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**Early lymphocyte recovery predicts clinical outcome after HSCT with mycophenolate mofetil prophylaxis in the Japanese population**

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**ABSTRACT**

Immune reconstitution affects clinical outcomes after allogeneic hematopoietic stem cell transplantation (HSCT), and it has been suggested that lymphocyte recovery affects survival after HSCT. However, few studies have examined lymphocyte recovery in Asian patients who received mycophenolate mofetil (MMF) prophylaxis for graft-versus-host disease. We retrospectively evaluated early lymphocyte recovery after HSCT among Japanese adults who received MMF prophylaxis. Patients were divided into two groups according to their median absolute lymphocyte count (ALC) on day 28 after HSCT as follows: the "low ALC group" ($\leq 0.22 \times 10^9$ cells/L) and the "high ALC group" ($>0.22 \times 10^9$ cells/L). With a median follow-up of 317 days, the high ALC group showed significantly better overall survival than the low ALC group (at 1 year: 62% vs. 46%, $P = 0.02$). The high ALC group also tended to have better non-relapse mortality than the low ALC group (at 1 year: 13% vs. 23%, $P = 0.08$). There was no significant difference in relapse rate between the high and low ALC groups (at 1 year: 29% vs. 35%, $P = 0.2$). We conclude that among Japanese patients who received MMF prophylaxis, ALC on day 28 after HSCT was effective in predicting overall survival and non-relapse mortality.

## INTRODUCTION

Immune reconstitution affects clinical outcomes after allogeneic hematopoietic stem cell transplantation (HSCT), as the donor lymphocytes help reconstitute the host's immune system, prevent infectious complications, and prevent disease relapse through a graft-versus-tumor effect. Thus, rapid lymphocyte recovery is generally associated with a survival benefit after HSCT [1-14]. However, previous studies incorporated HSCTs from different graft sources and covered a broad range of arbitrary post-transplant assessment time points and thresholds, which generated conflicting findings regarding relapse and survival. Furthermore, few studies have examined lymphocyte recovery in Asian cases with mycophenolate mofetil (MMF) prophylaxis for graft-versus-host disease (GVHD) [3, 5, 14]. Those analyses are important, as racial and ethnic diversity can affect clinical outcomes after HSCT. We usually use MMF as an alternative to methotrexate (MTX) in clinical practice, as 2 nationwide registry surveys of more than 1,000 Japanese patients showed that MMF was safe and effective for the prevention and treatment of GVHD after allo-SCT [15, 16]. Therefore, this multi-center study retrospectively evaluated early lymphocyte recovery after HSCT among Japanese adults who received MMF prophylaxis.

## PATIENTS AND METHODS

### Patients and transplant procedures

The study population consisted of adult patients undergoing allogeneic HSCT for hematological malignancies, who received MMF prophylaxis for GVHD, between January 2010 and March 2017 at the Hyogo Cancer Center and the Kobe University Hospital, Hyogo, Japan. Patients who died within 28 days after the HSCT were excluded. All patients completed either myeloablative conditioning (MAC) or reduced-intensity conditioning (RIC) regimens, and their intensities were based on the criteria from the Center for International Blood and Marrow Transplant Research [17].

The prophylaxis for GVHD primarily consisted of a calcineurin inhibitor (cyclosporine or tacrolimus) plus MMF (1,000 mg/body or 15 mg/kg) on day 0, with MMF treatments administered every 8 hours for bone marrow (BM) and peripheral blood stem cell (PBSC) transplantations or every 12 hours for cord blood transplantations [18]. The MMF dose was generally tapered over 3 weeks starting on day 30, as previously described [19]. Based on the clinical protocols, granulocyte-colony stimulating factor was usually started on day 1 after the HSCT to support neutrophil engraftment, and all patients received supportive care in accordance with institutional standards.

**Data**

Demographic, clinical, laboratory, and HSCT data were retrieved from the patients' medical records. All patients had provided informed consent for the use of protected health data, and the research protocol had been approved by the institutional review boards of the participating hospitals.

**Definitions**

Overall survival (OS) and relapse rate (RR) were defined as the time from HSCT until death from any cause and to disease relapse, respectively. Non-relapse mortality (NRM) was defined as death in a case without relapse. Other time-to-event measures (relapse, cytomegalovirus [CMV] reactivation, acute GVHD, and chronic GVHD) were calculated from the date of HSCT to the date of the event. Acute and chronic GVHD were diagnosed using established criteria [20, 21].

The patients were divided into two groups according to their median absolute lymphocyte count (ALC) on day 28 after HSCT: the "low ALC group" ($\leq 0.22 \times 10^9$ cells/L) and the "high ALC group" ($>0.22 \times 10^9$ cells/L). Disease risk was defined as low in cases with acute

leukemia during the first complete remission, myelodysplastic syndrome-refractory anemia, or chronic myeloid leukemia, while all other cases were considered high risk.

### Statistical analysis

Univariate categorical analyses were performed using Pearson's chi-square test or the Mann-Whitney U-test. The variables were analyzed for associations with OS using Kaplan-Meier curves and the log-rank test. The incidences of relapse, NRM, GVHD, CMV disease, and human herpes virus 6 (HHV-6) disease were calculated using Gray's test and considering competing events. The competing events were death before progression for relapse and relapse before NRM. Relapse and death were the competing events for GVHD, CMV, and HHV-6. Patients were censored if they did not experience any events. Variables with a *P*-value of <0.1 were included in the multivariate analysis. A Cox proportional hazard regression model was used for OS, while the Fine-Gray method was used for RR and NRM, considering the competing risks for each outcome. A stepwise selection algorithm was applied using the criteria for variable selection. The outcomes of the multivariate analyses were reported as hazard ratios (HR) and 95% confidence intervals (CI). Differences were considered statistically significant at a *P*-value of <0.05, and all analyses were performed using EZR and R Commander (version 1.35) [22].

## RESULTS

### Patient and transplant characteristics

The characteristics of the 88 included patients are summarized in Table 1. The median follow-up time for surviving patients was 317 days (range: 31–2341 days). Among the 88 included patients, 16 patients (18%) died without relapse or recurrence. The causes of deaths in the high ALC group were infectious pneumonia (n = 3), chronic GVHD (n = 1), and

hemorrhage (n = 1), while the causes of death in the low ALC group were infectious pneumonia (n = 4), multiple organ failure (n = 4), interstitial pneumonia (n = 2), and hemorrhage (n = 1).

**Factors associated with ALC**

Univariate and multivariable analyses were performed to assess the baseline factors' associations with ALC at day 28 after HSCT. Univariate analyses revealed that low ALC was not significantly associated with disease diagnosis ($P = 0.49$), donor source ($P = 0.94$), conditioning regimen ($P = 0.52$), or type of calcineurin inhibitors ($P = 1.00$). Furthermore, there were no significant risk factors for delayed lymphocyte recovery in the multivariable analysis.

**Effect of ALC on time-to-event outcomes**

The univariate analysis revealed that the high ALC group had significantly better OS, compared to the low ALC group (at 1 year: 62% vs. 46%, $P = 0.02$) (Figure 1a, Table 2). In addition, favorable OS was significantly associated with MAC conditioning regimens ($P = 0.03$). In the multivariable analyses, ALC at day 28 was independently associated with better OS ($P < 0.01$). Better OS was also independently associated with MAC regimen ($P = 0.01$) and BM transplantation ($P = 0.02$) (Table 3).

The univariate analysis revealed no significant difference in RR between the high and low ALC groups (at 1 year: 29% vs. 35%, $P = 0.2$) (Figure 1b, Table 2). Furthermore, increased RR was significantly associated with high-risk disease status ($P < 0.001$) and the RIC conditioning regimen ($P = 0.02$). The multivariable analysis revealed that RR was independently predicted by RIC regimens ($P = 0.001$) and high-risk disease status ($P < 0.001$) (Table 3).

The univariate analysis revealed a trend towards better NRM in the high ALC group, compared to the low ALC group (at 1 year: 13% vs. 23%, $P = 0.08$) (Figure 1c, Table 2). None of the other studied factors were significantly associated with NRM. The multivariable analysis revealed that a lower incidence of NRM was independently associated with ALC at day 28 ($P = 0.05$) and BM transplantation ($P = 0.007$) (Table 3).

The cumulative incidences of acute GVHD at 1 year after transplantation were 34% in the high ALC group and 34% in low ALC group ($P = 0.84$). There were also no significant differences in the cumulative incidences of grade II–IV acute GVHD (at 100 days: 18% vs. 7%, $P = 0.11$) or grade III–IV acute GVHD (at 100 days: 11% vs. 2%, $P = 0.1$) (Figure 2a). The cumulative incidence of chronic GVHD was significantly higher in the high ALC group, compared to the low ALC group (at 1 year: 35% vs. 13%, $P = 0.02$) (Figure 2b).

The incidences of CMV antigenemia were 64% (28 patients) in the high ALC group and 64% (28 patients) in the low ALC group ($P = 1.0$). However, the cumulative incidence of CMV disease was significantly higher in the high ALC group than in the low ALC group (at 1 year: 14% vs. 0%, $P = 0.01$). The cumulative incidence of HHV-6 infection tended to be higher in the low ALC group, compared to the high ALC group (at 1 year: 2% vs. 14%, $P = 0.05$).

**Serial changes in ALC after HSCT**

All patients had serial data regarding their post-transplantation ALC recovery. No significant difference was observed between the high and low ALC groups at their pre-transplantation assessments ($P = 0.39$). However, a significant difference in ALC was observed between the two groups starting at day 10 after HSCT ($P < 0.01$) and lasting until 2 months after HSCT. No significant differences between the two groups were observed at >2 months after transplantation (Figure 3).

## DISCUSSION

The present study revealed that early lymphocyte recovery after allogeneic HSCT was associated with better survival outcomes and a lower risk of NRM among Japanese patients who received MMF prophylaxis for GVHD. In this population, NRM is a major determinant of long-term survival that arises from early or late organ toxicities, GVHD, and various infections. However, previous studies have revealed conflicting results regarding the association between lymphocyte recovery and clinical outcomes after allogeneic HSCT. For example, Kim et al. performed a large cohort study that revealed low ALC ($\leq 0.2 \times 10^9$ cells/L) early after HSCT was an independent risk factor for increased NRM and poor survival [6]. Another study revealed that low ALC ($<0.3 \times 10^9$ cells/L) at day 30 was associated with a 3.76-fold greater risk of death within 100 days, although OS, RR, and NRM were not significantly different depending on ALC [11]. Furthermore, several studies have revealed associations between high ALC and better relapse-free survival [4, 6, 7], which seems logical, as donor lymphocytes play key roles in controlling the graft-versus-tumor effect [4]. In contrast, the present study failed to detect a significant difference in the cumulative RR between the two groups, although this could be the result of a relatively short follow-up period.

In terms of acute GVHD, the majority of previous reports demonstrated that the early lymphocyte recovery after HSCT was associated with a low incidence of acute GVHD [3, 11, 12]. Interestingly, the incidence of acute GVHD in the presented study was not significantly different between both groups. However, there was a tendency towards severe acute GVHD being more common in the high ALC group. In contrast to the cytotoxic effect of MTX against donor lymphocytes, MMF is a potent inhibitor of the proliferation and activation of donor lymphocytes [23, 24]. Therefore, more alloreactive donor lymphocytes could survive under MMF treatment as GVHD prophylaxis, which would become reactivated after tapering

of the MMF dose and subsequently induce GVHD. Furthermore, GVHD is primarily a T cell mediated disease [25], and the results of the present study might be acceptable.

Remarkably, CMV disease was seen more frequently in the high ALC group in this study. We suggest the following reasons for this result. First, there was a tendency towards severe acute GVHD tended to be more common in the high ALC group: 8 patients in the high ALC group and 3 patients in the low ALC group. Moreover, corticosteroids were used more frequently in the high ALC group than in the low ALC group (19 vs. 9 patients, $P = 0.04$). Furthermore, 3 of 6 patients in the high ALC group who experienced CMV disease had received high-dose corticosteroid treatments (methylprednisolone $\geq$ 1 mg/kg). Since both acute GVHD and corticosteroids are known as risk factors for CMV disease, we assume that the high frequency of these factors in the high ALC group could be one explanation for our result.

Previous reports have indicated that donor lymphocyte reconstitution is identified approximately 2 weeks after HSCT [26, 27]. In the present study, lymphocyte recovery in the low ALC group was delayed starting at day 10, although it normalized at 3 months after HSCT. Intriguingly, these patients received MMF prophylaxis for approximately 2 months after HSCT (median: 52 days, range: 11–105 days). Thus, MMF treatment may delay lymphocyte recovery, as it is an ester prodrug of mycophenolic acid (an immunosuppressant), which inhibits inosine monophosphate dehydrogenase and interferes with de novo purine synthesis in T and B lymphocytes.

The present study has several limitations. First, the small retrospective sample is prone to bias. However, the assessment time point and threshold of ALC reported in this study are compatible with those previously reported in a larger study [28]. Second, heterogeneous conditioning regimens were used for the various underlying diseases. Third, there were various donor sources for the included procedures. Nevertheless, the present study provides

the first information regarding ALC after MMF prophylaxis, and provides basic evidence for further research.

In conclusion, the present study revealed that, among Japanese patients who received MMF prophylaxis, ALC at day 28 after HSCT was effective for predicting OS and NRM.

**Figure legends**

**Table 1.** Patient and transplant characteristics according to absolute lymphocyte count at day 28 after hematopoietic stem cell transplantation

**Table 2.** Univariate analyses of overall survival, relapse rate, and non-relapse mortality

**Table 3.** Multivariable analyses of overall survival, relapse rate, and non-relapse mortality

**Figure 1.** Comparison of survival outcomes after allogeneic hematopoietic stem cell transplantation. **(a)** Superior survival was observed in the high absolute lymphocyte count (ALC) group, compared to the low ALC group ($P = 0.02$). **(b)** No significant difference was observed in the relapse rate between the high and low ALC groups ($P = 0.2$). **(c)** Increased non-relapse mortality was observed in the low ALC group, compared to the high ALC group ($P = 0.08$).

**Figure 2.** Comparing graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation. **(a)** No significant difference was observed in the cumulative incidence of grade II–IV acute GVHD ($P = 0.11$). **(b)** The increased cumulative incidences of chronic GVHD in the high and low ALC groups ($P = 0.02$).

**Figure 3.** Comparing the serial changes in absolute lymphocyte count (ALC) after hematopoietic stem cell transplantation between the high and low ALC groups. No significant difference was observed between the high and low ALC groups at their pre-transplantation assessments. *$P \leq 0.001$. **(a)** Significant differences in ALC were observed between the two groups at 30 and 60 days after HSCT, which were not observed at >2

months after HSCT. **(b)** A significant difference in ALC was observed between the two groups starting at day 10 after HSCT ($P < 0.01$) and lasting until 2 months after HSCT.

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| Characteristics | Total (n = 88) | High ALC (n = 44) | Low ALC (n = 44) | *P*-value |
|---|---|---|---|---|
| Sex (M : F) (%) | 56 (64) : 32 (36) | 29 (66) : 15 (34) | 27 (61) : 17 (39) | 0.83 |
| Median age (range), years | 52 (19-65) | 49 (19-65) | 52 (22-65) | 0.2 |
| median ALC (range) ($10^9$/L) | 220 (0-2408) | 448 (230-2408) | 146 (0-220) | < 0.001 |
| Diagnosis (%) | | | 17 (39) | 0.49 |
| AML | 42 (48) | 19 (43) | 23 (52) | |
| ALL | 17 (19) | 12 (27) | 5 (11) | |
| MDS | 10 (11) | 5 (11) | 5 (11) | |
| CML | 4 (5) | 2 (5) | 2 (5) | |
| NHL | 13 (15) | 6 (14) | 7 (16) | |
| MPN | 1 (1) | 0 (0) | 1 (2) | |
| Donor source (%) | | | | 0.94 |
| rBM | 2 (2) | 1 (2) | 1 (2) | |
| uBM | 37 (42) | 17 (39) | 20 (46) | |
| rPBSC | 12 (14) | 6 (14) | 6 (14) | |
| uPBSC | 1 (1) | 1 (2) | 0 (0) | |
| uCB | 36 (41) | 19 (43) | 17 (39) | |
| Conditioning (%) | | | | 0.52 |
| MAC | 40 (45) | 22 (50) | 18 (41) | |
| TBI-based | 34 (85) | 18 (82) | 16 (89) | |
| Bu-based | 6 (15) | 4 (18) | 2 (11) | |
| RIC | 48 (55) | 22 (50) | 26 (59) | |
| Flu-Bu±TBI | 24 (50) | 10 (46) | 14 (54) | |
| Flu-Mel±TBI | 21 (44) | 9 (41) | 12 (46) | |
| Others | 3 (6) | 3 (14) | 0 (0) | |
| GVHD prophylaxis (%) | | | | 1 |
| TAC : CSP | 79 (90) : 9 (10) | 39 (89) : 5 (11) | 40 (91) : 4 (9) | |
| Disease status (%) | | | | 0.83 |
| Low risk : High risk | 44 (50) : 44 (50) | 23 (52) : 21 (48) | 21 (48) : 23 (52) | |
| Neutrophil engraftment (days) | 15 (8-58) | 14 (8-24) | 17 (9-58) | < 0.001 |
| Median HCT-CI (range) | 2 (0-9) | 2 (0-8) | 2 (0-9) | 0.52 |
| Chimeric status at day 30 (donor, %) | | | | 0.38 |
| Complete (>95%) | 62 (70) | 34 (77) | 28 (64) | |
| Mixed (81-95%) | 14 (16) | 6 (14) | 8 (18) | |
| Mixed (20-80%) | 6 (7) | 1 (2) | 5 (11) | |
| Mixed (<20%) | 6 (7) | 3 (7) | 3 (7) | |

ALC, absolute lymphocyte count; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MDS, myelodysplastic syndrome; CML, chronic myeloid leukemia; NHL, non-Hodgkin's lymphoma; MPN, myeloproliferative neoplasm; rBM, related bone marrow; uBM, unrelated bone marrow; rPBSC, related peripheral blood stem cell; uPBSC, unrelated peripheral blood stem cell; uCB, unrelated cord blood; MAC, myeloablative conditioning; RIC, reduced intensity conditioning; Flu, fludarabine; Bu, busulfan; Mel, melphalan; TBI, total body irradiation; GVHD, graft-versus-host disease; TAC, tacrolimus; CSP, cyclosporine; HCT-CI, hematopoietic cell transplantation-comorbidity index

| Variable | 1-year outcome (%) | 95% CI | *P*-value |
|---|---|---|---|
| OS | | | |
| ALC at day 28 | | | |
| Low (≤0.22 x $10^9$/L) | 46 | 30-60 | 0.02 |
| High (>0.22 x $10^9$/L) | 62 | 45-76 | |
| Sex | | | |
| Male | 51 | 37-64 | 0.84 |
| Female | 59 | 39-74 | |
| Age (years) | | | |
| <40 | 60 | 29-81 | 0.37 |
| 40-59 | 55 | 39-68 | |
| ≥60 | 49 | 26-81 | |
| Conditioning regimen | | | |
| MAC | 63 | 45-76 | 0.03 |
| RIC | 47 | 31-61 | |
| Donor source | | | |
| Related | 32 | 10-57 | 0.16 |
| Unrelated | 57 | 39-72 | |
| uCB | 60 | 41-74 | |
| BM | 57 | 39-71 | 0.11 |
| PBSC | 31 | 8-58 | |
| CB | 60 | 41-74 | |
| Disease status | | | |
| Low risk | 63 | 46-76 | 0.07 |
| High risk | 45 | 28-60 | |
| HCT-CI | | | |
| 0 | 55 | 34-71 | 0.21 |
| 1-2 | 73 | 50-87 | |
| ≥3 | 40 | 22-56 | |
| GVHD prophylaxis | | | |
| TAC | 54 | 42-65 | 0.96 |
| CSP | 51 | 16-78 | |

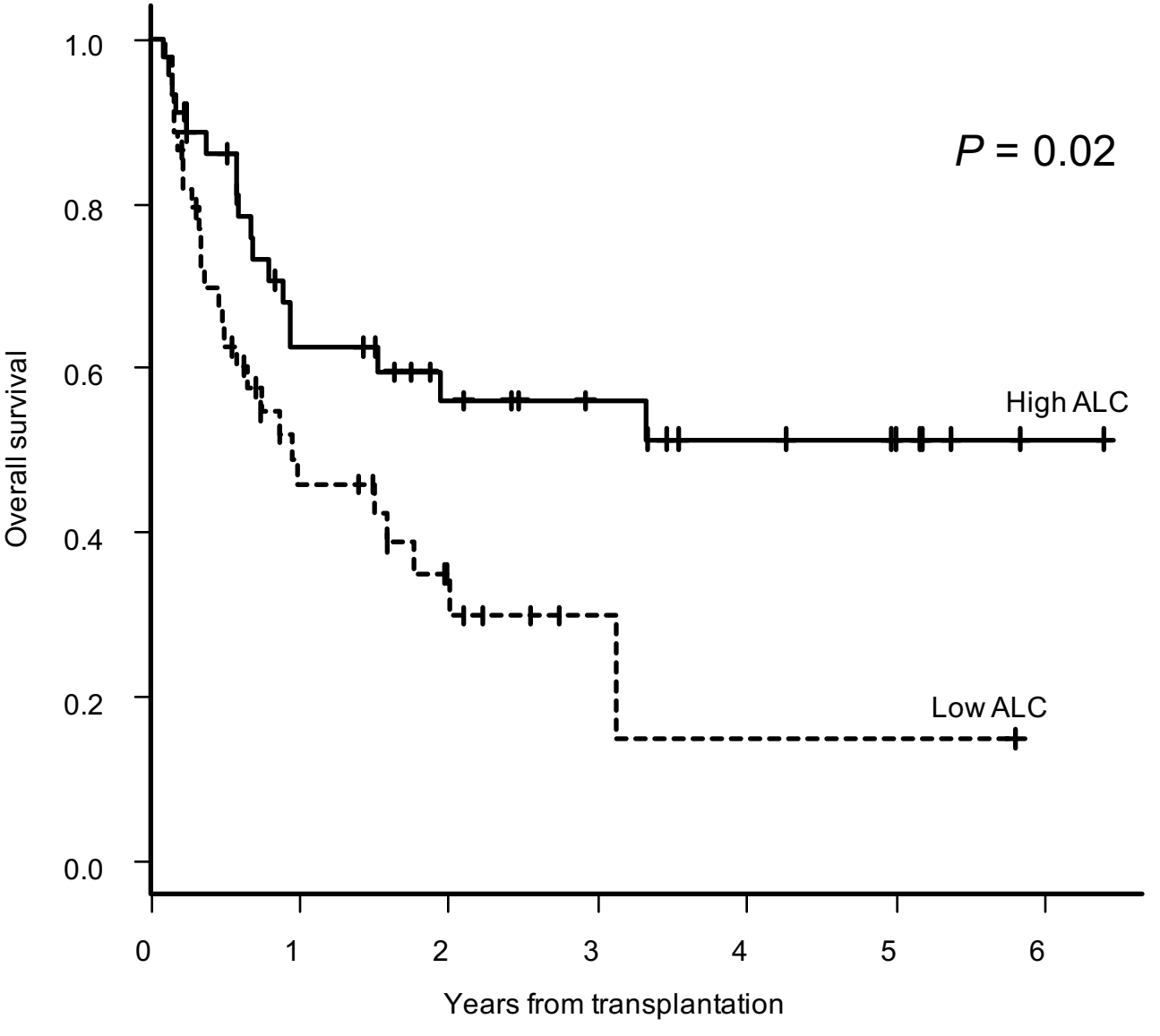
| **Variable** | **1-year outcome (%)** | **95% CI** | ***P*-value** |
|---|---|---|---|
| RR | | | |
| ALC at day 28 | | | |
| Low (≤0.22 x $10^9$/L) | 35 | 21-50 | 0.2 |
| High (>0.22 x $10^9$/L) | 29 | 16-44 | |
| Sex | | | |
| Male | 34 | 21-46 | 0.91 |
| Female | 30 | 15-47 | |
| Age (years) | | | |
| <40 | 15 | 23-50 | 0.27 |
| 40-59 | 37 | 23-50 | |
| ≥60 | 33 | 14-53 | |
| Conditioning regimen | | | |
| MAC | 21 | 10-35 | 0.02 |
| RIC | 42 | 27-56 | |
| Donor source | | | |
| Related | 38 | 13-63 | 0.74 |
| Unrelated | 36 | 20-51 | |
| uCB | 27 | 13-43 | |
| BM | 37 | 22-52 | 0.72 |
| PBSC | 32 | 9-58 | |
| CB | 27 | 13-43 | |
| Disease status | | | |
| low risk | 17 | 7-29 | <0.001 |
| high risk | 48 | 32-63 | |
| HCT-CI | | | |
| 0 | 33 | 16-52 | 0.35 |
| 1-2 | 21 | 8-40 | |
| ≥3 | 39 | 22-56 | |
| GVHD prophylaxis | | | |
| TAC | 32 | 22-43 | 0.94 |
| CSP | 37 | 7-68 | |

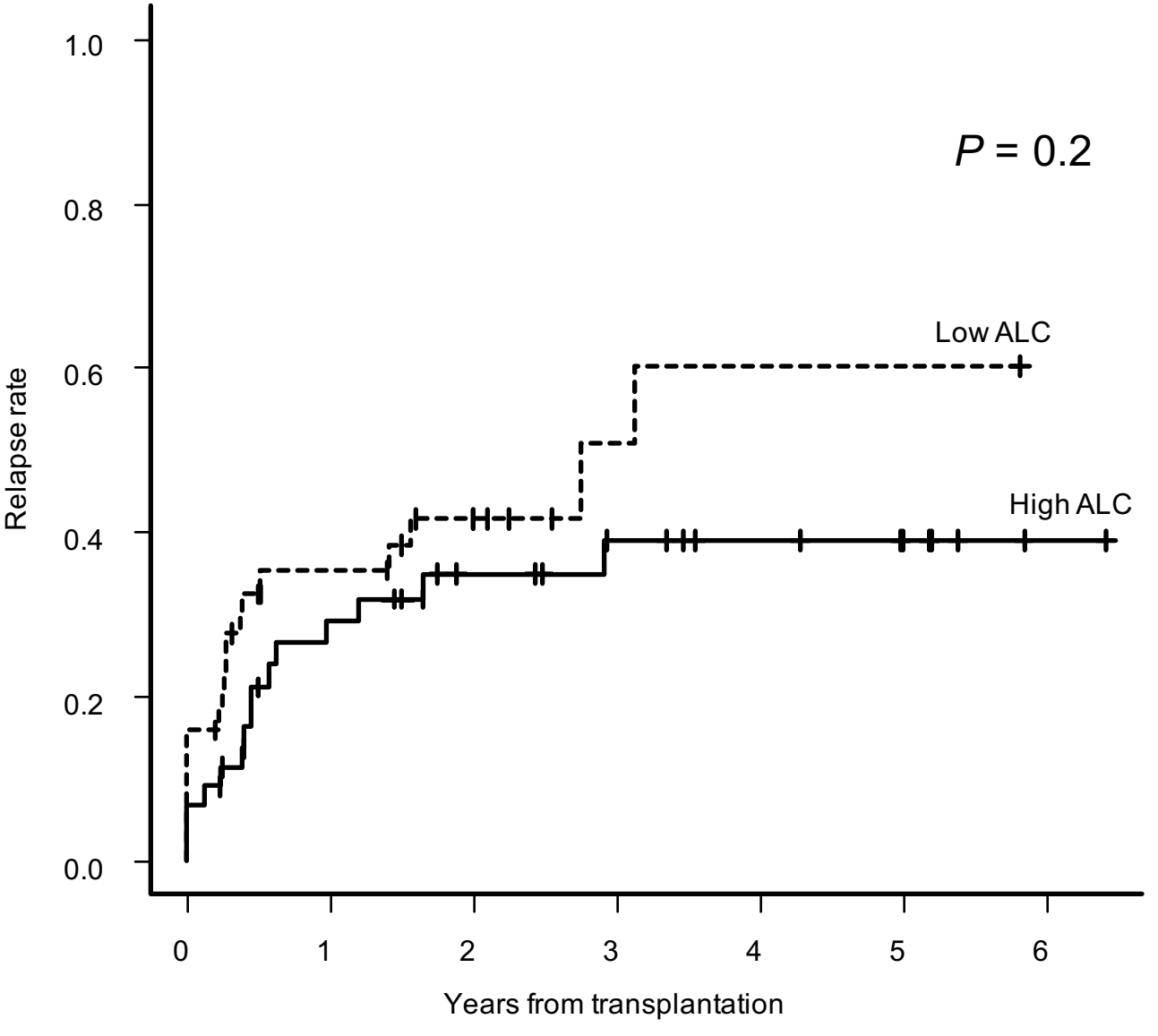
| Variable | 1-year outcome (%) | 95% CI | *P*-value |
|---|---|---|---|
| NRM | | | |
| ALC at day 28 | | | |
| Low (≤0.22 x $10^9$/L) | 23 | 11-37 | 0.08 |
| High (>0.22 x $10^9$/L) | 13 | 5-25 | |
| Sex | | | |
| Male | 16 | 7-27 | 0.61 |
| Female | 21 | 8-37 | |
| Age (years) | | | |
| <40 | 25 | 5-51 | 0.93 |
| 40-59 | 15 | 7-27 | |
| ≥60 | 19 | 5-38 | |
| Conditioning regimen | | | |
| MAC | 17 | 7-31 | 0.87 |
| RIC | 18 | 8-31 | |
| Donor source | | | |
| Related | 30 | 8-57 | 0.16 |
| Unrelated | 9 | 2-22 | |
| uCB | 21 | 9-37 | |
| BM | 9 | 2-21 | 0.08 |
| PBSC | 36 | 9-66 | |
| CB | 21 | 9-37 | |
| Disease status | | | |
| low risk | 23 | 11-37 | 0.32 |
| high risk | 12 | 4-25 | |
| HCT-CI | | | |
| 0 | 20 | 7-38 | 0.58 |
| 1-2 | 9 | 1-25 | |
| ≥3 | 22 | 9-38 | |
| GVHD prophylaxis | | | |
| TAC | 18 | 10-28 | 0.60 |
| CSP | 13 | 0-46 | |

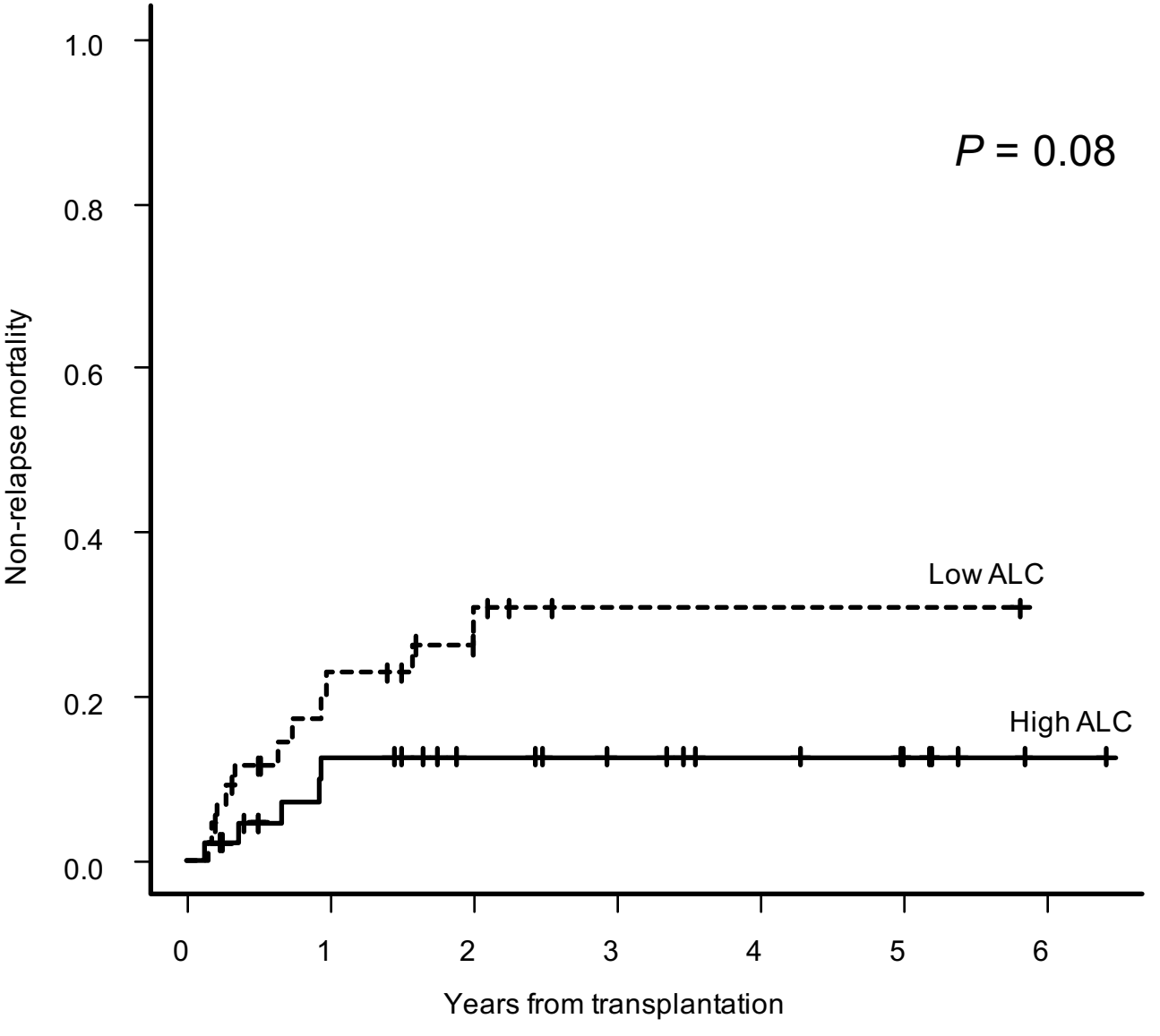
OS, overall survival; RR, relapse rate; NRM, non-relapse mortality; ALC; MAC, myeloablative conditioning; RIC, reduced intensity conditioning; absolute lymphocyte count; uCB, unrelated cord blood; BM, bone marrow; PBSC, peripheral blood stem cell; CB, cord blood; HCT-CI, hematopoietic cell transplantation-comorbidity index; GVHD, graft-versus-host disease; TAC, tacrolimus; CSP, cyclosporine

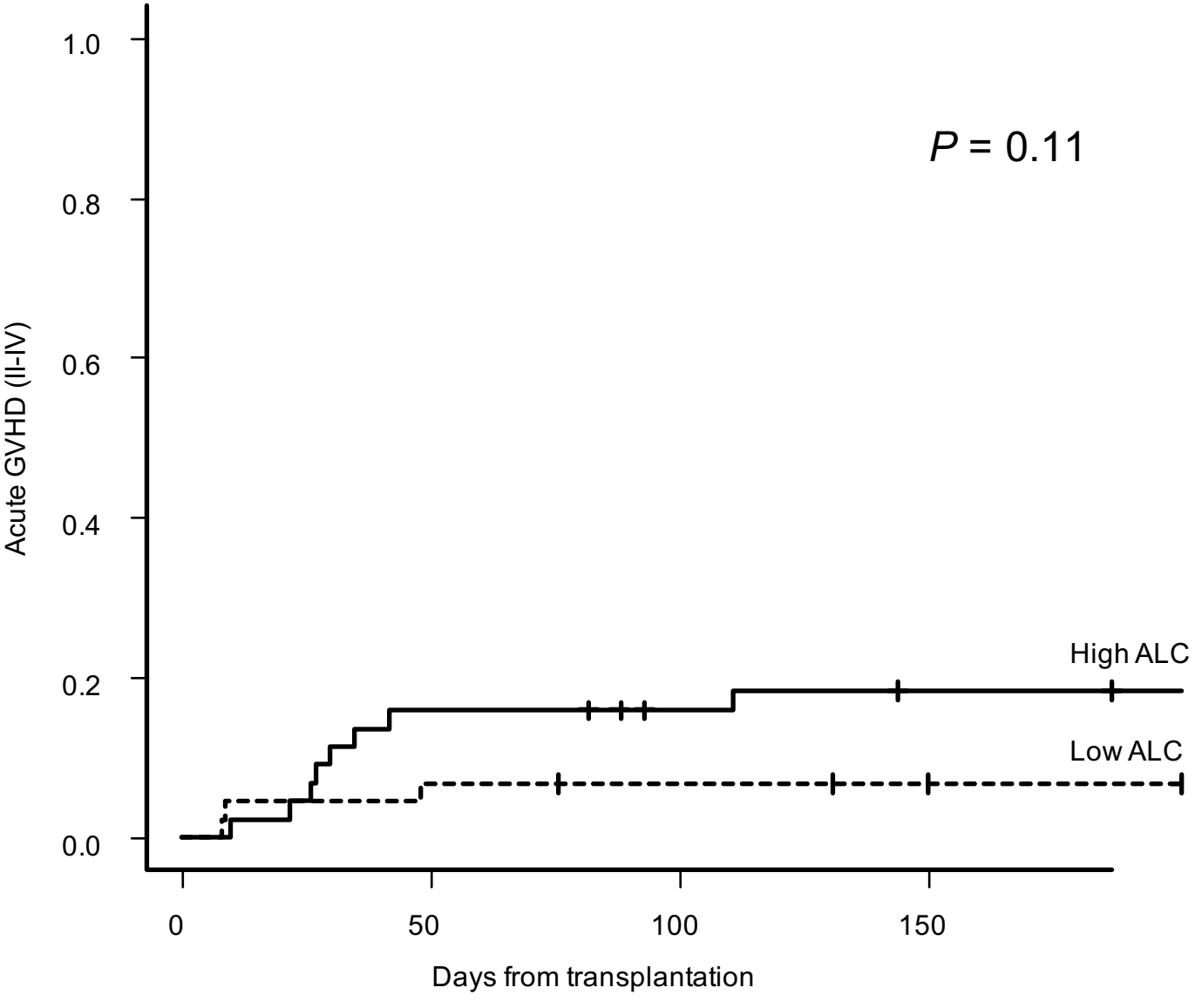
| Variable | Hazard ratio | 95% CI | *P*-value |
|---|---|---|---|
| **OS** | | | |
| ALC at day 28 | | | |
| Low (≤0.22 x $10^9$/L) | 2.43 | 1.26-4.69 | <0.01 |
| High (>0.22 x $10^9$/L) | 1 | | |
| Conditioning regimen | | | |
| MAC | 1 | | |
| RIC | 2.9 | 1.27-6.65 | 0.01 |
| Donor sources | | | |
| BM | 1 | | |
| PBSC | 4.31 | 1.25-14.8 | 0.02 |
| CB | 1.04 | 0.53-2.05 | 0.9 |
| **RR** | | | |
| Conditioning regimen | | | |
| MAC | 1 | | |
| RIC | 3.56 | 1.66-7.64 | 0.001 |
| Disease status | | | |
| Low risk | 1 | | |
| High risk | 4.33 | 2.18-8.64 | <0.001 |
| **NRM** | | | |
| ALC at day 28 | | | |
| Low (≤0.22 x $10^9$/L) | 3.02 | 1.02-8.93 | 0.05 |
| High (>0.22 x $10^9$/L) | 1 | | |
| Donor sources | | | |
| BM | 1 | | |
| PBSC | 3.77 | 1.45-9.79 | 0.007 |

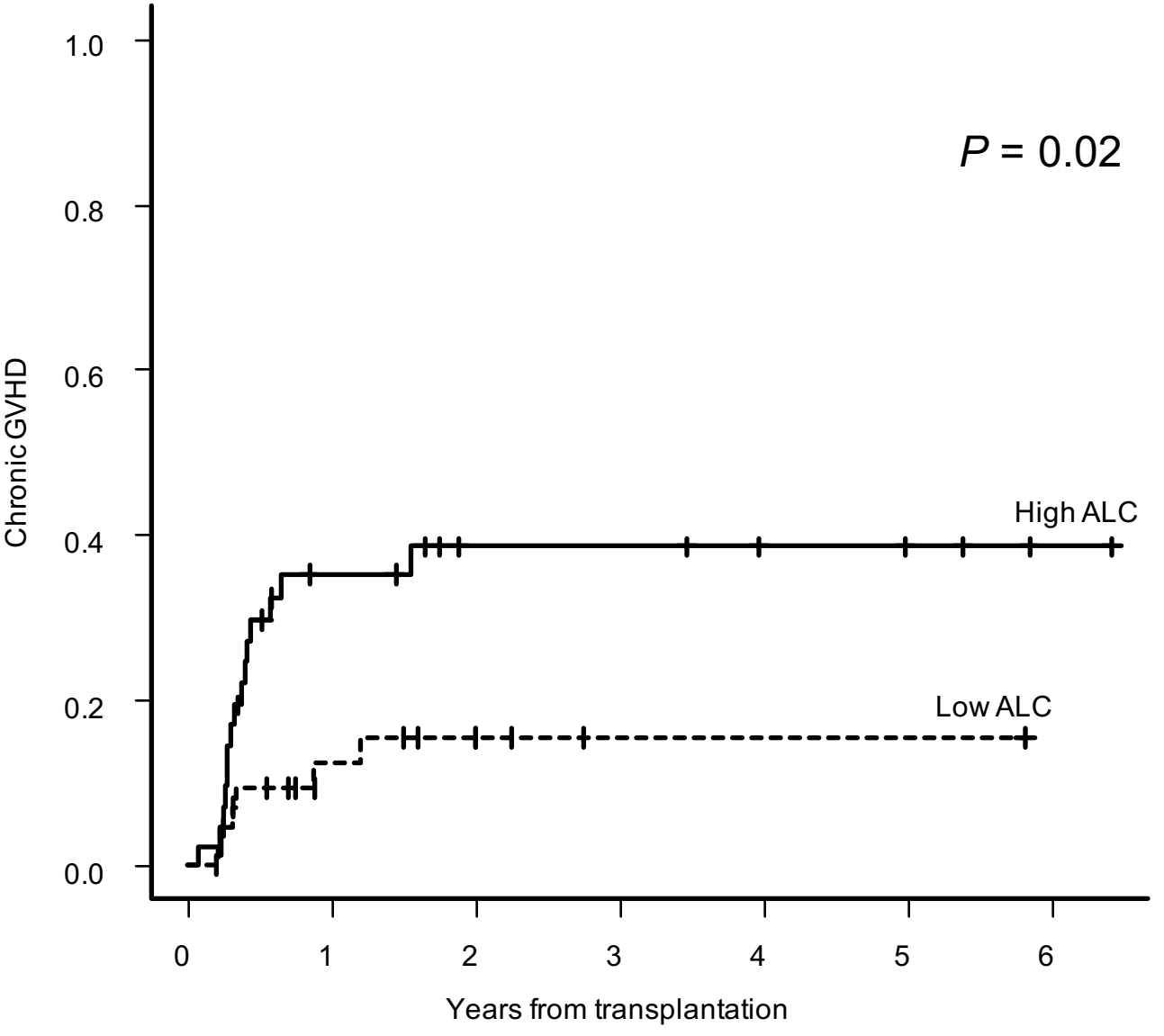
OS, overall survival; RR, relapse rate; NRM, non-relapse mortality; ALC; absolute lymphocyte count; MAC, myeloablative conditioning; RIC, reduced intensity conditioning; BM, bone marrow; PBSC, peripheral blood stem cell; CB, cord blood

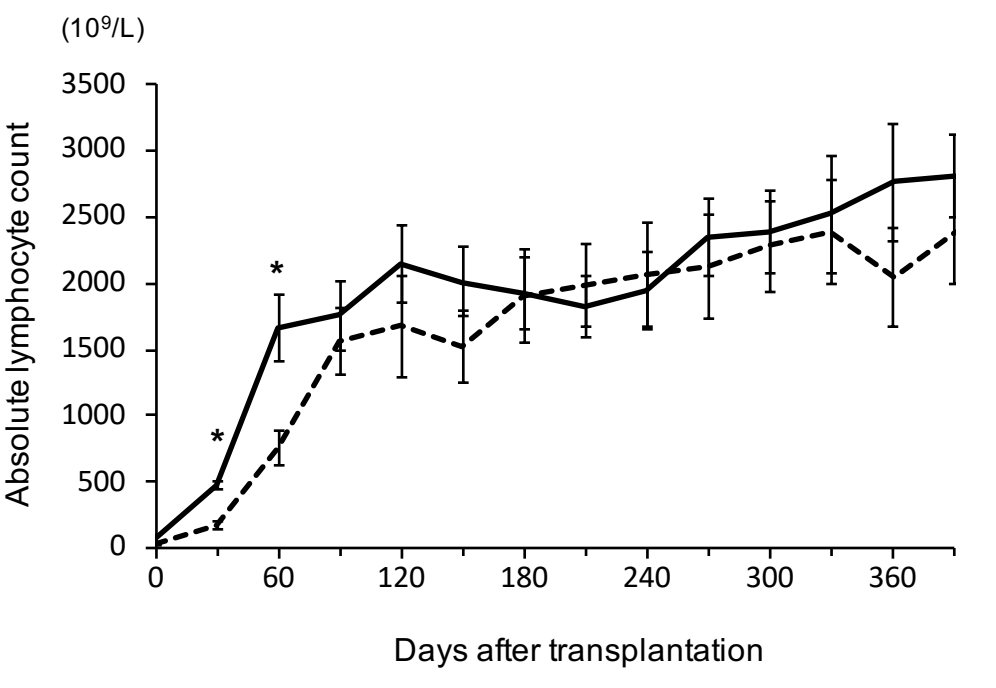

1.0
0.8
0.6
0.4
0.2
0.0
Overall survival
P = 0.02
High ALC
Low ALC
0
1
2
3
4
5
6
Years from transplantation

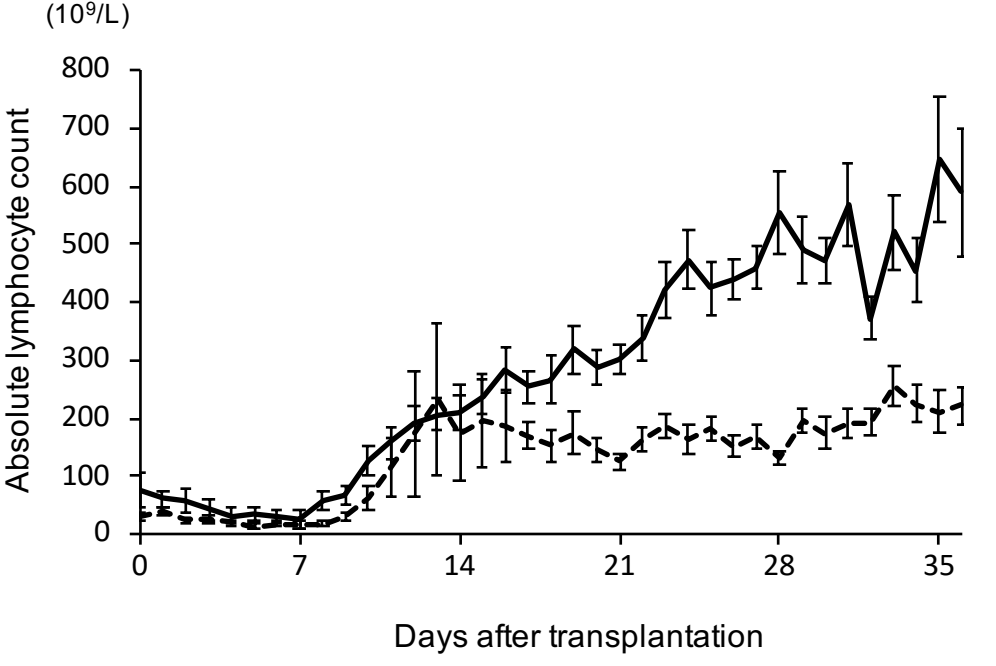

1.0
0.8
0.6
0.4
0.2
0.0
Relapse rate
P = 0.2
Low ALC
High ALC
0
1
2
3
4
5
6
Years from transplantation


1.0
0.8
0.6
0.4
0.2
0.0
Non-relapse mortality
P = 0.08
Low ALC
High ALC
0
1
2
3
4
5
6
Years from transplantation


1.0
0.8
0.6
0.4
0.2
0.0
Acute GVHD (II-IV)
P = 0.11
High ALC
Low ALC
0
50
100
150
Days from transplantation


1.0
0.8
0.6
0.4
0.2
0.0
Chronic GVHD
P = 0.02
High ALC
Low ALC
0
1
2
3
4
5
6
Years from transplantation


(10⁹/L)
3500
3000
2500
2000
1500
1000
500
0
Absolute lymphocyte count
*
*
0
60
120
180
240
300
360
Days after transplantation


(10⁹/L)
800
700
600
500
400
300
200
100
0
Absolute lymphocyte count
0
7
14
21
28
35
Days after transplantation