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HLA Typing and Hematopoietic Stem Cell Transplantation Outcome: Review

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Abstract

For many patients suffering from hematologic diseases, hematopoietic stem cell transplantation (HSCT) is a curative procedure. The plan is to use healthy hematopoietic stem cells from an HLA-compatible donor to replace the patient's immune and hematopoietic systems. For HSCT to be successful, genetic differences between the donor and recipient, particularly at HLA loci are crucial. Acute and chronic graft - versus - host diseases (GVHD) continue to be major causes of morbidity and mortality after HSCT despite improvements in genetic characterisation, immuno-suppressive medications, and supportive treatment. Along with genetic differences and GVHD, the source of the stem cells, conditioning regimens, and infection problems are linked to the success of HSC. Other donor-related factors, such as gender, age, and the presence or absence of cytomegalovirus (CMV) antibodies. HSCT outcomes may also be influenced by and ABO incompatibility, whose individual contributions have been investigated with varying degrees of success.

Keywords: Hematopoietic; Stem Cell; Transplantation

Introduction

The reactivation of CMV illness is still a significant source of morbidity and mortality despite preventative therapy. The development of reduced intensity conditioning (RIC) regimens has led to an increase in the number of people over 50 who undergo HSCT. Because of the regeneration potential of hematopoietic stem cells (HSC) and potential comorbidities, older related suitable donors are also accepted, and recent research have shown that donor age may be a risk factor for acute and chronic GVHD. Currently, ABO incompatibility is present in between 30 and 50 percent of HSCT procedures [1].

Although it is commonly known that ABO incompatibility raises the risk of hemolytic responses, recent research indicates that it has no impact on the results of HSCT. In this study, the effects of donor characteristics such age, gender, CMV status, cell source, ABO compatibility, and donor type (matched) were assessed. at the Hospital de Clinicas in Porto Alegre, southern Brazil, on the results of HSCT in a cohort of 347 patients who underwent transplantation. We were interested in learning whether these traits may be used to predict outcomes in this Latin American cohort of patients who underwent single-center transplants [2].

Methodical Aspects

Retrospective evaluations were performed on 347 patients who underwent allogeneic HSCT at a single location between January 1994 and December 2012. Acute and chronic GVHD, disease-free survival (DFS), and overall survival were all connected with the donor and recipient ages, gender, CMV status, ABO compatibility, type of donor (matched related and matched unrelated), and patient's disease status (OS). At the time of the procedure, each patient provided written informed permission, and the local ethics committee authorised the study. Refractory disease, a second or more remission from a cancerous condition, or a diagnosis of a benign condition more than a year old were all considered to have advanced disease status at HSCT [3]. Up until the year 2000, poor resolution DNA-based typing of HLA Class I (A, B, C) and Class II (DQ and DR) of patients and associated donors was used. Since 2005, unrelated donor HSCT procedures have been carried out in this facility. High resolution HLA typing was done for 6/6 matches up until 2008 and 8/8 or 10/10 matches after that. Peripheral granulocyte counts over 500/-L for three straight days were considered to be engraftment. When engraftment was not achieved in patients who survived more than 28 days following transplantation, it was referred to as a primary engraftment failure or rejection. Day 100 following the operation saw a calculation of the engraftment failure rate [4].

Impact of HLA-A and HLA-B Mismatches

Laminar high efficiency particulate air (HEPA) filters were used to keep all patients in a secure setting. All patients received standard prophylactic doses of acyclovir, fluconazole, and sulfamethoxazole along with trimethoprim. Weekly CMV monitoring was done via antigenemia assaying after 2005 and qualitative DNA-polymerase chain reaction (PCR) up until that point [5]. After two consecutive positive PCR results or one positive cell in the antigenemia assay, preventive 10 mg/kg ganciclovir was started. All blood components underwent irradiation and filtration. According to the guidelines issued by the hospital transfusion committee, minimum values were established to initiate platelet and red blood cell transfusions to maintain platelet counts above 20 109/L and haemoglobin levels above 7 g/dL, respectively [6]. Broad-spectrum antibiotics were used to treat neutropenic fever, according to base on our microbiological sensitivity profile and the Infection Dis- eases Society of America (IDSA) Guidelines for our hospital protocols Patients' and donors' characteristics are shown as frequencies for categorical variables and as medians and ranges for continuous variables [7]. The OS was the main outcome measure, and the incidence of acute and chronic GVHD, DFS,

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and transplant-related mortality served as secondary endpoints (TRM). The number and severity of organ involvement were used to stage and grade acute GVHD. Utilizing the Kaplan-Meyer method, OS was calculated [8]. The log-rank test was used to compare the curves. We compared categorical data using the Chi-square test. Age and gender of patients and donors, patient and donor gender combinations, patient and donor CMV-serological status, stem cell source [bone marrow (BM), peripheral blood stem cells (PBSC), and cord blood] were all were included in the studies. MAC vs. RIC, MUD vs. MRD, dosage of CD34+ cells, patient's illness condition, and stem cell. Multivariate analysis included factors with p-values 0.2. For multivariate analysis, the Cox proportional hazard regression model was employed. Based on the literature and the relatively lower age of patients and donors in our cohort, a cut-off value of 40 years was chosen in order to assess the impact of donor age on transplant outcomes. The HCPA Ethics Committee accepted this study, and the data were anonymized and analysed in accordance with the Declaration of Helsinki for human experimentation [9].

Mismatch Vector

Acute lymphoblastic leukaemia, 82 (23%) had chronic myeloid leukaemia, 18 (5.2%) had myelodysplastic syndrome, 21 (8.8 %) had lymphomas, 57 (16%) had aplastic anaemia, and 26 (7%) had additional diseases. In 151 (43.5%) individuals, the disease condition was progressed (beyond the second remission). In 265 (85.8%) of the patients and donors, respectively, and 218 (87.2%) of the donors, the CMV serological status was positive [10]. The median age of the donors was 33 (range: 1-65) years, 182 (52.2%) of them were men, and 282 (81.3%) of them were connected to the recipients by blood. The overall five-year OS was 49.1 percent [95% confidence interval (CI): 41-54 percent]. The average duration to engraft was 19 days, and 317 patients (92.4 percent) experienced engraftment (range: 8–45). The average dosage of CD34+ cells was 3.4 106/kg. Incompatibility with ABO was present in 113 (32.3%) transplants, with 65 (18.5%) having significant 48 (13.8%) minor incompatibilities, as well. Major and minor incompatibility had no effect on engraftment, which took place after 20.3 days (p-value = 0.293) and 18.6 days (p-value = 0.100), respectively, compared to 19.5 days for patients without incompatibility. Time to engraftment did not differ between younger (19.7 days) and older (18.7 days; p-value = 0.063) donors.

Result

185 patients had acute GVHD, while 131 had chronic GVHD (50.4 percent). Both the cumulative incidence of acute GVHD for MRD vs. MUD (147-57.5 percent and 39-65 percent, respectively; p-value = 0.358) and the cumulative incidence of chronic GVHD (110-52.6 percent and 20-46.7 percent, respectively; p-value = 0.573) did not differ. Donors older than 40 years had a considerably higher incidence of both acute and chronic GVHD [11]. Seventy-seven (65.6%) of the beneficiaries from the younger donors made up 52 percent of the sample in 92 (from donors under 40 years old) (p-value = 0.03). Chronic GVHD occurred in 64 (43%) recipients from younger donors and 54 (60%) recipients from older donors (p-value = 0.015).

Discussion

The occurrence of acute or chronic GVHD was unaffected by ABO incompatibility, donor gender, MRD or MUD, or CMV serological status. The findings of the univariate analysis of how key variables affect OS are outlined. The five-year OS of all transplanted patients according to donor age showed that recipients of younger donors had significantly higher survival rates (52 percent vs. 41 percent; p-value = 0.038). Acute GVHD negatively impacted the five-year OS in our research, with only 40.3% of patients with acute GVHD still living at that time-point compared to 69.1% of patients without acute GVHD (p-value = 0.001). A comparable difference in OS was seen depending on the kind of donor, with 41.5 percent of MUD transplant recipients and 50.9 percent of MRD recipients surviving for at least five years [12]. Only acute GVHD and donor age (RR: 1.8; 95 percent CI: 1.17-2.91; p-value = 0.008) had a significant detrimental influence on the five-year survival rate in multivariate Cox regression analysis. The recipient's age was included in the multivariate analysis in order to rule out any potential favourable effects of recipients who were children or younger recipients on the overall result. As a result, the five-year OS was no longer significantly influenced by donor age , and the RR was reduced from 1.68 to 1.47.

Conclusion

With the advent of non-myeloablative conditioning regimens, DNA-based high resolution HLA typing, and improved clinical support, much has been done in the last ten years to increase the efficacy of HSCT. As a result, there are more MUD transplants performed globally, and while acute and chronic GVHD rates are greater, survival rates are comparable to those seen with MRD transplants. 20 The ability to transplant older patients has increased thanks to the introduction of RIC regimens, which has led to an increase in donor age in the MRD scenario. Age of the donor and female-to-male transplants has been demonstrated to affect GVHD and survival, while these factors are still debatable. 6978 MUD transplants have involved elder donors more than 45 years increased GVHD and lowered OS.21 On the other hand, the results of MUD RIC transplants or those of patients were unaffected by donor age greater than 50 years.

References

1. Doherty PC, Zinkernagel RM (1975) A biological role for the major histocompatibility antigens. Lancet 1(7922):1406–9.
2. Chen C, Bain KB, Iuppa JA, Yusen RD, Byers DE, et al (2016) Hyperammonemia Syndrome After Lung Transplantation: A Single Center Experience. Transplantation 100(3):678-684.
3. Warrillow S, Fisher C, Bellomo R (2020) Correction and Control of Hyperammonemia in Acute Liver Failure: The Impact of Continuous Renal Replacement Timing, Intensity, and Duration. Crit Care Med 48(2):218-224.
4. Gupta S, Fenves AZ, Hootkins R (2016) The Role of RRT in Hyperammonemic Patients. Clin J Am Soc Nephrol 11(10):1872-1878.
5. Ames EG, Luckritz KE, Ahmad A (2020) A retrospective review of outcomes in the treatment of hyperammonemia with renal replacement therapy due to inborn errors of metabolism. Pediatr Nephrol 35(9):1761-1769.
6. Sharma R, Hawley C, Griffin R, Mundy J, Peters P, et al (2013) Cardiac surgical outcomes in abdominal solid organ (renal and hepatic) transplant recipients: a case-matched study. Interact Cardiovasc Thorac Surg 16(2):103-111.
7. Kohmoto T, Osaki S, Kaufman DB, Leverson G, DeOliveira N, et al (2018) Cardiac Surgery Outcomes in Abdominal Solid Organ Transplant Recipients. Ann Thorac Surg 105(3):757-762.
8. Delgado DDS, Gerola LR, Hossne NA, Branco JN, Buffolo E (2002) Myocardial revascularization in renal transplant patients. Arq Bras Cardiol 79(5):476-83.
9. Petersdorf EW (2017) In celebration of Ruggero Ceppellini: HLA in transplantation. HLA 89(2):71-76.
10. Petersdorf EW, Malkki M (2005) Human leukocyte antigen matching in unrelated donor Hematopoietic cell transplantation. Semin Hematol 42(2):76-84.
11. Petersdorf EW (2017) Which factors influence the development of GVHD in HLA-matched or mismatched transplants?. Best Pract Res Clin Haematol 30(4):333-335.
12. Dawkins RL, Lloyd SS (2019) MHC Genomics and Disease: Looking Back to Go Forward. Cells 8(9):944.