ORIGINAL RESEARCH

Cancer Rehabilitation: Impact of Physical Activity on Initial Clinical Assessments

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ABSTRACT

Background: Preconditioning and prehabilitation have been reported to ameliorate a host of health- and cancer-related issues, yet few studies have examined implications of past physical activity (PA) on physiological and psychological parameters in cancer survivors. Implications of prior PA on physiological and psychosocial variables in cancer survivors were acquired during an initial assessment prior to participation in a cancer rehabilitation program.

Methods: Cardiorespiratory fitness (VO_{2peak}), fatigue (Piper Fatigue Scale, PFS), and depression (Beck Depression Inventory, BDI) were measured ($N = 807$; 67 ± 13 years). PA groups were divided by self-reported prior PA history (Group 1 = none; Group 2 < 150 min/week; Group 3 ≥ 150 min/week).

Results: Significant ($P < 0.05$) main effects for PA were observed among all variables except the PFS affective subscale. Groups 1 and 3 were significantly ($P < 0.05$) different for BDI. Groups 1 and 3 were significantly ($P < 0.05$) different for the total, sensory, and cognitive subscales of the PFS. Finally, Groups 1 and 3, and Groups 2 and 3 differed significantly ($P < 0.05$) for the behavioral, sensory, and cognitive subscales of the PFS.

Conclusion: Cancer survivors with prior PA levels ≥ 150 min/week performed better on measures of VO_{2peak}, were significantly less fatigued and depressed at initial assessment. *Journal of Clinical Exercise Physiology*. 2018;7(1):1–7.

Keywords: exercise, preconditioning, oncology, survivorship

INTRODUCTION

Cancer is a global public health concern that continues to impact more people each year. A total of 1,685,210 new diagnoses and 595,690 deaths were estimated to have occurred in the United States in 2016. In addition, the probability of being diagnosed throughout the lifespan with an invasive cancer has been estimated at approximately 42% and 38% for males and females, respectively (1). Although cancer incidence and mortality rates are decreasing, approximately one-fifth (373,042) of the 2016 estimated cancer diagnoses have been reported to be related to obesity, inadequate nutrition, and an inactive lifestyle (1,2). Thus, this segment of cancer diagnoses could very well be considered preventable occurrences. Of particular importance to this investigation is the implications of history of physical activity (PA) on initial physiological and psychosocial variables

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in cancer survivors starting an exercise-based cancer rehabilitation program.

Physical inactivity has been reported to be among a list of substantial public health issues accounting for roughly a quarter of the causes of death worldwide (3). Physical inactivity has been linked to a multitude of health risks and diseases, including cancer (4). The costs to treat cancer are also increasing. For example, a medical expenditure panel survey of the United States revealed that between 2008 and 2011 the direct costs of medical treatment for cancer have increased from $183 billion in 2008 to $236 billion in 2011 (5). Although speculative, should trends continue as reported, the United States may potentially spend nearly $316 billion dollars in 2018 on medical treatment for cancer-related occurrences alone. However, a more recent review evaluating various types of prescriptive prehabilitation and the improvement of cancer-related health outcomes indicated that prescriptive prehabilitation interventions may reduce overall healthcare costs (6). The author suggested that prehabilitation may improve physical or psychological outcomes that may then help individuals undergoing treatment for cancer to function at a much higher level than their counterparts who are physically inactive prior to cancer diagnosis and treatment. In addition, by implementing more specifically targeted prehabilitation interventions, incidence reduction, reduced hospital stays, readmissions to hospitals, and reduced future impairments may improve health outcomes and thereby reduce medical costs associated with cancer (6).

Lifestyles that have been historically deficient of PA have been reported to be related to significant increases in cancer risk and mortality (7-9). Physical activity may reduce risk of primary cancer, increase survival rate, decrease recurrence, and reduce risk of secondary cancers and other life-threatening diseases (10). The American College of Sports Medicine (ACSM) (11) and the American Cancer Society (ACS) (2) recommend that cancer survivors accumulate at least 150 minutes of moderate-intensity activity each week. Recreational PA has also been linked to a 54% and 65% reduction in endometrial cancer risks for self-reported moderate-high and low-to-moderate intensities, respectively (12). A meta-analysis of PA and colon cancer prevention revealed an average of 24% decrease in colon cancer risk for individuals who had a history of occupational, recreational, and leisure time PA (13). Inactivity may result in muscular catabolism, physical performance decrements, psychological distress, fatigue, weight gain, changes in body image, and decreased quality of life (14). A physically active lifestyle meeting the ACSM and ACS recommendations (2,11,15) may act to more effectively regulate physiological quality of life pathways that are often linked to cancer development. These may include metabolic disorders, immunological function, inflammatory responses, hormonal dysfunction, cytokine and adipokine dysfunction, and apoptosis regulation (8). With activities that result in a maintenance of healthy body weight, a reduction in the risk of cancer linked to excessive adiposity and obesity is likely (16).

Within our clinic and others, it has been well-established that exercise is positively associated with increases in cardiovascular function, muscular endurance, and flexibility, as well as with reductions in resting heart rate. In addition, exercise has been shown to decrease inflammation, and improve total fatigue scores including behavioral, sensory, affective, and cognitive/mood subcategories in cancer survivors (17-21). Furthermore, moderate-intensity aerobic exercise during and after cancer treatment has been associated with increased vigor, overall physiological functioning, well-being, mental status, increased functional capacity, weight control, and reduced mortality risk (8). Using animal models, our laboratory has clearly shown that both long-term exercise preconditioning as well as an acute bout of exercise protect against chemotherapy-induced cardiotoxicity (22-24). Yet, little information exists on the role that history of PA prior to diagnosis and the start of a cancer rehabilitation program may have on functional capacity. Therefore, the purpose of this study was to examine the implications of self-reported PA on physiological and psychological variables in cancer survivors prior to the commencement of a 3-month exercise-based cancer rehabilitation program.

METHODS

Participants and Design

Eight hundred and seven cancer patients (67 ± 13 years; 75% female) completed initial physiological and psychosocial assessments prior to participating in an exercise-based cancer rehabilitation program. These patients were recruited from walk-ins and oncologist referrals at the University of Northern Colorado Cancer Rehabilitation Institute (UNC-CRI). The University Institutional Review Board approved all procedures, and written informed consent forms were signed by all subjects. Prior to initial screening assessment, each participant completed a lifestyle/activity evaluation that was composed of questions related to personal lifestyle choices regarding alcohol consumption, sleep habits, smoking, diet, and physical activity. Questions about current and previous PA that were specifically relevant to this study included whether they exercised, how many days per week they exercised, and how many minutes per week they exercised. Participant reports of physical activity were divided into 3 groups based on published ACSM and ACS guidelines: Group 1 (no regular physical activity, $n = 458$), Group 2 (less than 150 minutes of weekly activity, $n = 209$), Group 3 (greater than 150 minutes of weekly activity; $n = 140$) (15).

Theoretical Framework

The Health Belief Model guided the design of this study. Constructs that were most pertinent were susceptibility, cues to action, and seriousness as potential influencers on individual capacity to screen, act, or aim to prevent cancer (25). These model constructs influenced the direction of this study in a few ways: (1) numbers of people diagnosed with cancer are increasing, (2) there are greater numbers of people living longer with the outcomes of cancer and cancer treatment,

and (3) practitioners working with cancer patients and survivors are challenged to develop appropriately targeted rehabilitation programs for this population. By developing a greater understanding of how history of PA impacts variables often influenced by cancer and treatment, this information may increase PA among those seeking to reduce cancer risk, increase screening for cancer, or lead to action and implementation of prehabilitation to enhance treatment tolerance in those newly diagnosed. In addition, understanding the impacts of PA history on initial physiological and psychological values may influence first point of contact practitioners to better educate patients on their susceptibility and seriousness of cancer and cue them to action.

Physiological Assessment

Following initial screening and agreement to participate, participants completed a comprehensive physiological assessment (26). Initial values for heart rate, blood pressure, oxygen saturation (SpO_2), height, weight, body composition (skinfold measurements), circumference measurements, cardiovascular fitness (VO_{2peak}, UNCCRI protocol), balance (Bertec Balance Screener), pulmonary function (spirometry), estimated 1RM (Brzycki equation), muscular endurance (plate loaded cable assisted machines, chair squat test, and plank test), handgrip dynamometry, and flexibility measures (modified Sit and Reach and Shoulder Reach Behind Back) were collected as part of the standard UNCCRI physical assessment protocol. Cardiovascular endurance was assessed using the cancer-specific UNCCRI multistage treadmill protocol (26). This protocol starts at 1.0 mph and 0% grade, and the workload increased by approximately 0.5 metabolic equivalents every minute throughout the test. Instructions regarding the specific changes in speed and grade during each 1-minute stage were given, and the participant was encouraged to walk or run until exhaustion or volitional fatigue (to VO_{2peak}). Before each incremental treadmill test, participants were fitted with a heart rate monitor (Polar Inc., Lake Success, NY). Blood pressure was assessed at rest, every 3 minutes during exercise, immediately after exercise, and after 3 minutes of slow walking recovery. Rate of perceived exertion was assessed at the end of every 1-minute stage. ACSM metabolic equations were used to quantify VO_{2peak} at time of volitional fatigue (27).

Psychosocial Assessment

Fatigue was determined by using the Piper Fatigue Scale (PFS), which is composed of 22 items, numerically scaled from 0 to 10, that assesses 4 dimensions of subjective and total fatigue (28). The behavioral subscale includes 6 questions that assess impact of fatigue on school/work, social interaction, and the overall interference with enjoyable activities. The affective subscale includes 5 questions that assess the individual perception of experienced fatigue. The sensory subscale includes 5 questions that assess mental, physical, and emotional symptoms of fatigue. The cognitive/mood subscale includes 6 questions that assess fatigue impact on concentration, memory, and mental clarity. Higher total scores indicate greater severity of fatigue. Assessments of depression were determined by using the Beck Depression Inventory, where 21 items were numerically scaled from 0 to 3 (3 being the most severe) covering various gradations of experienced depression pertaining to daily living. Compiled scores created the overall depression score. The inventory assessed various physiological and psychological symptoms of depression. Higher total scores indicate a greater level of depression.

Statistical Analysis

Series mean imputations were applied (SPSS 21, Armonk, NY) to account for occurrences of missing data. Percentages of missing data that were imputed include Piper Affective (1%), Piper Sensory (0.12%), Piper Cognitive (0.5%), and Beck Depression (4%). Multiple 1-way Analyses of Variance (ANOVA) were conducted to compare the effect of prior physical activity on physiological and psychological outcomes in cancer survivors following the initial assessment. Tukey post hoc tests with Bonferroni corrections were conducted to evaluate pairwise comparisons among levels of prior activity, VO_{2peak}, fatigue, and depression. A familywise error rate of 0.05 was used to determine statistical significance.

RESULTS

There was a significant ($P<0.05$) main effect for prior PA and all initial assessment variables. Post hoc pairwise comparisons revealed significant ($P<0.05$) differences between Groups 1 (no regular PA) and 2 (less than 150 minutes of weekly activity), and Groups 2 and 3 (greater than 150 minutes of weekly activity) for VO_{2peak} (20.3 ± 6.5 vs 22.3 ± 7.1 vs 23 ± 7.2 $mL\cdot kg^{-1}\cdot min^{-1}$, respectively) (Figure 1).

Pairwise comparisons revealed significant ($P<0.05$) differences between Groups 1 and 3 for PFS total scores (5.1 ± 2.2 vs 4.4 ± 2.2, respectively) (Figure 2). Groups 1 and 3 Piper Behavioral sub-scores were significantly ($P<0.05$) different (5.1 ± 2.8 vs 4.3 ± 3.2, respectively). No significant ($P>0.05$) pairwise differences were observed for Piper Affective sub-scores. Significant ($P<0.05$) differences were observed between Groups 1 and 2, and Groups 2 and 3 for Piper Sensory sub-scores (5.6 ± 2.3 vs 5.1 ± 2.3 vs 5.0 ± 2.3, respectively) and for Piper Cognitive/Mood sub-scores (4.8 ± 2.1 vs 4.3 ± 2.0 vs 4.2 ± 2.1, respectively). Finally, there was a significant ($P<0.05$) difference in depression observed between Groups 1 and 3 (11.1 ± 7.0 vs 9.3 ± 6.0, respectively) (Figure 3).

DISCUSSION

The results of this study suggest that cancer survivors who had a PA history of at least 150 minutes per week yielded significantly higher baseline values for physical and psychological function and were better prepared to begin a cancer rehabilitation program than those who reported low or no PA. This information supports not only maintaining healthy PA levels but also a recommendation to practitioners that encounter newly diagnosed cancer patients to increase

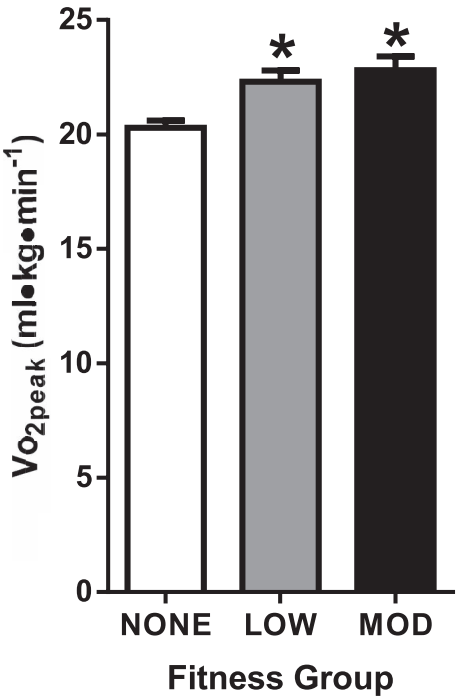

FIGURE 1. Comparisons of preconditioning fitness groups and initial VO_{2peak} values. Data are mean ± SEM. * significantly different from NONE ($P < 0.05$).

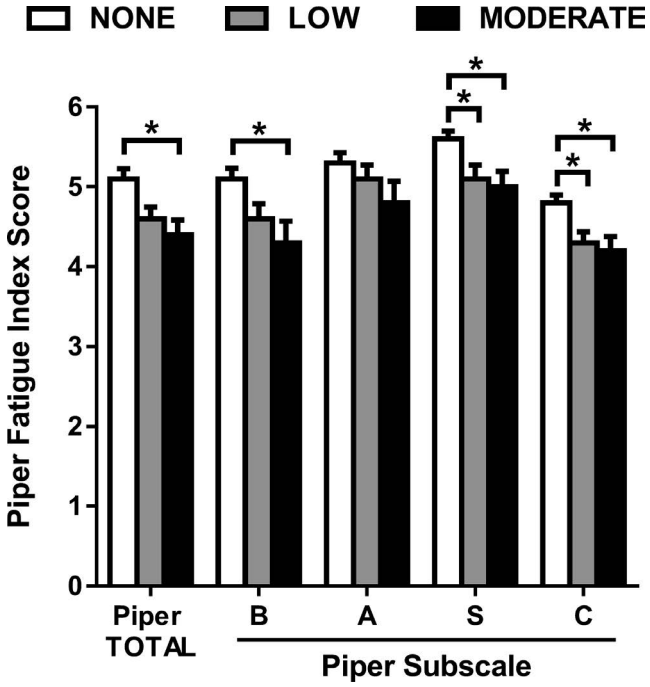

FIGURE 2. Group comparisons of preconditioning fitness groups and Piper Fatigue Scores. B, behavioral subscale; A, affective subscale; S, sensory subscale; C, cognitive/mood subscale. Data are mean ± SEM. * indicates significant differences ($P < 0.05$).

referral of patients to professionals trained to administer preconditioning or prehabilitation methodologies. Exercise or PA before, during, and following treatment for cancer has been associated with a vast number of physiological and psychological benefits in cancer patients/survivors (8,11,17-24). Studies have reported that exercise is safe and efficacious at any time point along the cancer continuum, with results of positive increases in physiological function, management of weight, and psychological outcomes in cancer survivors likely to occur (11,29). Investigations utilizing prescriptive prehabilitation methodologies also support the benefits of exercise for cancer patients (6,30). Yet, to our knowledge, this study is among the first to evaluate the implications of self-reported PA history on physiological and psychological variables in cancer survivors starting a cancer rehabilitation program.

Cancer-related fatigue and depression may act as barriers to exercise and, thus, the rehabilitation process. Zhu et al. reported that among 241 cancer patients who received psychological care that those with poor physical health tended to report greater levels of fatigue, depression, and anxiety (31). However, Tsimopoulou et al. (32) reported that studies incorporating psychological prehabilitation had positive impacts on quality of life, somatic symptoms, and psychological outcomes (i.e., total mood disturbances, anxiety, depression, fighting spirit) prior to undergoing surgery for cancer. Cancer survivors in this study who reported greater than 150 minutes of PA were significantly less depressed and fatigued than those who reported little or no PA. From a clinical standpoint, having patients begin rehabilitation with reduced fatigue and depression is not only of psychological

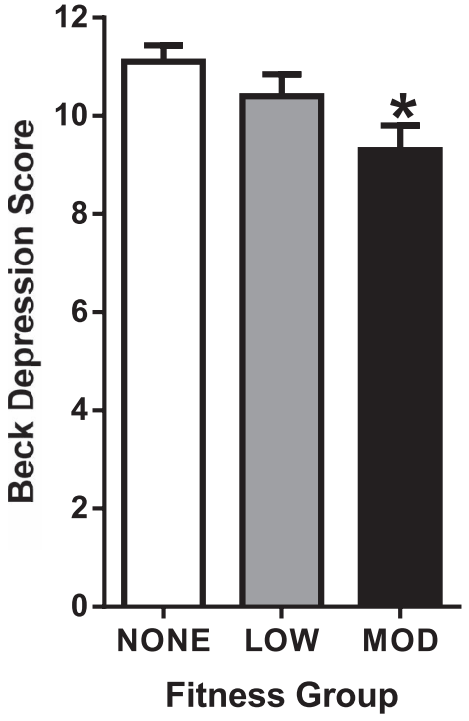

FIGURE 3. Comparisons of preconditioning group and initial Beck Depression scores. Data are mean ± SEM. * significantly different ($P < 0.05$) than NONE.

benefit to the patient, but it may also enhance the efficacy of an exercise intervention aimed at improving physical function and may improve attendance and adherence to rehabilitation programs. Finally, a reduction in psychological barriers can only increase the ability of the practitioner to develop high-quality individualized cancer rehabilitation.

Physical preconditioning and prehabilitation methodologies are not entirely novel concepts. For example, a review of literature on the effects of preoperative exercise therapy on postoperative outcomes revealed that preconditioning effectively reduced hospital stay and potential complications among patients who underwent abdominal and cardiac surgery (33). Chen et al. showed that colorectal cancer patients were physically able to complete an intervention consisting of 4 weeks of exercise, counseling, and nutritional supplementation. The patients significantly increased both the amount and intensity (moderate and vigorous) of PA prior to surgery in addition to improving 6-minute walk test times (30). The results of this study indicate that those who reported a history of greater than 150 weekly minutes of PA initially presented with significantly greater values of VO_{2peak} and, thus, cardiovascular function than those who had reported low or no history of PA. This is valuable information as PA has been linked with improvements in aerobic capacity while also linked to reductions in mortality and cardiovascular risk factors (34,35). An investigation of multiple cardiovascular parameters among colorectal cancer patients by Cramer et al. (36) reported that capacity to exercise was significantly impaired, parasympathetic tone and left ventricular ejection fraction were reduced, peak heart rate and VO_2 decreased, and markers of heart rate variability decreased to levels typically observed among chronic heart rate failure patients. In addition, the investigators noted that when chemotherapy began, cardiovascular function decreased further. Ideally, everyone would be attaining recommended levels of weekly PA as a precautionary measure to reduce cancer risk. Yet, the reality is quite the opposite. Only 49% of adults in the U.S. are meeting the guidelines for recommended daily levels of PA (37).

The findings of this study highlight the importance of implementing preparatory methods of increasing cardiovascular function, whether by prehabilitation or preconditioning with a trained clinician, or by personal efforts. Medical professionals should encourage regular PA and/or exercise prior to cancer treatment whenever possible because of their role of being the first points of patient contact. Specifically, medical professionals should increase the referral of newly diagnosed patients to certified clinicians trained to offer preconditioning or prehabilitation programs. It is plausible that cancer patients who start cancer rehabilitation at higher levels of overall functional capacity due to previous PA are more likely to physically and psychologically tolerate treatment better and invest greater effort, leading to improved prognosis and recovery from cancer and cancer treatment.

CLINICAL IMPLICATIONS

- Regardless of cancer status, maintaining lifestyles of at least 150 minutes of PA per week is further encouraged.
- A lifestyle that meets the physical activity recommendations of ACSM and ACS will provide a more favorable starting point for any individual that eventually receives a cancer diagnosis, which may allow them to better tolerate standard cancer treatment regimens.
- First point of contact medical professionals should increase referral of newly diagnosed cancer patients out to professionals trained to administer preconditioning or prehabilitation interventions.
- Increased integration between medical professionals and practitioners of cancer rehabilitation should stimulate improvements in the preparatory process for patients at cancer diagnosis throughout cancer rehabilitation.

CONCLUSION

Survivors with prior PA levels meeting or exceeding 150 minutes per week prior to their initial assessment and entry into an exercise-based cancer rehabilitation program recorded higher measures of VO_{2peak}, were significantly less fatigued, and reported less depression. Initiating a rehabilitation program with a higher level of overall functional capacity may positively impact the recovery process, whereas a history of no or low PA may disrupt or hinder the rehabilitation efforts of the participant, thereby negatively affecting the trajectory of the recovery process. Incorporating at least 150 minutes of PA prior to starting a cancer rehabilitation program, whether by prehabilitation/preconditioning or from active lifestyles, could result in increased cardiovascular function and decreased fatigue and depression measures that exceed outcomes from peers who report no or low levels of PA. By maintaining lifestyles meeting at least 150 minutes a week for physical activity, individuals are establishing a protective foundation should they receive a cancer diagnosis in their lifetime.

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