

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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1 **Title page**

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4 **Title**

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

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11 Running title:

12 Patient-reported physical functioning score of allo-HSCT patients

13

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49 **Abstract**

50

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

54

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

63

64 **Results:** The mean PF score at discharge of the patients was 76.5 (standard deviation:
65 15.2). Based on the results of screening by the single regression analysis, length of
66 stay, infections (+ / -), acute graft-versus-host disease grade, brief fatigue inventory
67 score (BFI), knee extensor strength, and 6-minute walk distance (6MWD) were
68 included in the multiple regression analysis. BFI ($B = -11.94$, $p < 0.001$), and 6MWD
69 (per 10m) ($B = 0.56$, $p = 0.001$) were extracted as significant independent variables
70 governing the PF at discharge in the multiple regression model (adjusted $R^2 = 0.59$).

71

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

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

75 (238 words)

76

77 **Keywords**

78

79 1. Allogeneic hematopoietic stem cell transplantation (allo-HSCT)

80 2. Quality of life (QOL)

81 3. The European organization for research and treatment of cancer quality of life

82 questionnaire core (EORTC QLQ-C30)

83 4. Physical functioning domain

84 5. Exercise tolerance

85 6. Acute graft-versus-host disease (acute-GVHD)

86 **Introduction**

87

88

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

101

102 A review that drew a large sample from a number of published studies showed
103 that the physical functioning (PF) scores of the disease-specific measure, namely, the
104 European Organization for Research and Treatment of Cancer (EORTC) quality of life
105 questionnaire core (QLQ-C) 30 declined in the acute phase after allo-HSCT and took
106 7 to 12 months to improve to pre-treatment levels [5]. PF, a subdomain of QLQ-C30,
107 would allow us to assess whether the interventions provided by the rehabilitation staff
108 are genuinely helpful to the recipients of allo-HSCT. Recently, several studies have
109 been published focusing on the association between objectively measured physical

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

131

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

134 HSCT.

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136

137 **Materials & Methods**

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139

140 ***Study design***

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

143

144 ***Subjects***

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

154

155

156 ***Data collection and measuring methods***

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~~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:

182 moderate, and 7-10: severe) and converted into dummy variables: mild: 1, moderate:
183 2, and severe: 3, respectively.

184

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

195

196 6MWD test was conducted as per the protocol recommended by the American
197 Thoracic Society [27]. Patients were requested to walk back and forth along a straight
198 30 m flat course indoors at the maximum effort for 6 minutes, and the walking distance
199 was recorded.

200 The order of the above measurements was random.

201

202 ***Rehabilitation protocols and assessment methods***

203

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

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

215

216 *Statistical analysis*

217

218 The normality of each continuous data was assessed using the Shapiro–Wilk
219 test. Simple linear regression analyses were used to calculate the unadjusted
220 determination coefficient (R^2), and the p value was used to explore the relationship
221 between post-PF (dependent variable) and each independent variable. Then, multiple
222 linear regression analysis was performed using variables with $p < 0.2$ in simple linear
223 regression analyses and confounding factors (sex, age, and pre-PF). All statistical
224 analyses were conducted using SPSS for Windows Version 17.0 (SPSS Inc., Chicago,
225 IL), and $p < 0.05$ was considered to be statistically significant.

226

227

228 **Results**

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231 ***Physical functioning scores during pre-conditioning regimens and at discharge***

232

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

237

238 ***Descriptive statistics of patient characteristics and treatment classifications (Table***
239 ***1)***

240

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

252

253 ***Simple regression model determining physical functioning score at discharge (Table***

254 2)

255

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

261

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

264

265 The multicollinearities were confirmed by observing a correlation matrix
266 table beforehand for the submitted independent or confounding variables, but there
267 were no variables that resulted in $r > 0.9$. BFI ($B = -12.11$, $p < 0.001$) and 6MWD (per
268 10m) ($B = 0.56$, $p = 0.001$) were extracted as significant independent variables
269 governing the post-PF score in the confounding adjusted multiple regression model (R
270 $= 0.77$, adjusted $R^2 = 0.59$, Durbin-Watson ratio = 1.76).

271

272

273 Discussion

274

275

276 The most important finding of this study was that exercise tolerance (6MWD)
277 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 ($R^2 = 0.21$ [$R = 0.45$]) and 6MWD ($R^2 = 0.38$ [$R = 0.61$]) (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] 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

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

338

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

349

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

355

356 ***Limitation***

357

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

371

372

373 **Conclusion**

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

383

(2,625 words)

384 **Declarations**

385

386 **Funding:** Not applicable.

387

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

390

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

394

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

397

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

400

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

403

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

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409 and editing: [Masanobu Murao, Ryota Hamada, Tadakazu Kondo, Junsuke Miyasaka,
410 Michiko Yoshida, Honami Yonezawa, Yasuyuki Arai, Junya Kanda, and Manabu Nankaku];
411 Supervision: [Tadakazu Kondo, Yasuyuki Arai, Junya Kanda, Manabu Nankaku, Ryosuke
412 Ikeguchi, Akifumi Takaori-Kondo, and Shuichi Matsuda].
413
414

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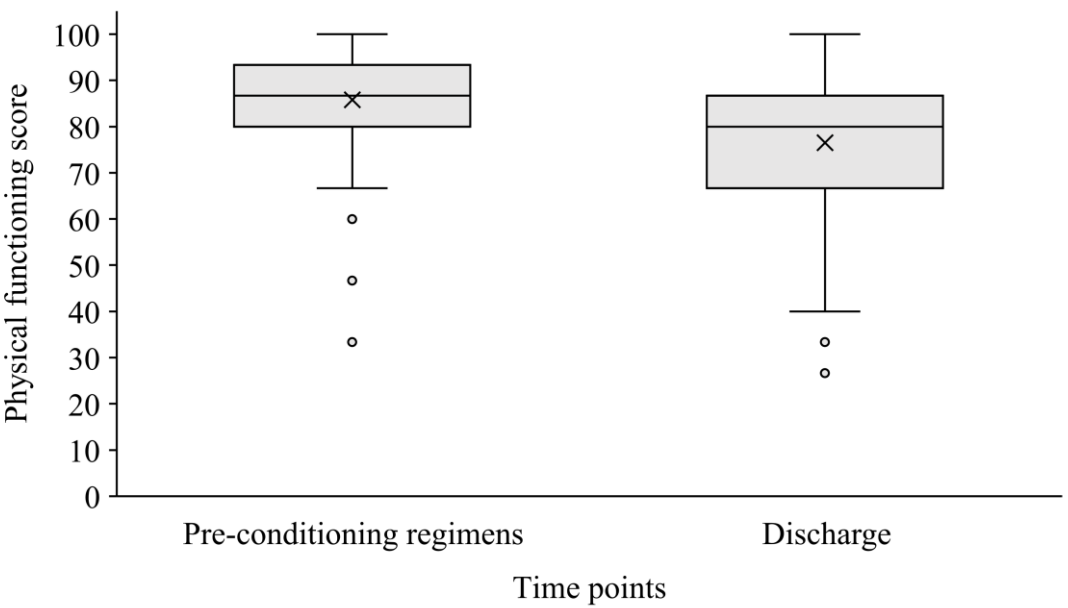
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554 **Figures & Figure captions**

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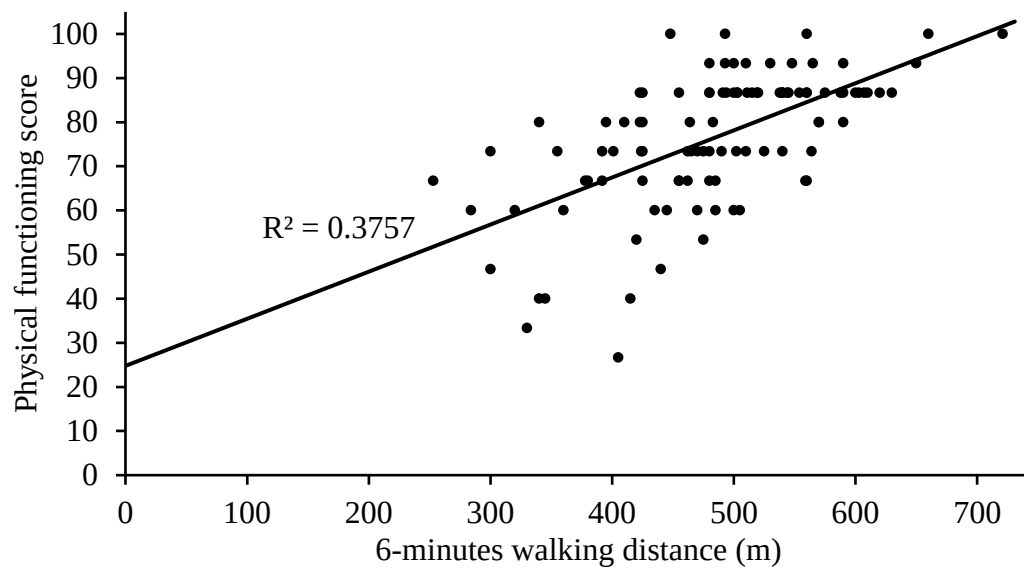


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558 Figure 1.

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

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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 $\pm$ SD (95% CI), or Number of incidences
Sex (Male / Female)	60 (58.3 %) / 43 (41.7%)
Age	47 (17 - 70)
Body mass index (kg / m²)	19.6 $\pm$ 2.8 (19.1 - 20.2)
Length of stay (days)	70.1 $\pm$ 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

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

Variables	R	R ²	<i>p</i>
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 / III: 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 $p < 0.2$

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

Adjusted R ²	Variables	Partial regression coefficient (B)	95% CI		Standard partial regression coefficient (β)	p
			Lower limit	Upper limit		
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 (-: 0 / +: 1)	2.10	-2.40	6.61	0.07	0.357
	Acute-GVHD grade (non-GVHD: 0 / I: 1 / II: 2 / II: 3 / IV: 4)	-1.80	-3.84	0.25	-0.12	0.084
	Brief Fatigue Inventory (mild: 1 / moderate: 2 / severe: 3)	-12.11	-16.65	-7.57	-0.39	<0.001*
	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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