Efficacy of physical exercise using the balance board game on physical and psychological function in patients with hematological malignancies confined to a bioclean room

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ABSTRACT. Objective: This study aimed to define the efficacy and features of physical therapy (PT) using the Nintendo Wii Fit U (Nintendo Inc., Kyoto, Japan) in patients with hematological malignancies confined to a bioclean room. Method: A total of 33 patients with hematological malignancies confined to a bioclean room were enrolled in this study. This study was designed as a randomized crossover test between two week-long interventions: PT program (Therapist PT) and Wii Fit U program (Wii PT). We compared the efficacy of Wii PT and Therapist PT with regard to physical and psychological function test scores. Results: Of the 33 patients, 22 were analyzed. The validity of the crossover design was demonstrated, as there were no significant differences in period and carryover effects between the two groups. Therapist PT resulted in significantly better improvements in fatigue scores and total mood disturbance (TMD) scores in the Profile of Mood States short-form Japanese version compared to Wii PT (fatigue score, -5.2 ± 8.3 vs 2.7 ± 8.2; TMD score, -22.5 ± 32.8 vs -2.6 ± 20.5; p<0.05). Physical function improved post-Wii PT and post-Therapist PT interventions (p<0.05), and there was no difference in treatment effect. Conclusion: Improvements in physical function were clearly observed following the use of Wii PT in patients confined to a bioclean room. However, compared to Therapist PT, Wii PT was less effective in improving the psychological function of patients. Key words: physical therapy, Virtual game, Hematological malignancies

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Patients with hematological malignancies are prone to infection, anemia, and bleeding due to cytopenia and require long-term treatment. Patients with hematological malignancies receive steroid medications during cytotoxic chemotherapy and have to remain in a limited tight space, such as a bioclean room, during intensive therapy, to prevent infection.

These patients are at risk for psychological disorders and physical disuse syndromes because they spend long periods bedridden due to neutropenic fever and general fatigue. Additionally, patients with hematological malignancies can lose physical and psychological conditioning because of the narrow space and their disease. Therefore, physical therapy (PT) interventions play an important role in the prevention of complications, including disuse syndrome and depression, especially in patients confined to a bioclean room. Previous studies on PT in patients with hematological malignancies have demonstrated that using a bicycle ergometer and strength training can successfully maintain a patient’s physical and psychological activities.

Despite this, patients often cannot undergo scheduled PT sessions conducted by a therapist because of nausea, diarrhea, and general fatigue, with high fever during and after intensive chemotherapy or total body irradiation before he-
matological stem cell transplantation. Although these symptoms are usually temporary, it is difficult for patients to fit themselves into the therapist’s schedule due to the effects of chemotherapy. Recently, the Nintendo Wii Fit (Nintendo Inc., Kyoto, Japan) has been recognized as a unique and effective tool for maintaining physical activity in patients. Previous studies have reported that PT using a virtual game was effective in improving physical and psychological function in older adults. Another study revealed that the Wii Fit was used successfully and safely as a form of PT for elderly patients with hematological malignancies.

The Wii Fit U is a virtual game that uses software and a balanced Wii board (wireless type Gravicorder; Nintendo Inc., Kyoto, Japan). Wii Fit U is relatively inexpensive, and exercises are performed on the balance Wii board using center-of-gravity transfer. The greatest advantage of using Wii Fit U for PT is that it requires only a 1.4 m × 1.4 m square area during use. Thus, we introduced Wii Fit U as a PT intervention, especially designed for use in the bioclean room in our hospital.

This study aimed to clarify whether PT using the Wii Fit U improved the physical and psychological function of patients with hematological malignancies confined to a bioclean room.

Method

1. Participants

Patients were included if they: 1) had a hematological malignancy, 2) received PT in the bioclean room at Saitama Medical Center, Saitama University, between April 2016 and March 2017; 3) were aged ≥ 18 years; 4) had an Eastern Cooperative Oncology Group Performance Status (ECOG-PS) score of 0 or 1, and 5) had no organ dysfunction. Performance status was evaluated by a physical therapist before hospitalization and in a bioclean room. Patients with grade 2 or worse Common Terminology Criteria for Adverse Events version 4.0 (CTCAE) were excluded. Written informed consent was obtained from all patients. Finally, 33 consecutive patients who were treated in the bioclean room at Saitama Medical Center, Saitama Medical University, were enrolled in this study. All patients had severe neutropenia with absolute neutrophil count < 500/μl after high-dose chemotherapy. We calculated the sample size using R software version 2.8.1 (The R Foundation for Statistical Computing, Vienna, Austria). With an α-error of 0.05, β-error of 0.8, effect size of 10, standard deviation of 25, and individual difference quotient of 1.5, the sample size was calculated as 32.

This study was approved by the local institutional review board of Saitama Medical Center, Saitama Medical University (permit number, 1403).

2. Design and study procedure

This was a randomized, open-label, crossover study. The interventions included 1 week of PT conducted by a therapist (Therapist PT) and 1 week of PT using the Wii Fit U (Wii PT). Each patient was randomly assigned to one of two groups using a random number table. A random number table was created by a computer operated by individuals unrelated to the study. In one group (Wii PT/Therapist PT), the patients received Wii PT for the first week (Period I) and Therapist PT the following week (Period II). In the other group (Therapist PT/Wii PT), the patients received PT for the first week (Period I) and Wii PT the following week (Period II) (Figure 1).

3. Intervention

Therapist PT comprised an aerobic exercise using a bike ergometer, strength training using a “TheraBand” and the patient’s own weight, stretching, and educational guidance regarding daily exercise. Aerobic exercise was performed with 40% to 60% intensity of target heart rate in the Karvonen formula and with an intensity between 11 and 13 on the Borg scale. Strength training was performed with an intensity between 11 and 13 on the Borg scale, and the number of exercises was 3 to 5 sets (10 exercises per set).

Wii PT comprised “cycling,” “table tilt,” and “balance Mii” and other activities based on the patients’ preference and if time permitted, including aerobic exercise, transverse and back-and-forth balancing, and strength training based on a previous study. Each intervention was conducted by a therapist, with an exercise duration of 30 min/day for 5 days a week. This program lasted a total of 2 weeks for each patient.

4. Outcome measures

We evaluated general characteristics, including age, sex, body mass index, disease diagnosis, disease treatment, period from start of treatment to Assessment I, patient’s stage according to CTCAE (fever, pain, malaise, vomiting, nausea, diarrhea, constipation), ECOG-PS, and Barthel index (BI) from patients’ medical records. We also measured general characteristics just before the start of PT (Assessment I).

To assess the physical function of patients, we used the Timed Up and Go (TUG) test, functional reach (FR) test, and 30-s chair stand test (CS-30) test as indicators of physical condition. The TUG test required participants to stand from a sitting position, walk for 3 m, turn 180°, walk back 3 m, and sit down again. The TUG walking speed was the maximum effort, and the time taken to complete the TUG test was measured. The FR test required the patient to stand with arms extended with 90° shoulder flexion. Then, the maximum forward reach was measured. The CS-30 test was performed with the patient’s arms in front of their chest, and the number of times the patient could sit and
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In the first week, 5 of 20 patients who received Therapist PT and 3 of 13 patients who received Wii PT dropped out of this study because of worsening general conditions due to chemotherapy for hematological malignancies and disease progression. In the second week, 3 of 15 patients who received Wii PT dropped out of this study because of worsening of general conditions due to chemotherapy and withdrawal of consent.

stand up from a chair in 30 s was measured. To assess the psychological function of patients, the Profile of Mood States short-form Japanese version (POMS-sf), which consisted of 30 questions graded on a five-stage scale (0 to 4), was used. The POMS-sf classifies questions into six dimensions: tension/anxiety (T-A), depression/defection (D), anger/hostility (A-H), vigor (V), fatigue (F), and confusion (C)\textsuperscript{14,15}. The total mood disturbance (TMD) score was calculated from the six dimensions as an index of the patient’s general psychological condition. In this study, the POMS-sf points were normalized for sex and age.

We measured TUG, FR, CS-30, and POMS-sf scores just before the start of PT (Assessment I) and on days 8 (Assessment II) and 15 (Assessment III) after PT.

### 5. Statistical analysis

In this study, we only included patients who completed the intervention. To ensure the validity of this crossover design, we compared the general characteristics of the patients in the two groups. Assessment I was analyzed using an independent t-test and \(\chi^2\) test.

We compared the general characteristics and Assessment I scores of the two groups using independent t-tests and \(\chi^2\) tests. Additionally, we examined the period and carryover effects to verify the validity of the crossover design. The period effect was calculated by subtracting the change values in Period I (subtract Assessment I from Assessment II) and Period II (subtract Assessment II from Assessment III). In Wii PT/Therapist PT, we subtracted Period II from Period I. In Therapist PT/Wii PT, we subtracted Period I from Period II. The values of each group were compared using an independent t-test. The carryover effect was calculated by comparing the sum of Period I and Period II between the two groups using an independent t-test.

Then, the effect of Wii PT and Therapist PT was assessed by comparing the pre- and posttreatment assessment values using a paired t-test. Moreover, the difference between the effects of Wii PT and Therapist PT was assessed by comparing the pre- and posttreatment change values using an independent t-test. The significance level was set at a P-value < 0.05 in all tests. Statistical analyses were conducted using SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY).

### Results

Of the 33 patients, 11 dropped out of the study because of worsening general condition due to chemotherapy.
for hematological malignancies (n=7), disease progression (n=3), and withdrawal of consent (n=1). A total of 22 patients who completed the treatment were included in the analysis: 10 in the Wii PT/Therapist PT group and 12 in the Therapist PT/Wii PT group. The average age of the patients was 44.7 ± 12.1 years. Eighteen men and four women were included in the study. Nineteen patients were diagnosed with acute myeloid leukemia, two with diffuse large B-cell lymphoma, and one with acute lymphoblastic leukemia. There was no significant difference in all items between the two groups (Table 1).

All subjects completed both exercise protocols (30 min/day, once daily, 5 days/week). There were no exercise protocol adverse events.

The validity of the crossover design is presented in Table 2. There was no difference in the period or carryover effect in any evaluation item between the groups (Table 2).

The treatment effects of Wii PT and Therapist PT are shown in Table 3. Patients showed significant improvement in TUG and CS-30 scores after Wii PT (p < 0.05). The POMS-sf scores showed no significant difference in any of the six dimensions. Patients showed significant improvement in TUG, CS-30, and POMS-sf (T-A, F, and C dimensions and TMD) scores after Therapist PT (p < 0.05; Table 3).

Differences in treatment effects between Wii PT and Therapist PT are shown in Table 4. The improvements in POMS-sf scores were significantly greater after Therapist PT compared to those after Wii PT (p < 0.05). There was no significant difference in physical function between the two PT methods (Table 4).

Discussion

In this study, we evaluated both the physical and psychological efficacies of PT using the Wii Fit U for patients with hematological malignancies confined to a bioclean room. Physical function improved with Wii PT and Therapist PT, and there was no difference in treatment effect. Regarding psychological function, Therapist PT improved the T-A, F, and C dimensions and TMD of POMS-sf, but Wii PT did not change in all items of POMS-sf. Therapist PT resulted in significantly better improvements in the F and TMD scores compared to Wii PT.

Previous studies have reported the efficacy of Wii PT in healthy elderly individuals, patients with spinal cord injury, and patients with stroke. In our study, the TUG and CS-30 test scores significantly improved after physical intervention with Wii PT. Compared with Therapist PT, Wii PT showed a similar effect in maintaining the physical function of patients confined to the bioclean room. Compared with patients in a previous study, the patients in our study were frail and had muscle atrophy, anemia, or hypoalbuminemia due to chemotherapy and malignant disease. However, Wii PT provided an exercise load to improve physical function in frail patients, even in such a small space.

Significant improvement in the depression score of the Depression Anxiety Stress Scales of physical disabilities through the use of Wii Fit has been reported. Furthermore, improvements in the Quick Inventory of Depressive Symptoms, MOS Short-Form 36-Item Health Survey, and RAND-36 Health Status Inventory using the Wii Fit have been previously reported in elderly patients and patients with back pain. This study did not recognize improvements in the POMS-sf with Wii PT, and this finding differed from those of previous studies. Additionally, the improvements in F and TMD scores were less in patients who received Wii PT compared to those who received Therapist PT. One potential reason for this phenomenon is that with Wii PT, the patient was unable to control their physical load, and perhaps this was not an appropriate load in psychological function. In contrast, during PT, the therapists evaluated the patient’s fatigue or mood and provided a more appropriate load for PT. The Wii PT lacks the perception that a therapist can provide. Moreover, communication between the patient and therapist is also crucial in the improvement of the patient’s mental stress.

The features of the Wii PT resulted in improvements in patients’ physical function; however, there was no improvement in psychological function, such as that observed in Therapist PT. Despite this, the advantages of the Wii PT remain: only a small space is required, the exercise load is simple to set in the game, and it can be used anytime without a therapist. In the future, therapists could design a self-training PT program for each patient based on the features of the Wii Fit U.

There were several limitations in this study. We did not include a washout period; thus, the treatment effect of Period I may have affected the treatment effect of Period II. Considering the poor health of the patients, it was unethical to include a washout period without PT, as this would be greatly disadvantageous for the patients. However, we demonstrate that there was no significant difference between the period and carryover effects in the two groups, and therefore, we were able to accurately assess the effect of the Wii Fit U and Therapist PT. Another limitation was that this study had 11 dropout patients; thus, in our study, small sample sizes may limit the generalizability of the results and must be consider β-error. Therefore, further studies are needed to clarify suitable Wii Fit U adaptations in patients with hematological malignancies confined to a bioclean room and assess more features of the Wii Fit U.

Conclusion

Wii Fit U is an effective PT tool for patients with hematological malignancies confined to a bioclean room.
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Table 1. Characteristics of participants

|                      | Wii PT/Therapist PT (n=10) | Therapist PT/Wii PT (n=12) | P-value |
|----------------------|----------------------------|----------------------------|---------|
| **General characteristics** |                            |                            |         |
| Age (years)          | 44.9±12.6                  | 44.6±12.3                  | 0.974   |
| Sex (male/female)    | 9/1                        | 9/3                        | 0.364   |
| BMI (kg/m²)          | 24.4±2.9                   | 23.4±3.6                   | 0.346   |
| **Disease**          |                            |                            |         |
| AML                  | 8                          | 11                         | 0.190   |
| DLBCL                | 2                          | 0                          |         |
| ALL                  | 0                          | 1                          |         |
| **Treatment**        |                            |                            | 0.388   |
| HD-AraC              | 5                          | 6                          |         |
| IDR-AraC             | 2                          | 5                          |         |
| CAG                  | 1                          | 0                          |         |
| MCVAC                | 1                          | 0                          |         |
| R-ESHAP              | 1                          | 0                          |         |
| TCCSG ALL L04-16     | 0                          | 1                          |         |
| **Period from start of treatment to Assessment I (day)** | 3.9±9.2                     | 0.5±5.1                     | 0.319   |
| **CTCAE**            |                            |                            |         |
| Fever (grade)        | 0.0±0.0                    | 0.0±0.0                    | 1.000   |
| Pain (grade)         | 0.0±0.0                    | 0.1±0.3                    | 0.974   |
| Malaise (grade)      | 0.1±0.3                    | 0.1±0.3                    | 0.974   |
| Vomiting (grade)     | 0.1±0.3                    | 0.0±0.0                    | 0.722   |
| Nausea (grade)       | 0.2±0.4                    | 0.2±0.3                    | 0.923   |
| Diarrhea (grade)     | 0.0±0.0                    | 0.1±0.3                    | 0.771   |
| Constipation (grade) | 0.1±0.3                    | 0.0±0.0                    | 0.722   |
| **ECOG-PS**          | 0.7±0.5                    | 0.6±0.5                    | 0.674   |
| BI (scores)          | 100±0.0                    | 100±0.0                    | 1.000   |
| **Assessment I**     |                            |                            |         |
| TUG (s)              | 5.9±1.1                    | 6.0±1.8                    | 0.801   |
| FR (cm)              | 43.2±6.1                   | 44.2±7.1                   | 0.738   |
| CS-30 (number of times) | 17.9±4.3                 | 20.6±6.1                   | 0.259   |
| T-A (points)         | 45.3±8.2                   | 52.3±8.9                   | 0.069   |
| D (points)           | 48.7±9.5                   | 53.2±12.0                  | 0.352   |
| A-H (points)         | 38.7±3.1                   | 41.8±7.1                   | 0.210   |
| V (points)           | 38.2±14.1                  | 36.8±9.8                   | 0.792   |
| F (points)           | 42.7±4.5                   | 48.3±11.3                  | 0.134   |
| C (points)           | 47.9±6.8                   | 50.9±8.9                   | 0.391   |
| TMD (points)         | 185.1±35.0                 | 209.8±45.3                 | 0.175   |

Data are presented as number of subjects or mean ± standard deviation.

BMI, body mass index; AML, acute myeloid leukemia; DLBCL, diffuse large B-cell lymphoma; ALL, acute lymphocytic leukemia; HD-AraC, high-dose cytarabine therapy; IDR-AraC, idarubicin and high-dose cytarabine therapy; CAG, low-dose cytarabine and aclacinomycin; MCVAC, high-dose raniomustine, cytarabine, etoposide and cyclophosphamide; R-ESHAP, rituximab, etoposide, cisplatin, cytarabine, and methylprednisolone; TCCSG ALL L04-16, Tokyo Children’s Cancer Study Group trial L04-16; CTCAE, Common Terminology Criteria for Adverse Events; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; BI, Barthel index; TUG, Timed Up and Go test; FR, functional reach test; CS-30, 30-s chair stand test; T-A, tension/anxiety; D, depression/defection; A-H, anger/hostility; V, vigor; F, fatigue; C, confusion; TMD, total mood disturbance.

However, the frequency of Wii Fit U use in this study was insufficient to improve the psychological function of pa-
Further studies are required to develop an effective program that combines the use of Wii Fit U and Therapist PT.

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| Table 4. Comparison of treatment effects for the two interventions |
|---------------------------------------------------------------|
|                  | Wii PT (n=22) | Therapist PT (n=22) | P-value |
| TUG (s)          | -0.3±0.7      | -0.3±0.6             | 0.876   |
| FR (cm)          | 1.6±5.1       | 1.9±4.9              | 0.835   |
| CS-30 (number of times) | 2.2±3.3     | 1.7±2.4              | 0.601   |
| T-A (points)     | -2.5±7.5      | -5.5±6.1             | 0.155   |
| D (points)       | -1.1±3.6      | -4.7±10.9            | 0.160   |
| A-H (points)     | 0.3±3.2       | -1.7±5.4             | 0.145   |
| V (points)       | 0.7±8.0       | 1.0±4.1              | 0.906   |
| F (points)       | 2.7±8.2       | -5.2±8.3             | 0.003 * |
| C (points)       | -1.3±6.3      | -4.5±8.3             | 0.159   |
| TMD (points)     | -2.6±20.5     | -22.5±32.8           | 0.021 * |

Data are presented as mean ± standard deviation.

TUG, Timed Up and Go test; FR, functional reach test; CS-30, 30-s chair stand test; T-A, tension/anxiety; D, depression/defection; A-H, anger/hostility; V, vigor; F, fatigue; C, confusion; TMD, total mood disturbance

*Significant difference between Wii PT and Therapist PT (p<0.05)

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