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# Second Allogeneic Stem Cell Transplantation in Hematologic Malignancies: A Single-center Experience

*Hee Won Chueh, MD,* Soo Hyun Lee, MD,† Ki Woong Sung, MD,†*
*Keon Hee Yoo, MD,† and Hong Hoe Koo, MD, PhD†*

**Summary:** Patients with hematologic malignancies who relapse after their first hematopoietic stem cell transplantation tend to have poor prognoses. One option for these patients is a second allogeneic hematopoietic stem cell transplantation (allo-HSCT). However, there are few reports of second allo-HSCT therapy in children with relapsed hematologic malignancies. Patient outcomes in 27 individuals with acute leukemia who received at least 2 allo-HSCTs at the Samsung Medical Center between May 1997 and September 2010 were analyzed retrospectively. After a median follow-up of 33 months, 11 of 27 patients (40.7%) were alive and in stable remission. The 5-year overall survival rate for all 27 patients was 32.6%. There was no statistically significant difference in the survival rates of patients differing in their sex, the stem cell source, the donor type, or the presence of acute or chronic graft-versus-host disease. Remission before the second allo-HSCT was the only prognostic factor that influenced the survival rates (44.1% vs. 11.1%, $P = 0.009$). Of 16 cases of mortality, 9 mortality cases (56.3%) were associated with relapse and 7 cases (43.7%) were associated with treatment-related mortality. Therefore, a second allo-HSCT offers the chance of stable remission for some patients with acute hematologic malignancies who relapse after their first allo-HSCT.

**Key Words:** leukemia, second allogeneic stem cell transplantation, relapse

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Patients with hematologic malignancies who relapse after the first allogeneic hematopoietic stem cell transplantation (allo-HSCT) tend to have poor prognoses.[1,2] Although effective treatment options for these patients are limited,[3] one potential therapy is a second allo-HSCT. However, reinduction chemotherapy and the consecutive hematopoietic stem cell transplantation (HSCT) poses a high risk because the patients are usually in poor general health and thus have difficulty coping with the adverse effects of these treatments.[4,5] There is no established standard therapy for these patients because of the high degree of controversy in the literature.[6,7] In addition, there exist few reports detailing outcomes of the second allo-HSCT in children.[7–12] Therefore, we analyzed the outcomes of patients with hematologic malignancies who received more than 2 allo-HSCTs after relapse, to elucidate the major factors that influence patients' outcomes and survivals.

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From the *Department of Pediatrics, Dong-A University Medical Center, Dong-A University College of Medicine, Busan; and †Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea.
The authors declare no conflict of interest.
Reprints: Hong Hoe Koo, MD, PhD, Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-Dong, Gangnam-Gu, Seoul 135-710, Republic of Korea (e-mail: hhkoo@skku.edu).


## PATIENTS AND METHODS

### Patients

Patients with acute lymphoblastic leukemia, acute myeloid leukemia (AML), and juvenile myelomonocytic leukemia who received their second allo-HSCTs at the Samsung Medical Center, Republic of Korea, between May 1997 and September 2010 were enrolled in the study. Medical records were analyzed retrospectively to collect data concerning the disease status, details of the first and second transplantations, and patient outcomes. Characteristics of the patient population are shown in Table 1.

### Methods

Patients were considered to be in complete remission (CR) if reinduction treatment resulted in the recovery of peripheral blood (PB) cell counts (absolute neutrophil count $\geq 750/\mu L$ and platelet count $\geq 75{,}000/\mu L$) and if bone marrow (BM) revealed an M1 status ($< 5\%$ blasts by BM aspirate) with no evidence of circulating blasts or extramedullary disease. Patients who did not achieve CR after the reinduction therapy were classified as having reinduction failure. Relapse was defined as a biopsy-confirmed M3 marrow ($\geq 25\%$ blasts) or the presence of leukemic cells in any other sites (eg, central nervous system, chloroma, PB) in a patient who had achieved CR previously, irrespective of any change in the molecular or the phenotypic characteristics. Patients who developed therapy-related AML due to secondary malignancy were included only when they received allo-HSCT at least twice because of the same disease. The status of minimal residual disease (MRD) was not checked during the treatment.

After reinduction chemotherapy, patients who achieved CR received an additional 1 to 2 cycles of consolidation chemotherapies before undergoing the second allo-HSCT. Granulocyte colony-stimulating factor and transfusions were administered during the period immediately after the reinduction therapy and consolidation chemotherapy. All treatment protocols were reviewed and approved by the Institutional Review Board.

Stem cell sources used in the HSCTs included matched sibling BM, matched sibling PB stem cells, haploidentical PB stem cells, matched unrelated BM, matched unrelated PB stem cells, and unrelated umbilical cord blood. If the patient had a suitable sibling donor, sibling BM or PB stem

**TABLE 1.** Characteristics of Patients

| Characteristics | N (%) |
|---|---|
| No. patients | 27 |
| Age (y) | |
| At diagnosis | 2.9 (0.2-17.4) |
| At the first allo-HSCT | 3.3 (0.6-18.3) |
| At the second allo-HSCT | 6.3 (1.2-19.0) |
| Sex | |
| Male | 18 (66.7) |
| Female | 9 (33.3) |
| Diagnosis | |
| AML | 13 (48.2) |
| ALL | 10 (37.0) |
| JMML | 3 (11.1) |
| Fanconi anemia | 1 (3.7) |
| Subgroup | |
| Infant leukemia | 5 (18.5) |
| t(8;21) | 5 (18.5) |
| t(1;19) | 1 (3.7) |
| MLL rearrangement* | 2 (7.4) |
| Monosomy 7† | 1 (3.7) |
| Other abnormality | 5 (18.5) |
| Normal karyotype | 10 (37.1) |
| Disease status before the first allo-HSCT | |
| First transplantation at CR1 | 21 (77.8) |
| First transplantation at CR2 | 5 (18.5) |
| First transplantation due to Fanconi anemia | 1 (3.7) |
| Stem cell source of the first allo-HSCT | |
| Bone marrow | 9 (33.3) |
| Peripheral blood stem cell | 12 (44.4) |
| Umbilical cord blood | 6 (22.2) |
| Conditioning regimen of the first allo-HSCT | |
| Myeloablative | 26 (96.3) |
| Nonmyeloablative | 1 (3.7) |
| GVHD prophylaxis | |
| CSA | 12 (44.4) |
| CSA + MTX | 8 (29.6) |
| CSA + MMF | 4 (3.7) |
| CSA + MPD | 3 (11.1) |

*Exclude infant leukemia with MLL rearrangement.
†This patient showed both t(8:21) and monosomy 7.
ALL indicates acute lymphoblastic leukemia; allo-HSCT, allogeneic hematopoietic stem cell transplantation; AML, acute myeloid leukemia; CR1, first complete remission; CR2, second complete remission after relapse; CSA, cyclosporine; GVHD, graft-versus-host disease; JMML, juvenile myelomonocytic leukemia; MMF, mycophenolate mofetil; MPD, methylprednisolone; MLL, myeloid/lymphoid or mixed-lineage leukemia; MTX, methotrexate.

cells were chosen preferentially. If the patient did not have a sibling donor, matched unrelated BM or PB stem cells were chosen with next priority. Umbilical cord blood stem cells were searched in the next step. Haploidentical stem cells were considered in special cases.

Myeloablative conditioning regimens were used with priority in patients with hematologic malignancies, but selective patients underwent second or third allo-HSCT with a nonmyeloablative or a reduced-intensity conditioning regimen according to their medical condition. Various busulfan or total body irradiation (TBI)-based regimens were used as the basic myeloablative regimen, but fludarabine–melphalan-based regimens were also used for the patients with AML. Commonly used conditioning regimens for acute lymphoblastic leukemia are as follows: TBI-Cy (TBI 333 cGy on days −6, −5, −4, cyclophosphamide 60 mg/kg on days −3, −2); BuCy (busulfan 0.8 to 1 mg/kg/dose q 6 h on days −9, −8, −7, −6, cyclophosphamide 50 mg/kg on days −5, −4, −3, −2), TBI-AraC-Cy (TBI 333 cGy on days −8, −7, −6, cytarabine 3000 mg/m$^2$/dose q 12 h on days −4, −3, cyclophosphamide 60 mg/kg on days −2, −1), and BuFlu (busulfan 0.8 to 1 mg/kg/dose q 6 h on days −6, −5, −4, −3, fludarabine 40 mg/m$^2$ on day −8, −7, −6, −5, −4). Conditioning regimens for AML also include BuCy, BuFlu, and TBI-FluMel (TBI 333 cGy on days −10, −9, −8, fludarabine 25 mg/m$^2$ on days −7, −6, −5, −4, −3, and melphalan 140 mg/m$^2$ on day −3).

Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporine alone for matche-related allo-HSCTs, cyclosporine plus methotrexate for unrelated donor allo-HSCTs, and cyclosporine plus mycophenolate mofetil for umbilical cord blood transplantation. The staging and grading of acute GVHD were performed using the modified Glucksberg consensus criteria[13] and occurred at the time of initiation of treatment, and the grading of chronic GVHD was performed using the clinical chronic GVHD grading system.[14]

## Statistics

Patient data were collected at the time of death or at the last follow-up appointment. Overall survival rates and event-free survival rates were calculated using the Kaplan-Meier method. Differences between the subgroups were compared by the log-rank and Wilcoxon tests to determine the statistical significance. Multivariate risk factor analysis was performed according to the Cox regression model.

# RESULTS

## Patient Characteristics

Twenty-seven patients underwent the second allo-HSCT between May 1997 and September 2010. Initial diagnoses of 26 patients were hematologic malignancies. However, 1 patient received the first allo-HSCT because of Fanconi anemia, but later developed AML as a secondary malignancy. He underwent his third allo-HSCT because of relapse after the second allo-HSCT. Chimerism statuses of the patients were checked after the allo-HSCT in all patients, and all patients showed mixed chimerism on relapse. One patient underwent second allo-HSCT because of graft failure, but relapsed after successful engraftment (data not shown). He received third allo-HSCT after reaching CR. Patient characteristics are listed in Table 1.

## Characteristics of the Pretransplantation Treatment and the Second Allo-HSCT

The median time span from the first allo-HSCT to the relapse was 144 days (range, 32 to 852 d). On average, 2 cycles (range, 1 to 4 cycles) of chemotherapy were given after the relapse, and a median of 91 days (range, 28 to 580 d) passed before the patients received their second allo-HSCT after the relapse. Twenty-seven patients underwent their second allo-HSCT, and 19 of these patients (70.4%) achieved complete hematologic remission before the second allo-HSCT. The remaining 8 patients (29.6%) had persistent disease before their second allo-HSCT, and each relapsed later. Characteristics of the second allo-HSCTs are shown in Table 2. For the patients who did not receive TBI at the first allo-HSCT, TBI was included in the conditioning for the second allo-HSCT. Stem cell sources included matched sibling BM, matched sibling PB, matched unrelated BM, matched unrelated PB, and unrelated umbilical cord blood.

**TABLE 2.** Characteristics of the Second Allogeneic Hematopoietic Stem Cell Transplantation

| | N (%) |
|---|---|
| Time from first allo-HSCT to relapse (range, d) | 144 (32-852) |
| Site of relapse | |
| BM | 27 (100) |
| Engraftment | 24 (88.8) |
| Days to neutrophil engraftment (ANC ≥ 1000/μL; range, d) | 12 (9-35) |
| Days to platelet engraftment (PLT ≥ 20,000/μL; range, d) | 21 (16-41) |
| Disease status before the second allo-HSCT | |
| CR | 19 (70.4) |
| Persistent disease | 7 (25.9) |
| Graft failure | 1 (3.7) |
| Donor type | |
| Matched related | 9 (33.3) |
| Matched unrelated | 13 (48.2) |
| Mismatched (haploidentical) | 5 (18.5) |
| Same donor for the first and second allo-HSCT | |
| Yes | 16 (59.3) |
| No | 11 (40.7) |
| Conditioning regimen | |
| Myeloablative | 25 (92.6) |
| Nonmyeloablative | 2 (7.4) |
| Stem cell source | |
| BM | 1 (3.7) |
| PBSC | 20 (74.1) |
| UCB | 2 (7.4) |
| PBSC + UCB | 4 (14.8) |
| GVHD prophylaxis | |
| CSA | 11 (40.7) |
| CSA + MTX | 10 (37.0) |
| CSA + MMF | 4 (14.8) |
| CSA + MPD | 2 (7.4) |

Allo-HSCT indicates allogeneic hematopoietic stem cell transplantation; ANC, absolute neutrophil count; BM, bone marrow; CR, complete remission; CSA, cyclosporine; GVHD, graft-versus-host disease; MMF, mycophenolate mofetil; MPD, methyl-prednisolone; MTX, methotrexate; PBSC, peripheral blood stem cell; PLT, pletelet; UCB, umbilical cord blood.

## Outcome of the Second Allo-HSCT

After a median follow-up of 33 months (range, 11 to 158 mo), 11 of 27 patients (40.7%) were alive and in stable remission. The 5-year overall survival rate of all patients was 32.6% (Fig. 1). The median time to neutrophil engraftment (neutrophil count over 1000/μL) was 12 days (range, 9 to 35 d), whereas the median time to platelet recovery (platelet count over 20,000/μL without transfusion over 7 consecutive days) was 21 days (range, 16 to 41 d; Table 2). BM biopsies and chimerism tests that were performed on day 28 showed complete engraftment in 24 patients (88.8%). However, 3 patients expired before the neutrophil engraftment because of early treatment-related mortality (TRM). Six patients showed grade 3/4 acute GVHD, but none of them was related to mortality. Extensive chronic GVHD was shown in 10 patients, and 4 of them suffered from lung GVHD (Table 5).

There was no statistical difference in the survival rates of patients differing in diagnosis, sex, stem cell source, donor type, or the presence of acute or chronic GVHD (Tables 3 and 4). The use of a TBI-based conditioning regimen in the first or the second allo-HSCT did not influence the survival. The use of the same donor at the second allo-HSCT did not influence the survival or relapse rates after the secondary

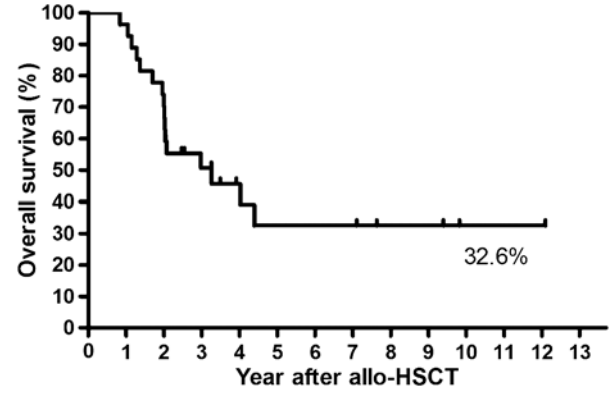


**FIGURE 1.** Overall survival rates of the patients. Allo-HSCT indicates allogeneic hematopoietic stem cell transplantation.

HSCT (38.1% vs. 25.0%, $P = 0.348$; Table 4). Similarly, early relapse (< 1 y after the first allo-HSCT) did not influence survival or relapse rates. Remission before the second allo-HSCT was the only prognostic factor that influenced the survival rate (44.1% vs. 11.1%, $P = 0.009$; Table 4; Fig. 2).

Six patients underwent a third allo-HSCT because of relapse after their second allo-HSCT. One patient used the same donor as the second allo-HSCT, and 5 patients

**TABLE 3.** Multivariate Analysis of Risk Factors Affecting the Survival

| | Hazard Ratio (95% CI) | P |
|---|---|---|
| No. transplantations | | |
| 2 | 1.0 | 0.405 |
| ≥ 3 | 0.254 (0.01-6.39) | |
| Relationship of donor | | |
| Sibling | 1.0 | 0.849 |
| Unrelated | 1.191 (0.19-7.22) | |
| Same donor of the first allo-HSCT | | |
| Same | 1.0 | 0.555 |
| Different | 2.236 (0.16-32.25) | |
| Sex | | |
| Male | 1.0 | 0.066 |
| Female | 11.24 (0.85-14.9) | |
| Subgroup | | |
| Standard or undetermined risk group | 1.0 | 0.144 |
| Groups with risk factor | 0.277 (0.05-1.55) | |
| Disease status before the second allo-HSCT | | |
| CR | 1.0 | 0.001 |
| Persistent | 0.036 (0.01-0.31) | |
| Time of relapse | | |
| Late (≥ 1 y) | 1.0 | 0.759 |
| Early (< 1 y) | 0.68 (0.06-7.81) | |
| Acute GVHD | | |
| No or mild (< Gr 3) | 1.0 | 0.833 |
| Severe (≥ Gr 3) | 1.24 (0.17-9.06) | |
| Chronic GVHD | | |
| No or localized | 1.0 | 0.171 |
| Extensive | 3.57 (0.17-9.06) | |
| TBI-based regimen | | |
| No | 1.0 | 0.212 |
| Yes | 0.17 (0.01-2.74) | |

Allo-HSCT indicates allogeneic hematopoietic stem cell transplantation; CI, confidence interval; CR, complete remission; Gr, grade; GVHD, graft-versus-host disease; TBI; total body irradiation.

**TABLE 4.** Comparison of the Overall Survival Between Subgroups

| | No. Patients (%) | Overall Survival (%) | *P* |
|---|---|---|---|
| Relationship of donor | | | 0.941 |
| Sibling | 9 (33.3) | 37.0 | |
| Unrelated | 13 (48.2) | 18.2 | |
| Haploidentical | 5 (18.5) | 40.0 | |
| Source of stem cell | | | 0.107 |
| PBSC | 20 (74.1) | 40.7 | |
| BM | 2 (7.4) | 0 | |
| UCB | 1 (3.7) | 0 | |
| Mixed | 4 (14.8) | 25.0 | |
| Same donor of the first allo-HSCT | | | 0.348 |
| Yes | 15 (55.6) | 38.1 | |
| No | 12 (44.4) | 25.0 | |
| Sex | | | 0.155 |
| Male | 18 (66.7) | 22.5 | |
| Female | 9 (33.3) | 58.3 | |
| Diagnosis | | | 0.998 |
| AML* | 14 (51.9) | 33.3 | |
| ALL | 10 (37.0) | 30.0 | |
| JMML | 3 (11.1) | 33.3 | |
| Risk group | | | 0.541 |
| Standard or undetermined | 20 (74.1) | 26.0 | |
| High risk | 7 (25.9) | 57.1 | |
| Disease status before the second allo-HSCT | | | 0.006 |
| CR | 18 (66.7) | 44.1 | |
| Persistent | 9 (33.3) | 11.1 | |
| Time to relapse | | | 0.432 |
| Early ( < 1 y after transplantation) | 15 (55.6) | 37.3 | |
| Late ($\geq$ 1 y after transplantation) | 12 (44.4) | 28.6 | |
| TBI-based conditioning regimen | | | 0.619 |
| Yes | 22 (81.5) | 40.1 | |
| No | 5 (18.5) | 31.0 | |
| Acute GVHD | | | 0.176 |
| $\geq$ Gr 3 | 21 (77.8) | 36.7 | |
| < Gr 3 | 6 (22.2) | 16.7 | |
| Chronic GVHD | | | 0.435 |
| Limited or none | 17 (63.0) | 29.8 | |
| Extensive | 10 (37.0) | 40.0 | |

*Includes a patient with Fanconi anemia who developed secondary AML.

ALL indicates acute lymphoblastic leukemia; allo-HSCT, allogeneic hematopoietic stem cell transplantation; AML, acute myeloid leukemia; BM, bone marrow; CR, complete remission; Gr, grade; GVHD, graft-versus host disease; JMML, juvenile myelomonocytic leukemia; PBSC, peripheral blood stem cell; TBI; total body irradiation; UCB, umbilical cord blood.

changed the donor. Donor leukocyte infusion (DLI) was performed in 4 patients when they relapsed after the second allo-HSCT, which did not change the course of mortality. Only 1 patient reached CR after the third allo-HSCT, followed by DLI, and is still alive.

Nonmyeloablative conditioning strategies were adopted in 3 cases (11.1%) of second HSCTs and in 2 cases (33.3%) of third HSCTs.

## Overall Survival and the Final Outcome

In total, 16 cases (59.3%) ended in patient mortality. Of these, 9 (56.3%) were associated with relapse and 7 (43.7%) were associated with TRM (Table 5). Of the TRM cases, 4 cases (57.1%) occurred within 100 days of the second allo-HSCT. The remaining 3 cases (42.9%) were associated with chronic GVHD and infection. Eleven patients (40.7%) survived in CR to the completion of the study.

**TABLE 5.** Analysis of the Cause of Death

| | N (%) |
|---|---|
| Total death | 16 (59.3) |
| TRM | 7/16 |
| Early events ($\leq$ day 100) | 3 |
| VOD | 1 |
| Cardiac Tamponade | 1 |
| ARDS | 1 |
| Acute GVHD | 0 |
| Late events (> day 100) | 4 |
| Chronic lung GVHD + organ failure | 1 |
| Chronic lung GVHD + fungal infection* | 3 |
| Relapse | 9 |

*Proven pathogens were *Aspergillus* species in all cases.

ARDS indicates acute respiratory distress syndrome; GVHD, graft-versus-host disease; TRM, treatment-related mortality; VOD, veno-occlusive disease.

## DISCUSSION

Patients who relapse after allo-HSCTs have few remaining treatment options. These patients have usually received prior chemotherapy with various agents, and they frequently show resistance to the chemotherapeutic agents used previously.[1] According to the literature, CR rates decrease as therapeutic attempts increase.[12,15–17] In addition, organ functions are usually impaired to their functional status at the time of the first allo-HSCT.[15,18] Donor selection also presents a problem. If patients have matched sibling donors, they are able to use their siblings as donors for a second or third HSCT. However, for the patients who received their first HSCT with umbilical cord blood or from an unrelated donor, it is difficult to use the same donor in a

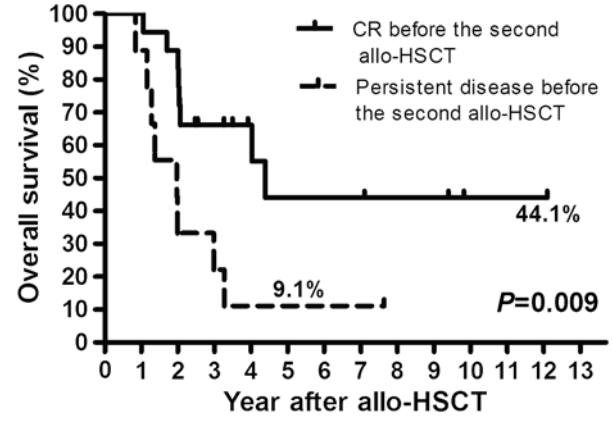


**FIGURE 2.** The Kaplan-Meier curve of survival comparison between the patient groups according to the disease status before the second allo-HSCT. Overall survival rates of the patients with persistent disease before the second allo-HSCT is lower than that of the patients with CR before the second allo-HSCT. Allo-HSCT indicates allogeneic hematopoietic stem cell transplantation; CR, complete remission.

second allo-HSCT. Therefore, this study aimed to assess the survival rates of patients who relapse after their first allo-HSCT and to elucidate the factors that influence the survival rates with the hope of establishing a strategy to improve the survival rates after relapse.

Although follow-up durations after the second allo-HSCTs were relatively short, patient outcomes reported here are similar to or even superior to those in other reports.[7–10,12,19] However, we were not able to determine the relationship between the survival rates and induction treatment because of the heterogenous induction therapy that patients received, particularly with subsequent treatment attempts.

The only factor that influenced the patient outcome was the status of CR before the second allo-HSCT. The CR rate after the first relapse was 70.4%, which is comparable to or higher than the CR rates reported by other studies.[2,7,12,16,20] Patients who failed to achieve CR were overcome by their primary disease and did not survive to the study's completion. This result implies that optimal induction and consolidation therapy is the key to improving the outcome of these patients. Although many efforts to improve the CR rate after relapse have been explored in numerous studies,[3,5,12,20–23] results remain unsatisfactory and require further study.

Overall survival rates did not differ between patients with varying age, diagnosis, times of relapse, durations between the first transplantation and the relapse, and TBI-based conditioning regimens. Among the various factors that may influence the survival rates, most studies focused on donor-related factors and graft-versus-leukemia effects.[3,24,25] There exists some controversy surrounding graft-versus-leukemia effects, and many studies aimed to demonstrate the positive effects of GVHD or HLA mismatches on preventing further relapse. Whereas some studies showed positive effects on survival rates,[3,22] others failed to demonstrate a benefit.[13,26,27] Here, we report that patients who received BM suffer from poorer outcomes compared with patients receiving PB stem cells or umbilical cord blood. However, the number of the patients who received the second allo-HSCT with BM ($n = 3$) was too small to attain statistical significance. In addition, no conclusive graft-versus-leukemia effect was seen in our study; acute or chronic extensive GVHD did not influence patient outcomes in this study.

Furthermore, there was no difference in survival rates between patients who underwent the second allo-HSCT with different donor types. The survival of patients who used the same donor for both transplantations did not differ from those of patients who received their second allo-HSCT from a new donor. Previous studies also failed to show the advantages of choosing a different donor.[8,15]

Some studies report that the time from the first allo-HSCT to the second allo-HSCT or to the time of relapse is an important prognostic factor and suggest that longer times are correlated with improved survival rates.[2,7,16] However, in our study, patients with late relapse did not show any improvement in overall survival rates compared with those with early relapse. This result differs significantly from previously published studies, necessitating the evaluation of the relationship between patient outcomes and the time to relapse. Some factors could contribute to this discrepancy; there were fewer patients with late relapse than the early relapsed patients. Also, MRD statuses of the patients who relapsed early or late are not available. Therefore, more data should be analyzed with a larger number of patients in future.

The toxicity of induction and consolidation chemotherapy was not significant in our study, but the incidence of TRM after the second allo-HSCT was relatively high. The majority of these TRMs consist of early TRM, which related to transplantation and chronic GVHD, especially lung GVHD. As other previous studies showed similar or slightly lower TRM rates after the second allo-HSCT,[6,15,16,28] TRM still seems to be the main problem in dealing with patients with relapse after the first allo-HSCT. Moreover, as more than half of the total deaths were cases of relapse, efforts to attain CR through intensive induction and allo-HSCT with an intensive conditioning regimen remains a reasonable possibility. The development of strategies to reduce patient mortality, especially transplantation-related mortality, is needed.

To date, the heterogeneity of therapeutic schemes and diversity of chemotherapeutic protocols limits the analysis of the risk factors influencing posttransplantation relapse and survival rates. Prospective studies with larger numbers of homogenous patients and a single chemotherapeutic schedule may yield more information in the future design of treatment protocols for patients with relapsed hematologic malignancies. Furthermore, statuses of MRD of the patients were not counted in this study because MRD was not included to routine evaluation until recently because of technical problem. We hope that more detailed results including MRD would be available within a few years.

In conclusion, a second allo-HSCT provides the opportunity for stable remission for some patients with hematologic malignancies who relapse after their first allo-HSCT. Being in remission before the second transplantation is the important factor influencing survival rates. Also, a myeloablative conditioning regimen could be applied for those patients. However, the type of conditioning regimen, attempts of DLI, and the donor type did not influence survivals. Therefore, new intensive induction chemotherapy followed by second allo-HSCT with a myeloablative conditioning regimen might be a reasonable strategy for those patients. Because high TRM remains a challenge, strategies to reduce the TRM should further be investigated.

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