



Original Article

Immediate effects of exercise intervention on cancer-related fatigue

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Abstract. [Purpose] To verify the immediate effects of exercise therapy on cancer-related fatigue (CRF) in cancer patients. [Subjects and Methods] Eighteen cancer patients who performed exercise therapy targeting a rating of 4 (somewhat strong) on the Borg category-ratio scale (CR-10) were enrolled. CRF was evaluated using the Cancer Fatigue Scale (CFS). CFS was evaluated in clinical practice immediately before and after exercise therapy on the 1st or 2nd day of physiotherapy for CRF management. CFS scores before and after exercise were compared to determine how CRF changed due to exercise therapy. [Results] CFS physical, CFS affective, CFS cognitive, and CFS total all decreased following exercise therapy, and the changes in CFS physical and CFS total were statistically significant. The effect sizes for CFS physical and CFS total were “medium”, and for CFS affective and CFS cognitive “small.” [Conclusion] These findings suggest that exercise therapy targeting a rating of 4 (somewhat strong) on the CR-10 can immediately reduce CRF in cancer patients.

Key words: Cancer-related fatigue, Cancer Fatigue Scale, Exercise therapy

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INTRODUCTION

The symptoms experienced by cancer patients are affected by a variety of factors related to the disease itself and the treatments used. Cancer-related fatigue (CRF) is one such symptom. According to the National Comprehensive Cancer Network (NCCN), “Cancer-related fatigue is a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning”¹). In total, 70–100% of cancer patients are said to experience CRF², and its presence can reduce their quality of life³, making managing CRF an important part of cancer therapy.

In the NCCN Guidelines¹, physical activity is a category-1 intervention for CRF management because “Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate”. Several studies have reported improved CRF as a result of exercise interventions^{4–6}. Segal et al.⁷ studied 24 bladder cancer patients receiving radiation therapy, and had them perform an aerobic exercise and strength training intervention for 24 weeks. They found that fatigue improved more in the intervention group than in the non-intervention group. While these studies showed that interventions are effective over a certain time period, in our clinic, we have observed patients who have experienced a reduction in fatigue immediately after an exercise intervention. However, the manner in which CRF changes immediately after an exercise intervention has not yet been described.

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With the above in mind, the objective of this study was to verify the immediate effects of exercise therapy on CRF in cancer patients.

SUBJECTS AND METHODS

The subjects were cancer patients hospitalized at the Cancer Center, Department of Radiology, Chemotherapy Center, or Department of Hematology at our hospital from August 1, 2012 to July 31, 2013. Patients were included if they underwent radiation and/or chemotherapy for cancer and performed exercise therapy in the form of leg strength and walking training under the guidance of a physical therapist. Patients were excluded if assessments were difficult because of reduced cognitive function, if they had difficulty performing exercise therapy, or if CRF was not evaluated.

CRF is normally evaluated in clinical practice immediately before and after exercise therapy on the 1st or 2nd day of physiotherapy for CRF management. We retrospectively collected the results of these CRF evaluations, as well as data regarding gender, age, body mass index, performance status (PS), type of cancer, types of treatment, and the Barthel index (BI) from electronic medical records. This study was approved by our university's ethics committee (No. H-25-162).

CRF was evaluated using the Cancer Fatigue Scale (CFS)⁸, which is a self-administered questionnaire developed to assess fatigue due to cancer. The CFS is a multidimensional scale consisting of three subscales: physical subscale (CFS physical), affective subscale (CFS affective), and cognitive subscale (CFS cognitive). The reliability, validity, and feasibility of the CFS were confirmed by a previous study⁹. The 15 questions included in the CFS are rated from 1–5 (1 no, 2 a little, 3 somewhat, 4 considerably, 5 very much) based on the patient's current condition. These scores are used to calculate scores for each subscale, as well as a total scale score (CFS total). For all scales, higher scores indicate more severe fatigue. The maximum scores are 28 points for CFS physical, 16 points for CFS affective, 16 points for CFS cognitive, and 60 points for CFS total. Patients whose CFS total is ≥ 19 points are considered to have severe fatigue⁹. The physical therapist in charge of each case handed the CFS questionnaire to the patient, and entered the score into the patient's electronic medical record.

The types of exercise therapy were standing-sitting training to strengthen the leg muscles and walking training to improve walking ability. For both exercises, intensity was set using the Borg category-ratio scale (CR-10), which is a subjective marker of exercise intensity¹⁰. In standing-sitting training, patients were asked to repeatedly stand up and sit down until they felt the intensity was equivalent to a rating of 4 (somewhat strong) on the CR-10. This number of repetitions was considered as one set, and each participant performed three sets in total. In walking training, patients were asked to walk continuously until they felt intensity equivalent to a rating of 4 (somewhat strong) on the CR-10. Again, this number of repetitions was considered as one set, and each participant performed three sets in total. The total duration of the exercise session was 20–40 min, including standing-sitting and walking.

After confirming the normality of the data with the Shapiro-Wilk test, the CFS scores before and after exercise were compared using a paired t-test. IBM SPSS version 21.0 for Windows (IBM Corp., Armonk, NY, USA) was used for the analysis. The significance level was set at 5%. G*Power 3.1.9.2¹¹ was used to calculate Cohen's d-values to determine the effect sizes in the paired t-tests. A Cohen's d-value of 0.20 was considered "small," 0.50 was considered "medium," and 0.80 was considered "large"¹².

RESULTS

Of the 24 patients who met the inclusion criteria, two were excluded because they did not take part in exercise therapy, one because CRF was difficult to assess due to reduced cognitive function, and three because CRF data were missing. This left 18 subjects with data suitable for analysis (Fig. 1). Table 1 shows the characteristics of these 18 patients. Before the exercise intervention, CFS physical was 10.9, CFS affective was 8.1, CFS cognitive was 4.8, and CFS total was 23.7. Fourteen patients were considered to have severe fatigue. After the exercise intervention, scores for CFS physical, CFS affective, CFS cognitive, and CFS total all decreased, and the differences in CFS physical and CFS total were statistically significant ($p=0.023$, $p=0.006$). The effect size was medium for CFS physical ($d=0.59$) and CFS total ($d=0.74$), and small for CFS affective ($d=0.05$) and CFS cognitive ($d=0.25$) (Table 2). CFS total decreased after exercise in 12 of 18 patients, increased in four patients, and did not change in two patients. Table 3 compares the characteristics of the groups with decreased CFS total (improved group) and increased/unchanged CFS total (non-improved group). Compared to patients in the non-improved group, those in the improved group tended to be older, and have higher PS and CFS total scores and lower BI.

DISCUSSION

In this study, we retrospectively investigated the immediate effects of exercise interventions on CRF in cancer patients hospitalized for radiotherapy and/or chemotherapy. Fourteen (78%) of the 18 subjects had severe fatigue. Hosokawa et al.¹³ evaluated cancer patients hospitalized in radiology departments using CFS, and found that 60.4% had severe fatigue. While the ratio of patients with severe fatigue was higher in the present study, all patients in our study were receiving radiotherapy or chemotherapy, while 14 patients (29.8%) in the previous study were not receiving either therapy.

Scores for CFS physical, CFS affective, CFS cognitive, and CFS total all decreased after exercise therapy, and the de-

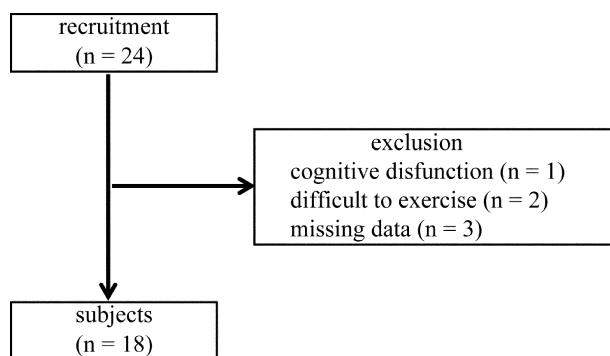


Fig. 1. Flowchart of subject enrollment.

Table 1. Characteristics of the study subjects

Age (yrs)	66.4 ± 16.6
Gender: Male/Female	11/7
Body mass index (kg/m ²)	19.8 ± 3.3
Performance status (grade)	2 (1–3)
Type of cancer:	
hematopoietic tumor/solid tumor	10/8
Type of therapy:	
radiation therapy/chemotherapy	10/8
Barthel index	85.2 ± 15.5

Gender, Type of cancer, Type of therapy are expressed as numbers.

Age, Body mass index, Barthel index are expressed as the mean ± standard deviation.

Performance status is expressed as the median with range.

Table 2. Cancer Fatigue Scale (CFS) values before (pre) and immediately (post) after exercise

	Pre	Post	Mean difference (95% CI)	p-value	Effect size
CFS physical	10.9 ± 4.9	8.3 ± 4.9	2.6 (0.4–4.8)	0.023	0.59
CFS affective	8.1 ± 2.8	7.9 ± 3.2	0.1 (–1.1–1.3)	0.847	0.05
CFS cognitive	4.8 ± 3.1	4.1 ± 3.4	0.7 (–0.7–2.0)	0.306	0.25
CFS total	23.7 ± 8.5	20.3 ± 8.7	3.4 (1.1–5.7)	0.006	0.74

Values are expressed as the mean ± standard deviation.
Effect size: Cohen's d.

Table 3. Differences in subject characteristics between the Cancer Fatigue Scale (CFS) total improved and worsened/unchanged groups

	Improved group (n=12)	Worsened/unchanged group (n=6)
Age (yrs)	67.5 ± 15.0	64.3 ± 20.8
Gender: Male/Female	8/4	3/3
Body mass index (kg/m ²)	20.9 ± 3.5	17.8 ± 1.5
Performance status (grade)	2 (1–3)	1 (1–2)
Type of cancer:		
hematopoietic tumor/solid tumor	4/8	6/0
Type of therapy:		
radiation therapy/chemotherapy	4/8	6/0
Barthel index	82.2 ± 17.8	91.2 ± 7.1
CFS total	25.8 ± 7.5	21.5 ± 10.8

Gender, Type of cancer, Type of therapy are expressed as numbers.

Age, Body mass index, Barthel index, CFS total are expressed as the mean ± standard deviation.

Performance status is expressed the median (minimum–maximum).

Increases in CFS physical and CFS total were statistically significant. Furthermore, the effect size of exercise therapy on CFS physical and CFS total was at least medium. These results suggest that exercise therapy immediately reduces CRF in cancer patients undergoing treatment.

Several studies have demonstrated that exercise therapy improves CRF. A meta-analysis by Brown et al.¹⁴⁾ concluded that exercise therapy was effective in improving CRF. However, the studies included in this meta-analysis described the long-term effects of exercise therapy, with exercise being performed for a mean of 3.5 days per week over a mean of 11.5 weeks. We were unable to find any previous studies that examined the immediate effects of exercise therapy on CRF. The novel findings of this study suggest that CRF improves immediately after exercise therapy.

Previous studies have used different exercise intensities for cancer patients. The studies in the meta-analysis published by Brown et al.¹⁴⁾ employed a mean exercise intensity of 4.5 METs for strength training, which is equivalent to moderate intensity (60–80% of 1 repetition maximum, 1-RM), and a mean exercise intensity of 5.6 METs for aerobic exercise (40–60% maximal oxygen consumption). Additionally, the American College of Sports Medicine (ACSM)¹⁵⁾ recommends 40–60% of 1-RM for strength training and 40–60% oxygen uptake reserve or heart rate reserve for aerobic exercise for cancer patients. In the present study, the intensity of strength training and aerobic exercise was set at a rating of 4 (somewhat strong) on the CR-10. Pincivero et al.¹⁶⁾ reported that this intensity of strength training is equivalent to 40% of 1-RM, which is lower than

the intensity of strength training used in the report by Brown et al.¹⁴⁾ but still within the ACSM's recommendations. For aerobic exercise, since we did not perform cardiopulmonary stress tests or other exams, it is difficult to compare the exercise intensity with that in previous studies or that recommended by the ACSM. However, Uwajima et al.¹⁷⁾ reported that a score of 13 on the Borg scale, which corresponds to a rating of 4 (somewhat strong) on the CR-10, is equivalent to the anaerobic threshold (AT). Furthermore, Zamunér et al.¹⁸⁾ reported that a rating of 5 (strong) on the CR-10 was equivalent to the AT, which indicates that the intensity of aerobic exercise in the present study was close to the AT-level intensity that is generally recommended. Moreover, when we compared the improved and non-improved groups after exercise, patients in the improved group had more severe CRF, greater age, and lower PS and BI. These findings suggest that exercise can immediately improve CRF in patients whose fatigue is more severe, who are older, whose general condition is worse, and whose daily activities are more limited. The reason for this was not clear. However, it may be that patients with these characteristics are generally bedridden for longer, and benefit more from exercise in terms of improved mood.

In clinical practice, patients with severe CRF tend to avoid exercise therapy. Such behavior can increase the risk of disuse syndrome. The findings of the present study suggest that exercise therapy targeting a rating of 4 (somewhat strong) on the CR-10 can be performed without aggravating CRF.

One limitation of this study is the lack of a control group, which made it impossible to demonstrate the true effects of exercise therapy. In addition, we did not clarify how exercise therapy caused the immediate decrease in CRF. Moreover, we did not consider the diurnal variation of CRF or the subjects' physical condition. We needed to select the time of CRF evaluation (e.g. morning, afternoon, and time of best or worst physical condition). Finally, the sample size of this study was small, and subjects with various types of cancer were included. We believe that despite these limitations, the results of this study are still clinically significant. In the future, investigations including control groups will be necessary to identify the factors involved in immediate reductions in CRF.

We investigated the immediate effects of exercise therapy on CRF in hospitalized cancer patients undergoing radiotherapy and/or chemotherapy. The results showed that CFS scores decreased immediately after exercise therapy, which suggests that exercise therapy targeting a rating of 4 (somewhat strong) on the CR-10 may produce an immediate decrease in CRF.

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