is a common complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT), which was mainly associated with BK virus and adenovirus (ADV). However, there still some patients developed LOHC without infection of BKV and ADV. Several retrospective studies showed that CMV infection was associated with LOHC. So, we design this prospective study to define the relationship between CMV infection and LOHC.

Design and Methods: Fifty consecutive patients who received allo-HSCT between October 2011 and December 2011 were prospectively investigated to screen BKV, ADV and CMV in the urine and plasma using Real-time Polymerase Chain Reaction (RT-PCR).

Results: Twenty-one out of the 50 patients developed LOHC with a cumulative incidence of 42%±7.1%.The median time from transplantation to onset of LOHC was 29 (range, 4-64) days. There are 34 patients and 21 patients developed CMV viremia and CMV viruria, respectively, within day 100. The cumulative incidence of LOHC in patients with CMV viremia was significantly higher than those without CMV viremia (58.8% vs. 6.3%, $P = .001$) on day 100 after transplantation. Patients with CMV viruria had a significant higher cumulative incidence of LOHC than those without CMV viruria (60.7% vs. 18.2%, $P = .006$). The cumulative incidence of CMV viremia and CMV viruria in patients with LOHC (n=21) versus those without LOHC (n=29) were 95.2% vs. 48.3% ($P = .001$) and 80.9% vs. 34.5% ($P = .001$), respectively. The cumulative incidence of LOHC in patients whose plasma BKV load increased more than or equal to 10^3-fold over baseline was significantly higher than those with plasma load increase less than 10^3-fold (67.9%±9.2%vs. 9.1%±6.3%, $P < .001$). The cumulative incidence of LOHC in patients whose urine BKV load increased more than or equal to 10^4-fold over baseline was significantly higher than those with urine load increase less than 10^4-fold (66.7% ±10.3% vs. 19.2%±7.9%, $P = .002$). ADV was positive in 4 patients including one patient with LOHC. Multivirariate analysis showed that CMV viremia (HR=10.496, 95% CI: 1.527-86.570, $P = .018$) and plasma BKV load increased more than or equal to 10^3-fold compared to baseline level (HR=10.669, 95% CI: 2.452-46.419, $P = .002$) were two independent risk factors for LOHC.

Conclusion: Our data suggest that CMV viremia is a risk factor for LOHC following allo-HSCT.

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Investigation of ADAMTS13 and VWF in the Patients with Thrombotic Complications Following Hematopoietic Stem-Cell Transplantation (HSCT)

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Objective: Plasma ADAMTS13 may play a role in the pathogenesis of hematopoietic stem-cell transplantation (HSCT) related thrombosis by cleaving the prothrombotic ultralarge VWF into less active VWF. This study was to investigate the alterations of ADAMTS13 and VWF in HSCT recipients during transplantation, and to evaluate their significance in transplantation-related thrombotic complications.

Methods: Plasma ADAMTS13 activity was detected by fluorescence resonance energy transfer substrate VWF73 (FRETS-VWF73) assay in 113 hematologic patients receiving allogeneic-HSCT. Of all the patients recruited for his study, 8 patients were diagnosed to have the thrombotic disorders and 49 patients were classified to have acute graft-versus-host disease (aGVHD). The alterations of ADAMTS13 activity and VWF level in the plasma of patients were analyzed during transplantation, and the correlation between ADAMTS13/VWF and transplantation-related thrombosis was evaluated using the SAS program (version 9.3).

Results: The average plasma ADAMTS13 activity in 113 cases following HSCT at each period were less than the healthy controls ($P < .01$), while the VWF antigen level in each period were higher than the controls ($P < .05$). Among all the patients after pretreatment, 69 showed decreased plasma ADAMTS13 activities (59.3%), including 9 patients with more than 60% (8.0%) decrease, while the average plasma VWF antigen level of this 69 patients was significantly increased in patients after pretreatment ($P < .05$). Considering thrombotic complications, the data showed that 8 patients with