IJBC 2016; 8(2): 52-55

Iranian Journal of Blood & Cancer

Journal Home Page: www.ijbc.ir

ORIGINAL ARTICLE

Preliminary Results of Allogenic Hematopoietic Stem Cell Transplantation of non-M3 Acute Myeloid Leukemia

Farhad Shahi[1], Marziye Ghalamkari[2*], Seyed Reza Safayi[1], Mehrzad Mirzania[1], Mahdi Khatuni[2], Faeze Almasi[2]

1. Department of Hematology and Medical Oncology, Cancer Research Center, Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
2. Internal Medicine Resident, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article History:
Received: 20.12.2015
Accepted: 30.02.2016

Keywords:
Prognostic factors
Karnofsky performance status scale
GVHD
2-year overall survival
Non-M3 AML
Allogenic stem cell transplantation
Autologous stem cell transplantation

*Corresponding author:
Marziye Ghalamkari, MD;Address: Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 912 6018502

ABSTRACT

Background: Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT) is used as treatment of choice for patients with acute myeloid leukemia (AML). We aimed to evaluate the prognostic factors in 2-year overall survival of patients with non-M3 AML who underwent allogenic HSCT.

Methods: This is a Cross sectional retrospective study. Demographic data and study of variables such as age, sex, complete remission status, Karnofsky performance status scale at baseline and at time of transplantation, occurrence of GVHD (acute and chronic), relapse and 2-year survival were extracted from records of 49 patients who underwent allogenic HSCT from years 2006-2013 at BMT center in Imam Khomeini Hospital. All Autologous SCTs and M3 cases were not included. All data were analyzed with SPSS software. $P<0.05$ was considered as statistically significant.

Results: The overall survival rate was 55% in the patients. There was no significant difference in overall survival between complete remission (CR) 1 and CR2. Relapse rate was 6%. Mean 2-year Karnofsky scale was 93.7. Mean admission time following BMT was 22 days which was significantly related to 2-year performance status ($P=0.02$). Admission complication rate was 22.5% (GVHD 12%). Rate of overall GVHD was 55%, 40% of whom developed chronic GVHD which had a positive effect on 2-year overall survival (OS2).The patient's first performance state (K1) had a significant correlation with 2-year performance state ($P<0.05$) and OS2 ($P<0.05$).

Conclusion: Chronic GVHD and initial Karnofsky performance status scale can be considered as good prognostic factors in patients with AML who undergo allo-HSCT.

Please cite this article as: Shahi F, Ghalamkari M, Safayi SR, Mirzania M, Khatuni M, Almasi F. Preliminary Results of Allogenic Hematopoietic Stem Cell Transplantation of non-M3 Acute Myeloid Leukemia. IJBC 2016; 8(2): 52-55.

Introduction

Acute myeloid leukemia (AML) is a malignant hematological disorder which is caused by clonal expansion of myeloid progenitors. However, chemotherapy is the frontline treatment approach in most hematologic malignancies such as acute lymphoblastic leukemia, is not much efficient in patients with AML.[1] As an alternative and practical method, hematopoietic stem cell transplantation, allogeneic or autologous, has been shown to lead to long-term remissions and cure for patients with AML. Although both approaches are associated with increased survival and improved quality of life,[1,2] the type of donor highly affects the outcome of the patient. Given the high risk of recurrence with autologous hematopoietic stem cell transplantation (HSCT), this method is not curative and progression is

inevitable.[3] In contrast, allogeneic HSCT (allo-HCT) is a potentially useful treatment option for patients with AML because of absence of contaminating tumor cells in the graft and the potential for a GVHD effect.[3,4]Although allo-HSCT improves the outcome of patients with AML, response to the treatment and survival rate varies in these patients. Age of the patient, karyotype, cytogenetic and molecular characteristics of each patient could be considered as prognostic factors.[5] However, the role of some important factors, such as impact of GVHD as a key determinate and performance status of the patients in the context of allo-HSCT have not yet been fully clarified. Therefore, we aimed to evaluate prognostic factors in 2-year overall survival of patients with non-M3 AML who had undergone allo-HSCT.

Patients and Methods

This was a cross-sectional retrospective study in patients who had been diagnosed with AML. The study was performed at the Bone Marrow Transplantation (BMT) center at Imam Khomeini Hospital, Tehran, Iran and was approved by the Hospital's Ethics Committee. The eligible patients were all patients who had been diagnosed with AML according to the World Health Organization classification and had received allo-HSCT during 2006-2013. The patients who had been diagnosed with other malignancies and/or M3-AML or those who had received autologous SCT were excluded from the study.

The patients who received allo-HSCT were fully HLA-matched with their donors. The preparative regimen for all patients was cyclophosphamide 5 mg/kg/d on days 1 and 2 and busulphan 4 mg/kg/d on days 3 to 6. Karnofsky performance status scale was used to evaluate the overall health and quality of life of the patients in initial manifestation of the disease and two years after transplantation. The scoring is a 0 to 100 scoring system in which zero score means the patient is dead and score of 100 means the patient is capable of doing normal activities and no special care is needed.

The description of complete remission (CR) and overall survival (OS) followed the recommended consensus criteria. OS was measured from the transplantation day until the day of event (such as relapse) and was documented.[6] Continuous variables included: donor age, sex, initial clinical sign, interval between initiation of chemotherapy and hybrid cell injection, flowcytometry status, interval between initial diagnosis and treatment and transplantation and the interval between SCT and relapse. Disease-free survival (DFS) rate, 2-year survival rate after allo-HSCT, and the patients' quality of life two years after transplantation were considered as dependent variables.

Categorical variables such as sex and donor type were indicated with counts and percentages. Descriptive statistics (proportions, percentages mean and standard deviation) was used to describe the demographic characteristics and frequency of symptoms. To assess the relationship between the frequency of clinical symptoms or variables listed in the methodology, the Chi-square or Fisher's exact tests were used. Quantitative variables were compared with two tailed Student's t-test. Statistical analyses were performed using the software package of SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

The number of allo-HSCT cases that were registered in the BMT center of Imam Khomeini Hospital during the study period were 49, of which 22 (49.1%) patients were male. 73.5% of the patients were younger than 40 years old. The percentage of patients receiving allo-HSCT was increasing during the last years of the study (2010-2013, figure 1).

Most patients (30.6%) were in their fourth decade of life. The youngest patient undergoing SCT was 15 years old and the eldest was 52 years. AML-M2 was the most common type in patients who received allo-HSCT. All patients (98%) except one, received the transplant from a fully-matched sibling donor.

Transplant Outcomes

The rate of 2-year overall survival was 55%. 55% of patients were in first complete remission (CR1), while

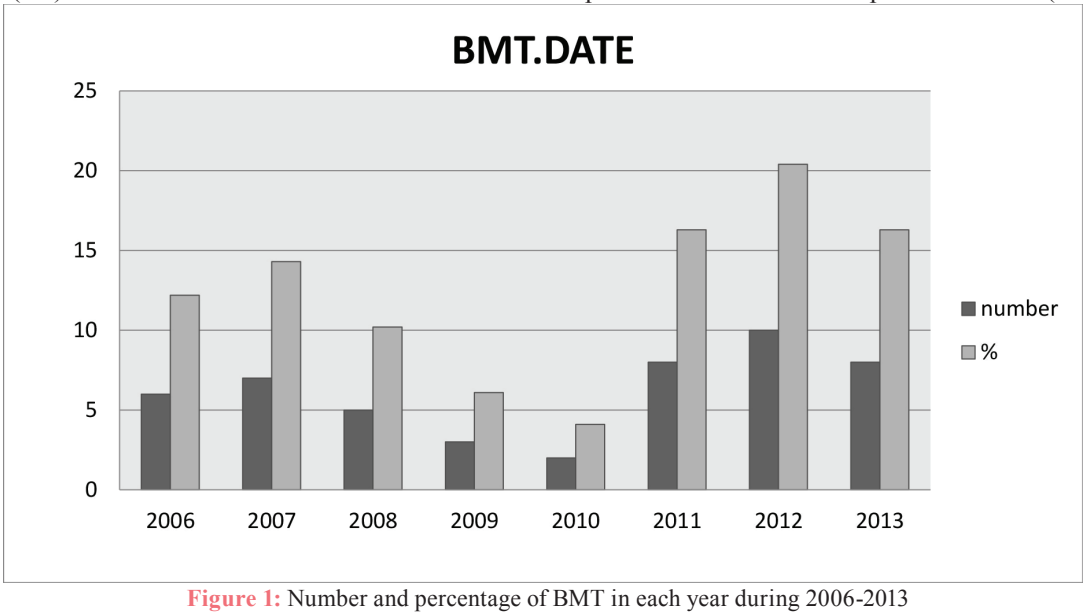

Figure 1: Number and percentage of BMT in each year during 2006-2013

45% received salvage chemotherapy (primary refractory) and were in CR2. There was no significant difference in OS between patients who were in CR1 or CR2. Relapse of disease was recognized in 6% of the patients following HSCT. Mean 2-year Karnofsky scale was 93.7. Mean admission time post BMT was + 22 days which was significantly correlated to 2-year performance status (P=0.02). 22.5% of the patients were admitted due to complications, half of which were related to acute graft versus host disease.

The overall rate of GVHD was 55%. The number of acute GVHD episodes was 15 (7 episodes occurred in one patient). 53% of acute GVHD cases progressed to chronic GVHD. The overall rate of chronic GVHD was 40% which had a positive effect on 2-year OS. The patient's first Karnofsky performance scale (K1) had a significant correlation with 2-year Karnofsky performance scale (P<0.05) and 2-year OS (P<0.05).

Discussion

The present study showed the practicability and usefulness of allo-HSCT in patients with AML. It also confirmed the support of beneficial effects of chronic GVHD and patient's performance status to progression of 2-year overall survival rate. The low relapse rate of patients (6%) can be considered as the main reason to consider allo-HSCT in AML patients who do have the indications to receive transplantation in our institution. Our results also showed that CR1 and CR2 did not affect 2-year overall survival rate. Our results were in contrast to Krauter and colleagues' study showing that a comparable outcome can be achieved when allo-HSCT is successfully performed in CR1, but deferring the transplant to a later time may compromise the survival of the patients.[7]

The incidence of GVHD as a major cause of non-relapse mortality was 55% with chronic GVHD in 40% of the patients. There was significant correlation between chronic GVHD and two-year OS in the patients; the patients with chronic GVHD do experience better outcome. Our results regarding beneficial effects of GVHD on 2-year OS was in contrast to another study showing that the occurrence of GVHD could not necessarily have a beneficial effect on reduction of mortality rate.[8] The inconsistency may be related to differences in patient characteristics enrolled in two studies; the researchers of the mentioned study had surveyed GVHD effect on 2-year survival rate in patients in CR2,[8] while in our study discrimination for CR1 or CR2 was not considered and we analyzed correlation of GVHD with 2-year survival rate in all patients.

Our results indicated that the Karnofsky performance status scale at the beginning of the study had a significant correlation with the corresponding 2-year scale and 2-year OS.

Krauter and colleagues reported age as a determining risk factor of outcome following allo-HSCT;[7] however, most of our patients were younger than 40 years old and this may explain the lack of correlation between age and 2-year survival rate.

Our study was also consistent with other studies that patients with active disease at the beginning of transplantation had a higher rate of relapse.[7,9,10]

Conclusion

Our results showed an acceptable profile for allo-HSCT in treatment of patients with AML, although relapse remains the main problem after allo-HSCT in patients with AML. Identifying the patients at risk before or after transplant would improve the results of allo-HSCT. Our results indicated that occurrence of chronic GVHD and initial Karnofsky performance status scale of the patients can be used as prognostic factors for estimation of 2-year survival rate.

Conflict of Interest: None declared.

References

References

1. Löwenberg B, Downing JR, Burnett A. Acute myeloid leukemia. N Engl J Med. 1999; 341(14):1051-62. doi: 10.1056/NEJM199909303411407. PubMed PMID: 10502596.
2. Armistead PM, de Lima M, Pierce S, Qiao W, Wang X, Thall PF, et al. Quantifying the survival benefit for allogeneic hematopoietic stem cell transplantation in relapsed acute myelogenous leukemia. Biol Blood Marrow Transplant. 2009; 15(11):1431-8. doi: 10.1016/j.bbmt.2009.07.008. PubMed Central PMCID: PMC4067765.
3. Russell N, Bessell E, Stainer C, Haynes A, Das-Gupta E, Byrne J. Allogenichaemopoietic stem cell transplantation for multiple myeloma or plasma cell leukaemia using fractionated total body radiation and high-dose melphalan conditioning. ActaOncol. 2000; 39(7):837–41. PubMed PMID: 11145442.
4. Nivison-Smith I, Bradstock KF, Dodds AJ, Hawkins PA, Szer J. Haemopoietic stem cell transplantation in Australia and New Zealand, 1992-2001: progress report from the Australasian Bone Marrow Transplant Recipient Registry. Intern Med J. 2005; 35(1):18–27. doi: 10.1111/j.1445-5994.2004.00704.x. PubMed PMID: 15667464.
5. Breems DA, Van Putten WL, Huijgens PC, Ossenkoppele GJ, Verhoef GE, Verdonck LF, et al. Prognostic index for adult patients with acute myeloid leukemia in first relapse. J ClinOncol. 2005; 23(9):1969-78. doi: 10.1200/JCO.2005.06.027. PubMed PMID: 15632409.
6. Cheson BD, Bennett JM, Kopecky KJ, Büchner T, Willman CL, Estey EH, et al. Revised recommendations of the international working group for diagnosis, standardization of response criteria, treatment outcomes, and reporting standards for therapeutic trials in acute myeloid leukemia. J Clin Oncol. 2003; 21(24): 4642–9. doi: 10.1200/JCO.2003.04.036. PubMed PMID: 14673054.
7. Krauter J, Wagner K, Stadler M, Dammann E, Zucknick M, Eder M, et al. Prognostic factors

in allo-SCT of elderly patients with AML. Bone Marrow Transplant. 2011; 46(4):545-51. doi: 10.1038/bmt.2010.145. PubMed PMID: 20548341.

8. Michelis FV, Atenafu EG, Gupta V, Kim DD, Kuruvilla J, Lambie A, et al. Duration of first remission, hematopoietic cell transplantation-specific comorbidity index and patient age predict survival of patients with AML transplanted in second CR. Bone Marrow Transplant. 2013; 48(11):1450-5. doi: 10.1038/bmt.2013.71. PubMed PMID: 23686095.
9. Schmid C, Schleuning M, Schwerdtfeger R, Hertenstein B, Mischak-Weissinger E, Bunjes D, et al. Long-term survival in refractory acute myeloid leukemia after sequential treatment with chemotherapy and reduced-intensity conditioning for allogeneic stem cell transplantation. Blood. 2006; 108(3):1092–9. doi: 10.1182/blood-2005-10-4165. PubMed PMID: 16551971.
10. Marks R, Potthoff K, Hahn J, Ihorst G, Bertz H, Spyridonidis A, et al. Reduced-toxicity conditioning with fludarabine, BCNU, and melphalan in allogeneic hematopoietic cell transplantation: particular activity against advanced hematologic malignancies. Blood. 2008; 112(2):415-25. doi: 10.1182/blood-2007-08-104745. PubMed PMID: 18451310.