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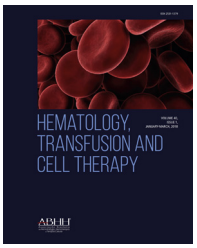

Original article

Donor characteristics and hematopoietic stem cell transplantation outcome: experience of a single center in Southern Brazil

Alessandra Paz[a,b], *Lisandra Rigoni*[a], *Gustavo Fischer*[a], *Monise Schittler*[b], *Annelise Pezzi*[b], *Vanessa Valim*[b], *Alice Dahmer*[a], *Bruna Zambonato*[b], *Bruna Amorin*[b], *Filipe Sehn*[b], *Maria Aparecida da Silva*[b], *Liane Daudt*[a], *Lucia Silla*[a,b,*]

[a] *Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, RS, Brazil*
[b] *Universidade Federal do Rio Grande do Sul (UFRS), Porto Alegre, RS, Brazil*

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ABSTRACT

Background: Hematopoietic stem cell transplantation is a curative treatment for many patients with hematological disorders. Donor–recipient genetic disparity, especially involving the human leukocyte antigen system is a critical factor for transplant outcome.
Objective: To evaluate retrospectively donor characteristics and correlations with the occurrence of acute and chronic graft-versus-host disease, disease-free survival and overall survival in a Brazilian population submitted to allogeneic hematopoietic stem cell transplantation between 1994 and 2012 in a single center.
Results: Three hundred and forty-seven consecutive transplantations were included. Related transplants (81.2%) were significantly more common than unrelated transplants (18.7%); donor and recipient median ages were 34 (range: 1–61) and 33 (range: 3–65) years respectively with donor HLAs being matched for 333 (95.9%) patients. Donor gender, cytomegalovirus status and ABO incompatibility did not influence the five-year overall survival. In univariate analyses, overall survival was negatively influenced by the presence of acute graft-versus-host disease (33% vs. 47%, respectively; p-value = 0.04), unrelated transplant (41.5% vs. 50.9%, respectively; p-value = 0.045) and donors aged over 40 years (41% vs. 52%, respectively; p-value = 0.03). Older donors were associated with a higher rate of acute (52% vs. 65.8%; p-value = 0.03) and chronic graft-versus-host disease (60% vs. 43%, respectively; p-value = 0.015). In multivariate analyses, acute graft-versus-host disease [relative risk (RR): 1.8; 95% confidence interval (CI): 1.1–29; p-value = 0.008] and older donors (RR: 1.6; 95% CI 1.11–2.24; p-value = 0.013) were associated with higher transplant-related mortality.

* *Corresponding author at*: Department of Hematology and Bone Marrow Transplantation, CTC-RS, Hospital de Clínicas de Porto Alegre, Rua Ramiro Barcelos, 2350 Room 2235, 90035-003 Porto Alegre, RS, Brazil.
E-mail address: lsilla@hcpa.ufrgs.br (L. Silla).
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Conclusions: In transplant patients, to have a donor older than 40 years of age seems to significantly increase the incidence of acute and chronic graft-versus-host disease and transplant-related mortality with no impact on disease-free survival and overall survival. In spite of the rather small cohort of patients, these findings are similar to what is described in the literature suggesting that a younger donor should be chosen whenever possible.

Introduction

Hematopoietic stem cell transplantation (HSCT) is a curative treatment for many patients with hematologic disorders.[1,2] Its goal is to replace both the immune and the hematopoietic systems with healthy hematopoietic stem cells obtained from a human leukocyte antigen (HLA) compatible donor.[3] Genetic disparity between donor and recipient, especially at HLA loci, is a critical factor for the outcome of HSCT.[4]

Despite advances in genetic characterization, immunosuppressive drugs and supportive care, acute and chronic graft-versus-host disease (GVHD) remain significant causes of morbidity and mortality after HSCT.[5,6] In addition to genetic disparities and GVHD, disease status at transplant, source of stem cells, conditioning regimens and infectious complications are associated to HSCT outcome. Some other donor-related aspects, such as gender, age, cytomegalovirus (CMV) serological status and ABO incompatibility may also be associated with HSCT outcomes with their individual roles having been explored with variable results.[7–10] In spite of pre-emptive treatment, the reactivation of CMV disease is still an important cause of morbidity and mortality.[11]

HSCT is being increasingly performed in over 50-year-old individuals due to the development of reduced intensity conditioning (RIC) regimens.[12] As a consequence, older related compatible donors are also being accepted and the regenerative capacity of hematopoietic stem cells (HSC) and possible comorbidities are becoming issues, as recent studies have demonstrated that increased donor age may be a risk factor for acute and chronic GVHD.[13]

Currently, about 30–50% of HSCTs are performed with ABO incompatibility.[14] It is well established that ABO incompatibility increases the risk of hemolytic reactions; however, according to recent data, it does not change the outcome of HSCT.[8,15]

This study evaluated the influence of donor characteristics such as age, gender, CMV status, cell source, ABO compatibility and type of donor (matched related – MRD or matched unrelated – MUD) on the outcome of HSCT in a cohort of 347 patients transplanted at the Hospital de Clinicas in Porto Alegre, southern Brazil. We wanted to know whether such characteristics would predict outcomes in this Latin American cohort of patients transplanted in a single center.

Methods

Three hundred and forty-seven patients submitted to allogeneic HSCT from January 1994 to December 2012 at a single center were evaluated retrospectively. The donor and recipient ages, donor gender, CMV status, ABO compatibility, type of donor (matched related, and matched unrelated) and patient's disease status were correlated with the occurrence of acute and chronic GVHD, disease-free survival (DFS) and overall survival (OS).

All patients had given their informed written consent at the time of the procedure and the study was approved by local Ethics Committee. Advanced disease status at HSCT was defined as refractory disease, second or more remission to malignant disease or more than one year of diagnosis of benign disease.

Donor selection and HLA typing

HLA Class I (A, B, C) and Class II (DQ and DR) typing of patients and related donors was performed by conventional serology until 2000 and low resolution DNA-based typing thereafter. For unrelated donor HSCT, performed in this center since 2005, high resolution HLA typing was performed for 6/6 matches up to 2008 and 8/8 or 10/10, thereafter.

Conditioning regimens

Standard myeloablative conditioning (MAC) consisted of 14–16 mg/kg oral busulfan (BU) plus 2×60 mg/kg cyclophosphamide (CY) or CY (2×60 mg/kg) plus total body irradiation (12 Gy fractioned dosage). The RIC regimens utilized were as follows: BU 8–10 mg/kg PO plus 90–120 mg/m^2 fludarabine (Flu), or Flu (120 mg/m^2) plus 140 mg/m^2 melphalan or CY 60 mg/kg. Patients submitted to MUD transplants also received rabbit thymoglobulin (7–14 mg/kg).

Graft-versus-host disease prophylaxis

Patients on MDR and MAC regimens received cyclosporin A (CYA) (3 mg/kg IV) starting on Day −1 and an additional short course of methotrexate (MTX) (15 mg/m^2) on Day +1 and 10 mg/m^2 on Days +3, +6 and +11. For those undergoing MUD transplants, tacrolimus (0.05 mg/kg IV) was associated with a short course of MTX. For RIC, GVHD prophylaxis was achieved with 2 g mycophenolate mofetil daily (Day +1 to Day +30) plus

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