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Combined aerobic and resistance training improves bone health of female cancer survivors

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ABSTRACT

Introduction: Cancer pathogenesis and resulting treatment may lead to bone loss and poor skeletal health in survivorship. The purpose of this investigation was to evaluate the influence of 26 weeks of combined aerobic and resistance-training (CART) exercise on bone mineral density (BMD) in a multi-racial sample of female cancer survivors.

Methods: Twenty-six female cancer survivors volunteered to undergo CART for 1 h/day, 3 days/week, for 26 weeks. The Improving Physical Activity After Cancer Treatment (IMPAACT) Program involves supervised group exercise sessions including 20 min of cardiorespiratory training, 25 min of circuit-style resistance-training, and 15 min of abdominal exercises and stretching. BMD at the spine, hip, and whole body was assessed using dual-energy X-ray absorptiometry (DXA) before and after the intervention. Serum markers of bone metabolism (procollagen-type I N-terminal propeptide, P1NP, and C-terminal telopeptides, CTX) were measured at baseline, 13 weeks, and at study completion.

Results: Eighteen participants, with the average age of 63.0 ± 10.3 years, completed the program. Mean duration since completion of cancer treatment was 6.2 ± 10.6 years. Paired *t*-tests revealed significant improvements in BMD of the spine (0.971 ± 0.218 g/cm^2 vs. 0.995 ± 0.218 g/cm^2, $p = 0.012$), hip (0.860 ± 0.184 g/cm^2 vs. 0.875 ± 0.191 g/cm^2, $p = 0.048$), and whole body (1.002 ± 0.153 g/cm^2 vs. 1.022 ± 0.159 g/cm^2, $p = 0.002$). P1NP declined 22% at 13 weeks and 28% at 26 weeks in comparison to baseline ($p < 0.01$) while CTX showed a non-significant decrease of 8% and 18% respectively.

Conclusions: We report significant improvements in BMD at the spine, hip, and whole body for female cancer survivors who completed 26 weeks of CART. This investigation demonstrates the possible effectiveness of CART at improving bone health and reducing risk of osteoporosis for women who have completed cancer treatment. The IMPAACT Program appears to be a safe and feasible way for women to improve health after cancer treatment.

1. Introduction

Improvements in cancer treatment and detection, as well as growth of the population, have led to increased survival rates among those diagnosed with cancer. As of 2014, there was an estimated 14.5 million cancer survivors in the United States, 64% who are 5-year survivors, while 15% are 20-year survivors [1]. Cancer survivors are living longer but experience greater comorbidity than age-matched peers who never had cancer. Survivors demonstrate comorbidities such as higher rates of obesity, type 2 diabetes, cardiovascular disease, and osteoporosis [2–4]. Osteoporosis is a chronic disease of low bone mass, characterized by skeletal fragility and increased risk for fracture. Women experience a greater burden of this disease accounting for 80% of people with osteoporosis.

Previous research reports that 12 months of treatment for a gynecological cancer can cause 6–10% reduction in bone mineral density (BMD) due to elevated resorption during treatment [5]. Elevated resorption and its associated loss in BMD increases risk for fracture. In fact, women with a history of breast cancer experience significantly more skeletal fractures than women who never had breast cancer [6]. Bone loss during cancer treatment appears to be in addition to losses experienced with cessation of ovarian function. Survivors of gynecological cancers, who were diagnosed before menopause and underwent

Abbreviations: BMD, bone mineral density; BTM, bone turnover marker; CART, combined aerobic and resistance training; CTX, C-terminal telopeptides; DXA, dual-energy X-ray absorptiometry; FFQ, food frequency questionnaire; IMPAACT, improving physical activity after cancer treatment; P1NP, procollagen-type I N-terminal propeptides; NTX, N-telopeptide cross-linked collagen type I.

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ovarectomy, demonstrate 7–9% lower BMD than similarly aged women who underwent an ovariectomy for non-cancerous reasons [7].

Cancer and its treatment may lead to poor skeletal health via several mechanisms. Secretions from tumors themselves can speed up osteoclast activity, increasing bone resorption [8]. This interference with normal bone signaling pathways is observed in both male and female cancer survivors and is frequently quantified as an elevated serum level of P1NP [9,10]. Subsequently, P1NP is valuable as both an indicator of risk for tumor invasion of the bone and as a traditional bone turnover marker (BTM) for measuring skeletal response to pharmacologic and non-pharmacologic interventions for poor BMD. For cancer patients, assessment of both the possibility for metastasis and normal/abnormal BMD are essential to promoting skeletal health during survivorship. In addition to the aforementioned burden of tumor interference, female cancer patients frequently encounter additional skeletal health challenge due to the surgery or chemotherapy necessary for cancer treatment which may also induce ovarian dysfunction and lead to early menopause and its associated bone loss [11]. Also, long-term use of antihormonal medications, which are often part of the cancer therapy, negatively impact bone health [6]. All of the mechanisms discussed here will have systemic influence on bone health, however radiation treatment can cause site-specific bone loss [12].

Multiple studies have demonstrated that weight-bearing exercise can improve or help maintain BMD and lower risk for fracture in pre and postmenopausal women [13,14]. Weight-bearing aerobic activities and resistance training performed multiple times per week are recommended to help preserve bone health during adulthood [15]. In addition, some research supports use of whole body vibration as a training method which may potentially be osteogenic [16,17]. Exercise is a nonpharmacological, low-cost approach, with the potential to improve or maintain bone health and additional likely benefits to cardiovascular fitness, body weight management, balance, and risk for falling. Exercise programming which combines aerobic and resistance training exercise may simultaneously help to address multiple comorbidities of cancer such as obesity, cardiovascular disease, type 2 diabetes, and osteoporosis. Little is known about the volume of exercise that is safe for cancer survivors and that is effective at maintaining or improving bone health [18]. With the recent increase in the number of cancer survivors and the multiple ways cancer and its treatment may affect the skeleton, there is a need to develop survivorship care plans which include exercise as a means to sustain bone health in women and reduce comorbidities. Therefore, the purpose of this investigation was to evaluate the influence of 26 weeks of combined aerobic and resistance-training (CART) exercise on bone mineral density (BMD) in a convenience sample of female cancer survivors.

2. Materials and methods

2.1. Ethical approval

The IMPAACT Study was approved by the Human Subject's Institutional Review Board at Loyola Marymount University. All research participants provided written informed consent. Procedures performed in this study involving human participants were in accordance with the ethical standards of the Loyola Marymount University Institutional Review Board which uses the 1964 Helsinki declaration and its later amendments as ethical standards.

2.2. Participants and anthropometrics

The Improving Physical Activity After Cancer Treatment (IMPAACT) Study recruited 26 female cancer survivors from the Los Angeles area to participate in the exercise intervention using convenience sampling and physician referral. Eighteen of the volunteers completed the 26-week intervention including testing at baseline and follow up. Volunteers were excluded if currently receiving intravenous chemotherapy or outpatient radiation therapy. Primary care physicians and oncologists were notified of their patient's participation. Weight and height were assessed in minimal clothing, without shoes, where weight was measured on an electronic scale (Tanita BWB-927A Tokyo, Japan) and height was assessed using a stadiometer (Seca Accu-Hite, Columbia, MD, USA). Body mass index (BMI) was calculated by dividing weight in kg by height in meters squared.

2.3. Assessments

Demographic characteristics and medical history were obtained at baseline via self-administered questionnaires. The Aerobic Center Longitudinal Study Physical Activity Questionnaire was used to assess regular physical activity by calculating metabolic equivalents in hours per week by using intensity of activity, age, body weight, and duration [19]. The Block 2005 Food Frequency Questionnaire (FFQ) was used to measure dietary intake over the previous year for nutrients important for bone health, including calcium and vitamin D. This questionnaire uses photos to help users more accurately estimate portion size and has been validated to assess dietary intake over the previous 12 months [20].

2.4. Bone health and body composition

Bone mineral density of the posterior-anterior spine, left hip, and whole body were measured using dual energy X-ray absorptiometry (DXA, Hologic Discovery A, Waltham, MA). One technician performed and analyzed all scans. This technician demonstrates 1.0% test-retest reliability for BMD at the hip and spine. The whole body DXA scan allows for analysis of lean mass and fat mass. Participants provided fasting blood samples early in the morning at baseline, 13 weeks, and 26 weeks. Serum samples were processed and stored at −20 °C within 2 h of collection and moved for long-term storage at −80 °C, 24 h later. Procollagen-type I N-terminal propeptide (P1NP, ng/mL) a measure of bone formation cleaved off in production of type I collagen was assessed by enzyme-linked immunosorbent assay (ELISA) kits from Cloud Clone Corp (Houston, TX). Serum levels of C-terminal telopeptides (CTX, ng/mL) were measured as a marker of bone resorption via ELISA kits from Immuno Diagnostic Systems (Fountain Hills, AZ). Bone turnover markers (BTMs) were assayed at the UCLA Bone Histomorphometry Laboratory with coefficients of variation (CV) as follows PINP inter-assay CV of <12%, P1NP intra-assay CV of <10%, CTX inter-assay CV of 2.5–10.9%, and CTX intra-assay CV of 1.8–3.0%.

2.5. Exercise program

The IMPAACT Study was a combined aerobic and resistance training program which occurred 1 h per day, 3 days per week, for 26 weeks. The supervised exercise intervention took place on the Loyola Marymount University campus in Los Angeles, CA following the academic calendar; beginning in August/September, taking a break for winter and spring holidays, then concluding in April/May. Therefore, the 26-week exercise program was actually spread over 32 weeks of the year. Prescribed in accordance with Guidelines for Exercise for Cancer Survivors from the American College of Sports Medicine (ACSM), each supervised exercise session includes a) 20 min of cardiorespiratory training, b) 25 min of circuit-style resistance training, and c) 15 min of exercises for the core musculature with dynamic and static stretching [21]. The IMPAACT study intervention incorporated both aerobic and resistance training components, in effort to meet the American College of Sports Medicine Guidelines on Exercise for Cancer Survivors and to help to reduce the multiple comorbidities exhibited by cancer survivors.

Cardiorespiratory training included walking although weather and fitness levels required the occasional inclusion of elliptical machines, or stationary bicycles at a prescribed target hear rate training zone of 35–80% heart rate reserve. In accordance with baseline activity levels,