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Impact of Disease Status and General Condition on Changes in Physical Function Before and After Allogeneic Hematopoietic Stem Cell Transplantation

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Abstract

Purpose

Physical function frequently declines after allogeneic hematopoietic stem cell transplantation (allo-HSCT). However, the influence of disease status and general condition at transplantation on longitudinal functional changes remains unclear.

Methods

This retrospective study included 135 adult patients with hematological malignancies who underwent their first allo-HSCT and completed physical function assessments before transplantation and at discharge. Handgrip strength and 6-minute walk distance (6MWD) were evaluated. Patients were stratified according to disease status (complete remission [CR] vs. non-CR) and general condition (performance status [PS]).

Results

Both handgrip strength and 6MWD decreased significantly after transplantation in all groups. No significant differences in functional changes were observed between the CR and non-CR groups. In contrast, patients with poor PS at transplantation tended to show a greater decline in 6MWD than those with good PS. Multiple regression analysis identified PS at transplantation, age, sex, and change in hemoglobin level as significant factors associated with changes in 6MWD.

Conclusion

Pretransplant PS was associated with a greater posttransplant decline in endurance capacity, regardless of disease status. PS may serve as a practical clinical indicator for identifying patients at higher risk of physical function deterioration and for guiding early targeted rehabilitation interventions.

Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is widely performed as a potentially curative treatment for hematologic malignancies [1, 2]. Advances in transplantation techniques and supportive care have improved survival outcomes in recent years [2]. However, intensive conditioning regimens, post-transplant complications, and prolonged hospitalization remain substantial burdens that may adversely affect patients' physical function and functional reserve [3].

Declines in physical function, including muscle strength and endurance, are frequently observed after allo-HSCT [4]. Such functional impairments are associated not only with prolonged hospitalization and

delayed recovery but also with reduced post-transplant functional independence and quality of life [5–7].

Disease status and general condition at the time of transplantation are well-established determinants of major transplant-related outcomes, including overall survival, relapse, and treatment-related mortality. Previous studies have demonstrated that patients who are not in complete remission (non-CR) at transplantation and those with poor performance status (PS) experience inferior post-transplant outcomes [8–11].

Patients with non-CR disease often undergo more intensive and complex pretransplant treatments because of refractory or relapsed disease, potentially resulting in cumulative treatment-related toxicity and diminished physiological reserves. These factors may influence physical function and functional vulnerability at the time of transplantation. PS is a widely used clinical indicator reflecting activities of daily living and overall health status [12], and poor PS at transplantation has been regarded as a marker of increased physical vulnerability and frailty [13] in allo-HSCT recipients.

Although associations between disease status or PS at transplantation and survival outcomes have been extensively investigated, limited data are available regarding their impact on longitudinal changes in physical function before and after transplantation. In particular, the extent to which remission status and general condition at transplantation influence post-transplant trajectories of muscle strength and endurance remains unclear.

Therefore, this study aimed to evaluate the effects of disease status and general condition at transplantation on changes in physical function before and after allo-HSCT in patients with hematological malignancies.

Patients and Methods

Study population

The study population comprised patients aged ≥ 16 years with hematologic malignancies who received their first allo-HSCT at our institution and underwent a pre-transplant physical therapy assessment.

The exclusion criteria were musculoskeletal disorders, severe cardiac dysfunction, severe pulmonary dysfunction, and the presence of bone metastases. Patients with myelodysplastic syndrome were excluded because many were untreated prior to transplantation in routine clinical practice, and because of the retrospective nature of data collection, detailed information regarding pretransplant disease status was insufficiently documented in a substantial proportion of cases.

Between March 2015 and March 2025, 233 patients underwent their first allo-HSCT at our institution. After excluding 21 patients based on the disease criteria and 12 who did not undergo pretransplant physical function assessment, 200 patients were included for analysis.

Disease status and PS

Disease status at transplantation was categorized as CR or non-CR. General condition at transplantation was assessed using the Eastern Cooperative Oncology Group PS.

Exercise intervention

Exercise therapy was initiated approximately 2 weeks before transplantation and supervised by physical therapists. Sessions were conducted 5–7 times per week for 20–40 min per session throughout the hospitalization period.

The exercise program comprised stretching, resistance training, balance training, and walking exercises. The intensity of resistance training was set to “somewhat hard” on the Borg Scale [14]. Endurance training intensity was determined using the Karvonen method, which targets approximately 60% of the maximal workload [15].

When patients experienced symptoms such as nausea, diarrhea, fever, or fatigue, low-intensity exercise interventions, including stretching and early mobilization, were implemented.

Physical function assessment

Physical function was assessed by measuring handgrip strength as an indicator of muscle strength and the 6-minute walk distance (6MWD) as an indicator of exercise tolerance.

Handgrip strength was measured using a handheld dynamometer (TKK 5101; TAKEI, Japan). The measurements were performed twice for each hand in the standing position, and the mean of the maximum values from the left and right hands was used for the analysis.

The 6MWD was measured according to American Thoracic Society guidelines [16]. The walking test was conducted on a straight 20-m course.

Clinical variables

Clinical variables included graft-versus-host disease (GVHD), cumulative steroid dose (mg/kg), number of febrile days (≥ 38°C), serum albumin, total protein, and hemoglobin.

The cumulative steroid dose was calculated as the prednisolone-equivalent dose, using the following conversion factors: prednisolone = 1.0, methylprednisolone = 1.25, and hydrocortisone = 0.25.

Acute GVHD was evaluated and graded according to established guidelines [17].

Adherence to exercise therapy

Adherence to exercise therapy was calculated as the proportion of scheduled exercise days on which patients completed at least 20 min of exercise therapy.

Timing of assessments

Physical function assessments were performed approximately 2 weeks before transplantation and at the time of hospital discharge.

Disease status and PS were evaluated at the time of transplantation. Laboratory data were obtained at the same time points as the physical function assessments.

Data were retrospectively extracted from electronic medical records and the Transplant Registry Unified Management Program, which is a nationwide registry database for hematopoietic cell transplantation and cellular therapy in Japan.

Patients were classified into two groups according to disease status (CR vs. non-CR) and PS (0 vs. ≥1), and changes in physical function before and after transplantation were compared between groups.

Statistical analysis

Normality of data distribution was assessed using the Kolmogorov–Smirnov test.

Differences in longitudinal changes in physical function according to disease status and general condition at transplantation were examined using repeated-measures analysis of variance, with patients stratified into CR vs. non-CR and PS = 0 vs. PS ≥ 1 groups.

Multiple regression analysis was performed to identify factors associated with changes in physical function. The independent variables included clinical variables, length of hospital stay, and adherence to exercise therapy. Variables with a p-value < 0.15 in univariate analyses were selected as candidates for inclusion in the multivariate models.

All statistical analyses were performed using EZR [18], and $p < 0.05$ was considered statistically significant.

Ethics

This study was approved by the Institutional Review Board of Imamura General Hospital (approval no. : NCR25-27) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients at the initiation of physical therapy. In addition, study information was made publicly available online, and patients were given the opportunity to opt out.

Results

Study population

Of the 200 enrolled patients, 11 who did not undergo post-transplant physical function assessment and 54 who died during transplant hospitalization were excluded. Consequently, 135 patients were included in the final analysis (Fig. 1).

The patient characteristics are summarized in Table 1. The study population consisted of 77 men and 58 women, with a median age of 57 years. Underlying diseases were acute myeloid leukemia in 55 patients, adult T-cell leukemia/lymphoma in 44, acute lymphoblastic leukemia in 20, malignant lymphoma in 7, and other hematologic malignancies in 9.

In comparisons according to disease status and general condition, the proportion of patients with PS ≥ 1 was higher in the non-CR group, and the proportion of non-CR patients was higher in the PS ≥ 1 group. The cumulative steroid dose was significantly higher in the PS = 0 group than in the PS ≥ 1 group (p = 0.034). Failure to undergo pre-transplant physical function assessment tended to be more frequent in the non-CR group (p = 0.056) and was significantly more frequent in the PS ≥ 1 group (p < 0.001). Failure to undergo post-transplant assessment was significantly more frequent in the non-CR group (p = 0.020), whereas no significant difference was observed according to PS (p = 0.610). In addition, dropout due to in-hospital death after transplantation was significantly more frequent in the non-CR group and the PS ≥ 1 group (detailed data not shown).

Physical function tests

Changes in physical function and clinical variables before and after allo-HSCT according to disease status

In the CR group, both handgrip strength (− 13.5%, p < 0.001) and 6MWD (− 5.7%, p = 0.002) declined significantly after transplantation. Similarly, in the non-CR group, significant declines were observed in handgrip strength (− 12.3%, p < 0.001) and 6MWD (− 7.3%, p < 0.001) (Table 2).

No significant differences in rates of change in physical function were observed between the CR and non-CR groups, and no significant interaction between disease status and time was found for handgrip strength (p = 0.555) or 6MWD (p = 0.666) (Table 2).

Changes in physical function before and after allo-HSCT according to PS

In the PS = 0 group, handgrip strength (− 13.0%, p < 0.001) and 6MWD (− 5.5%, p < 0.001) declined significantly after transplantation. In the PS ≥ 1 group, significant declines were likewise observed in handgrip strength (− 12.3%, p < 0.001) and 6MWD (− 14.7%, p < 0.001) (Table 2).

The decline in the 6MWD after transplantation tended to be greater in the PS ≥ 1 group than in the PS = 0 group (p = 0.062) (Table 2).

Multiple regression analysis of factors associated with changes in physical function

For changes in handgrip strength, graft source (B = 4.109, $p = 0.012$) and length of hospital stay (B = − 0.200, $p < 0.001$) were identified as significant associated factors (adjusted $R^2 = 0.209$).

In contrast, changes in 6MWD were significantly associated with PS at transplantation (B = − 7.475, $p = 0.039$), percentage change in hemoglobin (B = 0.141, $p = 0.023$), age (B = − 0.194, $p = 0.002$), and female sex (B = − 8.118, $p = 0.038$) (adjusted $R^2 = 0.220$) (Table 3).

Discussion

In this study, we investigated the effects of disease status and general condition at transplantation on changes in physical function before and after allo-HSCT. The results demonstrated no significant differences in changes in handgrip strength or 6MWD according to disease status at transplantation. In contrast, patients with a poor PS at transplantation tended to experience a greater decline in 6MWD after transplantation, suggesting that general condition at transplantation may be more closely associated with post-transplant functional changes than disease status.

Although patients with non-CR disease are generally presumed to have poorer general condition at transplantation because of residual disease activity or treatment resistance, pre-transplant handgrip strength and 6MWD were comparable between the CR and non-CR groups. This may partly explain the absence of differences in the rates of post-transplant functional decline between the two groups. In addition, only patients who were able to undergo pre-transplant physical function assessments were included. Failure to undergo pretransplant assessment tended to be more frequent in the non-CR group, suggesting possible exclusion of non-CR patients with poorer physical function or general condition. This potential selection bias may have contributed to the homogenization of baseline physical function between the groups, reducing the likelihood of detecting differences related to disease status.

Adherence to exercise therapy during hospitalization did not differ significantly between groups, although it tended to be higher in the non-CR group. Previous studies suggest that patients with lower baseline physical function may derive greater benefit from exercise interventions [19], which could partially attenuate the post-transplant functional decline in non-CR patients.

PS is a comprehensive clinical indicator reflecting activities of daily living and the degree of activity limitation [12], and decreased PS has been associated with impaired physical function in patients with cancer [20]. Poor PS at transplantation may represent underlying physiological vulnerability, including reduced activity levels, sarcopenia, and decreased cardiopulmonary reserve, which could influence subsequent changes in physical function. In addition, transplant-related factors, such as conditioning-related toxicity, systemic inflammation, prolonged hospitalization, and physical inactivity, may further exacerbate deconditioning in patients with poor baseline PS.

Fiala et al. reported that patients with PS ≥ 1 at transplantation experienced worse physical quality of life after transplantation [21], consistent with our findings. In our multiple regression analysis, PS at transplantation was independently associated with a decline in 6MWD. Patients with poor PS are likely to have reduced activity levels even before transplantation and may be more prone to prolonged bed rest and decreased spontaneous physical activity during transplant hospitalization. Consequently, declines in cardiopulmonary function and overall endurance capacity may become more pronounced, manifesting as greater reductions in the 6MWD.

In the present cohort, no significant differences were observed between the PS ≥ 1 and PS = 0 groups with respect to the incidence of posttransplant GVHD, adherence to exercise therapy, or length of hospital stay. However, despite a significantly higher cumulative steroid dose in the PS = 0 group, the decline in the 6MWD was greater in the PS ≥ 1 group. Steroid exposure is reportedly associated with muscle weakness and physical dysfunction in allo-HSCT recipients [22, 23]. Moreover, previous studies have shown that cumulative steroid dose is associated with a decline in 6MWD in patients receiving high-dose steroids for acute GVHD [24]. Nevertheless, the greater decline in the 6MWD observed in the PS ≥ 1 group despite lower steroid exposure suggests that PS at transplantation may independently influence post-transplant endurance decline. Importantly, our findings suggest that readily available clinical information, such as PS, may provide additional insights into post-transplant functional vulnerability beyond conventional disease-related factors at transplantation.

This study has several limitations. First, this was a single-center retrospective study, and patients with myelodysplastic syndromes were excluded; therefore, caution is required when generalizing the findings. Second, inclusion was limited to patients who completed pre-transplant functional assessments. Because patients who dropped out of the initial evaluation tended to have a poorer PS, the actual impact of poor PS on functional decline may have been underestimated. However, comparing the longitudinal changes between the pre- and post-transplant phases and restricting the analysis to patients with complete baseline data was a methodological necessity. Third, although treatment-related factors were considered, posttransplant physical activity levels and voluntary activity were not assessed. These factors may have influenced the changes in the 6MWD and may have partially contributed to the observed results.

In conclusion, this study suggests that PS at transplantation, as an indicator of general condition, may be associated with a post-transplant decline in endurance capacity. As a readily assessable clinical measure, PS may help identify patients at higher risk of functional decline, regardless of disease status. Strategies aimed at maintaining physical activity before transplantation and promoting early rehabilitation after transplantation may be particularly beneficial for patients with poor pretransplant PS.

Declarations

Ethics approval

This study was approved by the Institutional Review Board of Imamura General Hospital (approval no.: NCR25-27) and conducted in accordance with the Declaration of Helsinki.

Consent to participate

Written informed consent was obtained from all patients at the initiation of physical therapy. In addition, study information was made publicly available online, and patients were given the opportunity to opt out.

Clinical trial number

Not applicable.

Consent for publication

Not applicable.

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Author contributions

TT conceived and designed the study, collected the clinical data, performed the data analysis, and drafted the manuscript.

AU, YI, and KD contributed to the study conception and design; provided academic and clinical supervision, including patient management and rehabilitation oversight; and critically revised the manuscript.

NN, TM, MT, JO, SF, and SN contributed to patient management, clinical data collection, and manuscript review.

SS contributed to clinical data collection and critically revised the manuscript.

All authors read and approved the final manuscript.

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Data availability

The datasets generated and/or analyzed during the current study are not publicly available because of privacy and ethical restrictions but are available from the corresponding author upon reasonable request.

Competing interests

NN reports consulting fees and honoraria for lectures from Kyowa Kirin, and honoraria for lectures from Bristol Myers Squibb, Daiichi Sankyo, Novartis, Meiji Seika Pharma, and Takeda. YI reports honoraria for lectures from AstraZeneca, Genmab, AbbVie, Janssen, Amgen, MSD, Bristol Myers Squibb, Nippon Shinyaku, Chugai Pharmaceutical, and Otsuka Pharmaceutical.

The other authors declare no competing interests.

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Tables

Tables 1 to 3 are available in the Supplementary Files section.

Figures

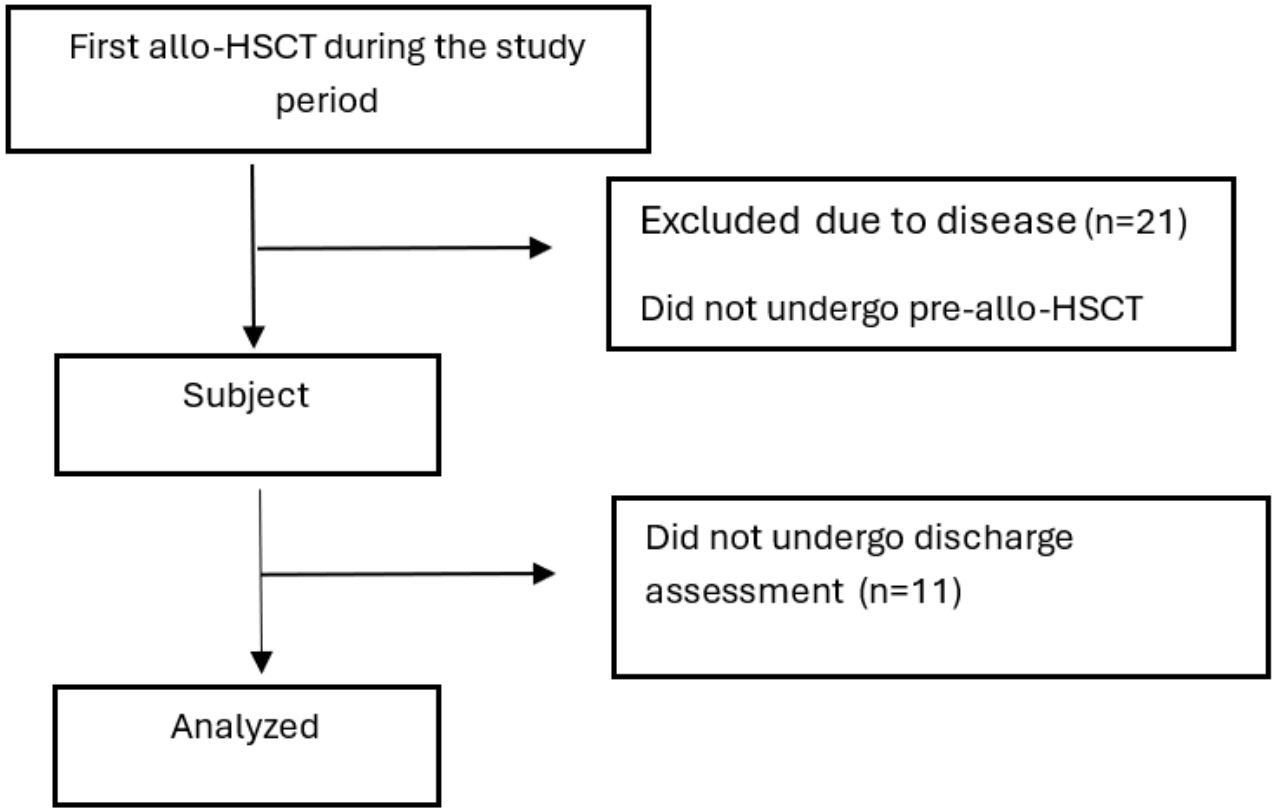


Figure 1

Study flow diagram

Allo-HSCT; allogeneic hematopoietic stem cell transplantation

Supplementary Files

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- Table1.xlsx
- Table2.xlsx
- Table3.xlsx