Conclusions: 3 independent factors — subsets of T cells, B cells, and total lymphocyte counts along with platelet counts — account for the majority of variability in IR in this cohort. CD4-CD8- T cells and NKT cells may be emerging biomarkers of chronic GVHD activity. Lymphocyte activation without overt GVHD adds to the complexity of the study of post-HCT IR. With more patient data, predictive classification of GVHD status by peripheral blood cell subset testing may become possible.

Table
Factor and Discriminant Analysis

<table>
<thead>
<tr>
<th>Factor</th>
<th>Percent of Variance</th>
<th>Cumulative Percent of Variance</th>
<th>Percent Misclassified on DA</th>
<th>Cumulative P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor 1 (CD4+, CD8+, CD45RO- T cells subsets)</td>
<td>33.91</td>
<td>33.91</td>
<td>41.9</td>
<td>0.54</td>
</tr>
<tr>
<td>Factor 2 (naïve B and switched memory B cell subsets)</td>
<td>28.19</td>
<td>62.10</td>
<td>35.0</td>
<td>0.10</td>
</tr>
<tr>
<td>Factor 3 (ALC + platelet count)</td>
<td>25.54</td>
<td>87.65</td>
<td>13.3</td>
<td>0.06</td>
</tr>
</tbody>
</table>

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Hypomethylating Agents for Relapse After Allogeneic Hematopoietic Cell Transplantation in Acute Myeloid Leukemia

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Background: Allogeneic hematopoietic cell transplantation (HCT) can be curative in patients with acute myeloid leukemia (AML), but relapse after HCT continues to be a leading cause of mortality. Treatment options for these patients are limited. Hypomethylating (HM) agents such as 5-azacytidine and 5-aza-2'-deoxycytidine (gemcitabine) have immunomodulatory properties including augmenting tumor antigen presentation that may enhance graft-versus-leukemia (GVL) effect. Moreover, inhibitory effects of these agents on T-cell activation and cytokine production may lead to low incidence of graft-versus-host-disease (GVHD). Our aim was to describe the outcomes, including response, survival, and incidence of GVHD, in patients treated with HM agents for relapsed AML or loss of donor chimerism (LDC) after HCT.

Methods: Subjects were patients with relapsed AML or LDC after allogeneic HCT for AML or high-risk myelodysplastic syndrome (MDS) who were treated with either 5-azacytidine or decitabine at the University of Pittsburgh Cancer Institute. Relapse was defined as a period of complete remission (CR) after HCT followed by re-occurrence of >5% myeloblasts or cytogenetic abnormalities on bone marrow biopsy. LDC was defined as <100% donor chimerism without relapse. Retrospective analysis was performed to determine response to HM agents, overall survival from time of relapse or LDC, and incidence of GVHD.

Results: Thirteen patients were identified, whose median age was 57 years (22-62), and median time to relapse after HCT was 124 days (30 to 847). Seven patients received myeloablative conditioning regimens, and 6 patients received reduced-intensity conditioning. Nine patients had relapsed AML, and 4 patients had LDC. Ten patients were treated with decitabine and 3 patients were treated with 5-azacytidine, with median cycles received of 4 (1-9). After hypomethylating agents, 9 of 12 (75%) evaluable patients had a CR, and 3 patients had progressive disease. Eight of 10 (80%) evaluable bone marrow biopsies revealed 100% donor chimerism after treatment with a HM agent. Grade I-IV acute GVHD of the liver occurred in 6 patients, 3 of whom had isolated liver involvement. Median survival was 308 days (44-857) from time of relapse or LDC, and 7 patients are alive at time of analysis and remain in CR.

Conclusions: HM agents in patients with relapsed AML can be effective in reversing loss of donor chimerism and inducing CR. This may be due to epigenetic changes and subsequent immunomodulatory effects that enhance GVL effect. There may be a relationship between use of these agents with development of acute liver GVHD, and further exploration into pathophysiology and predisposing factors are warranted. The use of HM agents as a maintenance strategy in patients at high risk of relapse after HCT should be further explored.

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Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) Is Predictive of Serious Adverse Events and Overall Survival in Older Allogeneic Transplant Recipients


Background: The Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) is predictive of non-relapse mortality (NRM) and overall survival (OS) after allogeneic stem cell transplant (SCT). However, the HCT-CI has been less well validated in the older SCT patient population. We hypothesized that the HCT-CI could have less discriminative ability in this population, where multiple comorbidities are common.

Methods: We performed a retrospective study of patients ≥50 years of age who underwent SCT at UCSF, where HCT-CI was recorded prospectively as part of routine clinical care starting in 2007. Outcomes measured included NRM and OS, as well as grade 3-4 non-hematologic adverse events to 100 days post-SCT, duration of hospital stay, and risk of re-hospitalization with the first 100 days. Kaplan Meier methods with log-rank tests were used for analysis of NRM and OS; Student’s t test or chi-square test were used for the remaining outcome measures.

Results: We identified 59 patients ≥50 years of age with complete HCT-CI data. The median age was 60 years (range 50-74) and 31 (53%) of the patients were male. Most SCTs were for AML (n=30, 51%) or MDS (n=9, 15%). SCTs were non-myeloablative in 24 patients (41%) and conditioning was fludarabine/busulfan-based in 53 patients (90%). Median follow up was 22 months.

Twelve patients had HCT-CI score of 0 (20%), 19 had HCT-CI score of 1-2 (32%) and 28 had HCT-CI score ≥3 (47%). High HCT-CI score (≥3) was associated with significantly decreased OS (median OS not reached for HCT-CI 0-2 vs 14 months for HCT-CI ≥3; hazard ratio 2.2, P = .02). This remained significant in multivariate analysis that included age, KPS, treatment intensity, and the presence or absence of...
GVHD as covariates (hazard ratio 2.2, \( P = .03 \) for HCT-CI; \( p = .NS \) for all other covariates). NRM was low in our patient population (12%), and was not significantly different between HCT-CI groups. Grade 3-4 non-hematologic adverse events within the first 100 days after SCT were significantly more common in the higher HCT-CI groups, \( P = .02 \). The most common adverse events were infectious and gastrointestinal. Risk of re-hospitalization within the first 100 days after SCT was not statistically different between groups (17%, 37% and 36% for HCT-CI = 0, 1-2 and \( \geq 3 \) respectively, \( P = .45 \)), although patients with HCT-CI = 0 did have a trend toward a lower risk than patients with HCT-CI = 0 (17% vs 36%, \( P = .2 \)). There was no difference in the duration of SCT hospitalization between HCT-CI groups.

Conclusion: Despite a high incidence of multiple comorbidities (HCT-CI score \( \geq 3 \)) in our older cohort, HCT-CI retained its ability to predict OS, specifically by distinguishing those with HCT-CI \( \geq 3 \) as having a particularly poor prognosis. HCT-CI score \( \geq 3 \) was a better predictor of OS than age or KPS. We conclude that HCT-CI remains a useful predictor of outcomes in older patients undergoing allogeneic SCT.

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The Impact of Continuity of Care on Survival Outcomes After Allogeneic Hematopoietic Stem Cell Transplantation (HCT)

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Continuity of care (COC) is acknowledged as a core quality measure in medicine. There is a little literature known about the impact of COC on OS after allogeneic hematopoietic stem cell transplantation Allo-HCT.

Method: Between July 2009 and May 2012, 74 consecutive Allo-HCT were performed at our center. The patient’s clinical care for the first consecutive 41 patients was shared between the physicians independent of primary transplant physician (Non-COC). We hypothesized that COC improve OS after Allo-HCT and the subsequent 33 patients (COC) were followed by their transplant physician both as in-patient and outpatient. Physician’s contribution into the care of each individual patient was calculated from physicians billing visits. Patient characteristics are shown in table I. Draft vs. host disease (GVHD) prophylaxis was Calcineurin inhibitor with MTX/Mycophenolate with the addition of Thymoglobulin for MUD and mismatched RD.

Results: The average contribution of the primary transplant physician into their patients care during the first year post-transplant was 49% vs. 80% for Non-COC and COC groups respectively (\( P = .01 \)). There was no difference in patient characteristics between COC and Non-COC groups except for older patients in Non-COC. With median duration of follow up of 815 days for Non-COC and 320 days for COC groups, the 1-year OS was 56% vs. 75% respectively (\( P = .07 \)). Similarly, there was a trend toward improved DFS for COC (1-year DFS of 68% vs. 48%, \( P = .11 \)). Both cumulative incidence of relapse and treatment related mortality (TRM) at 1-year were lower in COC compared to Non-COC groups; 9% vs. 25% and 17% vs. 25% respectively. The cumulative incidence of grade II – IV acute GVHD was 64% for Non-COC vs. 46% COC respectively. There was more patients with grade III/IV aGVHD: 13/41 (32%) in Non-COC compared to 6/33 (18%) in COC, however this difference was not statistically significant (\( p = .27 \)). Additionally, there was no difference in OS in patients with grade III/IV aGVHD in Non-COC (13 patients) vs. COC (6 patients), \( P = .85 \). In contrast, Patients without grade III/IV aGVHD had a statistical OS advantage in favor of COC (27 patients) vs. Non-COC (28 patients) with one year OS of 90% vs. 68% respectively, \( P = .05 \). Cumulative incidence of chronic GVHD at one year was 77% for COC and 48% for Non-COC patients, \( P = .02 \).

Conclusion: Continuity of care may favorably improve OS after Allo-HCT. COC did not improve OS in patients with severe aGVHD but may result in OS advantage in patients with grade II aGVHD. Personnel knowledge of the patients and promptness in initiating GVHD therapy in COC group may have contributed to the improved OS in patients with grade II aGVHD. Similarly, the more intense immune suppression for patients with severe GVHD in NCOC group may have contributed to higher relapse and TRM observed.

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Outcomes of Hematopoietic Cell Transplantation in Ethnic and Racial Minorities

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With the growing diversity in race and ethnicity of the American population, there is a need to characterize the disparities in access and outcomes of hematopoietic cell transplantation (HCT) for the racial and ethnic minorities. This single center study examined the association of ethnicity/race with outcomes after HCT. Clinical information of 301 adult patients who underwent single allogeneic HCT for a hematological disorder at Mayo Clinic in Arizona from 11/03 to 06/12 was obtained from the institutional database and retrospective chart review. Information about ethnicity was self-reported by patients. Median follow-up was 20 months (range 3-106 months). Overall survival was compared between the racial/ethnic groups using Cox regression while adjusting for other clinical factors.

The study included 224 white patients (75%) and 77 ethnic minority patients (25%). Non-whites/Hispanics were younger at HCT (median age 40 vs. 56, \( P = .001 \)). Use of myeloablative conditioning (61% vs. 31%, \( P < .001 \)) and related donors (50% vs. 35%, \( P = .01 \)) was more common in Non-whites/Hispanics. There were no differences in disease diagnosis and risk, gender distribution and HCT- comorbidity index between the two groups. More Non-whites/Hispanics were unemployed (51% vs. 25%, \( P < .001 \)). No statistically significant differences in the incidence of post-transplant complications including infections, veno-occlusive disease, grade II-IV acute and NIH chronic GVHD were seen between the two groups. Cumulative incidence of relapse at 5 years was higher in Non-whites/Hispanics (33% vs. 22%, \( P = .03 \)). Though the univariate analysis showed no differences in overall survival (5 year OS: 52% for Whites vs. 50% for Non-whites/Hispanics; \( P = .44 \)), a higher risk for mortality was seen in the multivariate analysis for ethnic minorities as compared to the white patients. (Table)