April th, 2021

Fred Ashbury
Editor-in-Chief
Supportive Care in Cancer

Dear Dr. Ashbury:

I wish to re-submit an original article for publication in *Supportive Care in Cancer*, titled "*Analysis of the factors associated with physical functioning domain of QLQ-C30 in allogeneic hematopoietic stem cell transplantation patients at discharge: A cross-sectional study*." The paper was coauthored by Ryota Hamada, Tadakazu Kondo, Junsuke Miyasaka, Michiko Yoshida, Honami Yonezawa, Yasuyuki Arai, Junya Kanda, Manabu Nankaku, Ryosuke Ikeguchi, Akifumi Takaori-Kondo, and Shuichi Matsuda.

This study to identified independent factors related to patient-reported physical functioning (PF) scores at discharge of patients who underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT). We found that higher exercise tolerance and lower fatigue of the patients who underwent allo-HSCT were independently associated with better patient-reported PF scores at discharge. We believe that our study makes a significant contribution to the literature because it highlights the objective exercise tolerance explains "patient-reported physical functioning score" independently with other factors in the acute phase after allo-HSCT.

We carefully considered comments by the reviewer and revised manuscript. Further, we believe that this paper will be of interest to the readership of *Supportive Care in Cancer* because our findings can be generalized other forms of cancer therapy.

This manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal. All study participants provided informed consent, and the study design was approved by the appropriate ethics review board. We have read and understood your journal's policies, and we believe that neither the manuscript nor the study violates any of these. There are no conflicts of interest to declare.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

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Title page

Title

Analysis of factors associated with patient-reported physical functioning scores at discharge of allogeneic hematopoietic stem cell transplantation patients: a cross-sectional study

Running title:

Patient-reported physical functioning score of allo-HSCT patients

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Abstract

Purpose: The purpose of this study was to clarify the independent factors related to patient-reported physical functioning (PF) scores at discharge of patients who underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT).

Methods: A total of 103 patients who underwent allo-HSCT were included in this cross-sectional study. As a screening method, a single regression analysis was conducted with the PF domain in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 at discharge as the dependent variable, and body mass index, adverse events related to HSCT, and objective physical functions as independent variables. Multiple regression analysis was performed with PF as the dependent variable, and variables that passed the screening by single regression analysis and confounders as independent variables.

Results: The mean PF score at discharge of the patients was 76.5 (standard deviation: 15.2). Based on the results of screening by the single regression analysis, length of stay, infections (+ / -), acute graft-versus-host disease grade, brief fatigue inventory score (BFI), knee extensor strength, and 6-minute walk distance (6MWD) were included in the multiple regression analysis. BFI ($B = -11.94$, $p < 0.001$), and 6MWD (per 10m) ($B = 0.56$, $p = 0.001$) were extracted as significant independent variables governing the PF at discharge in the multiple regression model (adjusted $R^2 = 0.59$).

Conclusion: Higher exercise tolerance and lower fatigue in patients who underwent

allo-HSCT were associated independently with patient-reported better PF scores at discharge.

(238 words)

Keywords

1. Allogeneic hematopoietic stem cell transplantation (allo-HSCT)
2. Quality of life (QOL)
3. The European organization for research and treatment of cancer quality of life questionnaire core (EORTC QLQ-C30)
4. Physical functioning domain
5. Exercise tolerance
6. Acute graft-versus-host disease (acute-GVHD)

Introduction

Quality of life (QOL) of the allogeneic hematopoietic stem cell transplantation (allo-HSCT) survivors have become progressively important due to the improved mortality rates of the patients [1-3]. Unfortunately, it is well-known that allo-HSCT noticeably reduces the patient's physical, psychological, and social QOL; and then, recovery takes a long time [4-6]. In recent years, the relationship between QOL and the physical function or the effects of rehabilitation on patients who have undergone allo-HSCT has been widely reported [5,7-14]. However, the concept of global health includes not only physical functions but also psychological, social, economic, and spiritual factors [15,16]. As a member of the medical care team, it is necessary to clarify the factors related to the aspects, i.e., subdomains of the QOL questionnaire, that are most relevant to each profession, so that interventions can be provided based on the most relevant aspects of the patient’s profession.

A review that drew a large sample from a number of published studies showed that the physical functioning (PF) scores of the disease-specific measure, namely, the European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire core (QLQ-C) 30 declined in the acute phase after allo-HSCT and took 7 to 12 months to improve to pre-treatment levels [5]. PF, a subdomain of QLQ-C30, would allow us to assess whether the interventions provided by the rehabilitation staff are genuinely helpful to the recipients of allo-HSCT. Recently, several studies have been published focusing on the association between objectively measured physical

function outcomes that can be altered by rehabilitation interventions (e.g., skeletal muscle strength, exercise tolerance) and patient-reported PF [10,17,18]. Morishita et al. [10] assessed objective and patient-reported PF in patients before HSCT and reported that exercise tolerance, fatigue, platelets, duration of disease, and sex were independently associated with patient-reported PF. Pidala et al. [17] reported an association between patient-reported PF and exercise tolerance in chronic graft-versus-host disease (GVHD)-affected HSCT recipients. Even in the early stages after HSCT, a significant correlation between patient-reported PF and knee extension strength and exercise tolerance, as reported by patients, has been reported [18]. However, the 36-item Short-Form Health Survey (SF-36) [19] , which asks about QOL in the last month, used in these studies may not be suitable for assessing the acute phase after allo-HSCT, where conditions can change within a short period of time. Although SF-36 is a comprehensive measure, it is not a disease-specific measure, and some questions are too advanced for patients who underwent allo-HSCT. Furthermore, based on our literature search, there are no reports validating patient-reported and objectively measured PF at discharge after HSCT, adjusted for the effects of other confounding factors associated with the disease-specific PF domain at discharge after HSCT. Indeed, the implementation of patient-reported QOL assessment in the acute phase after HSCT appears to have stalled, as concerns were raised in a recent review [20]. If these confounding factors can be identified, they could provide clues for rehabilitation interventions during the hospitalization period.

The aim of this study was to clarify the independent factors related to patient-reported physical functioning scores at discharge of patients who underwent allo-

HSCT.

Materials & Methods

Study design

This was a cross-sectional study conducted at a single institution.

Subjects

A total of 195 patients had undergone allo-HSCT at the Department of Hematology and Oncology of the Kyoto University Hospital between June 2011 and February 2020. Patients who died while hospitalized and missing evaluation cases were excluded. The participants of the study were 103 patients (median age: 47 years old, range: 17-70 years, mean body mass index [BMI]: 19.6 ± 2.8 kg/m2). The research protocols and procedures were approved by the ethics committee of Kyoto University Graduate School and Faculty of Medicine (Registration number: R0715), and written informed consent was obtained from each subject.

Data collection and measuring methods

~~The order of the measurements was random.~~

The QLQ-C30 for the Japanese [21] (version 3.0) was used with permission from the EORTC. The PF score is one of the domains of the QLQ-C30, which consists of 5 questions and indicates a score between 0 and 100 [22]. The PF scores were collected at just before the start of the conditioning regimens of allo-HSCT (pre-PF) and at discharge (post-PF).

Patient characteristics (sex, age, BMI) and treatment-related factors (length of stay [LOS] at the hospital, diagnosis, pre-conditioning regimens, performance status at pre-conditioning regimens, disease status at allo-HSCT, conditioning regimens, stem cell sources, total dose of total-body irradiation, hematopoietic cell transplantation-comorbidity index [HCT-CI], thrombotic microangiopathy [TMA], hepatic veno-occlusive disease or sinusoidal obstruction syndrome [VOD/SOS], infections that required interventions, chemotherapy side effects required intervention, and acute-GVHD grade) were collected from the database of the electronic medical chart. In addition, physical performance scores (brief fatigue inventory [BFI], knee extensor strength, and 6-minute walk distance [6MWD] for assessing exercise tolerance) were measured at discharge from the hospital.

BFI is a self-administered questionnaire consisting of 9 items (each with scores ranging from 0-10) for assessing fatigue in cancer patients [23], and its validity has been reported for the Japanese version used in this study [24]. The mean scores of all questions were calculated according to a previous study [24] (i.e., 1-3: mild, 4-6:

moderate, and 7-10: severe) and converted into dummy variables: mild: 1, moderate: 2, and severe: 3, respectively.

Knee extensor strength was evaluated during maximum voluntary isometric contraction for 3 seconds using an IsoForce GT-330 (OG Giken Co. Ltd., Okayama, Japan), according to the method described in a previous studies [25,26]. The measurement of knee extensor strength was conducted twice in the seated position (measure side knee joint flexion angle: 70°); the maximum value was used for analysis. The center of the force sensor was in contact with the lower legs at the upper 50 mm of the bilateral malleoli. The torque was calculated by multiplying the strength by the lever arm (distance between the position of the force sensor and the lateral epicondyle of the femur). Knee extensor strengths were expressed as the mean of the right and left side torque/body weight (Nm/kg).

6MWD test was conducted as per the protocol recommended by the American Thoracic Society [27]. Patients were requested to walk back and forth along a straight 30 m flat course indoors at the maximum effort for 6 minutes, and the walking distance was recorded.

The order of the above measurements was random.

Rehabilitation protocols and assessment methods

All patients received exercise therapy under the supervision of a registered physical therapist (PT) 5 times/week for 20-40 minutes from before the start of

conditioning regimens of HSCT until discharge from the hospital. The PT intervened by setting the goal of discharging the patient from the hospital after being able to perform physical functions independently, while constantly assessing the patient's activities of daily living (ADL). The ADL practice (standing, transfer, etc.), stretches, skeletal muscle strength training involving principally the lower extremity (half squat, heel raise, etc.), walking, and bicycle ergometry were included in the protocol. Rehabilitation was continued inside the ward (International Organization for Standardization 14644-1 Class 7) even during the aseptic management periods (neutrophil count < 500/μL).

Statistical analysis

The normality of each continuous data was assessed using the Shapiro–Wilk test. Simple linear regression analyses were used to calculate the unadjusted determination coefficient (R2), and the p value was used to explore the relationship between post-PF (dependent variable) and each independent variable. Then, multiple linear regression analysis was performed using variables with $p < 0.2$ in simple linear regression analyses and confounding factors (sex, age, and pre-PF). All statistical analyses were conducted using SPSS for Windows Version 17.0 (SPSS Inc., Chicago, IL), and $p < 0.05$ was considered to be statistically significant.

Results

Physical functioning scores during pre-conditioning regimens and at discharge

The mean ± SD of PF scores were 85.8 ± 12.9 and 76.5 ± 15.2, during pre-conditioning regimens (pre-PF) and at discharge (post-PF), respectively (Figure 1). There were 25 (24.3%) patients whose scores decreased beyond the previously reported clinically significant difference: 15 points on the QLQ-C30 [5].

Descriptive statistics of patient characteristics and treatment classifications (Table 1)

The ratio of sex (male/female), diagnosis (leukemia/myelodysplastic syndrome/lymphoma/others), performance status at pre-conditioning regimens (0-1/2-4), disease status at allo-HSCT (complete remission/non-complete remission), conditioning regimen (myeloablative/non-myeloablative), total dose of total-body irradiation (<4 Gy/4-8 Gy/8 Gy<), stem cell source (bone marrow/cord blood/peripheral blood), HCT-CI score (0-1/2-7), TMA (-/+), VOD/SOS (-/+), infections that required intervention (-/+), infection category, chemotherapy side effects that required intervention (-/+), chemotherapy side effects category, acute-GVHD grade (non-GVHD/I/II/III/IV), and BFI (mild/moderate/severe), the median (range) of age, or the mean ± SD (95% confidence interval [CI]) of BMI, LOS, knee extensor strength, 6MWD, pre-PF score, and post-PF score are shown in Table 1.

Simple regression model determining physical functioning score at discharge (Table

2)

The results of the simple regression analysis with the post-PF score as the dependent variable, and BMI, LOS, infection, complication, acute-GVHD, BFI, knee extensor strength, and 6MWD as independent variables are presented in Table 2. LOS, infections that required intervention, acute-GVHD grade, BFI, and 6MWD (Figure 2) were indicated $p < 0.2$.

Multiple regression model determining physical functioning score at discharge (Table 3)

The multicollinearities were confirmed by observing a correlation matrix table beforehand for the submitted independent or confounding variables, but there were no variables that resulted in $r > 0.9$. BFI ($B = -12.11$, $p < 0.001$) and 6MWD (per 10m) ($B = 0.56$, $p = 0.001$) were extracted as significant independent variables governing the post-PF score in the confounding adjusted multiple regression model ($R = 0.77$, adjusted $R2 = 0.59$, Durbin-Watson ratio = 1.76).

Discussion

The most important finding of this study was that exercise tolerance (6MWD) was significantly associated with PF score in the QLQ-C30 independently of other

278 factors at discharge after allo-HSCT (p =0.001). The result of fatigue in the acute phase
279 after HSCT was significantly associated with a PF score ($p < 0.001$) similar to that
280 from reports investigating long-term QOL after HSCT [28,29]. In contrast to previous
281 studies reporting that chronic-GVHD is associated with long-term PF [8,12,30], acute-
282 GVHD was not significantly independently associated with a PF score in the acute
283 phase ($p = 0.084$). Although it is difficult to substantially improve patient-reported PF
284 scores by improving exercise tolerance and reducing fatigue in patients after allo-
285 HSCT, rehabilitation staff may at least be able to contribute to raising the patient-
286 reported PF scores by adopting these measures.
287
288 ***Relationship between objective and patient-reported physical functioning***
289
290 Evidence that objective exercise tolerance (6MWD) is associated with
291 changes in patient-reported PF independently of other factors has already been
292 reported for patients scheduled for allo-HSCT [10] and from the time of discharge to
293 1 year after allo-HSCT [31]. The present study, for the first time, revealed that
294 objective exercise tolerance was significantly associated with patient-reported PF
295 independently of other factors, even in the acute phase after allo-HSCT. However, no
296 significant association was found between knee extensor strength, which is
297 representative of whole-body spontaneous muscle strength, and post-PF, in contrast to
298 a previous study [18]. Morishita et al. [18] reported a significant monocorrelation
299 between PF (subdomain of SF-36) and knee extensor strength (male/female: 0.54-
300 0.56/0.34-0.36) and between PF and 6MWD (male/female: 0.51/0. 60), in the early
301 phase after HSCT. In the present study, a simple regression model explaining post-PF

of EORTC-C30 also showed an association comparable to that reported by them with knee extensor muscle strength (R2 = 0.21 [R =0.45]) and 6MWD (R2 = 0. 38 [R = 0.61]) (Table 2). However, knee extensor strength adjusted by other factors in the multiple regression model was not considered a significant factor defining post-PF. The results suggest that the physical function demanded to the patients who underwent allo-HSCT is closely related to a complex function represented by the 6MWD, rather than instantaneous muscle strength. Exercise tolerance is regulated by systemic conditions such as blood status, central functions (pulmonary and cardiovascular), and peripheral functions (neuromuscular and muscle metabolism) [27]. Recently, associations between reduced skeletal muscle oxygenation capacity and exercise capacity [32] and between reduced skeletal muscle oxygenation capacity and fatigue [33] a after allo-HSCT have been reported. In addition to ergometry and walking, interventions to improve the oxidative metabolism of local skeletal muscles in the lower extremities to improve 6MWD in patients who underwent allo-HSCT should be urgently developed.

Stretton et al. [34] reported that objective PF and patient-reported QOL assessed different concepts in the frail elderly and that each was related to self-efficacy. Therefore, we hypothesize that self-efficacy is potentially involved in exercise tolerance and PF score. Future studies should investigate the real-life self-efficacy of patients who underwent allo-HSCT to fill in the gaps between health care providers' and patients' perceptions of physical function.

Other factors related to patient-reported physical functioning

Previous studies have suggested that fatigue after allo-HSCT is associated with long-term global QOL [28,29]. The present study revealed that similar factors were associated with only one subdomain of QLQ-C30 in the acute phase after allo-HSCT. Fatigue was assessed immediately before hospital discharge and was not associated with the adverse effects of pre-conditioning regimens (R = -0.07: no data were shown in the Results section). Fatigue in patients after allo-HSCT is an important adverse outcome that can be improved by exercise therapy during the hospitalization period [35]. In the present study, all patients were provided with physiotherapist-supervised exercise therapy. The same is true for other factors, but the effect of exercise therapy interventions would have altered the influence of independent factors on PF at discharge.

Although we defer to other literature for a specialized discourse on the treatment of GVHD, the importance of GVHD in defining the life prognosis of transplant patients [36] and global QOL [12,30] is well-known. In our recently presented data [37], at discharge, differences in the severity of acute-GVHD were not associated with objective exercise tolerance in patients who underwent allo-HSCT. Similarly, the present study showed no significant association between acute-GVHD grades and patient-reported PF. These results indicate that the relationship between GVHD and patient-reported PF may be fluid depending on the time after HSCT, suggesting the need for medical intervention and / or care appropriate for each treatment stage.

In the present study, 24.3 % of patients were observed to have reduced PF over the clinically significant difference from the pre-conditioning regimen to discharge. If we can predict the patients who would reduce their scores before HSCT, it might give some hints for intervention strategies. The search for factors that predict PF decline is required for future research.

Limitation

There are several limitations to this study. First, this was a cross-sectional study, and we did not standardize the order of the assessments. Therefore, the results do not strictly demonstrate a causal relationship between the dependent and independent variables. Further, the results of the earlier conducted 6MWD test or muscle strength test might have influenced the responses to the subsequently conducted QOL questionnaire. Second, as shown in the present results, in clinical practice, fatigue is an important factor associated with PF among after-HSCT patients; however, there is no consensus on an objective assessment for fatigue. Therefore, the BFI, a subjective questionnaire, was unavoidably included in the regression model. Third, the present study did not assess any QLQ-C30 domain other than PF as the dependent variable. The possibility that these factors are interrelated cannot be ruled out. Finally, there is a risk of potential selection bias, as 92 subjects ultimately dropped out of this study.

Conclusion

Independent factors associated with PF, a subdomain of QLQ-C30, were examined at the time of discharge from the hospital in patients who underwent allo-HSCT. Exercise tolerance and fatigue in the acute phase of the patients who underwent allo-HSCT were found to be associated with patient-reported PF scores. Further research is needed to identify other subdomains of QOL questionnaire and associated objective factors to ensure that each staff member in the health care team provides appropriate care to patients who underwent allo-HSCT.

(2,625 words)

Declarations

Funding: Not applicable.

Conflicts of interest/Competing interests: The authors declare that they have no conflict of interest.

Ethics approval: This study was approved by the Institutional Review Board of Kyoto University Hospital conducted in accordance with the international ethical recommendations stated in the Japanese Good Clinical Practice Guidelines.

Consent to participate: Consent to participate were obtained by signature from each subject.

Consent for publication: Consent to publication were obtained by signature from each subject.

Availability of data and material: The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

Authors' contributions: Conceptualization: [Masanobu Murao, Ryota Hamada, Junsuke Miyasaka, Michiko Yoshida, and Honami Yonezawa]; Methodology: [Masanobu Murao, Ryota Hamada, and Tadakazu Kondo]; Formal analysis and investigation: [Masanobu Murao, Ryota Hamada, and Tadakazu Kondo]; Writing-original draft

preparation: [Masanobu Murao, Ryota Hamada, and Tadakazu Kondo]; Writing-review and editing: [Masanobu Murao, Ryota Hamada, Tadakazu Kondo, Junsuke Miyasaka, Michiko Yoshida, Honami Yonezawa, Yasuyuki Arai, Junya Kanda, and Manabu Nankaku]; Supervision: [Tadakazu Kondo, Yasuyuki Arai, Junya Kanda, Manabu Nankaku, Ryosuke Ikeguchi, Akifumi Takaori-Kondo, and Shuichi Matsuda].

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554 **Figures & Figure captions**

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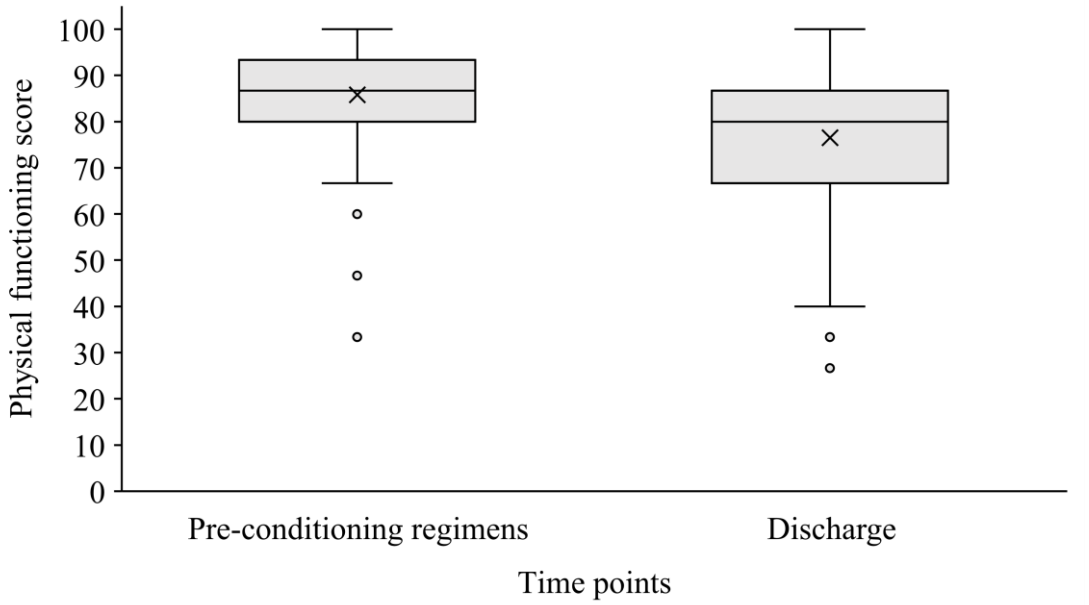

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558 Figure 1.

559 Boxplot of the physical functioning score at pre-conditioning regimens and discharge.

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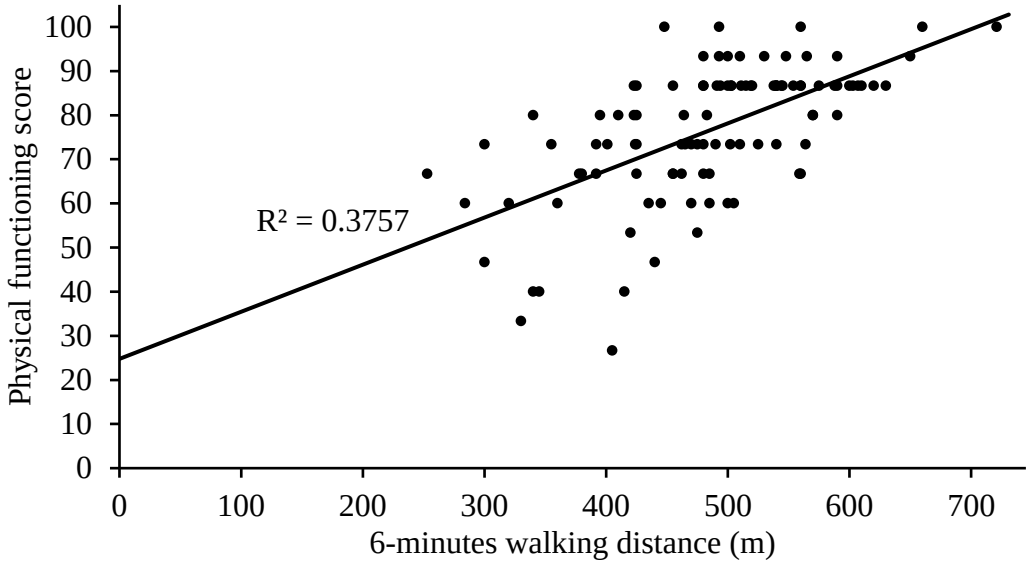

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562 Figure 2.

563 Relationship between physical functioning score 6 minute walking distance at

564 discharge. R^2: determination coefficient

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566 **Tables**

567

Table 1. Patient characteristics and treatment classifications

Variables	Ratio (percentage), Median (range), Mean ± SD (95%CI), or Number of incidences
Sex (Male / Female)	60 (58.3 %) / 43 (41.7%)
Age	47 (17 - 70)
Body mass index (kg / m^2)	19.6 ± 2.8 (19.1 - 20.2)
Length of stay (days)	70.1 ± 25.8 (65.2 - 75.1)
Diagnosis (Leukemia / MDS / Lymphoma / Others)	62 (60.2 %) / 20 (19.4 %) / 17 (16.5 %) / 4 (3.9 %)
Performance status at pre-conditioning regimens (0-1 / 2-4)	99 (96.1 %) / 4 (3.9 %)
Disease status at allo-HSCT (Complete remission / Non-complete remission)	66 (64.1 %) / 37 (35.9 %)
Conditioning regimens (Myeloablative / Non-myeloablative)	67 (65.0 %) / 36 (35.0 %)
Total dose of total-body irradiation (<2 / 2-8 / 8<) (Gy)	51 (49.5 %) / 15 (14.6 %) / 37 (35.9 %)
Stem cell sources (Bone marrow / Cord blood / Peripheral blood)	53 (51.5 %) / 39 (37.9 %) / 11 (10.7 %)

HCT-CI (0-1 / 2-7)	82 (79.6 %) / 21 (20.4 %)
Thrombotic microangiopathy (- / +)	92 (89.3 %) / 11 (10.7 %)
Hepatic veno-occlusive disease or sinusoidal obstruction syndrome (- / +)	102 (99.0 %) / 1 (1.0 %)
Infections that required interventions (Include multiple infection: - / +)	58 (56.3 %) / 45 (43.7 %)
Hemorrhagic cystitis	20
Pneumonia or Respiratory inflammation	17
Enteritis	8
Human herpesvirus - 6 encephalitis	7
Bacteremia	2
Pulmonary aspergilloma	3
Sinusitis	4
Upper gastrointestinal inflammation	5
Chemotherapy side effects required interventions (- / +)	18 (17.5 %) / 85 (82.5 %)
Nausea or Vomit	73
Mucosal damage	20
Diarrhea	9
Neuropathy	4
Acute-GVHD grades (non-GVHD / I / II / II / IV)	57 (55.3 %) / 16 (15.5 %) / 25 (24.3 %) / 3 (2.9 %) / 2 (1.9 %)
Discharge Brief Fatigue Inventory (mild / moderate / severe)	71 (68.9 %) / 31 (30.1 %) / 1 (1.0 %)

Discharge Knee extensor strength (Nm / kg)	2.05 ± 0.78 (1.75 - 2.34)
Discharge 6-minute walk distance (m)	482.6 ± 89.3 (379.4 - 585.9)
Pre-conditioning regimens QLQ-C30 Physical Functioning score	85.8 ± 12.9 (83.3 - 88.2)
Discharge QLQ-C30 Physical Functioning score	76.5 ± 15.2 (73.6 - 79.4)

SD: Standard deviation

CI: Confidence interval

MDS: Myelodysplastic syndrome

allo-HSCT: allogenic-hematopoietic stem cell transplantation

HCT-CI: Hematopoietic cell transplantation-comorbidity index

GVHD: Graft-versus-host disease

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Table 2. Simple regression model determining physical functioning score at discharge

Variables	R	R^2	*p*
Body mass index	0.23	0.05	0.851
Length of stay (days)	**0.30**	**0.09**	**0.002**
Conditioning regimens (Myeloablative: 0 / Non-myeloablative: 1)	0.05	<0.01	0.646
Thrombotic microangiopathy (-: 0 / +: 1)	0.07	0.01	0.509
Infections that required interventions (-: 0 / +: 1)	**0.15**	**0.02**	**0.131**
Chemotherapy side effects required interventions (-: 0 / +: 1)	0.06	0.04	0.532
Acute-GVHD grades (non-GVHD: 0 / I: 1 / II: 2 / II: 3 / IV: 4)	**0.23**	**0.05**	**0.019**
Brief Fatigue Inventory (mild: 1 / moderate: 2 / severe: 3)	**0.58**	**0.34**	**<0.001**
Knee extensor strength	**0.45**	**0.21**	**<0.001**
6-minute walk distance	**0.61**	**0.38**	**<0.001**

GVHD: Graft-versus-host disease

Boldface: Independent factors with $p < 0.2$

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Table 3. Multiple regression model determining physical functioning score at discharge

Adjusted R^2	Variables	Partial regression coefficient (B)	95% CI Lower limit	Upper limit	Standard partial regression coefficient (β)	*p*
0.56	***Constant***	40.51	16.38	64.64		0.001
	Control variable					
	Male: 0 / Female: 1	-0.14	-5.17	4.89	0.00	0.228
	Age	0.09	-0.06	0.24	0.08	0.955
	Pre-Physical Functioning	0.25	0.08	0.41	0.21	0.005
	Independent variable					
	Length of stay	-0.05	-0.13	0.04	-0.08	0.291
	Infections required intervention	2.10	-2.40	6.61	0.07	0.357
	(-: 0 / +: 1)					
	Acute-GVHD grade	-1.80	-3.84	0.25	-0.12	0.084
	(non-GVHD: 0 / I: 1 / II: 2 / II: 3 / IV: 4)					
	Brief Fatigue Inventory	-12.11	-16.65	-7.57	-0.39	<0.001*
	(mild: 1 / moderate: 2 / severe: 3)					
	Knee extensor strength	1.60	-2.28	5.49	0.08	0.415
	6-minute walk distance	0.56 (per 10m)	0.23	0.89	0.32	0.001*

CI: Confidence interval

GVHD: Graft-versus-host disease

*: Significant factors determining physical functioning score at discharge ($p < 0.05$).

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