

Physical Exercise for Patients Undergoing Allogeneic Haematopoietic Stem Cell Transplantation

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Allogeneic haematopoietic stem cell transplantation (allo-HSCT) has been increasingly used in the treatment for malignant and non-malignant haematopoietic diseases [1], especially owing to the constant advances in treatment technology. This has resulted in reduced morbidity and increased life expectancy [2], with disease-specific 5-year survival rates for this treatment ranging from 5% to 80% [2]. The standard procedure for myeloablative allo-HSCT entails a conditioning regime of high-dose chemotherapy, often in combination with total-body irradiation, followed by the infusion of stem cells harvested from donor bone marrow or peripheral blood [3]. Currently, complications for patients with haematological malignancies are still frequently reported [4], and allo-HSCT treatments are themselves associated with numerous somatic, psychological, and psychosocial side effects [5]. Complications caused by the transplantation emerge at different stages of the treatment. During the pretransplant (conditioning) phase, side effects of high-dose chemotherapy and/or radiation include nausea, emesis, diarrhoea, loss of hair, cystitis/bladder infection, and mucositis [6]. During the posttransplant phase, complications resulting from graft versus host disease include skin rash, bronchiolitis, nausea, emesis, diarrhoea, and jaundice, which results in weakness [7]. As a result of graft versus host disease and its treatment process, patients are often subjected to prolonged periods of immobilization and bed rest that lead to loss of strength and endurance [8]. In a previous study, we confirmed that transplant patients who stayed in isolation rooms for several weeks exhibited deteriorated physical function [9]. We also showed that allo-HSCT patients had lower quality of life (QOL) as well as deteriorated physical function after transplantation than before transplantation [10].

Over the past few years, the number of studies describing the promising role of physical exercise programs performing as nonpharmacologic adjuvant therapy for patients with cancer has been on the rise. Here, we introduce the effects of physical exercise on the QOL, fatigue levels, psychological function, and physical function of allo-HSCT patients.

Physical Exercise Intervention Period

The onset timing of physical exercise intervention for allo-HSCT patients varies, and can occur in 1 of 3 phases: conditioning (before HSCT) [11-17], post engraftment (after HSCT) [18,19], or hospital discharge phase [20-24]. Recently, physical exercise intervention has reportedly been increasingly initiated during the conditioning phase (chemotherapy and radiation therapy regimen). In a previous study, we observed that patients who underwent allo-HSCT had significantly lower body mass index and physical function than the normal population, even before undergoing the transplantation [25]. We also showed that roughly half of the study population had sarcopaenia before undergoing allo-HSCT [26]. On the basis of these findings, we concluded that physical exercise should be initiated as soon as possible during the hospitalization of allo-HSCT patients. Recent guidelines for cancer survivors' exercise prescription provided by the American College of Sports Medicine did not report any contraindications to starting an exercise program for patients undergoing either autologous or allogeneic HSCT [27]. The ideal time for safely and effectively starting an exercise program for HSCT patients, as well as the appropriate

type, frequency, intensity, and duration of the program have not been identified. In a previous study, we showed that physical exercise is beneficial and can be performed safely and feasibly in patients with cytopaenia who are undergoing allo-HSCT [9]. Physical exercise, even if only mild exercise, should be performed by allo-HSCT patients as early as during the conditioning period, since it possibly helps prevent the deterioration of physical function after transplantation.

Types of Exercise Intervention

Physical exercise intervention is usually fully [11,13-21] or partially supervised [12] in patients undergoing allo-HSCT. Interestingly, Shelton et al. [22] reported higher endurance and gait speeds in supervised training groups than that in patient-directed training groups. Physical exercise intervention for patients undergoing allo-HSCT typically involves a combination of aerobic training (treadmill, cycle, walking or stair climbing) and resistive exercises with weights or elastic bands [11-13,18,19,21,22]. Other common physical exercise programs have incorporated educational [22] and psychoeducational [11] elements with low intensity bed exercises for stretching and relaxation breathing [14,15]. In our study, we performed one-on-one (physical therapist and patient) physical therapy involving resistance, stretching, and aerobic exercises for cytopaenic patients during their hospitalization [9]. Physical therapists can usually vary exercise frequency, intensity, and duration based on patient conditions and complaints on a given day. For allo-HSCT patients, a physical exercise regimen combining different types of exercise might be recommended. On the other hand, if the patient is unable to execute a self-directed exercise regimen, one-on-one physical therapy may be more appropriate.

Quality of Life

Several studies have examined the effects of physical exercise on the QOL of patients undergoing allo-HSCT [11,12,16,17,19,21,23]. Most of these studies used the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [11,12,16,17,21], while one study used the Cancer Rehabilitation Evaluation System [19], and another used the Medical Outcomes Study 36-Item Short Form [23]. Some studies revealed significantly higher QOL scores for the allogeneic intervention group than those for the allogeneic control group [11,12,17,19]. On the other hand, Hacker et al. [16] and Knols et al. [21] observed no significant differences between the QOL scores of the physical exercise and control groups following physical

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exercise intervention. Wilson et al. [23] observed higher QOL scores pertaining to 'vitality/fatigue' outcomes; however, their results were not compared to a control group. We also investigated the QOL of patients undergoing allo-HSCT using the Medical Outcomes Study 36-Item Short Form questionnaire, and demonstrated that the frequency of physical therapy corresponded with the extent of decline in QOL [9]. Several reports have examined the effects of physical exercise on QOL; however, to date, these effects have not been confirmed in patients with HSCT.

Fatigue

The effect of physical exercise on fatigue in patients undergoing allo-HSCT was assessed using the following questionnaires: the Functional Assessment of Cancer Therapy-Anaemia scale [11,21], Functional Assessment of Cancer Therapy-Fatigue [20] scale, Brief Fatigue Inventory [20,22], Multidimensional Fatigue Inventory [12], Piper Fatigue Scale [14], and Fatigue Symptom Inventory [23]. Knols et al. [21] did not observe a statistically significant decline in fatigue between the intervention and control groups. Moreover, Shelton et al. [22] reported that the decline in fatigue observed after physical exercise was not statistically significant, and the favourable changes in the intervention group's fatigue levels observed by Jarden et al. [11] also were not statistically significant. On the other hand, Wilson et al. [23] and Carlson et al. [20] reported significant improvement in fatigue symptoms following physical exercise, and Wiskemann et al. [12] demonstrated significant differences in fatigue levels between the intervention and control groups at the end of the physical exercise intervention. Moreover, Kim et al. [14] described a significant decline in the level of fatigue in the relaxation breathing exercise group compared to the control group. We also investigated fatigue using the Piper Fatigue Scale, and observed that post-HSCT fatigue levels are significantly higher than pre-HSCT levels in allo-HSCT patients. Increased fatigue is often observed in allo-HSCT patients, and physical exercise intervention might be useful and beneficial in alleviating this increased fatigue.

Psychological Function and Distress

Few studies have examined the effects of physical exercise on the psychological function and distress levels of patients undergoing allo-HSCT [11,12,20]; in these studies, psychological function was evaluated using the Profile of Mood States [12,20], or the Hospital Anxiety and Depression Scale [11,12]. Wiskemann et al. [12] demonstrated a significant reduction in anxiety and depression levels in the intervention group compared to the control group. Conversely, Jarden et al. [11] observed no significant difference in the anxiety and depression levels of both groups following physical exercise intervention. Additionally, Carlson et al. [20] did not observe a reduction in depression levels following physical exercise intervention. We investigated anxiety and depression levels in patients undergoing allo-HSCT using the Hospital Anxiety and Depression Scale, and observed no differences in these levels pre-HSCT and post-HSCT [10]. It seems that anxiety and depression levels are not significantly increased in allo-HSCT patients, and physical exercise does not seem to significantly affect these levels.

Physical Functioning

Physical functioning has been evaluated through various methods that usually involve 3 aspects: aerobic capacity [11,13,18,20,23], muscle strength [11,13,18,21], and functional capacity [11,12,21,22,24]. In previous studies, aerobic capacity was evaluated using a treadmill or bicycle. A significant increase in aerobic fitness was observed after the physical exercise intervention compared to before the intervention

[20,23]; furthermore, the physical exercise group demonstrated significantly better aerobic fitness than the control group [11,13,18]. Muscle strength was evaluated as upper and lower body strength using a hand-held dynamometer and resistance equipment; a significant increase in muscle strength was observed in the physical exercise group compared to the control group, following physical exercise intervention [11,13,18,21]. Functional capacity was evaluated using the 6-min walk test, 50-foot walking time, and repeated sit-to-stand movement. While one study reported no significant increase in functional capacity after physical exercise intervention [24], several other studies described a significant increase in functional capacity among the physical exercise group compared to the control group, following physical exercise intervention [11,12,21,22]. In our study, we showed that the high-frequency physical therapy group of allo-HSCT patients exhibited significantly less decline in muscle strength and functional capacity than the low-frequency physical therapy group [9]. Overall, physical exercise intervention may be useful and beneficial to maintaining physical functioning in allo-HSCT patients.

Conclusion

Based on previous research, physical exercise may help patients reduce the loss of, or maintain, aerobic and functional capacity, as well as muscle strength. Some studies have also indicated that physical exercise interventions have multidimensional benefits, including improving QOL and reducing fatigue. Therefore, physical exercise may not only help allo-HSCT patients maintain physical function during treatment but also improve their QOL and alleviate their fatigue symptoms.

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