

Effects of a Supervised Exercise Intervention on Recovery From Treatment Regimens in Breast Cancer Survivors

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Purpose/Objectives: To investigate the effects of supervised exercise training on cardiopulmonary function and fatigue in cancer survivors undergoing various clinical treatments.

Design: Pretest and post-test quasiexperimental.

Setting: Outpatient oncology rehabilitation center.

Sample: 96 breast cancer survivors undergoing various clinical treatments.

Methods: Subjects were divided into four groups based on the specific type of clinical treatment: surgery alone ($n = 22$); surgery and chemotherapy ($n = 30$); surgery and radiation ($n = 17$); and surgery, chemotherapy, and radiation ($n = 27$). Following a comprehensive screening and medical examination, cardiovascular endurance, pulmonary function, and fatigue were assessed, leading to the development of an individualized exercise prescription and a six-month exercise intervention. Repeated-measures analysis of variance and covariance were used to compare the effectiveness of the intervention and differences among treatment groups.

Main Research Variables: Systolic and diastolic blood pressure, resting heart rate, forced vital capacity, forced expiratory volume, predicted oxygen consumption, time on treadmill, and fatigue.

Findings: Cardiopulmonary function (predicted maximal oxygen consumption and time on treadmill) significantly increased in all groups after exercise training. In addition, resting heart rate and forced vital capacity significantly improved in those receiving surgery, chemotherapy, and radiation. Psychologically, the exercise intervention resulted in significant reductions in behavioral, affective, sensory, cognitive and mood, and total fatigue scale scores in all three groups who received treatment with surgery. The breast cancer survivors in the surgery-alone group showed significant reductions in behavioral, affective, and total fatigue scale scores but not in sensory and cognitive and mood fatigue scale scores.

Conclusions: The results suggest that moderate intensity, individualized, prescriptive exercise maintains or improves cardiopulmonary function with concomitant reductions in fatigue regardless of treatment type. Moreover, cancer survivors receiving combination chemotherapy and radiotherapy following surgery appear to benefit to a greater extent as a result of an individualized exercise intervention.

Implications for Nursing: Clinicians need to be aware of adjuvant therapies such as moderate exercise that attenuate negative side effects of cancer treatments. Symptom management recommendations should be given to cancer survivors concerning the effectiveness of exercise throughout the cancer continuum and the importance of participating in a cancer rehabilitation exercise program.

Key Points . . .

- Cancer therapy not only impacts tumors and mutant cells but also can cause deleterious side effects on healthy tissue, resulting in acute and chronic physiologic and psychological negative symptoms.
- Research indicates that the severity of cancer treatment-related symptoms may depend on the type of treatment.
- Exercise training results in many positive physiologic and psychological benefits.

merous therapeutic modalities such as surgery, chemotherapy, and radiotherapy. The type and technique of therapy used, alone or in combination with another treatment, are selected based on factors such as response rate, drug sensitivity, and side effects (Schneider, Dennehy, & Carter, 2003).

However, the impact of surgery, chemotherapy, or radiation is not limited to tumors or mutant cells; these treatments also cause deleterious effects on healthy tissues, resulting in acute and chronic physiologic and psychological negative symptoms in cancer survivors (Chabner & Longo, 2001; Gianni et al., 2001). Surgery has been correlated with fatigue in breast cancer survivors (Cimprich, 1993), whereas chemotherapy often

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The American Cancer Society ([ACS], 2008) estimated that 1,437,180 people will be diagnosed with new cases of cancer in 2008. Advances in technology and the effectiveness of cancer treatments have helped to significantly increase cancer survival rates. Cancer treatments include nu-

Participants

Subjects were chosen from women who were referred by local oncologists to the Rocky Mountain Cancer Rehabilitation Institute (RMCRI) for rehabilitative exercise immediately following treatment for breast cancer. The university institutional review board approved all study procedures. Informed consent was obtained prior to participation in the study.

Assessment and Reassessment

Trained, certified cancer exercise specialists completed all assessments, exercise interventions, and reassessments. Cancer exercise specialists complete coursework, assessment observations, shadowing, and reliability testing before working with cancer survivors.

The cancer survivors received comprehensive screening followed by an initial medical examination prior to inclusion in the study. Cardiovascular endurance, pulmonary function, and fatigue were assessed leading to the development of individualized exercise prescriptions. Cardiovascular endurance (the ability of the heart, lungs, and circulatory system to supply oxygen to working muscles efficiently, therefore allowing for the production of energy for activities of daily living) was evaluated using the three-minute stage of the Bruce Treadmill Protocol, a multistage, variable speed, and elevation treadmill protocol. The Bruce protocol correlation coefficient is $r = 0.91$ with a standard error of estimate of 2.7 ml/kg per minute. Heart rate, blood pressure, oxygen consumption (predicted VO_{2max}), time on treadmill, and oxygen saturation were obtained from the Bruce protocol results. Participants continued to a predetermined heart rate or voluntary fatigue, dependent on the recommendation of the medical director of the institute.

Pulmonary function was assessed using a Flowmate™ spirometer, which measures forced vital capacity (FVC) and forced expiratory volume (FEV_1). Three tests were performed and were reproducible within 5% of each other. The participant's measured result was compared to predicted normative data tables for FVC and FEV_1 based on the participant's age, gender, height, and weight to obtain the percentage of predicted ($FVC \%_{pred}$ and $FEV_1 \%_{pred}$). An $FVC \%_{pred}$ less than 75% suggests a restrictive disorder, and an $FVC \%_{pred}$ less than 60% suggests ventilatory disorder. Likewise, an $FEV_1 \%_{pred}$ less than 75% suggests an obstructive disorder and less than 60% suggests a ventilatory disorder.

The revised Piper Fatigue Scale (Piper et al., 1998) was used to assess cancer-related fatigue. The behavioral fatigue subscale includes six questions and was used to assess the impact of fatigue on school and work, interacting with friends, and the overall interference with activities that are enjoyable. The affective fatigue subscale includes five questions and was used to assess the emotional meaning attributed to fatigue. The sensory fatigue subscale includes five questions and was used to assess the mental, physical, and emotional symptoms of fatigue. The cognitive and mood fatigue subscale includes six questions and was used to assess the impact of fatigue on concentration, memory, and the ability to think clearly. The average score on the 22 total questions from the subscales provided the total fatigue score (Piper et al.). Patients are to circle the number that best describes the fatigue they are experiencing now. The Likert scale on the Piper Fatigue Scale ranges from 0 (none) to 10 (a

leads to general fatigue (Byar, Berger, Bakken, & Cetak, 2006; de Jong, Kester, Schouten, Abu-Saad, & Courtens, 2006) and impaired exercise tolerance (Pihkala et al., 1995). Nail, Jones, Greene, Schipper, and Jensen (1991) reported that fatigue afflicts up to 96% of cancer survivors receiving chemotherapy. Radiation therapy has been implicated in the occurrence of interstitial myocardial fibrosis (Renzi, Straus, & Glatstein, 1992) and coronary and carotid artery arteriosclerosis (Rubin, Finkelstein, & Shapiro, 1992). Hickok, Morrow, McDonald, and Bellg (1996) demonstrated that radiotherapy resulted in fatigue in 78% of cancer survivors. Chemotherapy and radiation have been linked to impairments in left ventricular function, often manifested as altered ventricular morphology, abnormal pressure and volume relationships, and decreased left ventricular ejection fraction (d'Avella et al., 1998; Rubin et al.). When used concomitantly, the effect of these therapies on the cardiovascular and muscular systems appears to be magnified (Bezwada et al., 1998). The magnitude and variability of these alterations suggest that cancer treatment-related fatigue is the result of a myriad of factors and specifically may be affected by the course of treatment.

Studies have shown that exercise training results in many positive physiologic and psychological benefits in cancer survivors (Coleman et al., 2003; Dimeo, Stieglitz, Novelli-Fischer, Fetscher, & Keul, 1999; Drouin et al., 2006; Mock et al., 1997, 2001; Mutrie et al., 2007; Pinto, Clark, Maruyama, & Feder, 2003; Schneider, Hsieh, Sprod, Carter, & Hayward, 2007; Schwartz, 1999, 2000; Segal et al., 2001; Turner, Hayes, & Reul-Hirche, 2004). Researchers have investigated the benefits of exercise training in breast cancer survivors receiving surgery, chemotherapy following surgery, radiotherapy following surgery, or chemotherapy and radiotherapy following surgery. For example, Gaskin, LoBuglio, Kelly, Doss, and Pizitz (1989) and Turner et al. investigated the effects of an exercise intervention on breast cancer survivors after surgery. Others (Dimeo et al., 1997, 1999; Schwartz, 1999, 2000; Segal et al.) have reported the effects of exercise intervention on breast cancer survivors receiving chemotherapy following surgery. In addition, studies (Mock et al., 1997, 2005) have reported the effects of exercise on breast cancer survivors receiving radiotherapy following surgery. Moreover, the effects of exercise have been studied in breast cancer survivors who had completed surgery, chemotherapy, and/or radiation (Courneya et al., 2003; Mock et al., 2001; Mutrie et al.; Pinto et al.).

Initial research indicates that the severity of cancer treatment-related symptoms may be dependent on the type of treatment. For example, chemotherapeutic agents each impart unique side effects and long-term sequelae. In addition, chemotherapy and radiotherapy produce distinct detriments in cancer survivors that may be partially responsible for the variance in reported fatigue levels. Cancer survivors who had received a combination of chemotherapy and radiotherapy following surgery experienced higher levels of fatigue and scored lower during a functional capacity assessment than those survivors receiving chemotherapy or radiotherapy exclusively (Woo, Dibble, Piper, Keating, & Weiss, 1998). However, no investigation has specifically determined if the benefits of supervised exercise intervention are influenced by the type of treatment received by cancer survivors. Therefore, the purpose of the present study was to investigate the effects of supervised exercise training on cardiopulmonary function and fatigue in cancer survivors undergoing differing clinical treatments.

great deal) of fatigue. The higher the score, the greater the patient fatigue. The revised Piper Fatigue Scale has a standardized Cronbach alpha of 0.97 with subscales reliability estimates ranging from 0.92–0.96. Reassessments were obtained following a six-month individually prescribed exercise intervention. The same physiologic and psychological parameters were assessed using identical protocols during the initial assessment and reassessment to obtain program effectiveness outcomes.

Exercise Prescription and Intervention

Certified cancer exercise specialists developed individualized exercise prescriptions and exercise interventions to meet the specific needs of each breast cancer survivor based on results from the medical and cancer history, the physical examination, and the initial physiologic and psychological assessments. Participants attended individually supervised exercise sessions two or three days per week for six months. Prior to each training session, the cancer exercise specialists asked each participant a series of questions that would clarify the need to alter the exercise intervention, if necessary. Questions focused on how participants felt after the last exercise session, if participants had any soreness or specific problems that would affect training, and if changes in medication or treatment had been implemented since the last exercise session. The exercise sessions lasted 60 minutes and were based on a “whole-body” approach (Schneider et al., 2003). Each exercise session was individualized for the cancer survivor but generally included a 10-minute warm-up, 40 minutes of aerobic exercise, resistance training and stretching, and concluded with a 10-minute cooldown. Exercise intensity was based on the cancer survivors’ treadmill assessment results, and ranged from 40%–75% of heart rate reserve depending on the participants’ health status. The Karvonen or percent heart rate reserve method was used to determine exercise heart rate intensity using the formula (exercise target heart rate = [(220–age) – resting heart rate] x percent of exercise intensity + resting heart rate). The mode of aerobic exercise selected for each participant was based on the mode offering the greatest anticipated benefit. Options included outdoor or treadmill walking, stationary cycling, recumbent stepping, or walking on an AquaCiser® underwater treadmill. Resistance training and flexibility consisted of exercises emphasizing all of the major muscle groups. The exercise sessions concluded with an extremely low-intensity cooldown targeting all of the major muscle groups. Follow-up examinations revealed that participants’ adherence to the exercise intervention was approximately 90%, which can be attributed to cancer exercise specialists who prescribed individualized cancer interventions that fit patients’ circumstances.

Statistical Analyses

Participants’ characteristics in the four groups were compared using one-way analysis of variance (ANOVA). The main effect of supervised exercise training was determined before and after the exercise intervention using repeated-measures ANOVA. Following main effects significance, Tukey honestly significant difference post-hoc tests were used to determine where significance occurred. The primary analyses compared changes from before and after the exercise intervention and between treatment groups using univariate analyses of covariance procedures in which the post-value was the dependent variable, the prevalue of the same variable was the covariate, and treatment group was the grouping variable. Statistical analyses were performed using SPSS®. Significance was set at a probability of ≤ 0.05 .

Results

The study included 96 breast cancer survivors with a mean age of 57.9 ± 10.4 years. The convenience sample of participants was divided into four groups based on the type of clinical treatment they had received: surgery alone ($n = 22$); surgery and chemotherapy ($n = 30$); surgery and radiation ($n = 17$); and surgery, chemotherapy, and radiation ($n = 27$). All participants had surgery, with 53% having a mastectomy, 28% lumpectomy, and 16% bilateral mastectomy. Twelve percent of the women were on antidepressants. Skinfold body fat averaged $33.4 \pm 6.7\%$ before the exercise intervention and $33.4 \pm 5.8\%$ following the exercise intervention. The cancer survivors’ initial characteristics are shown in Table 1. No significant differences were observed in age, height, and weight between groups. Table 2 shows cardiopulmonary function changes in all four groups before and after the exercise intervention. Following the six-month exercise intervention, predicted $\text{VO}_{2\text{max}}$ and time on treadmill in all four treatment groups ($p < 0.05$) improved significantly. In addition, breast cancer survivors in the surgery, chemotherapy, and radiation group showed significant reductions in resting heart rate ($p < 0.05$) and concurrent increases on FVC $\%_{\text{pred}}$ after the supervised exercise intervention. Although the four treatment groups showed varying levels of improvement in cardiopulmonary function, no significant differences were noted between the four groups in regard to before exercise versus after exercise improvement.

Table 3 displays alterations on the four fatigue domains and total fatigue before and after the exercise intervention for all treatment groups. The exercise intervention resulted in significant reductions in behavioral fatigue, affective fatigue, sensory fatigue, cognitive and mood fatigue, and total fatigue in the surgery and chemotherapy; surgery and radiation therapy; and surgery, chemotherapy, and radiation therapy groups ($p < 0.05$). However, the breast cancer survivors in the surgery alone group

Table 1. Characteristics of the Breast Cancer Population

Characteristic	Surgery Alone (N = 22)		Surgery and Chemotherapy (N = 30)		Surgery and Radiation Therapy (N = 17)		Surgery, Chemotherapy, and Radiation Therapy (N = 27)	
	\bar{X}	SD	\bar{X}	SD	\bar{X}	SD	\bar{X}	SD
Age (years)	55.6	11.3	55.6	11.0	57.2	9.4	63.1	9.8
Height (inches)	64.4	3.1	63.7	3.0	64.2	2.7	64.4	2.4
Weight (pounds)	167.4	31.0	164.2	38.1	164.9	42.0	173.5	40.4

Table 2. Cardiopulmonary Function Before and After the Exercise Intervention

Variable	n	Before Exercise		After Exercise		% Change
		\bar{X}	SD	\bar{X}	SD	
Systolic blood pressure (mmHg)						
Surgery	22	132	17	127	12	-3.79
Surgery and chemotherapy	30	125	19	123	13	-1.60
Surgery and radiation therapy	17	126	17	121	14	-3.97
Surgery, chemotherapy, and radiation therapy	27	125	11	123	10	-1.60
Diastolic blood pressure (mmHg)						
Surgery	22	80	7	76	8	-5.00
Surgery and chemotherapy	30	78	10	76	11	-2.56
Surgery and radiation therapy	17	78	10	76	8	-2.56
Surgery, chemotherapy, and radiation therapy	27	79	8	78	8	-1.27
Resting heart rate (bpm)						
Surgery	22	81	11	80	11	-1.23
Surgery and chemotherapy	30	86	13	83	13	-3.49
Surgery and radiation therapy	17	83	10	81	10	-2.41
Surgery, chemotherapy, and radiation therapy	27	86	13	81	11	-5.80*
FVC %_{pred}						
Surgery	22	98	18	102	19.4	3.36
Surgery and chemotherapy	30	96	20	100	20.6	4.81
Surgery and radiation therapy	17	96	18	95	21.0	-0.73
Surgery, chemotherapy, and radiation therapy	27	90	16	95	14.6	4.70*
FEV₁ %_{pred}						
Surgery	22	92	24	99	21.1	6.95
Surgery and chemotherapy	30	91	22	99	19.3	9.17
Surgery and radiation therapy	17	90	19	88	22.7	-1.67
Surgery, chemotherapy, and radiation therapy	27	87	19	91	13.5	4.38
pVO_{2max} (ml/kg/minute)						
Surgery	22	20	5	25	5.2	23.00*
Surgery and chemotherapy	30	21	6	24	5.4	15.17*
Surgery and radiation therapy	17	20	7	24	6.0	19.70*
Surgery, chemotherapy, and radiation therapy	27	21	7	25	5.2	18.93*
Treadmill time (minutes and seconds)						
Surgery	22	4:56	2:40	6:46	2:32	37.16*
Surgery and chemotherapy	30	5:33	2:06	7:03	2:02	27.03*
Surgery and radiation therapy	17	5:08	2:47	6:36	2:34	28.57*
Surgery, chemotherapy, and radiation therapy	27	5:28	2:33	7:18	2:31	33.54*

* $p < 0.05$

bpm—beats per minute; FEV₁ %_{pred}—forced expiratory volume percent of predicted; FVC %_{pred}—forced vital capacity percent of predicted; pVO_{2max}—predicted maximal oxygen consumption

showed significant reductions in fatigue on the behavioral and affective subscales and the total fatigue score ($p < 0.05$) but not on sensory and cognitive and mood subscales ($p > 0.05$) after exercise training. Moreover, no significant differences were observed between groups on any of the fatigue domains.

Discussion

The present study is the first to compare the effects of an exercise intervention on cardiopulmonary function and fatigue in breast cancer survivors who received different types of clinical treatments. Cardiovascular toxicity, pulmonary toxicity, and extreme debilitating fatigue often are experienced by breast can-

cer survivors following surgery with adjuvant chemotherapy or radiotherapy. The study found that moderate intensity, individualized, prescriptive exercise could alleviate negative side effects of cancer treatment, as evidenced by an improvement in pVO_{2max} and the length of treadmill exercise time in all groups.

The side effects of cancer treatments can last days, months, and even years. Breast cancer survivors in the study were assessed within weeks following the end of treatment. The results showed that the breast cancer survivors did not experience prolonged decrements in physiologic or psychological parameters following treatment but were able to maintain their cardiovascular fitness (systolic blood pressure, diastolic blood pressure, resting heart rate) and pulmonary fitness (FVC

Table 3. Fatigue Before and After the Exercise Intervention

Variable	n	Before Exercise		After Exercise		% Change
		\bar{X}	SD	\bar{X}	SD	
Behavioral fatigue						
Surgery	22	49.60	2.79	2.39	1.62	-51.81*
Surgery and chemotherapy	30	4.40	2.69	2.82	2.29	-35.91*
Surgery and radiation therapy	17	4.29	2.36	2.10	2.22	-51.05*
Surgery, chemotherapy, and radiation therapy	27	5.21	2.64	3.08	2.49	-40.88*
Affective fatigue						
Surgery	22	5.29	2.52	3.96	2.27	-25.14*
Surgery and chemotherapy	30	5.52	2.52	3.85	2.98	-30.25*
Surgery and radiation therapy	17	5.39	2.49	3.43	2.28	-36.36*
Surgery, chemotherapy, and radiation therapy	27	5.90	1.92	3.99	2.04	-32.37*
Sensory fatigue						
Surgery	22	5.20	2.44	4.05	1.78	-22.12
Surgery and chemotherapy	30	5.53	2.36	4.18	2.29	-24.41*
Surgery and radiation therapy	17	5.54	2.16	2.99	2.07	-46.03*
Surgery, chemotherapy, and radiation therapy	27	5.80	1.71	3.71	1.64	-36.03*
Cognitive and mood fatigue						
Surgery	22	5.08	2.48	4.26	1.78	-16.14
Surgery and chemotherapy	30	4.77	1.97	3.93	1.95*	-17.61
Surgery and radiation therapy	17	4.64	2.08	3.42	1.99*	-26.29
Surgery, chemotherapy, and radiation therapy	27	5.25	1.99	3.29	1.25*	-37.33
Total fatigue						
Surgery	22	5.12	2.40	3.63	1.55*	-29.10
Surgery and chemotherapy	30	4.97	1.99	3.59	2.16*	-27.77
Surgery and radiation therapy	17	4.89	1.97	2.96	2.01*	-39.47
Surgery, chemotherapy, and radiation therapy	27	5.40	1.82	3.29	1.44*	-39.07

* $p < 0.05$

and FEV₁) in the surgery alone, surgery with chemotherapy, and surgery with radiation groups as a result of the exercise intervention. Interestingly, breast cancer survivors in the group who had completed surgery plus adjuvant chemotherapy and radiotherapy showed significant improvements in resting heart rate (-5.8%) and FVC (+4.7%) as a result of the exercise intervention, whereas systolic blood pressure, diastolic blood pressure, and FEV₁ maintained their initial levels.

The results are, to some extent, consistent with the findings of Courneya et al. (2003) who observed a beneficial effect of a structured training intervention on peak oxygen consumption (+17.4%) compared with a control group in breast cancer survivors who started the intervention several months after surgical treatment and adjuvant chemotherapy. In addition, MacVicar, Winningham, and Nickel (1989) also showed improved pVO_{2max} following a 10-week interval-training cycle ergometer protocol compared with a stretching and flexibility exercise program in breast cancer survivors following chemotherapy. Similarly, an increase in pVO_{2max} between 15%–23% among all clinical treatment groups was observed. In addition, the significant improvements in resting heart rate and FVC%_{pred} in the surgery, chemotherapy, and radiation group imply that individualized exercise training can benefit cancer survivors independent of treatment type.

The pVO_{2max} of breast cancer survivors improved as result of exercise training in the study, regardless of the type of treat-

ment. The mechanism by which exercise training increased pVO_{2max} and time on treadmill in breast cancer survivors following surgery and adjuvant chemotherapy and/or radiotherapy remains elusive. During exercise training, more than 80% of the consumed oxygen is used by working skeletal muscle. Maximum oxygen uptake is an integrative indicator of the maximum working capacity of the cardiopulmonary and muscular systems (lungs, heart, blood, working skeletal muscles) involved in the aerobic process from the delivery of atmospheric oxygen to the mitochondria of the muscle fibers. Therefore, any increase in maximum oxygen uptake brought about by exercise training involving large muscle mass is mostly attributable to an improvement of cardiopulmonary function, but also of blood oxygen transport and muscle aerobic capacity (McArdle, Katch, & Katch, 2001). In addition, Chicco, Schneider, and Hayward (2006) and Hayward et al. (2004) found that exercise training preserved intrinsic cardiovascular function following treatment with various chemotherapeutic agents. These cardioprotective effects were associated with an exercise-induced increase in endothelial nitric oxide synthase, myocardial heat shock protein content, and attenuation in chemotherapy-induced myocardial lipid peroxidation. Therefore, several mechanisms may have contributed to the physiologic adaptations observed in this investigation.

Fatigue is a common effect of cancer treatment (Portenoy & Itri, 1999). Prevalence rates of fatigue as high as 96% have

been reported following chemotherapy and radiotherapy. Fatigue may be described as lack of energy, muscle weakness, somnolence, dysphoric mood, or impaired cognition. Possible causes of fatigue include pain, sleep problems, infection, poor nutrition, side effects of medications, anemia, and deconditioning (Berger, 2003). Fatigue has been considered the most prevalent and distressing symptom of cancer therapies, as well as the most common unmanaged symptom. The presence of one or a combination of the symptoms has the potential to adversely affect quality of life and general well-being. For example, the presence of fatigue often leads to a decrease in daily activity level, which in turn lowers an individual's capacity to perform daily tasks in the future. As breast cancer survivors become too tired to participate fully in the roles and activities that make life meaningful, quality of life is adversely influenced.

Limitations

The convenience sample was a limitation of the study as well as the sample composition of women from one geo-

graphic area. In addition, the strength of the study could have been enhanced if a nonexercise group was included.

Implications for Nursing

The results of the study suggest that moderate intensity, individualized, prescriptive exercise maintains or improves cardiopulmonary function with concomitant reductions in fatigue regardless of treatment received for breast cancer. Nurses can help cancer survivors improve their quality of life by making appropriate referrals to initiate supportive therapies such as exercise interventions to help cancer survivors combat the side effects of cancer treatments whether surgery, chemotherapy, radiation, or combination therapy. The present study investigated moderate intensity exercise; future research must determine if higher intensity exercise also is safe for cancer survivors.

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