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LONG-TERM SURVIVAL AND QUALITY OF LIFE (QOL) ASSESSMENT AFTER ALLOGENEIC STEM-CELL TRANSPLANTATION (SCT) FOR ACUTE LEUKEMIA AND MDS; COMPARABLE RESULTS WITH MYELOABLATIVE AND REDUCED-INTENSITY CONDITIONING

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Allogeneic SCT is a curative therapy for patients (pts) with acute leukemia and MDS. SCT is associated with substantial mortality during the first 2 years after SCT whereas after 2 years survival curves often reach a plateau. The pattern of late events and QOL was reported in myeloablative conditioning (MAC) but there is limited data in the reduced intensity (RIC) setting. We analyzed SCT results in a cohort of 457 pts with acute leukemia and MDS. Pts meeting standard eligibility criteria were given MAC (BuCy or Cy/TBI)). Pts considered at excessive risk for non-relapse mortality (NRM) were given reduced toxicity myeloablative conditioning (RTC) such as fludarabine (F) with high-dose busulfan (Bu) or treosulfan or RIC with F and reduced Bu. The 5-year overall survival (OS) rate was 38% (95CI, 33-43); similar with the various regimens. 131 pts, median age 52 (17-72) were alive and leukemia-free 2 years after SCT, with RIC (n = 41), RTC (n = 42) or MAC (n = 48). The probability of remaining alive for the next 5 years was 81% (95CI, 71-90). OS was 75%, 87%, and 83%, respectively (p = NS). There were 18 deaths beyond 2 years. 7 pts had NRM due to solid cancers (n = 2), myocardial infarction (n = 2) and chronic GVHD (n = 3); cumulative incidence 7% (3-16). 11 pts died of relapse; cumulative incidence 12% (7-23). Relapse risk was 16%, 9% and 6% beyond 2, 3 and 5 years after SCT, respectively. Advanced age (> 50) and comorbidity score > 2 at SCT correlated with shortened OS. OS was 70% and 93% in the older and younger groups, respectively (p = 0.02). Chronic GVHD predicted reduced late relapse rate while advanced age predicted late NRM. The regimen used was not correlated with any of these outcomes. QOL was assessed by the EORTC QLQ-C30 questionnaire. Mean QOL score was 67, 67 and 68 after RIC, RTC and MAC, respectively. A low QOL score (20 points lower than the median) was reported by 25%, 37% and 33%, respectively (p = NS). There was no difference in any of the other domains of QOL assessment as well. Multiple regression analysis identified continuous need for immune suppressive therapy (IST) and depression as factors correlated with a low score. Pts given RIC/RTC had shorter duration of IST and were more likely to stop it (78%, 73% and 62%, p = 0.06, respectively). This may be associated with better QOL. In conclusion the pattern of late outcome is similar after MAC and RIC/RTC. Younger pts who are leukemia-free 2 years after SCT can expect a good outcome and relatively good QOL.

LEUKEMIA

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PROGNOSTIC IMPLICATION OF GENE MUTATIONS IN ADULT ACUTE MYELOID LEUKEMIA PATIENTS RECEIVING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Several gene mutations have been shown to have clinical implications in patients with acute myeloid leukemia (AML). However, the prognostic impact of gene mutations in AML patients receiving allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains unclear. We retrospectively evaluated the clinical implication of 10 gene mutations in 325 adult AML patients; 100 of them received allo-HSCT and 225 did not. The genetic alterations analyzed included NPM1, FLT3-ITD, FLT3-TKD, CEBPA, N-RAS, K-RAS, MLL-PTD, IDH1, AML1/RUNX1, and WT1. In patients who did not receive allo-HSCT, older age, higher WBC count, unfavorable karyotype, FLT3-ITD, and AML1/RUNX1 mutation were significantly associated with poor overall survival, while CEBPA mutation and NPM1mut/FLT3-ITDneg were associated with good outcome in both univariate and multivariate analyses. However, in allo-HSCT patients, preHSCT disease status, karyotype, use of HLA-identical sibling donor, CEBPA double mutation, and AML1/RUNX1 mutation were five independent factors that affect post-HSCT overall survival (OS) and relapse-free survival (RFS). The prognostic impacts of FLT3-ITD and NPM1mut/FLT3-ITDneg were lost in AML patients receiving allo-HSCT. Interestingly, AML1/RUNX1 mutation had a trend to be associated with good, rather than poor, prognosis in this group of patients (p = 0.073). The few patients with K-RAS or WT1 mutation also had poor OS and RFS after HSCT. In conclusion, different types of gene mutations might have unique prognostic impact on allo-HSCT outcome in AML patients. These results need to be confirmed by further studies in more patients.

LYMPHOMA/MULTIPLE MYELOMA

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ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MULTIPLE MYELOMA

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Background: Allogeneic hematopoietic cell transplantation (allo HCT) is a potentially curative therapy for multiple myeloma (MM), but has high treatment-mortality (TRM). In addition, disease relapse occurs in a significant number of patients. We sought to evaluate if the recent advances in the field of HCT and MM have impacted the results of allo HCT for MM. We present the results of allo HCT performed at a single center over last 25 years.

Methods: 149 patients with MM who underwent allo HCT between 11/1985 and 6/2010 using myeloablative (MA) N = 52, or reduced intensity conditioning (RIC) N = 97 at our institution were retrospectively analyzed.

Results: Patient characteristics and pertinent outcomes are summarized in the Table. 62 (42%) were female. Median age was 50 (28-70) years. Median follow up is 2.4 years [11.3 years for the patients who received allo HCT prior to year 2000(< 2000); 2 years for the patients who received allo HCT in the year 2000 and onwards (≥ 2000)]. TRM at 2 year was 37%. TRM was significantly lower for year ≥ 2000, recipients of RIC regimens, recipients of peripheral blood stem cells (HPC-A), and disease status at transplant PR or better. There was no difference between TRM for patients above or below age 50 years (p 0.08). Grade II-IV acute and limited or extensive chronic graft-versus host disease was seen in 31%, and 37% patients, respectively. Progression free survival (PFS) at 2 year and 5 year was 23% (95% CI: 16-30) and 15% (95% CI: 9-21), respectively. Overall survival (OS) at 2 year and 5 year was 40% (95% CI: 32-48) and 21% (95% CI: 13-29), respectively. At the time of last follow up 40 patients are still alive and 28 are in remissionn, longest for 166 months. On univariate analysis the OS was significantly better for year ≥ 2000 versus year < 2000; recipients of HPC-A versus HPC-M; primary responsive disease versus relapse or primary refractory disease at HCT; disease status at HCT PR or better; and patients without poor risk cytogenetic features at diagnosis. OS was longer in patients who received maintenance therapy post allo HCT (N = 12) versus the patients who did not, although it did not reach statistical significance (2.9 years versus 8.4 months; p 0.06).

Conclusions: Allo HCT for MM can offer long term disease control in a subset of MM patients. TRM has declined and outcomes have significantly improved over the last decade. Maintenance therapy may have a role post allo HCT.