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Randomized Trial of Exercise and an Online Recovery Tool to Improve Rehabilitation Outcomes of Cancer Survivors

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Abstract

Purpose—The purpose of this study was to test the effects of a cancer survivor exercise program and an online recovery awareness program (Restwise) on physical outcomes of aerobic capacity and muscle strength.

Design—Randomized controlled trial design. Setting: Treasure Valley Family YMCA, Boise, ID. Sample: Fifty cancer survivors.

Methods—Subjects were randomly assigned to the 12-week exercise program or the exercise program and Restwise. Restwise required users to complete daily objective and subjective ratings. Restwise compiles these data to provide individualized feedback recommending the exercise dose to maximize recovery and minimize fatigue.

Main Research Variable—Baseline and posttest measures of physical performance (6-minute walk, 1-repetition maximum of lower and upper body strength).

Findings—The exercise plus Restwise group demonstrated significant improvements ($P < 0.001$) that were found on all 3 physical measurements of strength and endurance. The exercise-only group demonstrated significant within-group improvement only on the 6-minute walk. The exercise plus Restwise group demonstrated an 18.5% greater improvement in the 6-minute walk, and a 35.2% and 45%, respectively, greater improvement on the leg and chest press than the exercise-only group. However, the between-group differences were not significant.

Conclusion—Cancer survivors who use the Restwise online recovery program in conjunction with an exercise program demonstrated minimal clinically important differences compared with other clinical populations on all 3 measures, whereas the exercise-only group had improvements only on the 6-minute walk. Patient adherence to the Restwise program was good, and patients provided positive feedback.

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Keywords

cancer; rehabilitation; recovery; physical activity; exercise

Introduction

Cancer and its treatment are arduous and cause many lingering acute, late, and long-term side effects.^{1,2} These side effects include fatigue, muscle weakness, lowered aerobic capacity, poor balance, reduced flexibility, and many other factors that affect quality of life. Fatigue is the most common problem reported by cancer survivors; it begins during treatment and often persists many years after treatment is complete.³ Physical inactivity after cancer treatment is common; it accounts for significant declines in aerobic capacity and muscle strength in cancer survivors and contributes to persistent fatigue and weakness.⁴⁻⁸

Physical exercise, both aerobic and resistance, is a recognized intervention to improve fatigue and many other side effects including weakness, muscle strength, aerobic capacity, balance, flexibility, and many aspects of quality of life.^{1,2,6,9} Although there is strong research to support the benefits of exercise for cancer survivors both during and after cancer treatment, the rate of recovery from treatment is limited by survivors' ability to monitor and manage their fatigue and energy, as well as regulate their exercise dose and energy expenditure. Cancer survivors tend to overdo their activity on days they feel good, often resulting in several days of exhaustion, which has led to strategies and recommendations for energy conservation for fatigue management rather than exercise.^{3,10} Cancer survivors could potentially benefit from an intervention to help them learn not only how to manage their fatigue and energy expenditure but also how to adjust their exercise dose to improve and hasten recovery.

The concept of energy management or recovery is difficult, even for an elite athlete who is prone to overexerting. The science of exercise training has identified specific indicators of overtraining (eg, changes in heart rate, mood, appetite, sleep), and athletes use these, to varying degrees of success, to reach their peak performance.¹¹ Competitive athletes often monitor deviations from their baseline values to determine their risk of overexerting and make informed decisions on training load based on this feedback. Similarly, cancer survivors seek an optimal level of functioning. Although many approaches to energy conservation have been tested, and some have demonstrated efficacy, no approach has applied the science of overtraining or overexerting in athletes to cancer survivors who tend to overexert when they feel good and then have several days of exhaustion.¹⁰

Restwise (Recovery Science & Technology, LLC; Concord, MA) is an online recovery program that has demonstrated preliminary efficacy with Olympic and collegiate athletes (unpublished data) and uses various physiological and subjective markers to provide an individualized exercise recommendation each day it is used. A similar approach to monitoring fatigue or overexertion in cancer survivors could provide an effective self-help guide to making informed decisions to improve cancer recovery. This approach may prove superior to simple advice to exercise from oncology professionals who, even with published

guidelines to manage fatigue that focus on physical activity, continue to recommend energy conservation and often do not advocate exercise.³

The purpose of this pilot study was to test the effect of an online recovery and feedback system (Restwise) on cancer survivors who were participating in a YMCA cancer survivor exercise program, Cancer Fitness Fundamentals. The hypothesis was that survivors randomized to the Restwise intervention would be guided in their exercise prescription by the online recovery program and have greater improvements in physical outcomes than the exercise alone group.

Materials and Methods

Study Design

A 12-week randomized controlled design was used. This time frame was selected as it was thought to provide sufficient time to see changes in the physical outcomes; it also is the length of the Cancer Fitness Fundamentals program. Institutional review board approval was obtained for all study procedures, and study staff received training in human subject protection. After consent was obtained, subjects were randomly assigned to exercise alone or exercise plus Restwise. The project manager informed subjects of their group assignment and explained the study procedures. Subjects in the Restwise group were given step-by-step instruction on how to log on, access, and use the program.

Participants

Cancer survivors were recruited through referral by oncologists, oncology nurses, physical therapist, and fliers placed in the Treasure Valley Family YMCA, Boise, ID. Sixty cancer survivors volunteered to participate in the 12-week exercise study with or without the recovery program (Restwise). Eligible subjects were 18 years old, had a diagnosis of cancer, and had received or were currently receiving chemotherapy and/or radiotherapy. None of the subjects were participating in a regular exercise program at entry into the study. All subjects were informed of the study expectations and possible risks of participating before providing written informed consent.

Exercise Intervention Program

The Cancer Fitness Fundamentals program is a 12-week supervised 1-on-1 exercise program conducted by cancer trainer specialists at Treasure Valley Family YMCA, Boise, ID. The Cancer Fitness Fundamentals program is a blend of supervised and unsupervised exercise sessions. Once a week, all participant receive a 1-hour, 1-on-1 supervised exercise session and specific instructions on exercises (aerobic and resistance) to complete 2 or 3 additional days a week on their own either at the YMCA or at home.

Supervised exercise training followed a standardized protocol that included a period of progressive warm-up, 20 minutes of aerobic exercise on a machine of the subject's choosing beginning at an intensity of 60% to 70% of aerobic capacity, and 3 to 5 resistance (muscle strengthening) exercises for both the upper and lower body. Individuals were given specific exercise instructions to follow a similar workout on their own the other days of the week. On

the days participants exercised on their own, they were encouraged to follow the specific instructions they received for resistance exercises that were individualized to each person's ability or physical limitations. In general most subjects were instructed to engage in 4 upper body exercises, 3 lower body exercises, 1 core strengthening exercise, and an aerobic exercise that they enjoyed (eg, cycling, walking, swimming). The dose of exercise (sets/repetitions/weight for resistance exercise and duration and intensity) progressively increased over time. Workload intensity was individualized based on the abilities and limitation of each subject as determined at baseline on tests of aerobic capacity (6-minute walk) and upper and lower body muscle strength (1-repetition-maximum [1-RM] tests). The workload intensity and volume progressed following the American College of Sports Medicine exercise guidelines for cancer survivors and recommendations for exercise progression for people at risk for lymphedema.^{9,12} All study participants received a free membership to the YMCA, which included the use of all equipment (eg, weight machines, free weights, treadmills, recumbent and upright stationary bicycles, rowing machines), swimming pools, and group exercise classes.

Recovery Intervention

Subjects in the exercise plus Restwise group participated in the Cancer Fitness Fundamentals exercise program and were given access and instruction to use the online recovery tool. All Restwise subjects received a pulse oximeter, training in how to use it properly, and instruction on how to log on to Restwise and record their information every day. Restwise is an online recovery assessment tool that requires the user to input daily data for resting heart rate, oxygen saturation by pulse oximeter, weight, mood state, energy level, sleep, training performance, muscle soreness, appetite, and hydration. The data is weighted to provide a daily recovery score, which then provides users with individualized specific guidance and recommendations on the optimal training load for that day. For example, based on the information that subjects enter, they may receive feedback to reduce their exercise duration and intensity, or even to take the day off and recover. The information is also color-coded, with green indicating good to exercise, yellow to exercise with caution, and red to rest. Subjects were instructed to use the feedback to guide their exercise intensity and duration. Exercise trainers were not blinded to group but did not receive the feedback from Restwise for subjects in that group. At the end of the study, user access to Restwise was open for 3 weeks and users were able to continue using the program and were invited to provide comments about their experience using Restwise. At the conclusion of the study, Restwise users were asked to provide positive and negative feedback about their experience using the program to help further refine the program for cancer survivors.

Physical Performance Measures

Aerobic capacity was assessed by the 6-minute walk—a safe, valid, and reliable measure used in healthy and chronically ill populations.¹³ All subjects were asked to walk as fast and as far as they could for 6 minutes over a premeasured area following standard guidelines.¹² Maximum upper and lower body strength was assessed by a 1-RM test on a chest press and leg press machine. The same machines were used at baseline and posttest. The machines did not require calibration; seat height and equipment positioning were constant at both testing periods. The equipment increased in weight by 5-pound increments. A familiarization trial

included proper lifting technique and practice before the maximum load was determined. The 1-RM test is a safe, clinically relevant, and valid method to assess changes in muscle strength for fit and unfit people, the elderly, and cancer survivors.^{14–16}

Analyses

All analyses were conducted using SPSS version 21.0 (SPSS Inc., Chicago, IL). Demographic characteristics of participants at baseline were summarized using frequencies and descriptive statistics. To compare the 2 groups (exercise only vs exercise plus Restwise) on baseline characteristics, independent-sample *t* tests were used for numerical variables and χ^2 tests for categorical variables.

To assess whether change from baseline to 12-week follow-up was different between the 2 groups, multivariate regression analyses were conducted with the physical measures (6-minute walk and 1-RM strength testing). First, the overall main effect for group membership on the outcomes was evaluated. Second, contrasts of the interaction of group (exercise only vs exercise plus Restwise) by time (from baseline to 12-week follow-up) tested to examine the difference in change for each outcome variable between groups over time.

Results

Baseline Characteristics

Sixty subjects volunteered to participate, 50 of whom completed the pilot study (38 women and 12 men). The 10 subjects who did not complete the study (8 women and 2 men) were evenly divided between the 2 groups. Reasons for quitting were being too sick or required additional treatment (*n* = 5) and work or family obligations that prevented participation (*n* = 5). Three subjects signed consent but did not complete baseline measures; the 7 others quit within the first 2 weeks of beginning the program. Scores on baseline demographics and physical performance measures were not statistically significantly different between the dropouts and those who completed the study; consequently, the dropouts were eliminated from the analyses.

A total of 50 cancer survivors completed the intervention, 25 in each group. All participants who completed the baseline testing also completed the follow-up. On the 12 outcome measures across 2 time points and 50 participants, only 7 total data points were missing (99.42% complete, 0.58% missing). Baseline characteristics are summarized in Table 1. The most common cancer was breast cancer (*n* = 27, 54%), followed by hematologic cancer (eg, leukemia, lymphoma; *n* = 12, 24%), prostate (*n* = 3, 6%), melanoma (*n* = 3, 6%), colorectal (*n* = 2, 4%), bladder (*n* = 2, 4%), and head/neck cancers (*n* = 1, 2%). Mean duration of survivorship was 2.2 years. At baseline, on average, participants were 52.4 years old (± 12.95), 76% were female, and 14.3% were on treatment. The baseline 6-minute walk distance was 445 meters (m) (± 105). The mean leg press across all participants was 127.8 $\pm$ 70.82 lb and the chest press was 91.5 $\pm$ 45.66 lb. None of the demographic characteristics or outcome variables was significantly different between the 2 groups at baseline, suggesting that randomization was successful.

Adherence to Exercise and Restwise

Adherence to the Cancer Fitness Fundamentals program was 92% for both groups. Exercise plus Restwise subjects recorded their online data in Restwise 82% of the time (mean = 69 days, range = 0–84 days). Subjects were asked to complete the online assessment every day, but only 82% of subjects completed the assessment > 5 days a week. Two subjects never used the Restwise program and only 1 subject entered scores < 4 days a week. Scores on the program ranged from 100 (highest composite score, indicating complete recovery) to 27 (a low composite score indicating that rest and recovery is needed) and guided subjects in changing their exercise. When subjects received a score of 80% to 100% they were encouraged to follow their usual exercise routine. Scores in the 70s advised subjects to be cautious with their exercise and consider reducing their exercise dose. Scores < 70 recommended reductions in exercise or rest. Restwise recommended subjects exercise with caution 16% of the time, reduce their exercise dose 17% of the time, and rest 5% of the time.

Exercise plus Restwise users reported that the program was easy to use and that the feedback was useful and allowed them to learn the relationship between the way they felt (symptoms reported) and how hard to exert themselves. They reported it was “reassuring to be told I am OK to exercise” when they did not think they should. Users reported that they learned to increase hydration, rest, or exercise based on the simple feedback and learned that they were misinterpreting some symptoms. Three users were surprised that a program developed for athletes could help them at their low level of exercise. More than half the users recommended tailoring the feedback to be specific to cancer survivors. Thirty-two percent of users continued using the program after the study ended.

Changes from Baseline to Follow-Up

From baseline to follow-up, there was an overall significant improvement across the entire sample on the outcome measures. The overall multivariate test for change in the outcomes was significant ($F[df = 3] = 19.77, P < 0.001$). Within each group, improvements were seen across the board, although the pattern was slightly different in each group (Table 2). For the Exercise plus Restwise group, significant improvements ($P < 0.001$) were found on all 3 physical measurements of strength and endurance. Participants improved their 6-minute walk distance by an average of 68.8 to 507 m, an improvement of 15.7%; and improved on the leg press by 28.0% (36.8 lb) and the chest press by 30.1% (30 lb). For the exercise-only group, significant within-group improvement was found on the 6-minute walk, but not on the chest press and leg press. When these changes are compared and expressed in proportions, the exercise plus Restwise group demonstrated an 18.5% greater improvement in the 6-minute walk, a 35.2% greater improvement in the leg press, and a 45% greater improvement on the chest press than the exercise-only group. Although these differences may not be statistically significant between groups, they fall within the range to be considered minimal clinically important differences, which are estimated to be 25 m for patients following acute coronary syndrome, to 50 m for community-dwelling older adults, to 86 m for patients with cardiorespiratory disorders.^{17–19}

Between Group Contrasts Over Time

Despite the slightly different patterns of within-group improvements from baseline to 12-week follow-up, contrasts of the time (from baseline to 12-week follow-up) by group (exercise only vs exercise plus Restwise) interaction revealed that only 1 of the outcome variables, 1-RM leg press, improved marginally more among the exercise plus Restwise group compared with the exercise-only group (36.8 lb improvement compared with 13.3 lb improvement, $P = 0.071$ for comparison).

Discussion

Fatigue and weakness are the most common and troubling side effects of treatment for cancer survivors. Cancer treatment causes profound weakness, fatigue, deconditioning, and debilitation.^{20,21} Recovery from cancer can take many months, and survivors are often faced with lingering side effects that interfere with meaningful activities. Exercise is an intervention that helps restore physical and psychological health of cancer survivors.⁹ Yet, even today, most cancer survivors with weakness, fatigue, and deconditioning are counseled in energy conservation strategies that focus on rest and relaxation and not exercise.^{3,22} Research demonstrates that muscle weakness and inactivity predict fatigue, and a consistent association is observed among inactivity, aerobic capacity, muscle strength, weakness, and fatigue.^{23–29}

The baseline 6-minute walk distance demonstrates the poor fitness level of the cancer survivors in this study and the profound effect of inactivity. All subjects in this study were in worse physical condition at baseline than is observed in community-dwelling adults in general. For example, among nonsmoking community-dwelling adults, Steffen and colleagues³⁰ found an average distance walked of 572 m for men and 538 m for women aged 60 to 69 years. Even after the 12-week exercise program, subjects in this study had not attained the average aerobic fitness level of community-dwelling adults who were, on average, 10 years older than the cancer survivors in this study. This finding points to the critical need for rehabilitation programs to improve the functional capacity and ability of cancer survivors.

This pilot study was community based, and as such, used the 6-minute walk distance as a convenient, clinically reliable measure of aerobic capacity. Although some may argue that the 6-minute walk test is more of a functional test than a measure of aerobic capacity, we selected this measure because of the community-based nature of this study. A laboratory measure of oxygen uptake would have given a more comprehensive measure, but the feasibility of oxygen uptake testing is limited by resources and the functional ability of the subject.

Although both groups benefited from exercise, the exercise plus Restwise group demonstrated greater improvements, a nonsignificant finding that reflects the limitations of the small sample size. In this pilot study, we suspected, but did not measure, that the Restwise program may have had a positive effect by helping cancer survivors learn to regulate their energy and exercise dose, which led to greater physical performance improvements. Restwise may have helped users learn not only to balance their energy

expenditure but also to become more aware of their symptom interpretation. Use and adherence with Restwise was consistent, and many users continued using the program after the study ended, suggesting that the feedback provides survivors with useful information that may have promoted greater symptom awareness, ultimately offering the potential to facilitate a quicker recovery from cancer treatment. However, future research is needed to examine this relationship.

This pilot study demonstrated the feasibility of Restwise, but further research is needed to examine the mechanism of how Restwise works, which we believe to be self-regulation.³¹ Restwise appears to help users become more aware of their state of recovery and learn to translate that knowledge and understanding into decisions about their current fatigue state and the energy they could expend. After the subjects submitted daily recordings of resting heart rate, a scientifically determined algorithm analyzed the subjects' oxygen saturation, body mass, mood state, energy level, sleep, training performance, muscle soreness, appetite, and hydration, and the user received specific feedback about their level of recovery and how hard to exert themselves during the day. We believe that the daily input of symptoms into the Restwise program may hasten behavioral awareness and ultimately self-regulation. The individualized instructional information provided by Restwise makes the cancer survivor aware of how their current state influences how much they can and should do to improve their physical fitness without getting overextended. This self-monitoring appears to help cancer survivors make better decisions about not just exercise, but also, perhaps, about how much they can do on good days and bad days, and increases awareness about hydration and symptoms that can often be ignored. The Restwise information may eliminate the self-doubt that often drives cancer survivors to do too much and ultimately feel exhausted or conversely to protect themselves and rest and become more debilitated.

This pilot study demonstrated that cancer survivors who use the online Restwise recovery program in conjunction with an exercise program had minimal clinically important differences in physical performance. It is unclear whether these survivors actually exercised more often or whether Restwise guided them to rest and exercise more efficiently, such as with greater intensity, on "good" days. These survivors were able to access the recovery program and use the recommendations to adjust their daily activities according to the feedback they received. This individualized feedback was more specific than what they would typically receive from their oncology team or a personal trainer and is focused on improving survivors' performance and ability to pursue activities that are meaningful. Restwise goes beyond an energy conservation intervention in that the tool recommends exercise dose or load, and it encourages hard exercise or rest and recovery as appropriate. Exercise logs were not maintained, so we do not know if the survivors in this group actually exercised more, or rested more and were then able to exercise at a higher intensity or volume because they were rested. This is a question for future study.

Although this pilot study was limited in its focus to physical outcomes, learning to attend to present-moment body experiences and developing an ability to interpret and understand their meaning may be helpful in recovery. The Restwise recovery program may have helped survivors make a constructive shift in their symptom interpretation and learn how to dose not only their exercise but also their energy expenditure in daily activities. Much like the

self-regulation and coping research that demonstrates how information processing can help with stressful experiences,^{32,33} Restwise may increase awareness of one's physical and emotional state, which may hasten the physical recovery of cancer survivors. This shift in awareness may explain why cancer survivors who followed the exercise program and used the Restwise recovery program had clinically greater improvements in aerobic capacity and muscle strength.

Study Limitations

This pilot study suffered from the lack of a usual-care control group, which would have added depth to the results. However, because a large body of evidence supports exercise as a clinical recommendation to improve the physical health of survivors, we felt that using a control group posed an ethical challenge.^{34–37} Additionally, we felt the most rigorous test of Restwise was a study examining the differences between subjects enrolled in the same exercise program. In spite of this, results from exercise studies using control groups consistently demonstrate that the usual-care control groups do not improve in aerobic capacity or muscle strength over time.^{4,5,7,8} Actually, most studies demonstrate a significant decline in aerobic capacity and muscle strength.^{4,6,7} The aerobic capacity of usual-care groups demonstrates declines in activity level over time when measured by number of steps per day, metabolic equivalent levels, 12-minute walking distance, and peak oxygen consumption over 12- and 15-week time periods.^{4–6} These declines are even greater over longer periods of time.

Another limitation is that the subjects were self-selected and could be called “health-seekers.” These highly motivated cancer survivors were willing to participate in the program and may not represent the community of cancer survivors as a whole. Finally, the study lacked a measure of fatigue. Although we speculate that Restwise may have benefits for energy conservation and symptom interpretation, further study is warranted prior to drawing any conclusions about these relationships.

Conclusion

Rehabilitation outcomes from cancer may be positively affected by the use of an online recovery program, such as Restwise. This pilot study demonstrates that the program is easy to use and feasible. Although statistically significant differences were not observed between the exercise groups, the Restwise group demonstrated clinically important increases in aerobic capacity and functional ability. Exercise and energy conservation approaches have demonstrated efficacy, but none has been able to help survivors interpret and manage their symptoms in a systematic and easy manner. The use of an online tool is feasible and may improve outcomes, but further research is needed to refine the Restwise program, tailor the messaging feedback to cancer survivors, and confirm these findings in a larger sample of cancer survivors. Further research is needed to examine how Restwise influences exercise adherence and self-management.

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Table 1
Baseline Characteristics of Participants in the Exercise Intervention and Restwise Intervention

Variable	Total (SD or %)	N	Exercise (n = 25)	Exercise + Restwise (n = 25)	P value
<i>Demographic variables:</i>					
Age (years)	52.42 ($\pm$ 12.95)	50	53.96 ($\pm$ 11.45)	50.88 ($\pm$ 14.36)	0.406
<i>Sex</i>					
Female	38 (76.0%)	38	21 (84.0%)	17 (68.0%)	0.185
Male	12 (24.0%)	12	4 (16.0%)	8 (32.0%)	
On treatment	7 (14.3%)	49	4 (16.0%)	3 (12.5%)	0.726
<i>Physical measures:</i>					
6-minute walk (meters walked)	445.2 ($\pm$ 105.5)	50	445.5 ($\pm$ 87.1)	444.8 ($\pm$ 123.1)	0.984
1-repetition-maximum leg press (lb)	127.8 ($\pm$ 70.8)	50	128.2 ($\pm$ 74.6)	127.4 ($\pm$ 68.3)	0.969
1-repetition-maximum chest press (lb)	91.5 ($\pm$ 45.7)	48	85.6 ($\pm$ 47.9)	97.0 ($\pm$ 43.8)	0.392

Table 2

Changes in Physical Fitness Indicators from Baseline to 12-Week Follow-Up of Participants in the Exercise Intervention and Restwise Intervention

Variable	Exercise (n = 20)		Change	Exercise + Restwise (n = 23)		Change	F-test ^a value	P value ^a
	Baseline (SD)	Follow-up (SD)		Baseline (SD)	Follow-up (SD)			
<i>Physical measures:</i>								
6-minute walk (meters walked)	451.6 (± 81.6)	514.0 (± 106.7)	+62.4 ^b	438.2 (± 126.0)	507.0 (± 97.1)	+68.8 ^b	0.12	0.752
1-repetition-maximum leg press (lb)	139.5 (± 76.4)	152.8 (± 70.6)	+13.3	131.5 (± 69.7)	168.3 (± 82.8)	+36.8 ^b	2.33	0.071
1-repetition-maximum chest press (lb)	84.4 (± 50.1)	99.8 (± 31.6)	+15.4	99.6 (± 44.5)	129.6 (± 57.3)	+30.0 ^b	1.11	0.165

^aF-test and P value for comparison of change from baseline to 12-week follow-up between groups (group by time interaction) based on multivariate generalized linear model.

^bSignificant at $P < 0.001$.