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Early-phase differences in health-related quality of life, psychological status, and physical function between human leucocyte antigen-haploidentical and other allogeneic haematopoietic stem cell transplantation recipients

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A B S T R A C T

Purpose: This study investigated the differences between allogeneic haematopoietic stem cell transplantation (allo-HSCT) patients receiving HSC from human leucocyte antigen (HLA)-haploidentical donors (HID) and other donors that included HLA-matched sibling, matched unrelated, and unrelated umbilical cord blood donors in the 6 weeks after HSCT with respect to quality of life (QOL), psychological status, and physical function.

Methods: The study included 126 patients (HID group, n = 100; other donor group, n = 26) who underwent allo-HSCT between July 2007 and December 2012. Patients were evaluated for health-related QOL using the Medical Outcome Study 36-item Short Form Health Survey. Psychological status was measured by Hospital Anxiety and Depression Scale. Physical function was assessed using tests for handgrip strength, knee extensor strength, and the 6-min walk test.

Results: After HSCT, the HID group showed significantly greater improvements in the general health subscale and Mental Component Summary (MCS) of QOL than the other donor group ($P < 0.01$). Multivariate analysis confirmed that complete remission and age were associated with changes in the general health subscale before and after HSCT ($P < 0.05$). With regard to physical function, the HID group showed significantly more decline than the other donor group with respect to handgrip strength and knee extensor muscle strength after HSCT ($P < 0.05$). Total corticosteroid dose was associated with decreased handgrip strength before and after HSCT ($P < 0.05$).

Conclusions: The donor type affects QOL, psychological status, and physical function in allo-HSCT recipients; these findings may provide insights for customised rehabilitation strategies for HSCT recipients.

Introduction

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is a potentially curative treatment for patients with haematological malignancy (Koreth et al., 2009; Pidala et al., 2011) and is increasingly being used in the treatment of haematopoietic diseases worldwide (Yoshimi et al., 2010; Passweg et al., 2012). One difficulty with this procedure is that a human leucocyte antigen (HLA)-matched sibling donor (MSD) is available to fewer than 30% of patients in Japan (Okamoto, 2002). Therefore, for 70% of patients without a fully matched donor, the only feasible option is to

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identify an alternate matched unrelated donor (MUD), unrelated umbilical cord blood donor (CBD), or an HLA-haploidentical donor (HID) (Aversa et al., 2012). MUD is considered to be the most appropriate alternative donor in allo-HSCT for patients who lack an HLA-matched sibling donor. However, it is difficult to find an MUD for patients with rare haplotypes, and the coordination period from the start of the donor search application until the actual receipt of grafts takes a median of 5 months in Japan (Kanda et al., 2014). CBD is also an option for many patients and is sometimes the preferred option. Cord blood units do not need to match the patient's HLA type as closely as bone marrow or peripheral blood stem cells from an adult donor. They can also be made available more quickly for transplant. CBD has the specific advantage of lower incidence and severity of graft versus host disease. However, CBD has the disadvantage of an increased rate of graft failure and longer time to engraftment as well as insufficient number of stem cells for some larger patients (Ruggeri et al., 2010; Ballen and Spitzer, 2011; Ballen et al., 2012). On the other hand, the use of HSCs from relatives who are only partially HLA haploidentical provides some advantages for patients lacking a fully HLA-matched sibling or unrelated donor. Virtually all patients have at least 1 HLA-haploidentical parent or child who can serve as an immediate donor. Furthermore, the immediate availability of a mismatched family member could be advantageous, because patients are not lost to early relapse (Koh and Chao, 2008). Although rapid and near universal donor availability is the major advantage of allo-HSCT over HID, HLA-haploidentical HSCT has the disadvantage of the host and donor T-cell response to allogeneic HLA molecules, which results in increased incidences of graft failure, graft-versus-host disease (GVHD), and non-relapse mortality (Luznik et al., 2012). Haploidentical HSCT has recently become available as a treatment option with a better preventive protocol for GVHD (Ogawa et al., 2006).

The importance of health-related quality of life (QOL) (Grulke et al., 2012; Morishita et al., 2012a), psychological status (Sun et al., 2011; Rischer et al., 2009; Bevans et al., 2011), and physical function (Van Haren et al., 2013, Morishita et al., 2012b), before and after transplantation has been recognised in allo-HSCT recipients. Our previous studies indicate that allo-HSCT recipients have lower QOL (Morishita et al., 2013c) and lower physical function (Morishita et al., 2013a) after transplantation than before transplantation. Recently the number of HLA-haploidentical HSCT is expanding after the development of new strategies for GVHD prophylaxis including in vivo T-cell depletion and post-transplant high-dose cyclophosphamide (Reisner et al., 2011; Wolschke et al., 2014). As HLA-haploidentical HSCT has unique features of HLA disparities and special transplant strategies compared with other standard HSCT, QOL, psychological status, and physical function need to be assessed in HLA-haploidentical HSCT. Mo et al. (Mo et al., 2012) investigated and compared health-related QOL between patients receiving allo-HSCT from HLA-haploidentical related donors and HLA-identical sibling donors. Patients with an HLA-haploidentical related donor had higher QOL scores than those with an HLA-identical sibling donor. However, this was a cross-sectional, not cohort, study, and QOL was only evaluated 48 months after transplantation. Also, the change in QOL from pre-transplantation to post-transplantation was not evaluated. Furthermore, this study did not evaluate physical function. To our knowledge, no study has investigated the differences in QOL, psychological status, and physical function between patients receiving allo-HSCT from HID and other donors in the early phase. Clarification of these differences would be useful for developing rehabilitation strategies after transplantation. Information about the QOL in patients receiving allo-HSCT from HID is limited (Mo et al., 2012), and additional data from these patients is necessary.

Therefore, we investigated the differences in QOL, psychological status, and physical function between patients receiving allo-HSCT from HID and other donors (e.g. MSD, CBD, and MUD) both before and in the early phase after HSCT. We also investigated the clinical factors affecting the differences with respect to health-related QOL, psychological status, and physical function between the 2 groups.

Materials and methods

Study design

This was a prospective observational study investigating changes before and after HSCT.

Patients and methods

The patients with haematologic diseases who underwent allo-HSCT at the Hyogo College of Medicine Hospital in Japan from July 2007 to December 2012 (5 years, 6 months) were included. The transplantation protocol was performed as described previously (Morishita et al., 2013c, 2013a). The inclusion criteria were as follows: (1) age $\geq$18 years, (2) capable of speaking and reading Japanese, and (3) able to undergo evaluation of physical function before and after HSCT. Patients who received re-transplantation in the same hospital, experienced graft failure or relapse, or could not tolerate evaluation after HSCT were excluded. Thus, out of the 471 consecutive patients admitted during the study period, 126 were enrolled in this study and divided into the HID group (n = 100) and other donor group (n = 26). A detailed study flow chart is shown in Fig. 1. Ethical approval of the study was obtained from the Institutional Committee on Human Research of the Hyogo College of Medicine. One of the authors (S.M) obtained written informed consent from each patient prior to participation.

Pre-transplantation evaluation was performed before the start of conditioning, and post-transplantation evaluation was performed after bone marrow recovery and decreased immunosuppressant dose in the physiotherapy room. Patients were evaluated up to 3 weeks before and 6 weeks after transplantation. The following information was collected from patients' medical records: age, sex, height, body weight, upper- and lower-limb dominance, marital status, employment status, underlying haematological diagnosis, number of days from initial diagnosis to hospitalisation, type of transplantation, donor–recipient relationship, conditioning, complete remission (CR) before HSCT, and history of previous HSCT. Furthermore, data on total corticosteroid dose, GVHD, and presence of infection were collected from medical records. Acute GVHD was defined as symptoms including abdominal pain or cramps, nausea, vomiting, and diarrhoea, dry or irritated eyes, jaundice, and rash, itching, or redness within the first 3 months after transplantation. Patients who received corticosteroids were treated with methylprednisolone and prednisolone. Total cumulative corticosteroid doses are expressed as mg prednisolone (1 mg methylprednisolone = 1.25 mg prednisolone) per kg body weight.

Patients' health-related QOL was assessed using the Medical Outcome Study 36-item Short-Form Health Survey (SF-36). Fatigue and psychological status were measured using the Piper Fatigue Scale (PFS) and Hospital Anxiety and Depression Scale (HADS), respectively. Physical strength was assessed using handgrip strength and knee extensor strength, and the 6-min walk test (6MWT) was used as a measure of exercise capacity. All measures including patient-reported health-related QOL, PFS, HADS, handgrip strength, knee extensor strength, and 6MWT were assessed on the same day.