What are Factors Influencing on Life Space Mobility in Cancer Survivors after Hematopoietic Stem CellTransplantation? -Physical and Psychological Function, Physical Symptoms, Environment, or Employment Status?

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Abstract

Purpose: The amount of physical activity in daily life is important to maintain the physical and mental health of cancer survivors after hematopoietic stem cell transplantation (HSCT). As the physical activity is considered to be limited by the life space mobility (LSM), it is more important to maintain and expand the LSM in post-HSCT survivors. The purpose of this study was to clarify the factors that affect the LSM in post-HSCT survivors.

Methods: Thirty cancer survivors after HSCT (14 women, mean age 52.0±12.3 years, 196-3,017 days post-HSCT) were included in this cross-sectional study. Patient characteristics, employment status, life space (Life Space Assessment; LSA), physical function (grip strength, isometric knee extension strength, 5 chair stand test, walking speed), depression (Self-rating Depression Scale; SDS), fatigue (Cancer Fatigue Scale), and neighborhood environment (Walk Score). The association between LSA and each factor was compared by correlation analysis. Then, multiple regression analysis was conducted, with LSA as the dependent variable and age, gender, and outcome measures that showed significant correlation with LSA in the correlation analysis as the independent variables.

Results: The variables that showed significant correlation with LSA were SDS (r= 0.65, p<.01), employment status (r= 0.60, p<.01), grip strength (r=0.43, p=0.02), and isometric knee extension strength (r=0.40, p=0.03). Results of multiple regression analysis shows that SDS (β= 0.52, p<.01), employment status (β=0.49, p<.01), and isometric knee extension strength (β=0.29, p=0.02) were significantly associated with LSA (R2=0.75)

Conclusion: Depression, employment status, and isometric knee extension strength were found to be related to the LSM in post-HSCT survivors.

Introduction

Hematopoietic stem cell transplantation (HSCT) is a well-established standard treatment for patients with a variety of hematological malignancies and is associated with good clinical outcomes with longer post-transplant life expectancy being observed over the years [1]. However, during the treatment, physical activity levels are markedly reduced in patients undergoing HSCT due to the conditioning regimen, such as the administration of total body irradiation, high-dose chemotherapy, immunosuppressive therapy for graft-versus-host disease (GVHD), transplant-related toxicities including infections and GVHD, and prolonged bed rest in a bioclean room. Therefore, deconditioning is commonly observed in patients undergoing HSCT [2–4] and physical function, represented by muscle strength and aerobic capacity, is decreased after HSCT [4–6]. Deconditioning that occurs during treatment limits patients' leisure and occupational activities and resumption of daily activities after discharging from hospital becomes difficult and negatively affects patients' health-related quality of life (HRQOL) [7]. Previous studies reported a period of up to one year for complete recovery of physical function in 40% of patients undergoing allogeneic HSCT (allo-HSCT). Moreover, stamina loss prevented 32% of survivors from return

to work during the first 2 years after allo-HSCT [8]. Therefore, it is very important for HSCT patients to increase physical activity level and improve their physical function for their healthy life even after discharging from hospital.

Recently, the life space mobility (LSM) has been considered as one of the factors affected on the daily physical activity level [9–10]. LSM is defined as the spatial area where a person travels over a specified period in daily life, and is considered not only the extent of movement but the frequency of movement and any assistance needed [11]. Restricted LSM leads to reduction of participation in social activities [12], poor HRQOL [13], and increase mortality [14]. On the other hand, increasing of LSM provides individuals with a variety of daily activities and well-being [15], so maintaining or expanding of LSM is essential for cancer survivors to live their healthy lives.

Although to date, the factors influencing on LSM in cancer survivors after HSCT remains unclear. We made a hypothesis that LSM would be affected by physical and psychological function, and physical symptom as physical and psychological factors, and neighborhood environment and employment status as environmental factors, and investigated the factors influencing on LSM in post-HSCT survivors.

Methods

Participants

This cross-sectional single center study included 30 cancer survivors with hematological malignancies who underwent HSCT and presented for outpatient medical follow-up after discharge at Kobe University Hospital in Japan between August 2018 and February 2019. The exclusion criteria included the presence of musculoskeletal disorders, declining of consent, or any missing values. This study was performed in accordance with the ethical standards established by the 1964 Declaration of Helsinki and later amendments and was approved by the Ethics Committee of Kobe University Graduate School of Medicine (approval number: B200223). Written informed consent was obtained from all participants.

Measures

Demographic and transplant characteristics

The following data were obtained from the medical records: age, sex, body mass index (BMI), primary diagnosis, graft type (autologous/relative allogeneic/non-relative allogeneic), donor type (bone marrow/peripheral blood/umbilical cord blood), presence of chronic GVHD, and duration (days) from transplantation to study enrollment.

Life space mobility (LSM)

LSM was measured using the Japanese version of the Life-Space Assessment (LSA) [16], which is used to evaluate an individual’s pattern of mobility across five levels of his/her life space (from within the home to outside of their town), during the month prior to evaluation and whose validity and reliability

have been confirmed. For each life space level, participants were asked how often they moved or traveled within a given area (less than once a week, 1-3 times each week, 4-6 times each week, or daily) and whether they required any assistance from another person or an assistive device (yes or no). LSA scores range from 0 (restricted to one's bedroom) to 120 (traveling outside of one's town daily without any assistance). The higher scores indicate the greater life space mobility [16].

Physical and psychological factors

Physical function

Handgrip strength, isometric knee extension strength, 5 chair standing test, and walk speed were evaluated as variables of physical function.

Handgrip strength was measured using a standard adjustable-handle dynamometer (Grip-D, Takei Scientific Instruments Co. Ltd., Niigata, Japan) in accordance with the method previously described by Mathiowetz et al. [17]. The grip dynamometer was set to the second grip position. The test was performed twice on each hand and the highest value was selected for analysis.

Isometric knee extension strength was measured using a hand-held dynamometer (microFET2 ; Nihon Medix, Chiba, Japan) based on the method described by Andrews et al. [18]. The test was performed with the patient seated and the knee flexed to approximately 90°. The dynamometer was applied proximal to the malleoli. The maximum force observed during 10 s of effort was recorded. The test was performed twice on each leg, and the highest value was selected. The value divided by body weight was used for analysis.

The 5 chair standing test and walk speed test were performed based on the short physical performance battery (SPPB), and the time required for 5-repetition sit-to-stand for 5 chair standing test and the speed for 4 meter walk for walk speed test were recorded [19].

Psychological function

As a substitute of psychological function, depression was assessed with the Self-Rating Depression Scale (SDS) [20]. SDS is a 20-item self-report questionnaire that is widely used as a screening tool covering affective, psychological, and somatic symptoms associated with depression. Each item is scored on a Likert scale with scores ranging from 1-4. The total score is obtained by calculating the sum of individual item scores and ranges from 20-80. Most patients with depression score between 50 and 69 points, and scores of >70 indicate severe depression.

Physical symptom

As a substitute of physical symptom, fatigue was assessed with the Cancer Fatigue Scale (CFS) [21]. CFS is a 15-item self-rating scale to assess fatigue of cancer patients. The scale consists of 3 subscales (scales evaluating the physical, affective, and cognitive aspects of fatigue) and assesses the

multidimensional nature of fatigue. The patients are instructed to circle a number that describes their present state on a scale of 1 (not at all) to 5 (very much). The response range for each subscale score is 0-28 for the physical and 0-16 for each of the affective and cognitive subscales. The total fatigue score is calculated as the sum of these individual scores. The maximum total score is 60 and the higher scores indicates more severe fatigue.

Environmental factors (Neighborhood walkability)

As an indicator of environment assessment, the neighborhood walkability was measured using the Walk Score®. Walk Score® is a free, web-based, and publicly available estimate of neighborhood walkability that can minimize the limitations of observational, self-reported, and geographic information system (GIS) measures (website link: www.walkscore.com) [22]. Walk Score® is first calculated by determining a raw score for each geographic location based on the network distance to nine amenity categories of walking destinations, namely grocery stores, restaurants, shopping, coffee shops, bank services, schools, entertainment, bookstores, and parks. These raw scores are then normalized from 0 to 100 adjusting for the “intersection density” and “block length” around each location [23]. Previous studies showed a positive association between walk score and walking behavior, sedentary behavior and overall physical activity [24-27]. Moreover, the walk score is negatively related to health outcomes such as risk of obesity [28] and cardiovascular diseases [29,30].

Employment status

Employment status (employed or unemployed) was asked by the questionnaires at the study enrollment. Both full-time and part-time works were included into “employed”.

Statistical analysis

The association between LSA and each outcome measure was compared by correlation analysis using Pearson’s (in the case of normal distribution) and Spearman’s (in case of non-normal distribution) correlation coefficients. Then, multiple regression analysis was conducted, with LSA as the dependent variable and age, gender, and outcome measures that showed significant correlation with LSA in the correlation analysis as the independent variables. All statistical analyses were performed with the JMP software, version 14.0.1 (SAS Institute Japan, Tokyo, Japan). A p value < .05 was considered statistically significant.

Results

Demographic and transplant characteristics of the 30 participants in this study are summarized in Table 1 and the measures of LSA, physical function, depression, fatigue, neighborhood walkability and employment status in Table 2. The median age of the participants was 52.0 years (standard deviation: 12.3) and 46.7% were women. The mean duration from HSCT to study enrollment were 1,253.4 days (standard deviation: 760.0).

As a result of correlation analysis, the variables that showed significant correlation with LSA were SDS (r= 0.65, p<.01), employment status (r= 0.60, p<.01), grip strength (r=0.43, p=0.02), and isometric knee extension strength (r=0.40, p=0.03) (Table 3). Results of multiple regression analysis shows that SDS (β= 0.52, p<.01), employment status (β=0.49, p<.01), and isometric knee extension strength (β=0.29, p=0.02) were significantly associated with LSA (R^2=0.75) (Table 4).

Table 1

Demographic and transplant characteristics of participants

Variables		n=30
Mean age, years (SD)		52.0 (12.3)
Sex, women (%)		14 (46.7)
BMI, kg/m^2 (SD)		21.2 (2.5)
Primary diagnosis at HSCT (%)	AML	11 (36.7)
	ALL	6 (20.0)
	CML	2 (6.7)
	MDS	1 (3.3)
	MM	1 (3.3)
	Lymphoma	7 (23.3)
	Others	2 (6.7)
Graft type (%)	Autologous	4 (13.3)
	Relative Allogeneic	8 (26.7)
	Non-relative Allogeneic	18 (60.0)
Donor type (%)	BM	11 (36.7)
	PBSC	11 (36.7)
	UCB	8 (26.7)
Presence of chronic GVHD + (%)		11 (36.7)
Duration from HSCT, mean days SD)		1,253.4 (760.0)
Emplyment status, employed (%)		15 (50.0)

BMI: Body Mass Index, HSCT: hematopoietic stem cell transplantation

AML: acute myelogenous leukemia, ALL: acute lymphoblastic leukemia, CML: chronic myelogenous leukemia, MDS: myelodysplastic syndrome, MM: multiple myeloma

BM: bone marrow, PBSC: peripheral blood stem cell UCB: umbilical cord blood

GVHD: graft-versus-host disease, SD: standard deviation

Table 2

Measures of life space mobility, physical function, depression, fatigue, neighborhood walkability and employment status

Variables		n=30
LSA, points (SD)		88.5 (27.8)
Handgrip strength, kg (SD)		27.9 (8.3)
Isometric knee extension strength,	kgf (SD)	29.8 (6.2)
	kgf/kg (SD)	0.52 (0.08)
5 chair standing test, sec. (SD)		7.65 (1.31)
Walk speed, m/s (SD)		0.79 (0.15)
SDS, points (SD)		36.8 (7.2)
CFS, points (SD)		14.2 (6.5)
Walk Score®, points (SD)		64.1 (25.1)

LSA: Life Space Assessment, SDS: Self-rating Depression Scale

CFS: Cancer Fatigue Scale, SD: standard deviation

Table 3

Association between life space mobility and each outcome measure by correlation analysis

Variables	γ	ρ	95% CI
Age	-0.21	0.27	-0.53; 0.16
Sex	-0.30	0.12	-0.59; 0.07
BMI	-0.07	0.73	-0.42; 0.30
Presence of chronic GVHD	-0.03	0.86	-0.39; 0.33
Duration from HSCT	0.37	0.05	0.01; 0.64
Employment status	-0.60	<.01 *	-0.79; -0.31
Handgrip strength	0.43	0.02 **	0.08; 0.68
Isometric knee extension strength	0.40	0.03 **	0.04; 0.67
5 chair standing test	-0.30	0.11	-0.60: 0.06
Walk speed	-0.09	0.64	-0.44; 0.28
SDS	-0.65	<.01 *	-0.82; -0.38
CFS	-0.32	0.09	-0.61; 0.05
Walk Score®	-0.12	0.53	-0.46; 0.25

95% CI: 95% confidence intervals, BMI: Body Mass Index, GVHD: graft-versus-host disease

SDS: Self-rating Depression Scale, CFS: Cancer Fatigue Scale

Table 4

Association between life space mobility and each outcome measure by multiple regression analysis

Variables	β	ρ	95% CI
Age	-0.03	0.84	-0.67; 0.55
Sex	0.21	0.32	-5.89; 17.14
Employment status	0.49	<.01 *	5.70; 20.70
Handgrip strength	-0.14	0.51	-2.02; 1.04
Isometric knee extension strength	0.29	0.02 **	16.52; 189.91
SDS	-0.52	<.01 *	-2.99; -1.08

R^2=0.75, p<.0001

* <.01, ** <.05, 95% CI: 95% confidence intervals, SDS: Self-rating Depression Scale

Discussion

Maintaining and increasing physical activity in daily life is essential for cancer survivors after HSCT to lead their physically and mentally healthy lives. The LSM has been considered as one of the important factors affecting on the physical activity [9–10], however, there is little information on the LSM among cancer survivors in the previous studies. In the present study, we investigated the factors affecting on LSM in cancer patients after HSCT, and the results shows that the LSM, assessed with LSA, may be affected by the physical function (isometric knee extension strength), psychological function (SDS), and employment status in post-HSCT survivors. The present study is the first to identify the factors influencing on the LSM in post-HSCT survivors. In fact, this study is one of only a handful of studies on the LSM among patients with cancer [31–34] and the first focused on post-HSCT survivors.

First, in terms of physical factor, isometric knee extension strength was significantly associated with the LSM. In the previous studies, lower physical function was related to lower LSM among the community-dwelling older adults [11, 35–37]. Kuspinar et al found that worse performance in walking speed and grip strength associated with lower LSM [36], and Portegijs et al found that poorer performance in Short Physical Performance Battery (SPPB) was associated with lower LSM score [37]. In the present study focusing on post-HSCT survivors, performance in handgrip strength, chair standing test, and walk speed were not associated with the LSM but only knee extension strength was associated with the LSM. The value of knee extension strength in the participants in the present study was 29.8 kgf. Morishita et al reported that the mean knee extension strength was 204.0 N (20.8 kgf) at the time of hospital discharge in patients undergoing HSCT [38]. In contrast, previous studies that investigated healthy volunteers in their 50s reported that the mean knee extension strength was 507 N (51.7 kgf) for men and 442 N (45.1 kgf) for women [39]. In HSCT patients, lower extremity muscle strength is decreased at discharge, but it would gradually improve after discharge. However, the values of their muscle strength are lower than those of healthy people, so this might be associated with LSM in the post-HSCT survivors.

Second, in the psychological factor, depression (SDS) was significantly associated with the LSM in the present study. Our finding that post-HSCT survivors with high depression, sometimes due to fear of infection, are more likely to experience low LSM, because post-HSCT survivors with shorter interval between transplantation and study enrollment may take immunosuppressive medication. Depression is considered to be one of the most influential factors on LSM [35]. It has also been reported that cancer survivors have a high frequency of depression, and especially in HSCT patients, 43% of patients after allo-HSCT was reported to develop depression within one year [40]. The presence of depression was related to low LSM among the community-dwelling older people [41], and the similar result was observed in the post-HSCT survivors.

Third, in our study, employment status was significantly associated with the LSA. This is the first study to show the association between employment status and LSA in cancer survivors. Since the target subjects in most of previous studies on LSA have been the older adults, no previous study showing the association between employment status and LSA has been recognized. However, Miyashita et al reported that the participation in social activities was associated with the LSA in the community-dwelling independent older people [42], so the social participation, including employment, might be important to maintain and expand the LSA in cancer survivors.

Some few systematic reviews and meta-analyses have reported that physical exercise reduced depression, anxiety and fatigue and improved HRQOL in patients undergoing HSCT [43–45]. Exercise improves physical function and HRQOL and reduces depression, therefore, positive rehabilitation after discharge is useful in post-HSCT survivors. Early introduction of a rehabilitation program including physical exercise and vocational counseling is important to facilitate early return to work in post-HSCT survivors. A study performed by De Boer et al reported that rehabilitation intervention, such as vocational counseling combined with patient education and biofeedback-assisted behavioral training or physical exercise, achieved higher return-to-work rates in cancer patients [46].

While, the environmental factors assessed with neighborhood walkability was not associated with the LSM. Environmental factors are being increasingly taken into account in mobility research. Previous studies showed the influence of different environmental features on the LSM. Examples of mobility barriers are a poor infrastructure, uneven sidewalks, loud traffic, the absence of a possibility to take a break during walking, and long ways to various service facilities [47, 48]. Mobility facilitators are green spaces [49], pavements, the attractiveness of the neighborhood [50], and the variety of amenities [51]. However, in the present study, no associations between neighborhood walkability and LSM could not be found. This might be due to the lower age of the study participants without restriction of mobility skill including driver’s license, as the participants of the above-mentioned previous studies were almost all community-dwelling older people.

This study has several limitations. First, the sample size was very small. Second, due to the cross-sectional design, it was impossible to establish causal relationship between LSM and physical and psychological function, physical symptom, neighborhood environment and employment status. LSM has

been found to be a predictor of cognitive decline [52], 90-day hospital readmission [53], falls [54], mortality [55], HRQOL [56], and admission to nursing home [57]. Therefore, even in post-HSCT survivors, the further longitudinal follow-up study in larger samples is needed.

Conclusion

Our findings suggest that the LSM might be affected by isometric knee extension strength, depression, and employment status in post-HSCT survivors. Positive rehabilitation after discharge may be useful to promote LSA in post-HSCT survivors. Further longitudinal study in larger samples is needed to validate our findings.

Declarations

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Author contribution

J.I., T.S., D.M., H.D., K.Y. contributed to conceptualization and data curation. J.I. and R.O. contributed to the evaluation of data analysis. All authors contributed to the writing of the original draft, review, and editing. Y.S. contributed to the final approval of the article.

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Data availability Not applicable.

Code availability Not applicable.

Ethic approval

This study was performed in accordance with the ethical standards established by the 1964 Declaration of Helsinki and later amendments and was approved by the Ethics Committee of Kobe University Graduate School of Medicine (approval number: B200223).

Consent to participate

Written informed consent was obtained from all participants.

Consent for publication

Patients signed informed consent regarding publishing their data.

Competing interests

The authors declare no competing interests.

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