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Peripheral Blood as a Preferable Source of Stem Cells for Salvage Transplantation in Patients with Graft Failure after Cord Blood Transplantation: A Retrospective Analysis of the Registry Data of the Japanese Society for Hematopoietic Cell Transplantation

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To compare the different stem cell sources used in salvage transplantation for graft failure (GF) after cord blood transplantation (CBT), we retrospectively analyzed data of 220 patients who developed GF after undergoing CBT between January 2001 and December 2007 and underwent a second hematopoietic stem cell transplantation (HSCT) within 3 months. The donor sources for salvage HSCT were cord blood (n = 180), peripheral blood stem cells (PBSCs; n = 24), and bone marrow (BM; n = 16). The cumulative incidence of neutrophil engraftment on day 30 after the second HSCT was 39% with CB, 71% with PBSCs, and 75% with BM. Multivariate analysis revealed that PBSC and BM grafts were associated with a significantly higher engraftment rate than CB (hazard ratio [HR], 7.77; $P < .001$ and HR, 2.81; $P = .016$, respectively). Although the incidence of grade II-IV acute graft-versus-host disease was significantly higher in the PBSC group than in the CB group (HR, 2.83; $P = .011$), the incidence of 1-year nonrelapse mortality was lower in the PBSC group than in the CB group (HR, 0.43; $P = .019$), and 1-year overall survival was superior in the PBSC group compared with the CB group (HR, 0.45; $P = .036$). Our results suggest that PBSC is the preferable source of stem cells in salvage HSCT for GF after CBT.

Biol Blood Marrow Transplant 18: 1407-1414 (2012) © *2012 American Society for Blood and Marrow Transplantation*

KEY WORDS: Engraftment, Second transplant, Peripheral blood stem cells

INTRODUCTION

Graft failure (GF) is one of the lethal complications of allogeneic hematopoietic stem cell transplantation (HSCT) [1]. Recently, the incidence of GF has increased with the introduction of cord blood transplantation (CBT), HLA-mismatched transplantation, and reduced-intensity conditioning (RIC)

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Financial disclosure: See Acknowledgments on page 1413.

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Received December 1, 2011; accepted February 25, 2012

1083-8791/$36.00
doi:10.1016/j.bbmt.2012.02.014

regimens. The GF rate after HSCT with conventional myeloablative conditioning (CST) regimens is <5% for peripheral blood stem cell transplantation (PBSCT), ~5%-10% for bone marrow transplantation (BMT), and ~20% for CBT [2-5]. Rocha et al. [4] reported GF rates of 10% for unrelated BMT and 22% for CBT. Atsuta et al. [5] reported GF rates of 6% and 23% in patients with acute myelogenous leukemia (AML) treated with unrelated BMT and CBT, respectively, and corresponding GF rates of 3% and 20% in patients with acute lymphoblastic leukemia (ALL). These results indicate that GF is not a rare complication.

The survival rate of patients who developed GF after allogeneic HSCT but did not undergo a second salvage transplantation has been <10% [4-6]. In a recent investigation of the feasibility of a second HSCT with an RIC regimen for GF, Guardiola et al. [7] reported the clinical outcomes of 82 patients with GF who underwent a second transplantation, most from an HLA-matched sibling donor. The 3-year overall survival (OS) rate in these patients was 30%, significantly better than that reported in a previous study in which the patients did not undergo a second HSCT. Waki et al. [8] analyzed the clinical outcomes of 80 patients with GF who underwent salvage CBT and found a 1-year OS rate of 33%, with nonrelapse mortality (NRM), especially infectious diseases, as the major cause of death [8]. This OS rate was higher than that reported in a previous study in which patients did not undergo a second HSCT; however, the low engraftment rate and high NRM rate after salvage CBT are not acceptable results. Schriber et al. [9] obtained clinical data of 122 patients who underwent unrelated HSCT as salvage treatment for GF from the database of National Marrow Donor Program. The engraftment rate of 74% in this series was markedly greater than that reported by Waki et al. [8], possibly attributable to differences in stem cell sources. However, the high engraftment rate did not improve the outcome because of a high NRM rate (86%). Infectious disease was the major cause of death in that study.

Given that infectious diseases are a main cause of failure after second HSCT, peripheral blood stem cells (PBSCs) may be the preferred stem cell source for the second transplantation. However, acute and chronic graft-versus-host disease (GVHD) is a concern after PBSCT, especially after HLA-mismatched transplantation. The effect of the stem cell source in a second HSCT has not yet been clarified, because previous studies had insufficient statistical power to analyze the effect of this factor using multivariate analysis.

In the present study, we retrospectively analyzed the clinical outcomes of patients who had undergone salvage HSCT after GF, using registry data of the Japanese Society for Hematopoietic Cell Transplantation (JSHCT). We compared outcomes by stem cell source: PBSCs, cord blood (CB), or bone marrow (BM).

MATERIALS AND METHODS

Patients

This study was approved by the Institutional Review Board of Izumisano Municipal Hospital, Rinku General Medical Center, Osaka, Japan. The patients' clinical data were obtained from the JSHCT database [10]. The following patients were included in the study: (1) patients who developed primary or secondary GF after allogeneic HSCT performed between January 2000 and December 2007, (2) patients who underwent a second HSCT for GF within 3 months after the diagnosis of GF, and (3) patients who did not demonstrate progression of the primary disease before the second HSCT. Neutrophil engraftment was defined as an absolute neutrophil count (ANC) $>500/mm^3$ in the first 3 consecutive days after HSCT. Primary GF was defined in accordance with a previous report as an ANC not exceeding $500/mm^3$ or the absence of donor T cells (<5%) before relapse, disease progression, second HSCT, or death [11]. Secondary GF was defined as a decrease in ANC of $<100/mm^3$ at 3 determinations or absence of donor T cells (<5%) after the initial engraftment without recovery before relapse, disease progression, second HSCT, or death. Chimerism was assessed using polymerase chain reaction for short tandem repeats or variable number tandem repeats. Sex chromosome chimerism in sex-mismatched donor–recipient pairs was assessed using fluorescence in situ hybridization.

Data of 382 patients were obtained from the JSHCT database. Of these 382 patients, 67 were excluded because of relapse or disease progression before the second HSCT, autologous hematopoietic recovery, autologous HSCT, or missing data on, for example, stem cell source, engraftment, and OS. Furthermore, patients who received PBSCs (n = 24) or BM (n = 71) for the first HSCT were excluded, to focus on CBT in this study. The data of the remaining 220 patients were subjected to further analysis.

Statistical Analysis

We first performed a statistical analysis of the differences in the 3 stem cell sources. Patients and transplantation characteristics in the different groups were compared using the χ^2 test to determine the difference in proportions. One-way analysis of variance was used to compare mean values. The primary endpoint of this study was the engraftment rate after second HSCT. Secondary endpoints included the probabilities of OS and progression-free survival (PFS) and the cumulative incidents of NRM, acute GVHD, and infectious diseases after the second HSCT. OS and PFS were estimated using the Kaplan-Meier method. The cumulative incidents of engraftment, relapse, GVHD, and infectious diseases were evaluated using

the method of Gray. In the competing-risk models for engraftment, relapse, GVHD, and infectious diseases, death before these events was defined as a competing risk. The competing-risk regression model of Fine and Grey was used for univariate and multivariate analyses of cumulative incidence. A Cox proportional hazards regression model was used to analyze OS and PFS. Factors associated with a 2-sided P value of $<.10$ in the univariate analysis were included in a multivariate analysis. A backward-stepwise selection algorithm was used, and only the statistically significant variables were retained in the final model. A 2-sided P value of $<.05$ was considered statistically significant.

The following variables were evaluated in these analyses: sex, age at time of HSCT, disease risk (standard risk versus high risk), conditioning regimen for the first HSCT (CST versus RIC versus nonmyeloablative [NMA]), conditioning regimen for the second HSCT (CST versus RIC versus NMA), use of fludarabine (Flu), use of an alkylator-containing regimen, use of total body irradiation (TBI), use of antithymocyte globulin (ATG), stem cell source (PBSCs, BM, or CB) for the second HSCT, immunosuppressive drugs (primary drug: none, cyclosporine, or tacrolimus [TAC]; secondary drug: methotrexate [MTX], mycophenolate mofetil [MMF], neither MTX nor MMF, steroid, or no steroid), HLA disparities (in both graft-versus-host and host-versus-graft directions), and type of GF (primary versus secondary). Standard risk was defined as the first complete remission of acute leukemia or malignant lymphoma, the first chronic phase of chronic myelogenous leukemia, or nonmalignant disease. High risk was defined as other stages of hematologic malignancies and solid tumors. The definitions of conditioning regimens were similar to those used in previous studies [12,13]. Myeloablative conditioning regimens included at least 1 of the following: >8 Gy TBI, >140 mg/m^2 melphalan, or >6.4 mg/m^2 i.v. busulfan (or >8.0 mg/m^2 oral busulfan). NMA conditioning included conditioning regimens with 2 Gy TBI plus a purine analogue, Flu + cyclophosphamide + ATG, Flu + cytarabine + idarubicin, cladribine + cytarabine, or total lymphoid irradiation + ATG. RIC included all other conditioning regimens. Infectious diseases included both clinically and microbiologically documented infections diagnosed by a physician. Statistical analyses were performed using Stata version 11.1 (StataCorp, College Station, TX).

RESULTS

Patients

Recipient and transplantation characteristics are summarized in Table 1. Because of the limited availability of stem cell grafts in Japan, all CB recipients received only single CB unit. The median age of the recipients was 42.5 years (range, 0-75 years). Their diagnoses included AML (n = 71), ALL (n = 40), myelodysplastic syndrome (MDS; n = 52), malignant lymphoma (n = 31), nonmalignant diseases (n = 14), and others (n = 12). Eighty-two patients were classified as standard risk, and 138 were classified as high risk. The conditioning regimen at the first HSCT was CST in 137 patients, RIC in 80 patients, and NMA in 2 patients. Of the 220 patients who had GF, 200 (90.9%) had primary GF and 19 (8.7%) had secondary GF. In these 220 patients, GF was diagnosed after a median of 29 days (range, 12-176) after the first HSCT.

The median interval between the diagnosis of GF and the second HSCT was 11 days (range, 0-89 days). The stem cell source for the second HSCT was CB in 180 patients, BM in 16 patients, and PBSCs in 24 patients. In the BM and PBSC recipients, all except 1 patient with BM received stem cells from a related donor. The patients who underwent PBSCT received stem cells from an HLA 1-locus mismatched donor (n = 1; 4.5%) or a haploidentical donor (n = 21; 95.5%). The patients undergoing BMT received stem cells from an HLA-matched donor (related, n = 2; unrelated, n = 1) or an HLA 1-locus mismatched (n = 2; 12.5%) or haploidentical donor (n = 11; 68.8%). For conditioning, 5, 122 and 77 patients received CST, RIC and NMA, respectively. As for GVHD, prophylaxis included cyclosporine in 79 patients, TAC in 118 patients, and ATG in 38 patients. A short course of MTX was added in 57 patients, and a short course of MMF was added in 21 patients. No patient received posttransplantation cyclophosphamide as GVHD prophylaxis.

Neutrophil Engraftment

The cumulative incidents of neutrophil engraftment according to stem cell source are shown in Figure 1. Engraftment was achieved by day 30 after second HSCT in 39% of CBT recipients, 71% of PBSCT recipients, and 75% of BMT recipients. Engraftment was achieved at median intervals of 21 days (range, 12-97) after CBT, 18 days (range, 0-37 days) after PBSCT, and 14.5 days (range, 9-26 days) after BMT. In the univariate analysis, PBSCT and BMT were associated with a significantly higher probability of engraftment (hazard ratio [HR], 2.5; 95% confidence interval [CI], 1.5-4.3; P = .001 and HR, 2.5; 95% CI, 1.2-5.0; P = .01, respectively). In the multivariate analysis, PBSCT and BMT remained significant variables after adjustment for other independently significant variables, including the use of alkylating agents, HLA disparities, and administration of additional immunosuppressive drugs (Table 2).

Table 1. Patient and Transplantation Characteristics

	CB	BM	PBSCs	Total	*P* Value
Number of patients	180	16	24	220	
Conditioning regimen for first HSCT, n					
CST	114	9	14	137	
RIC	63	7	10	80	
NMA	2	0	0	2	
Unknown	1	0	0	1	.968
Sex of recipient, n					
Male	97	13	11	121	
Female	83	3	13	99	.069
Age of recipient, years, median	44	14	28.5	42.5	.0016
ABO mismatch, n					
Match	57	6	12	75	
Minor	42	3	5	50	
Major	51	4	3	58	
Major/minor	29	0	3	32	
Unknown	1	3	1	5	<.001
HLA disparities (graft-versus-host direction), n					
0	22	3	0	25	
1	59	2	1	62	
2	96	9	13	118	
3	2	2	8	12	
Unknown	1	0	2	3	<.001
HLA disparities (host-versus-graft direction), n					
0	14	5	0	19	
1	60	2	4	66	
2	102	7	8	117	
3	3	2	10	15	
Unknown	1	0	2	3	<.001
Disease risk, n					
0	65	6	11	82	
1	115	10	13	138	.652
Disease, n					
ALL	30	4	6	40	
AML	59	3	9	71	
MDS	45	5	2	52	
Chronic myelogenous leukemia	6	1	1	8	
Lymphoma	28	0	3	31	
Plasma cell disorder	1	0	0	1	
Nonhematologic malignancies	2	0	1	3	
Nonmalignant disease	9	3	2	14	.402
Conditioning regimen, n					
None	10	1	2	13	
CST	4	1	0	5	
RIST	105	8	9	122	
Mini	60	6	11	77	
Unknown	1	0	2	3	.074
TBI, n					
No	123	13	17	153	
Yes	56	2	4	62	
Unknown	1	1	3	5	.001
Alkylating agent, n					
No	59	5	7	71	
Yes	120	10	14	144	
Unknown	1	1	3	5	.005
Flu/cladribine, n					
No	22	2	3	27	
Yes	157	13	18	188	
Unknown	1	1	3	5	.005
Calcineurin inhibitor, n					
None	13	0	2	15	
Cyclosporine	76	1	2	79	
TAC	84	15	19	118	
Unknown	7	0	1	8	.053
Additional immunosuppressive drugs, n					
None	122	4	8	134	
MTX	32	12	13	57	
MMF	19	0	2	21	
Unknown	7	0	1	8	<.001
Steroids, n					
No	160	13	18	191	
Yes	13	3	5	21	
Unknown	7	0	1	8	.147
ATG, n					
None	153	11	13	177	
Yes	26	4	8	38	
Unknown	1	1	3	5	<.001
Engraftment failure of previous transplantation, n					
Primary	162	16	22	200	
Secondary	17	0	2	19	
Unknown	1	0	0	1	<.001
Time from graft failure to transplantation, days, median (range)	12 (0-89)	7 (0-83)	9 (0-34)	11 (0-89)	.115

There were no significant differences between PBSCT and BMT.

OS and PFS

The median follow-up period for surviving patients after second HSCT was 481 days (range, 82-1825 days). The probability of 1-year OS after the second HSCT was 58% with PBSCs, 38% with BM, and 28% with CB (Figure 2A). In the multivariate analysis, after adjustment for age, disease risk, use of calcineurin inhibitors, and use of steroids in GVHD prophylaxis, the probability of 1-year OS was significantly greater after PBSCT than after CBT (HR, 0.45; 95% CI, 0.21-0.95; $P = .036$). The probability of 1-year PFS after the second HSCT was 48% with PBSCs, 34% with BM, and 24% with CB (Figure 2B). After adjustment

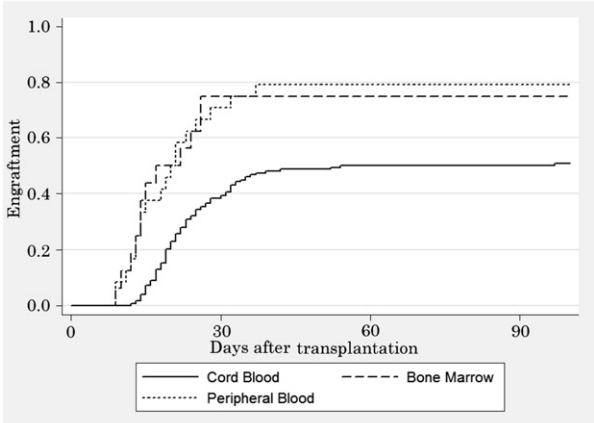

Figure 1. Cumulative incidence of engraftment after a second HSCT in patients according to stem cell source.

Table 2. Multivariate Analysis for Engraftment, OS, and PFS

	HR (95% CI)	*P* Value
Engraftment		
Stem cell source		
CB	Reference	
BM	2.81 (1.21-6.53)	.016
PBSCs	7.77 (4.16-14.51)	<.001
Alkylating agent		
None	Reference	
Yes	2.69 (1.64-4.41)	<.001
HLA disparities (host-versus-graft direction)		
0	Reference	
1	0.47 (0.22-1.03)	.06
2	0.46 (0.22-0.97)	.041
3	0.21 (0.08-0.61)	.004
Additional immunosuppressive drugs		
None	Reference	
MTX	0.19 (0.06-0.63)	.006
MMF	0.99 (0.66-1.48)	.945
OS		
Stem cell source		
CB	Reference	
BM	0.95 (0.46-1.95)	.881
PBSCs	0.45 (0.21-0.95)	.036
Disease risk		
Normal	Reference	
High	1.74 (1.21-2.49)	.003
Steroids		
None	Reference	
Yes	2.31 (1.37-3.91)	.002
Each additional year older	1.01 (1.00-1.02)	.003
Calcineurin inhibitor		
Cyclosporine	Reference	
None	0.97 (0.53-1.75)	.915
TAC	0.63 (0.44-0.90)	.011
PFS		
Stem cell source		
CB	Reference	
BM	0.95 (0.46-1.96)	.886
PBSCs	0.52 (0.25-1.05)	.066
Disease risk		
Normal	Reference	
High	1.85 (1.29-2.66)	.001
Calcineurin inhibitor		
Cyclosporine	Reference	
None	0.99 (0.55-1.79)	.971
TAC	0.61 (0.43-0.88)	.008
Steroids		
None	Reference	
Yes	2.01 (1.19-3.40)	.009
Each additional year older	1.01 (1.00-1.02)	.014

for age, disease risk, use of calcineurin inhibitors, and use of steroid as GVHD prophylaxis, the multivariate analysis indicated a trend toward a higher probability of 1-year PFS after PBSCT than after CBT (HR, 0.52; 95% CI, 0.25-1.05; $P = .066$) (Table 2). There were no statistically significant differences in OS and PFS between recipients of BMT and recipients of CBT.

NRM and Transplantation-Related Complications

The cumulative incidence of NRM at 1 year after the second HSCT was 29% with PBSCs, 38% with BM, and 60% with CB (Figure 2C). After adjustment for age and use of steroids, the incidence of 1-year NRM was significantly lower after PBSCT than after CBT (HR, 0.43; 95% CI, 0.21-0.87; $P = .019$). The cumulative incidents of grade II-IV acute GVHD were 47% after PBSCT, 31% after BMT, and 19% after CBT (Figure 2D), and the corresponding cumulative incidents of grade III-IV acute GVHD were 44%, 0%, and 12% (Figure 2E). After adjustment for the use of TBI in multivariate analysis, PBSCT was associated with a significantly higher incidence of grade II-IV (HR, 2.8; 95% CI, 1.3-6.3; $P = .011$) (Table 3). After adjustment for the use of steroids as GVHD prophylaxis and the type of conditioning regimen in multivariate analysis, PBSCT was associated with a significantly higher incidence of grade III-IV (HR, 7.3; 95% CI, 2.9-18.7; $P < .001$).

The cumulative incidents of infectious disease at 1 year after the second HSCT were 23% with PBSC, 15% with BM, and 58% with CB (Figure 3). PBSCT and BMT were associated with a significantly lower incidence rate of infectious disease (HR, 0.33; 95% CI, 0.14-0.81; $P = .015$ and HR, 0.21; 95% CI, 0.05-0.87; $P = .032$, respectively). The significant risk factors in the multivariate analyses are listed in Table 3. The major cause of death in our cohort was infectious disease (n = 72); other causes of death were relapse or progression of primary disease (n = 31), organ failure (n = 26), acute GVHD (n = 8), and others (n = 15).

DISCUSSION

In this study, we retrospectively analyzed the outcomes of 220 patients who underwent a second allogeneic HSCT after GF. The largest sample size found in the literature allowed us to analyze the effect of stem cell source on outcome. Neutrophil engraftment was significantly faster after PBSCT and BMT than after CBT. Patients with GF are at increased risk for developing a lethal infectious disease because of prolonged severe pancytopenia, and thus the faster neutrophil recovery after PBSCT and BMT is a highly beneficial effect. The differences in engraftment rate of stem cells from different sources in the present study may be greater than those observed after the first HSCT in previous studies [2-5], possibly because many patients died before engraftment after the second CBT. Infectious disease was the main cause of death in our cohort.

The clinical outcomes after salvage CBT in the present study are comparable to those reported by Waki et al. [8]. The 1-year OS was 28% in the present study and 33% in the study of Waki et al. The engraftment rate was lower in our cohort; however, this difference may be attributable to the fact that Waki et al. excluded patients who died before engraftment within 28 days after second HSCT. Our engraftment rate after PBSCT was comparable to that reported in the

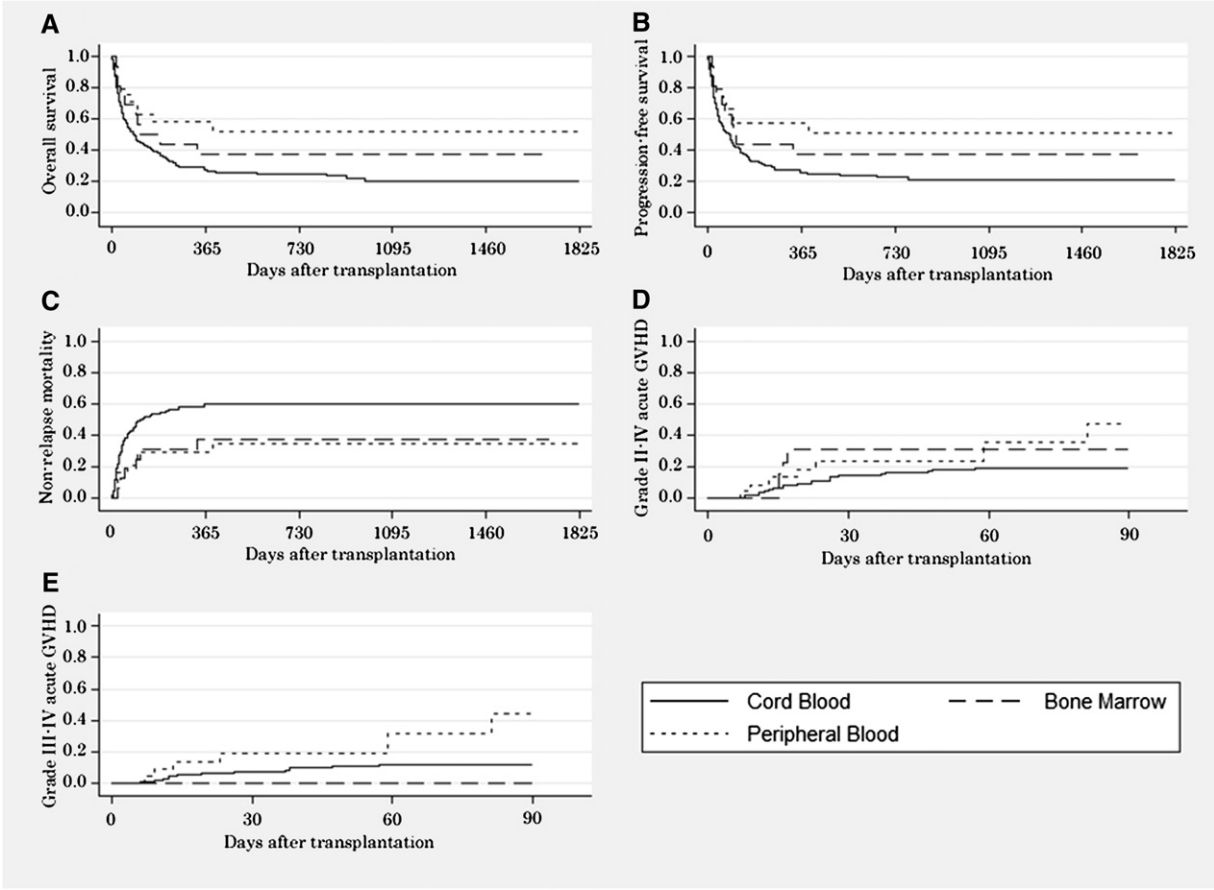

Figure 2. Probability of 1-year OS (A), probability of 1-year PFS (B), cumulative incidence of NRM (C), cumulative incidence of grade II-IV acute GVHD (D), and cumulative incidence of grade III-IV acute GVHD (E) in patients according to stem cell source.

previous NMDP study, but our OS was greater [9]. The poor OS in the NMDP study might be attributable to the longer interval between the diagnosis of GF and the second HSCT (median, 48 days) because they included only patients who underwent unrelated HSCT, which takes more time to coordinate. In addition, the proportion of patients who received a conventional conditioning regimen was significantly higher in the NMDP study than in the present study, possibly contributing to the higher NRM rate in the NMDP study [14]. Most patients in the present study received an RIC or NMA regimen, which might have reduced the incidence of NRM.

The risk of severe GVHD is a major concern when selecting HLA-mismatched PBSCs as the stem cell source for a second HSCT, even with the advantage of faster engraftment. In fact, PBSCT was associated with significantly higher rates of grade II-IV and grade III-IV acute GVHD, as expected given that the majority of PBSC grafts were obtained from HLA-mismatched donors. The incidence rate of NRM was significantly lower after PBSCT, however. In addition, 21 of 22 PBSCT recipients with available HLA information (95%) received stem cells from a 2-3 HLA antigen-mismatched donor. The main cause of death after second HSCT, especially before engraftment, was infectious disease; therefore, an early, significant reduction in the rate of infectious disease after the second HSCT contributed to the reduction in NRM. In addition, our study cohort comprised exclusively Japanese patients, who have a lower incidence of acute GVHD compared with Caucasian patients and can better tolerate HLA-mismatched HSCT without ex vivo T cell depletion [15-17]. The superiority of PBSC compared with CB awaits confirmation in Caucasian patients.

Regarding the conditioning regimen for salvage PBSCT, we performed univariate analysis only because of the limited number of patients. The cumulative incidents of engraftment were 100% with a Flu-based regimen including an alkylator, 78% with a Flu-based regimen without an alkylator, and 0% without any conditioning regimen. The use of a Flu-based regimen including an alkylator was associated with a significantly higher probability of engraftment compared with a Flu-based regimen without an alkylator (HR, 4.5; 95% CI, 1.6-12.8; $P = .0051$). The probability of 1-year OS was 82% with a Flu-based regimen including an alkylator, but only 44% with a Flu-based regimen without an alkylator ($P = .27$). Alkylators

Table 3. Multivariate Analysis for NRM, Acute GVHD, and Infectious Disease

	HR (95% CI)	*P* Value
NRM		
Stem cell source		
CB	Reference	
BM	0.54 (0.25-1.15)	.111
PBSCs	0.43 (0.21-0.87)	.019
Steroids		
None	Reference	
Yes	2.41 (1.59-3.66)	<.001
Each additional year older	1.01 (1.00-1.02)	.015
Grade II-IV acute GVHD		
Stem cell source		
CB	Reference	
BM	1.74 (0.54-5.62)	.352
PBSCs	2.83 (1.27-6.27)	.011
TBI		
None	Reference	
Yes	2.43 (1.29-4.61)	.006
Grade III-IV acute GVHD		
Stem cell source		
CB	Reference	
BM	<0.01	<.001
PBSCs	7.34 (2.87-18.74)	<.001
Steroids		
None	Reference	
Yes	<0.01	<.001
Conditioning regimen		
None	Reference	
CST	16.12 (1.34-193.80)	.028
RIST	1.93 (0.20-18.75)	.573
Mini	0.94 (0.09-9.60)	.961
All infectious diseases		
Stem cell source		
CB	Reference	
BM	0.21 (0.05-0.87)	.032
PBSCs	0.33 (0.14-0.81)	.015
Additional immunosuppressive drugs		
None	Reference	
MTX	1.09 (0.64-1.85)	.748
MMF	2.25 (1.23-4.10)	.008
Disease risk		
Normal	Reference	
High	0.63 (0.41-0.98)	.039

included cyclophosphamide in 7 patients and melphalan in 3 patients. The majority of patients (79%) received TAC-based GVHD prophylaxis. Therefore, PBSCT with a Flu + alkylator combination regimen followed by TAC-based GVHD prophylaxis seemed to be the preferable course of treatment.

Some limitations of this study warrant considereation. A major limitation is the study's retrospective nature and use of registry data, which make it impossible to identify the decisions made by the physicians regarding stem cell source, conditioning regimen, timing of second HSCT, and so on. Consequently, our analysis might include uncontrolled confounding variables, even though we performed multivariate analysis. Another important limitation is the lack of chimerism data at the time of GF, which prevented us from differentiating GF without donor hematopoiesis from GF with donor hematopoiesis but poor graft function.

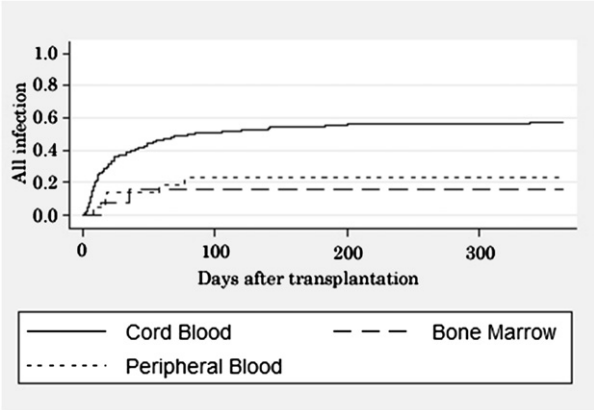

Figure 3. Cumulative incidence of infectious disease in patients according to stem cell source.

In conclusion, this retrospective analysis found that PBSCT was associated with greater and faster engraftment than CBT and led to a significantly better survival, although it did have a higher rate of acute GVHD. Considering the difficulty in performing a randomized controlled trial to compare the effects of stem cell source in patients with GF, PBSCT with a conditioning regimen including Flu and an alkylator may be the preferable salvage therapy, even using PBSCs from a mismatched related/haploidentical donor if necessary, in the emergent situation of GF after CBT.

ACKNOWLEDGMENTS

We thank the medical, nursing, data processing, laboratory, and the clinical staff at the participating centers for their important contributions to this study and their dedicated care of the patients. This study was supported in part by grants from the Ministry of Health, Labor and Welfare, Japan.

Financial disclosure: The authors have no conflicts of interest to disclose.

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