Accepted Manuscript online: 2023-10-17 Article published online: 2024-01-30

EXERT-BC: Prospective Study of an Exercise Regimen After Treatment for Breast Cancer

OPEN ACCESS

Authors

Colin E. Champ[1,5], Chris Peluso[1], David J. Carenter[2,7], Jared Rosenberg[3], Frank Velasquez[1], Adam Annichine[1], Krista Matsko[1], Parker N. Hyde[4], Alexander K. Diaz[2,8], Sushil Beriwal[5], Christie Hilton[6]

Affiliations

1 Exercise Oncology and Resiliency Center, Allegheny Health Network, Pittsburgh, United States
2 Radiation Oncology, Duke University Medical Center, Durham, United States
3 Department of Exercise Science, Syracuse University, Syracuse, United States
4 Department of Kinesiology, University of North Georgia, Dahlonega, United States
5 Department of Radiation Oncology, Allegheny Health Network, Pittsburgh, United States
6 Medical Oncology, Allegheny Health Network, Pittsburgh, United States
7 Department of Radiation Oncology, Wellstar Paulding Medical Center, Hiram, GA
8 Department of Radiation Oncology, Murray-Calloway County Hospital, Murray, KY

Key words

breast cancer, exercise, cancer, ressitance training

received 28.07.2023
revised 09.10.2023
accepted 10.10.2023
accepted manuscript online 17.10.2023

Bibliography

Sports Medicine International Open 2024; 8: a21930922
DOI 10.1055/a-2193-0922
ISSN 2367-1890

Georg Thieme Verlag, Rüdigerstraße 14, 70469 Stuttgart, Germany

Correspondence

Dr. Colin E. Champ
Allegheny Health Network
Exercise Oncology and Resiliency Center
100 S. Jackson Ave.
15202 Pittsburgh
United States
Tel.: (878) 332-4049
colin.champ@ahn.org

ABSTRACT

Purpose EXERT-BC is a dose-escalated resistance training regimen created to improve body composition, strength, and balance in women treated for breast cancer (BC). Herein, we report the interim analysis. Women treated for BC underwent this 3-month exercise regimen in an exercise oncology facility with continual monitoring of load and strength. Twenty women completed the IRB-approved protocol, with a mean age of 57 years (range 41–74). Concurrent therapies included anti-estrogen therapy (73 %), chemotherapy (14 %), and radiotherapy (23 %). 27 % of women endorsed prior exercise. Subjects missed an average of 1.75 classes (range 0–7), with all meeting adherence over 75 %. No injuries or adverse events were reported aside from muscle soreness and 2 days of knee pain. Significant differences in body composition at completion included reduced body fat (38.2 % vs. 36.7 %, $p = 0.003$), and increased muscle mass (33.1 % vs. 37.1 %, $p < 0.001$), functional mobility screening (9.82 vs. 11.73, $p = 0.018$), and Y-balance (left: 72.4 vs. 85.3, $p = 0.001$; right: 70.3 vs. 85.2. $p < 0.001$). Significant increases in load were demonstrated: split squat ($p < 0.001$), trap bar deadlift ($p = 0.035$), inclined dumbbell press ($p < 0.001$), and bird dog rows ($p < 0.001$). Dose-escalated resistance training in women with BC is safe and feasible, endorsing significant improvements across body composition, balance, and strength.

Introduction

Obesity is a risk factor for both breast cancer and disease recurrence after treatment [1]. Furthermore, weight gain during and after treatment for breast cancer is associated with a higher risk of recurrence, distant metastases, and death [2]. Yet, most women gain significant weight during and after breast cancer treatment, potentially compromising outcomes.

Conversely, increased activity levels have been repeatedly associated with decreased breast cancer incidence as well as improved outcomes after breast cancer treatment, including breast cancer-specific and overall survival [3]. Many breast cancer survivors do not meet adequate daily activity level recommendations, potentially compounding issues with weight gain during and after breast cancer treatment [4]. As a result, attempts are underway to both quantify and increase activity levels during treatment and survivorship [5].

Studies in non-cancer populations reveal that aerobic exercise, when unaccompanied by other health changes, is generally minimally effective for weight loss, and specifically fat loss [6]. Breast cancer survivors achieving weight loss through aerobic exercise may risk loss of lean mass and muscle tissue [7] and the potential metabolic and functional benefits that accompany both. In contrast, resistance training at an appropriate intensity level may help support lean mass maintenance or even muscle gains during weight loss, which has been shown to simultaneously increase resting metabolic rate to increase fat oxidation and improve body composition [8, 9]. Such changes may be more advantageous in the oncologic setting than previous aerobic-based exercise strategies to increase caloric expenditure.

Historically, resistance training regimens among breast cancer survivors limited training intensity and progression in an effort to minimize the risk of exacerbating treatment-related lymphedema [10]. Yet, multiple studies have now confirmed no increase, and potentially improvement, in lymphedema in women undergoing resistance training after breast cancer treatment [11–14]. For safety measures, many home interventions in breast cancer patients also utilize light-weight free-weight, or open kinetic chain (OKC) movements where the body is fixed and the distal extremities are mobile, both of which can often limit activation of core and accessory muscles, leading to a less intense regimen that may limit functional and mobility benefits and hypertrophy [15, 16]. Closed kinetic chain (CKC) exercises, also known as compound exercises, involve fixation of the distal aspect of the extremity (as opposed to proximal isolation) and therefore require involvement of multiple joints and co-contraction of multiple simultaneous muscles to stabilize the body during movement. Such CKC exercises include lunges, squats, deadlifts, and power cleans; in contrast, examples of OKC exercises are bench press, seated leg curls and extensions, and machine curls. Closed kinetic chain and compound exercises also mimic athletic movements, thus positively impacting mobility and function.

Studies in non-cancer patients reveal that resistance training routines that expose muscle tissue to extensive mechanical tension with subsequent muscle damage and metabolic stress promote training-induced muscle growth [17]. Resistance training has been shown to combat cachexia and augment muscle mass in individuals with cancer via an array of mechanisms [18]. While resistance training has shown significant improvements in quality of life after treatment for cancer, reports on improvements in body composition have been underwhelming thus far [19].

While weight training has clear advantages over aerobic training for improving body composition and several measurable metabolic variables, there have been barriers to its implementation in exercise regimens for the breast cancer patient, including concerns of safety and lymphedema risk [20]. However, as stated above, these risks have been largely disproved by the current available research [21]. Adverse effects (AEs) reported in prior exercise studies include typical self-limiting musculoskeletal issues, including muscle strains, joint and back pain, shin splints, and tendinitis [22]. Overall, AEs are minimal. Furthermore, an observed environment with supervision by trained exercise personnel can further reduce the risk of injury [23, 24], as can adaptation of a workout regimen that accounts for individuals' functional movement abilities, mobility, and function [25].

Additionally, studies reveal that observed exercise programs lead to enhanced strength gains and hypertrophy [26], and successful exercise interventions tend to be those that involve direct supervision [27]. Finally, many of the exercise regimens tested include prolonged exercise regimens like treadmill and aerobic sessions lasting 90 minutes or more. More intense weight training generally lasts a fraction of the time and therefore may serve as a time-effective method of exercise.

Thus, the EXERT-BC protocol (a prospective study of an exercise regimen designed to improve functional mobility, body composition, and strength after treatment for breast cancer) was designed to assess the safety and feasibility of an observed exercise regimen utilizing high-load resistance training via compound CKC and functional resistance exercises with the goal of improving physical and metabolic function, mobility, muscle mass, and body composition in women with breast cancer utilizing guidelines from the National Strength and Conditioning Association (NSCA). Herein, we report an interim analysis of body composition and exercise parameters for an initial cohort following an initial three-month resistance training regimen.

Methods

Participants

Women aged 20–89 with biopsy-proven ductal carcinoma in situ (DCIS) or breast cancer were eligible for this trial. Additionally, participants were required to be able to get up and down from the ground, squat their body weight, and be able to participate in a group exercise regimen. Individuals with severe arthritic, joint, cardiovascular, or musculoskeletal condition deemed unsafe to engage in resistance training were excluded. Participants currently treated with systemic cytotoxic chemotherapy were excluded from the study, while radiation therapy, anti-estrogen and targeted systemic therapy were allowed. Participants were screened by study personnel at the time of oncologic consultation or follow-up. Treatment and medical records were manually curated.

Recruitment occurred between September 15, 2022, and April 13, 2023, at the Allegheny Health Network (AHN) departments of surgical, medical, and radiation oncology, along with the AHN Cancer Institute Exercise Oncology and Resiliency Center. Consent was obtained for each participant. The study was approved by the institutional review board (protocol 2022–269-SG) and registered at ClinicalTrials.gov (NCT05747209).

Experimental design

All participants were enrolled in a 3-month thrice-weekly dose-escalated exercise regimen utilizing multi-joint compound movements and linear progression balanced with resistance training volume to elicit hypertrophy, as previously published [28]. The co-primary outcomes were regimen adherence and safety, which were recorded throughout the regimen. Secondary endpoints, reported in the present interim analysis, included change in body composition, functional mobility, and balance, resting metabolic rate, phase angle, quality of life, and activity levels.

Body composition and resting metabolic rate

Prior to initiation of the exercise regimen and at completion, each participant underwent body composition analysis via an InBody 970 bioimpedance analysis (BIA) machine (InBody Co., Seoul, South Korea). InBody testing is noninvasive and requires no ionizing radiation. The individual simply stands on the machine while holding handles. Reliability and agreement of the InBody device is high with small error risk [29]. To confirm changes over differing modalities, an ultrasound (US) was also utilized to measure muscle and adipose tissue thickness to provide additional metrics for body composition with fat mass, fat-free mass, percent body fat, and resting metabolic rate calculated utilizing BodyMetrix software (BodyMetrix, Brentwood, CA, USA) and measurements at the triceps, suprailiac, abdominal, and thigh area utilizing the Jackson & Pollock calculation[30]. US is a valid and reliable method to assess body composition [31, 32]. Both devices utilize the body metrics and Cunningham equation to calculate resting metabolic rate, which has been shown to be relatively accurate [33].

Functional movement and balance

Prior to initiation of the exercise regimen and at completion, each participant underwent a seven movement Functional Movement Screen (FMS) and Y-balance test. The FMS is a tool used prior to the initiation of an exercise protocol to assess individual mobility and movement patterns. These patterns are general accompanied by compensatory mechanisms that may predispose participants to injury but can be improved through specific exercises that can reduce the risk of chronic injury. During the test, seven movement patterns are assessed and each one is rated between 0 and 3 by an examiner. These movements include the deep squat, hurdle step, inline lunge, shoulder mobility test, active straight leg raise, trunk stability push up, and rotary stability test. Normal values in the general population range from a score of 12.56 in individuals over the age of 65 to 14.79 in individuals aged 20–39, and women generally have a slightly higher score [34]. The FMS has an acceptable degree of inter-rater reliability and is currently the most well-researched movement screen available.

The Y-balance test has the participant stand on one leg while reaching out in three different directions with the other lower extremity. They are anterior, posteromedial, and posterolateral. When using the Y-Balance test kit, the three reaches yield a “composite reach distance” or composite score used to predict injury.

Strength and load lifted

Prior to initiation of the exercise regimen and at completion, each participant underwent bilateral grip strength assessment with the arm in the neutral position and overhead utilizing a Jamar Hand Dynamometer grip strength measurement device (Patterson Medical, Warrenville, IL, USA). Load was calculated continuously and throughout the regimen as volume load and by multiplying weight lifted (lbs) by repetitions and sets. These calculations occurred at the fourth week of the exercise regimen to ensure proper form, movement, and adaptation to the exercise, and then again at the eighth and final week of the exercise regimen. Split squat, trap bar deadlift, incline dumbbell bench press, and bird dog row were compared as these encompass squat, hip hinge, push, and pull movement patterns.

Quality of life and activity levels

Prior to initiation of the exercise regimen and at completion, each participant completed EQ-5D-5L and Godin Leisure-Time Exercise Questionnaires, which strongly correlate with activity levels and quality of life [35].

Phase angle

Phase angle, which reflects the health of cellular membranes, was assessed via the InBody 970 bioimpedance analysis (BIA) machine (InBody Co., South Korea).

Exercise intervention

The exercise regimen utilized a mixture of compound movements focusing on CKC movements, utilizing linear progression, and following guidelines from the NSCA. Each individual exercise workout progressed from most intense, CKC, compound, and athletic movements like squats and dead lifts, to least intense and more isolated exercises throughout the workout to maximize safety. Additionally, each workout provided full body resistance training focusing on the basic movement patterns of push, pull, hip hinge, squat, and core activation. The entire program lasted 3 months, and each exercise session ranged from 45–60 minutes. Activation and reset exercises focusing on mobility, muscle activation, and range of motion were performed prior to each workout to reduce the risk of injury. There was a 2-week ramp up period at the start of the program, and weights lifted utilized a combination of repetition speed, number “left in the tank”, and rating of perceived exertion (RPE). See ▶ **Fig. 1** for an example of the program.

The study took place at the Exercise Oncology and Resiliency Center. The center is a state-of-the-art 3,000-square-foot exercise and research facility where the exercise regimens are created and monitored by Certified Strength and Conditioning Specialists (CSCSs) utilizing exercise principles to improve strength, conditioning, performance, and overall health.

Exercise class attendance was recorded for each class. Planned missed days were able to be performed remotely if the individual had access to similar workout equipment only after the first month of the regimen. The initial 2 weeks of the regimen were considered the run-in period with strength and movement assessments to help ascertain proper weight usage and individual lifts. Exercises were progressed or regressed around specific core movement patterns (push, pull, hip hinge, squat, and core). For example, if an individual was unable to split squat body weight, they would be assisted in the movement until they could progress to the weighted lift. Weight lifted, repetitions, sets, and notes were recorded, and load was calculated throughout (volume load = weight lifted × repetitions × sets).

DAY 1		DAY 2		DAY 3	
	EXERCISE		EXERCISE		EXERCISE
A1	SPLIT SQUAT 3-4x8	A1	GOBLET SQUAT 3-4x8	A1	HEX DL 3-4x8
A2	SIDE PLANKS 20 s each side +5SPB	A2	BAND PULL APARTS 3x10	A2	TRX ROW 3x10
B1	BIRD DOG ROW 3x10	B1	HIP THRUST on 12" plyo box 3x10	B1	BOX STEP UP 6, 12 or 18" bx 3x10
B2	1-LEG GLUTE BRIDGE 3x10	B2	INCLINE DB PRESS 3x10	B2	PUSH UP 3x10 *W/KNEES/BOX *ASSIST W/BAR
C1	1/2 KNEELING SHLD PRESS 3x10	C1	DB SKULL CRUSHERS 3x10	C1	SUIT CASE CARRY turf distance x 3
C2	BICEP DB CURLS 3x10	C2	DB LATERAL RAISE 3x10	C2	DB HEEL TOES turf distance x 3

▶ **Fig. 1** Workout regimen during month one.

▶ **Table 1** Patient characteristics.

Age, years (mean, range)	57	41–74
Breast cancer stage	N = 20	
DCIS	1	(5 %)
Early stage	10	(45 %)
Locally advanced	7	(32 %)
Locally recurrent	3	(14 %)
Metastatic	1	(5 %)
Lymphedema	N = 5	(23 %)
Worse	0	(0 %)
Better	1	(5 %)
Concurrent Therapies	N = 24	
Antiestrogen	16	(73 %)
Chemotherapy	3	(14 %)
Radiotherapy	5	(23 %)
Prior Exercise	N = 6	(27 %)
Coach Rating (mean, SE)	2.45	0.14

DCIS, ductal carcinoma in situ; SE, standard error.

Statistics

All of the anthropometric, metabolic, fitness and QOL measurements were analyzed as continuous variables. Pairwise comparisons were assessed via the Wilcoxon signed-rank test. For each compound exercise, total load across months 1–3 was assessed via the Freidman test, with intragroup comparison using Wilcoxon signed rank testing with Bonferroni correction. All statistical analyses were performed using R version 4.1.2 (R Project for Statistical Computing).

Results

In total, 52 women were referred to the EOC to be screened for this study. Nine did not choose to participate, with the most common reason being work and scheduling conflict. Two were referred to physical therapy due to concerns of joint impingement or musculoskeletal disorders. Forty women were enrolled in the study, and the first twenty have completed the exercise regimen. Patient characteristics are listed in ▶ **Table 1**. Mean age was 57 (range 41–74) and half of the participants were diagnosed with DCIS or early-stage breast cancer. Nearly 75 % were undergoing treatment with antiestrogen therapy during the study, and 23 % were actively receiving irradiation. Twenty-seven percent of participants had engaged in prior exercise before enrolling and all participants continued a resistance training regimen after the protocol.

Adherence at interim analysis revealed 1.75 missed classes per participant (range 0–7), with all 20 participants meeting adherence over 75 %. No injuries or adverse events were reported, besides muscle soreness and, in one participant, 2 days of knee pain.

Body composition

Large improvements were seen in body composition in both BIA and US (▶ **Table 2**). On BIA, mean body fat percent decreased from 38.22 ± 2.0 to 36.66 ± 2.5 ($p = 0.003$) and body fat (lbs) decreased from 72.60 ± 6.56 to 68.22 ± 6.89 ($p = 0.020$). Muscle mass (lbs) and percent muscle mass increased from 58.04 + /−1.66 to 59.58 + /−1.63 ($p = 0.002$) and 33.07 + /−1.22 to 37.14 + /−2.27 ($p < 0.001$), respectively. On US, percent body fat decreased from 37.19 + /−1.30 to 32.7 + /−1.42 ($p < 0.001$), while fat free mass increased from 28.73 + /−1.20 to 31.66 + /−1.15 ($p = 0.011$). Bone mineral concentration was maintained throughout the regimen with no changes.

Resting metabolic rate (kcal/day) was unchanged on BIA but was increased from 1440.27 + /−36.81 to 1513.32 + /−41.6 ($p = 0.017$) on US. Additionally, phase angle was increased 4.85 to 5.11 ($p = 0.011$).

Functional movement and balance

Significant improvements were seen in balance and functional movement. Mean FMS scores increased from 9.82 + /−0.51 to 11.73 + /−0.7 ($p = 0.018$). Mean Y-balance on the left increased from 72.37 + /−2.69 to 85.26 + /−2.4 ($p = 0.001$) and mean Y-balance on the right increased from 70.33 + /−2.60 to 85.24 + /−2.42 ($p < 0.001$).

▶ **Table 2** Mechanisms of interaction between exercise and improved cancer-specific outcomes.

	Baseline		Month 3		
	Mean	**SE**	**Mean**	**SE**	**Wilcoxon signed-rank p value**
Height (inches)	65.11	0.44	-	-	-
Weight (initial)	177.38	8.54	176.93	8.88	0.834
InBody body fat (lbs)	72.60	6.56	68.22	6.89	0.020
InBody body fat %	38.22	2.00	36.66	2.15	0.003
InBody muscle mass (lbs)	58.04	1.66	59.58	1.63	0.002
InBody muscle mass %	33.07	1.22	37.14	2.27	< 0.001
InBody fat-free mass	106.79	3.41	108.72	2.79	0.108
BMC	6.45	0.17	6.48	0.17	0.223
Whole-body phase angle	4.85	0.11	5.11	0.12	0.011
US % BF	37.19	1.30	32.7	1.42	< 0.001
US essential fat (lbs)	53.34	2.87	53.9	3.67	0.442
US excess fat	13.22	2.93	9.68	2.5	0.108
US FFM	28.73	1.20	31.66	1.15	0.011
InBody RMR	1426.41	30.81	1435.05	27.42	0.108
US RMR	1440.27	36.81	1513.32	41.6	0.017
Grip strength RH	19.50	1.16	22.73	0.93	0.261
Grip strength RL	23.32	1.30	24.77	0.99	0.304
Grip strength LH	20.27	1.16	23.82	1.16	0.016
Grip strength LL	21.68	1.32	24.68	1.09	0.143
Godin	27.36	5.07	38.41	2.42	0.152
EQ5D1	4.91	0.06	4.86	0.1	1.000
EQ5D2	5.00	0.00	5	0	-
EQ5D3	4.91	0.06	4.86	0.07	1.000
EQ5D4	4.36	0.14	4.23	0.17	0.824
EQ5D5	4.68	0.10	4.82	0.08	0.773
EQ5D6	73.09	4.42	81.95	3.51	0.097
FMS initial	9.82	0.51	11.73	0.7	0.018
Y-balance L	72.37	2.69	85.26	2.4	0.001
Y-balance R	70.33	2.60	85.24	2.42	< 0.001

SE, standard error; BMC, bone mineral concentration; US, ultrasound; lbs, pounds; FFM, fat-free mass; RH, right high; RL, right low; LH, left high; LL, left low; FMS, functional movement screen.

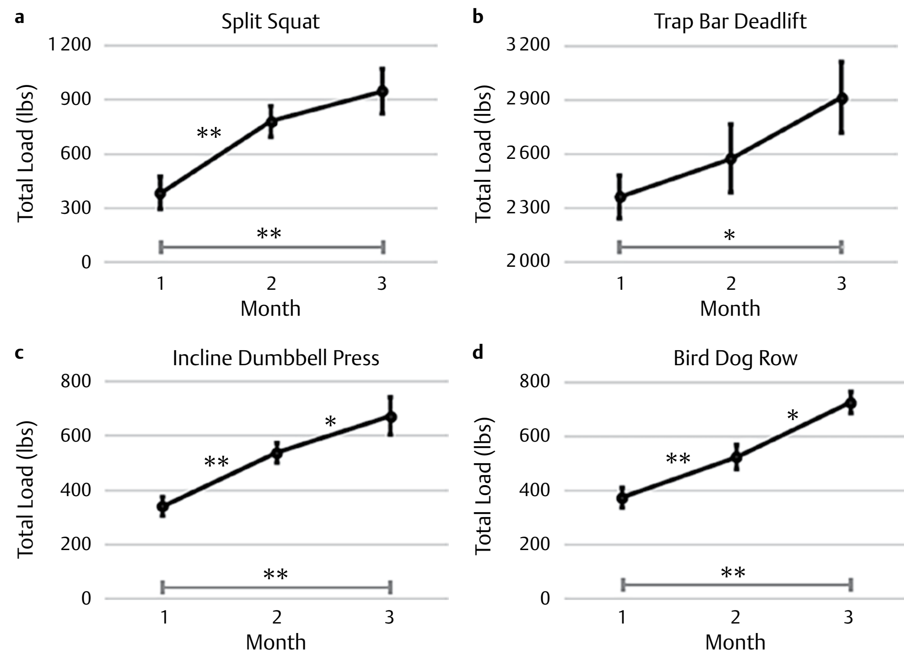
▶ **Table 3** Changes in load lifted, reported as mean and standard error. Following Friedman testing with $p < 0.05$, pairwise comparisons across months 1 vs. 3, 1 vs. 2, and 2 vs. 3 were performed via Wilcoxon signed rank testing with Bonferroni correction.

	Month 1		Month 2		Month 3		p value		
Exercise	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Month 1 vs. 3**	**Month 1 vs. 2**	**Month 2 vs. 3**
Split squat	383.0	89.4	782.4	84.8	951.0	123.9	< 0.001	< 0.001	0.268
Trap bar DL	2363.4	117.4	2576.1	189.9	2913.0	195.2	0.035	0.238	0.155
Incline DB bench	341.4	34.5	538.2	37.1	673.3	69.7	< 0.001	< 0.001	0.047
Bird dog row	374.2	36.3	523.9	43.4	725.2	40.4	< 0.001	< 0.001	0.002

SE, standard error; DL, dead lift; DB, dumbbell.

Strength and load lifted

Significant increases were seen in strength and load lifted on conclusion of the exercise regimen (▶ **Table 3**, ▶ **Fig. 2**). Hand grip strength did not significantly change except on the left with arm overhead ($p = 0.016$). Load calculations for split squat, trap bar deadlift, bird dog row, and incline dumbbell press increased significantly throughout the workout, with mean deadlift loads of 2900 lbs. For all compound exercises, the Friedman test was significant with an overall difference in load across months 1, 2, and 3. Accordingly, pairwise comparisons were performed, showing significant increase in load from completion of month 1 to month 3 for each exercise even after multiple hypothesis correction (▶ **Table 3**, ▶ **Fig. 2**).



▶ **Fig. 2** Load lifted over time (sets x repetitions x lbs), shown at the end of each successive month of training as mean values with standard error bars. Abbreviations: *P<0.05; **P<0.001 on pairwise Wilcoxon signed-rank testing with Bonferroni correction.

Quality of life and activity levels

Godin levels of activity increased from 27.36 + /−5.07 to 38.41 + /−2.42, but this was not statistically significant. Quality of life scores were similarly high for EQ-5D questions before and after exercise, though with a numeric increase in self-rating of heath from 73.09 + /−4.42 to 81.95 + /−3.51 (p = 0.097).

Phase angle

Phase angle increased from 4.85 + /−0.12 to 5.11 + /−0.12 ° (p = 0.011).

Discussion

Interim analysis of the EXERT-BC study assessing a novel dose-escalated resistance training regimen for women with breast cancer reveals significant and impactful improvements in balance, functional movement, strength, muscle mass, and fat mass, even though half of participants had locally advanced, recurrent, or metastatic breast cancer. This was achieved in a short period of 3 months utilizing an intense linear progression resistance training regimen with a focus on multipoint movement compound and closed chain exercises.

In comparison to prior studies, these data reveal considerable increase of muscle mass with an average increase of 1.5 lbs. of muscle mass on BIA and 3 pounds of fat-free mass on US [36]. With the considerable amount of adipose tissue lost during the intervention, percent body fat dropped 2.5 and 4.5 % on BIA and US, respectively. Additionally, phase angle was significantly improved after the resistance training regimen (▶ **Table 3**). Phase angle reflects the health of cellular membranes and muscle function and correlates with outcomes after the treatment for cancer [37]. Significant improvement was seen in phase angle in just 3 months of resistance training, raising the question as to whether this one mechanism exercise may improve cancer-specific outcomes [38].

The age and functional status of the women in this study varied significantly, with a minority already engaged in a resistance training or exercise regimen prior to enrollment in the protocol. Additionally, the majority had chronic musculoskeletal, joint, or orthopedic issues yet were capable of engaging in an intense exercise regimen utilizing compound movements and heavy weights. Half of the women were experiencing joint pain from endocrine therapy or lymphedema from axillary surgery on enrollment in the study. Yet, the load lifted was able to produce significant increases in strength and considerable improvements in functional movement assessments and balance scores, the latter of which improved by around 20 % for each leg. Such profound changes could have large downstream impact on both health and cost-saving by reduced risk of falls and fractures and generally improved overall physical function, which correlates strongly with outcomes after the treatment of breast cancer, particularly within the first two years after treatment.[39] Of note, lymphedema did not worsen in any participants and improved in one based on fluid measurements (data not shown).

A recent large study published in the *Journal of Clinical Oncology* found that breast cancer patients randomized to a strength training regimen did not exhibit a reduced fall risk [40]. However, their weight training regimen utilized 1–3 sets of 8–10 exercises at a weight performed at 8–12 repetitions with weighted vests providing resistance, with planned progression increases of 1–3 % body weight up to a target of 15 % by 6 months. Several similar regimens appear within the breast cancer exercise oncology literature utilizing low loads [41]. In EXERT-BC, we aimed to stress the neuromuscular and musculoskeletal systems with linear progression to elicit the maximum potential neuroadaptation and increase in strength utilizing a regimen that has shown benefits in noncancer patients. Additionally, the present regimen was designed to achieve around 10 sets per muscle group or movement pattern per week, as studies reveal this may promote hypertrophy [42].

While the above is an interim assessment of EXERT-BC, it may suggest that a higher dose of resistance training utilizing compound multi-joint movement may be more efficacious in improving functional capacity and reducing fall risk.

It is important to note that studies in noncancer and athletic populations have revealed doses of exercise that are generally required to elicit physical improvements like increases in bone density, muscle mass, and strength [28]. Data reveal that these thresholds are rarely met in exercise oncology literature. Other data have questioned whether women with a history of breast cancer or undergoing treatment for breast cancer may achieve similar physiologic changes to those of a noncancer population [36]. The data from the interim analysis of EXERT-BC appear to support this hypothesis.

Limitations of the study should be addressed. Firstly, this was a single arm study with no comparison or control group, future studies should include a randomization. Assessing body composition while maximizing terms of safety, efficacy, convenience, and cost is difficult. All sources, including bioimpedance analysis and ultrasound, have limitations. However, to minimize these issues, we performed both tests to confirm consistent changes across two modalities. The average age was 57 years, so the results of this study may not be applicable to all individuals with breast cancer. Additionally, the training age of the participants was quite low, and most had never engaged in prior resistance training. However, it should be noted that entrance criteria were broad, with the major stipulation being the ability to get up and down from the ground, squat body weight, and participate in a group exercise regimen. The expertise of the Certified Strength and Conditioning Specialists to progress or regress exercise choice based on movement patterns likely accounted for the ability to train a broad range of skill levels with heavy weights and compound movements. Future studies utilizing this method are underway and can further elucidate these methods in more general cancer populations. Lastly, studies assessing more experienced individuals may attempt to progress to full range of motion in a shorter amount of time, which may produce greater strength and hypertrophy gains.

Conclusion

Interim analysis of a dose-escalated resistance training exercise program in women with breast cancer demonstrates favorable rates of safety and compliance while showing significant improvements in body composition, balance, and strength. Future exercise protocols in women with breast cancer should incorporate dose-escalated resistance training and linear progression to achieve improvements in muscle mass, fat mass, and functional capacity.

Conflict of Interest

C. E. Champ receives compensation for health-related books and is on the scientific board of Simply Good Foods and was a scientific advisor for Biosense (relationship no longer present).

References

[1] Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological evidence and proposed mechanisms. Nat Rev Cancer 2004; 4: 579–591. DOI: 10.1038/nrc1408

[2] Champ CE, Volek JS, Siglin J et al. Weight gain, metabolic syndrome, and breast cancer recurrence: Are dietary recommendations supported by the data? Int J Breast Cancer 2012; 2012: 9. DOI: 10.1155/2012/506868

[3] Borch KB, Braaten T, Lund E et al. Physical activity before and after breast cancer diagnosis and survival – the Norwegian women and cancer cohort study. BMC Cancer 2015 151 2015; 15: 1–10. DOI: 10.1186/s12885-015-1971-9

[4] Irwin ML, McTiernan A, Bernstein L et al. Physical activity levels among breast cancer survivors. Med Sci Sports Exerc 2004; 36: 1484–1491

[5] Champ CE, Ohri N, Klement RJ et al. Assessing changes in the activity levels of breast cancer patients during radiation therapy. Clin Breast Cancer 2018; 18: e1–e6. DOI: 10.1016/j.clbc.2017.08.009

[6] Fogelholm M, Kukkonen-Harjula K. Does physical activity prevent weight gain--a systematic review. Obes Rev 2000; 1: 95–111

[7] Weiss EP, Racette SB, Villareal DT et al. Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction but not with exercise-induced weight loss. J Appl Physiol 2007; 102: 634–640. DOI: 10.1152/japplphysiol.00853.2006

[8] Westcott WL. Resistance training is medicine. Curr Sports Med Rep 2012; 11: 209–216. DOI: 10.1249/JSR.0b013e31825dabb8

[9] Shaibi GQ, Cruz ML, Ball GDC et al. Effects of resistance training on insulin sensitivity in overweight Latino adolescent males. Med Sci Sport Exerc 2006; 38: 1208–1215. DOI: 10.1249/01.mss.0000227304.88406.0f

[10] Dos Santos WDN, Gentil P, de Moraes RF et al. Chronic effects of resistance training in breast cancer survivors. Biomed Res Int 2017; 2017: 8367803. DOI: 10.1155/2017/8367803

[11] Schmitz KH, Troxel AB, Dean LT et al. Effect of home-based exercise and weight loss programs on breast cancer–related lymphedema outcomes among overweight breast cancer survivors. JAMA Oncol 2019; 5: 11: 1605–1613. DOI: 10.1001/jamaoncol.2019.2109

[12] Schmitz KH, Ahmed RL, Troxel A et al. Weight lifting in women with breast-cancer–related lymphedema. N Engl J Med 2009; 361: 664–673. DOI: 10.1056/NEJMoa0810118

[13] Schmitz KH, Ahmed RL, Troxel AB et al. Weight lifting for women at risk for breast cancer–related lymphedema. JAMA 2010; 304: 2699. DOI: 10.1001/jama.2010.1837

[14] Ahmed RL, Thomas W, Yee D et al. Randomized controlled trial of weight training and lymphedema in breast cancer survivors. J Clin Oncol 2006; 24: 2765–2772. DOI: 10.1200/JCO.2005.03.6749

[15] Stensdotter A-KK, Hodges PWPW, Mellor R et al. Quadriceps activation in closed and in open kinetic chain exercise. 2003; 35: 2043–2047. DOI: 10.1249/01.MSS.0000099107.03704.AE

[16] Rivera JE. Open versus closed kinetic chain rehabilitation of the lower extremity: A functional and biomechanical analysis. J Sport Rehabil 1994; 3: 154–167. DOI: 10.1123/jsr.3.2.154

[17] Schoenfeld BJ. The mechanisms of muscle hypertrophy and their application to resistance training. J Strength Cond Res 2010; 24: 2857–2872. DOI: 10.1519/JSC.0b013e3181e840f3

[18] Gould DW, Lahart I, Carmichael AR et al. Cancer cachexia prevention via physical exercise: molecular mechanisms. J Cachexia Sarcopenia Muscle 2013; 4: 111. DOI: 10.1007/S13539-012-0096-0

[19] Clifford B, Koizumi S, Wewege MA et al. The effect of resistance training on body composition during and after cancer treatment: A systematic review and meta-analysis. Sport Med 2021; 52(2): 287–300

[20] Phillips SM, Winett RA. Uncomplicated resistance training and health-related outcomes: evidence for a public health mandate. Curr Sports Med Rep 2010; 9: 208–213. DOI: 10.1249/JSR.0b013e3181e7da73

[21] Singh B, Spence RR, Steele ML et al. A systematic review and meta-analysis of the safety, feasibility, and effect of exercise in women with stage II+ breast cancer. Arch Phys Med Rehabil 2018; 99: 2621–2636. DOI: 10.1016/j.apmr.2018.03.026

[22] Fairman CM, Focht BC, Lucas AR et al. Effects of exercise interventions during different treatments in breast cancer. J Community Support Oncol 2016; 14: 200–209. DOI: 10.12788/jcso.0225

[23] Myer GD, Quatman CE, Khoury J et al. Youth versus adult "weightlifting" injuries presenting to United States emergency rooms: accidental versus nonaccidental injury mechanisms. J strength Cond Res 2009; 23: 2054–2060. DOI: 10.1519/JSC.0b013e3181b86712

[24] Hamill BP. Relative safety of weightlifting and weight training. J Strength Cond Res 1994; 8: 53–57

[25] Cook G, Burton L, Hoogenboom B. Pre-participation screening: the use of fundamental movements as an assessment of function – part 1. N Am J Sports Phys Ther 2006; 1: 62–72

[26] Mazzetti SA, Kraemer WJ, Volek JS et al. The influence of direct supervision of resistance training on strength performance. Med Sci Sport Exerc 2000; 32: 1175–1184. DOI: 10.1097/00005768-200006000-00023

[27] Grimmett C, Corbett T, Brunet J et al. Systematic review and meta-analysis of maintenance of physical activity behaviour change in cancer survivors. Int J Behav Nutr Phys Act 2019; 16: 37. DOI: 10.1186/s12966-019-0787-4

[28] Champ CE, Carpenter DJ, Diaz AK et al. Resistance training for patients with cancer: A conceptual framework for maximizing strength, power, functional mobility, and body composition to optimize health and outcomes. Sports Med 2023; 53: 75–89. DOI: 10.1007/S40279-022-01759-Z

[29] McLester CN, Nickerson BS, Kliszczewicz BM et al. Reliability and agreement of various InBody body composition analyzers as compared to dual-energy X-ray absorptiometry in healthy men and women. J Clin Densitom 2020; 23: 443–450. DOI: 10.1016/J.JOCD.2018.10.008

[30] Jackson A, Pollock M, Ward A. Generalized equations for predicting body density of women. Med Sci Sport Exerc 1980; 12: 175–182

[31] Smith-Ryan AE, Blue MNM, Trexler ET et al. Utility of ultrasound for body fat assessment: validity and reliability compared to a multicompartment criterion. Clin Physiol Funct Imaging 2018; 38: 220–226. DOI: 10.1111/CPF.12402

[32] Miclos-Balica M, Muntean P, Schick F et al. Reliability of body composition assessment using A-mode ultrasound in a heterogeneous sample. Eur J Clin Nutr 2020 753 2020; 75: 438–445. DOI: 10.1038/s41430-020-00743-y

[33] Jagim AR, Camic CL, Kisiolek J et al. Accuracy of resting metabolic rate prediction equations in athletes. J Strength Cond Res 2018; 32: 1875–1881. DOI: 10.1519/JSC.0000000000002111

[34] Perry FT, Koehle MS. Normative data for the functional movement screen in middle-aged adults. J Strength Cond Res 2013; 27: 458–462. DOI: 10.1519/JSC.0b013e3182576fa6

[35] Craig BM, Pickard AS, Lubetkin EI. Health problems are more common, but less severe when measured using newer EQ-5D versions. J Clin Epidemiol 2014; 67: 93–99. DOI: 10.1016/J.JCLINEPI.2013.07.011

[36] Clifford B, Koizumi S, Wewege MA et al. The effect of resistance training on body composition during and after cancer treatment: A systematic review and meta-analysis. Sport Med 2021

[37] Arab A, Karimi E, Vingrys K et al. Is phase angle a valuable prognostic tool in cancer patients' survival? A systematic review and meta-analysis of available literature. Clin Nutr 2021; 40: 3182–3190. DOI: 10.1016/J.CLNU.2021.01.027

[38] Sardinha LB, Rosa GB. Phase angle, muscle tissue, and resistance training. Rev Endocr Metab Disord 2023 243 2023; 24: 393–414. DOI: 10.1007/S11154-023-09791-8

[39] Sehl M, Lu X, Silliman R et al. Decline in physical functioning in first 2 years after breast cancer diagnosis predicts 10-year survival in older women. J Cancer Surviv 2013; 7: 20–31. DOI: 10.1007/S11764-012-0239-5

[40] Winters-Stone KM, Horak F, Dieckmann NF et al. GET FIT: A randomized clinical trial of Tai Ji Quan versus strength training for fall prevention after chemotherapy in older, postmenopausal women cancer survivors. J Clin Oncol 2023; 3384–3396: JCO2201519. DOI: 10.1200/JCO.22.01519

[41] Rosenberg J, Hyde PN, Yancy WS et al. Quantity of resistance exercise for breast cancer patients: Does the dose match the objective? J Strength Cond Res 2021; 35: 1467–1476. DOI: 10.1519/JSC.0000000000003996

[42] Schoenfeld BJ, Ogborn D, Krieger JW. Dose-response relationship between weekly resistance training volume and increases in muscle mass: A systematic review and meta-analysis. J Sports Sci 2017; 35: 1073–1082. DOI: 10.1080/02640414.2016.1210197