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Technical Note

Effects of Aerobic Exercise Modality on Cognition and Fitness in Breast Cancer Survivors

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ABSTRACT

International Journal of Exercise Science 12(3): 1023-1033, 2019. Although cognitive dysfunction is a common occurrence among breast cancer survivors, there is no widely recognized intervention for this debilitating condition. The purpose of this study was to determine whether floor/step aerobics (FSA) and/or treadmill walking (TMW) interventions can improve outcomes when compared to standard care (STC). Recent breast cancer survivors participated in 12 weeks of FSA (n=8), TMW (n=7), or STC (n=10) with pre/post assessments of cognition and fitness. Interaction effects between group and time were assessed with repeated measures ANOVA. Throughout the extent of cognitive and fitness assessments, there were found to be no statistically significant interactions between group and time. Because of the small sample size, these results should not be taken to mean that exercise cannot improve cognition in recent breast cancer survivors, but this study should be used as a baseline for designing similar studies with a longer intervention, more intense exercise program, or another alteration that might increase effectiveness of the intervention. More research is needed in this area, but until more specific study results are available, healthcare providers should continue to encourage breast cancer survivors to regularly participate in aerobic exercise to maintain physical function.

KEY WORDS: Chemobrain, Chemofog, Memory, Physical Activity, Quality of Life, Treatment

INTRODUCTION

An estimated 65% of breast cancer survivors suffer from dysfunction in a variety of cognitive domains (23), as described by the term “cancer-induced cognitive dysfunction” (CICD). Although cognition improves over time in many women, researchers have demonstrated that some breast cancer survivors who are 20 years post-treatment still score lower on neuropsychological assessments of verbal learning, executive function, and psychomotor function than do their age-matched counterparts (12). Other cognitive domains that are commonly hindered in this population include memory, processing speed, and attention. In general terms, breast cancer survivors often describe their symptoms as a change in memory, fogginess in the brain, difficulty focusing, decreased ability to follow directions, and trouble with multitasking (16). Because of their effect on daily tasks, these symptoms are likely to reduce quality of life in breast cancer survivors.

In accordance with the International Cognition and Cancer Task Force (ICCTF) guidelines (24), some researchers report the percentage of their participants who experienced objective cognitive decline from pre-treatment to post-treatment, rather than only reporting statistical data. By using the Mini-Mental State Exam to determine cognitive ability, Biglia and colleagues found that the number of breast cancer survivors (n = 40) who scored below the mean increased from 19.5% before treatment to 30.8% immediately post-treatment (4), which indicates that treatment for breast cancer decreases basic cognitive functions in a subset of survivors. Debess and colleagues found that 15.4% of their 120 breast cancer survivor participants demonstrated cognitive decline on at least two tests (5), which was considered to be a clinically significant decline. Vearncombe and colleagues reported that 16.9% of their 136 breast cancer survivor participants had significant cognitive decline post-chemotherapy (21). Stewart and colleagues found that 31% of their 61 patients who were treated with chemotherapy showed reliable cognitive decline, while only 5% showed reliable improvement (20). These studies show that one sixth to one third of breast cancer survivors appear to suffer from clinically significant cognitive decline. However, since there are more than 3.5 million breast cancer survivors alive today (1), it could be extrapolated that ½ million to 1 million women in the United States alone have previously, or are currently, suffering from CICD.

While it seems that treatment for breast cancer does not adversely impact cognition in all breast cancer survivors, there is enough evidence that it can significantly negatively impact many cognitive domains in a large number of women. Based on this evidence, it is important to consider whether interventions could reduce CICD to improve quality of life in those breast cancer survivors who are affected by this disorder.

Chemotherapy-induced cognitive dysfunction can be reduced in rats by regular participation in physical activity. In a study by Fardell and colleagues, healthy adult rats were treated with a chemotherapy regimen that is known to cause cognitive dysfunction (8). Their control group remained sedentary while the intervention group was provided with access to a running wheel for four weeks. After this time, the physically active rats scored significantly higher than their sedentary counterparts on spatial reference memory and novel object recognition tests ($p < .05$). These results provide support for conducting a similar study with humans to determine if aerobic exercise is an effective intervention for reducing CICD. However, a recent Cochrane review reported that there is a substantial lack of conclusive data from well-designed, adequately sized studies regarding the impact of aerobic exercise on cognitive function in breast cancer survivors (9).

In another study, 41 breast cancer survivors completed 12 weeks of cognitive training or a wait-list control period (11). Those in the intervention group had significantly improved post-intervention scores in the Wisconsin Card Sorting Test (p = .008), letter fluency (p = .003), and the symbol search test (p = .009), demonstrating the effectiveness of cognitive training in this population. A cognitively challenging exercise intervention could potentially function similarly to a cognitive training program, enhancing cognition while also increasing cardiorespiratory fitness.

The aforementioned studies demonstrate that aerobic exercise and cognitive training both have the potential to improve cognitive function in breast cancer survivors. However, published research does not indicate whether there are additional benefits from combining these interventions.

The primary purpose of this study was to determine whether aerobic exercise improves cognition in recent breast cancer survivors compared to a sedentary lifestyle or standard care (STC), and to identify whether floor/step aerobics (FSA) improves cognition more than does treadmill walking (TMW). FSA involves following frequently changing upper and lower body movement patterns from verbal cues by a group exercise leader, which adds a cognitive stimulus to the exercise program when compared to treadmill walking monotonously in a straight line. The secondary purpose of this study was to compare effects of FSA, TMW, and STC on cardiorespiratory fitness among breast cancer survivors to ensure that fitness benefits of aerobic exercise participation are maintained when a cognitive stimulus is added.

METHODS

Participants

Participants were female, with a mean age of 60 years old, who reported being sedentary at enrollment. Study inclusion criteria required that they be within 3 months following completion of primary treatment for breast cancer. Ongoing treatments, such as tamoxifen and Herceptin, were allowed. Exclusion criteria included current pregnancy, participation in a concurrent exercise program, reconstructive surgery or surgery rehabilitation during the study, inability to obtain medical clearance, and inability to speak English fluently. The study design was approved by the Institutional Review Board at Washington State University (WSU) before recruitment began.

Effect sizes are not readily available for exercise interventions on cognition among recent breast cancer survivors. Among adults, in general, the effect size of exercise on cognitive function is approximately 0.30 (3). Therefore, a power analysis demonstrated that 30 women were needed for this study, with 10 assigned to each group, in order to distinguish interaction effects. Within the allotted time frame, 25 women gave informed consent to participate and completed the study. Assessed subject characteristics did not differ significantly between groups at baseline (see Table 1).

Table 1. Participant demographics. Shown as mean ± standard deviation.

	FSA (n=8)	TMW (n=7)	STC (n=10)	*p*-value
Age	60.38 ± 10.07	58.71 ± 6.99	60.82 ± 11.54	0.908
Education	15.38 ± 1.19	14.86 ± 2.55	14.40 ± 3.66	0.275
Resting Heart Rate	71.67 ± 12.35	68.14 ± 7.47	72.15 ± 9.37	0.680
Systolic Blood Pressure	122.67 ± 15.13	111.14 ± 11.13	125.54 ± 17.01	0.144
Body Mass Index	31.24 ± 8.19	29.89 ± 7.15	29.23 ± 6.32	0.809
Percent Body Fat	40.00 ± 6.17	39.77 ± 5.82	39.67 ± 7.09	0.993
Timed Up & Go	8.28 ± 1.54	8.88 ± 1.05	9.17 ± 1.88	0.485
Perceived Stress Scale	14.56 ± 7.54	11.29 ± 6.07	14.38 ± 5.68	0.528

FSA: Floor/step aerobics, TMW: Treadmill walking, STC: Standard care.

Protocol
All participants who met inclusion and exclusion criteria were enrolled into the study in one of three groups: FSA, TMW, or STC. They were assigned to a group based on the class time that they selected. To reduce the risk of home-based exercise as a confounding variable, all participants were asked to maintain their normal level of physical activity, except for attending designated exercise classes at the study site. Participants were asked to complete and return an exercise log to confirm their offsite physical activity.

Women in the STC group were instructed to remain sedentary throughout the study, but were invited to attend 12 weeks of free exercise classes following post-testing as an incentive to submit exercise logs and complete post-testing. TMW and FSA participants attended exercise classes for 12 weeks at WSU's Health Sciences Campus. The exercise prescription (frequency, intensity, time, and type) was based on the American College of Sports Medicine recommendations for this population (2): 30-50 minutes, three to five days per week of moderately intense aerobic exercise that uses large muscle groups.

Frequency: Breast cancer survivors attended classes each Monday, Wednesday, and Thursday. Participants were allowed to miss three exercise classes; additional missed class days were required to be rescheduled. Intensity: All classes were held at a moderate intensity, which was monitored throughout class using heart rate (HR) and Borg's ratings of perceived exertion (RPE) scale (7) in which exertion is rated between 6 and 20. Moderate intensity is classified as an RPE of 12-13 or HR of 40%-<60% of heart rate reserve (2). If exercising HR or RPE were not in the desired range at any checkpoint, participants were assisted with making modifications to intensity. Time: Exercise classes were 50 minutes long to allow participants to utilize the free one-hour parking on campus. By scheduling three classes per week, this duration also met the minimum national recommendations for weekly physical activity volume (2). Type: Participants were assigned to FSA or TMW classes for the duration of the study. The first half of each FSA class focused on step aerobics, and the second half of each class focused on floor aerobics. A single instructor designed and taught all classes using a standard 32-count design. In this format, movements are organized into 32-count blocks that are gradually learned throughout the session and then repeated until the class can perform them without any instructor cues. TMW classes began with a slower walk at an incline and concluded with a rapid walk with no incline, mimicking the speed and grade changes in the FSA classes. Treadmill speeds varied between individuals, but were set at a level that kept heart rates within the goal range.

Data was collected during a separate testing appointment the week prior to and the week following the 12-week intervention, on non-exercise days, to reduce risk of a false positive cognitive improvement from acute exercise. To prepare for test days, participants were instructed to maintain their normal activities and intake, and to avoid products containing alcohol, caffeine, or tobacco. Assessments were conducted at a standard room temperature and humidity. A thorough explanation of test procedures was given prior to each test. Where standard protocols indicate, a demonstration or practice test were also given.

Cognition was assessed using a battery of traditional cognitive assessments to test all primary cognitive domains. The Trail Making Test-A (TMT-A) and Trail Making Test-B (TMT-B) (14) involve participants connecting numbered dots as quickly as possible, and rapidly alternating between numbered and lettered dots, respectively. TMT-A is an assessment of attention and processing speed; TMT-B assesses executive function. The Controlled Oral Word Association Tests (COWAT) (including FAS, category, and switching trials) (14) require participants to name as many words as possible, within certain criteria, in one minute. These assessments show verbal fluency. Design Fluency (DF) tests involve participants drawing a variety of shapes by connecting dots, also within one minute. Condition 1 involves connecting black dots, Condition 2 involves connecting white dots, and Condition 3 involves alternating between black and white dots. Conditions 1 and 2 assess attention and processing speed, while Condition 3 assesses executive function. The Grooved Pegboard Test (GPT) requires participants to place odd shaped pegs into a pegboard as quickly as possible, which shows psychomotor function. This was selected as a control test; results should not change with an exercise intervention. In order to determine cardiorespiratory fitness for exercise prescription, as well as to assess improvement following the intervention, fitness was estimated using the Ebbeling Submaximal Single-Stage Treadmill Walking Test (15, 22). In this test, participants walk on a treadmill at a self-selected speed and a 5% grade for four minutes, at which point exercising heart rate is assessed. Maximal VO_2 was predicting using the standard Ebbeling equation, which uses age, gender, walking speed, and exercising heart rate as variables. Based on previous experience (13) treadmill speed was held constant during pre- and post-testing, leaving exercising HR as the only test variable between tests.

Statistical Analysis

Repeated measures analysis of variance (SPSS 23) indicated whether there was an interaction between group and time. Assessments were considered statistically significant if the interaction *p*-value was less than or equal to .05. All data is reported as mean ± standard deviation.

RESULTS

Trail Making Tests: The statistical interaction between group and time for the TMT-A test was not significant (FSA: 26.00±6.17, 22.11±7.28; TMW: 25.08±9.36, 22.05±4.50; STC: 27.13±7.72, 26.21±9.18; p = .637). Results are shown in Figure 1. The TMT-B also showed no interaction between group and time (FSA: 62.58±8.95, 51.77±15.46; TMW: 58.77±24.32, 57.79±22.70; STC: 57.36±16.34, 48.54±16.51; p = .292).

Verbal Fluency: There was no significant interaction of exercise group over time on verbal fluency scores when measured with the FAS test (FSA: 11.75±3.62, 13.69±3.51, TMW: 13.57±4.50, 14.14±3.93, STC: 11.57±2.23, 10.86±4.02; p = .296), as shown in Figure 2, with the "category" trials (FSA: 44.00±11.77, 48.63±11.56; TMW: 42.00±12.65, 45.57±11.69; STC: 36.20±7.24, 37.80±10.02; p = .662), or with the "switching" trial (FSA: 15.13±2.42, 14.00±2.39; TMW: 15.00±3.27, 16.43±3.21; STC: 13.10±2.56, 13.70±4.50; p = .369).

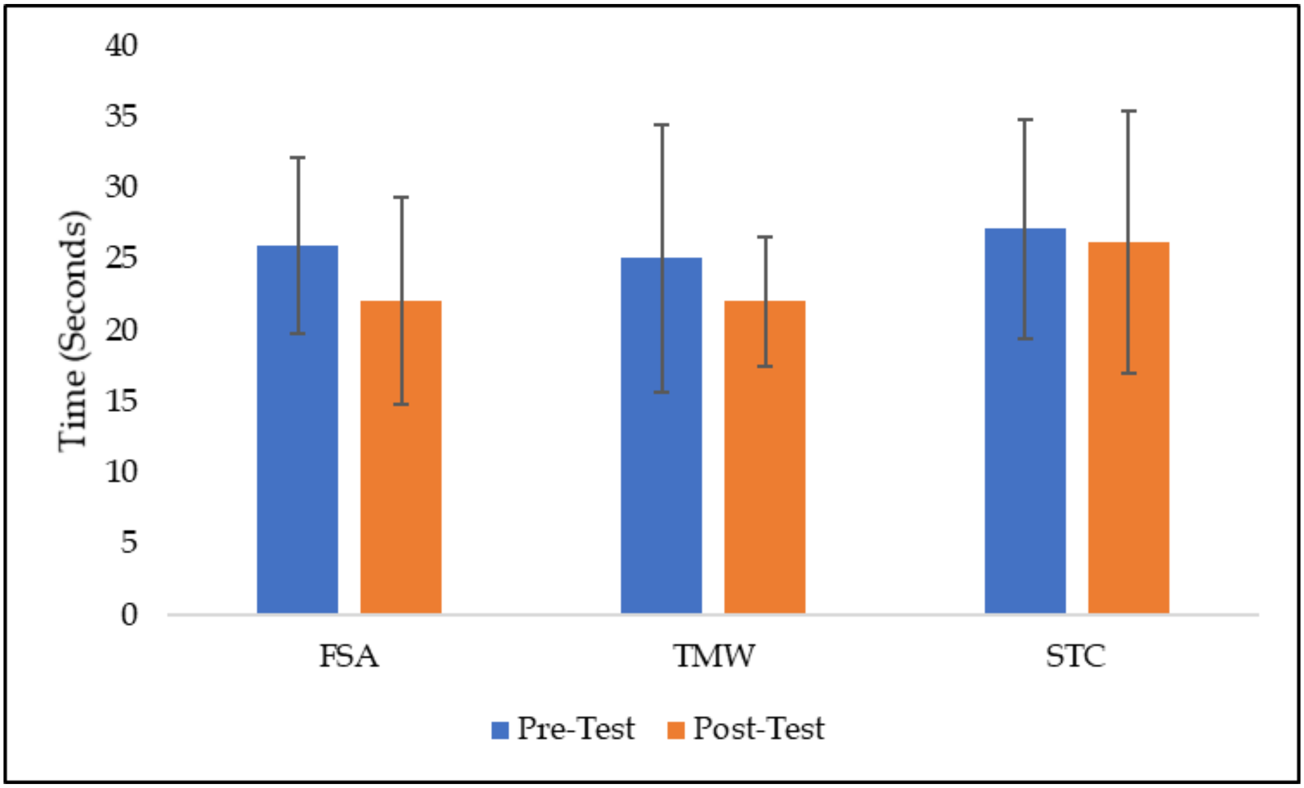

Figure 1. Effect of exercise modality over time on attention and processing speed during the TMT-A.

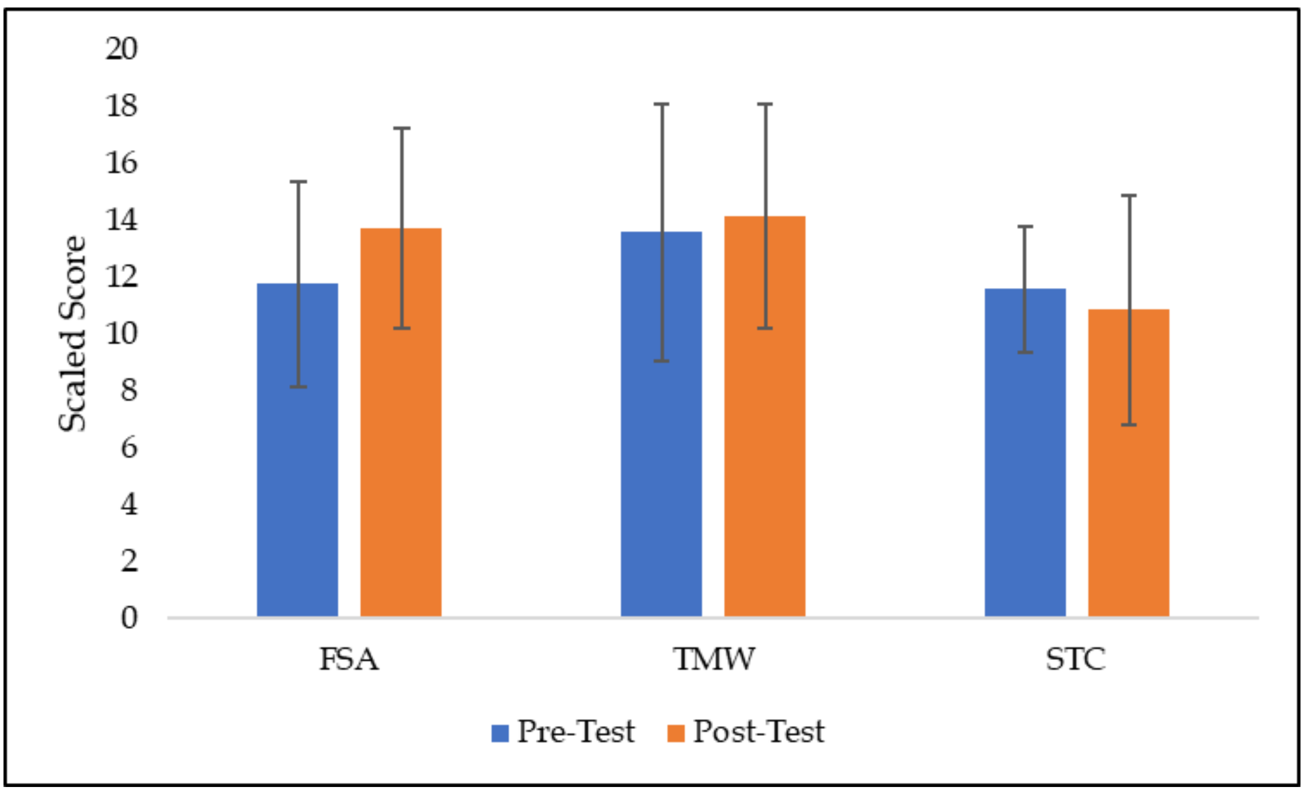

Figure 2. Effect of exercise modality over time on verbal fluency.

Design Fluency: When assessing results from the DF test, it is standard to add scaled scores from Condition 1 and Condition 2, and then scale that sum. Using this procedure, the interaction between group and time on DF results was not statistically significant (FSA: 12.75±3.69, 14.25±2.25; TMW: 11.71±2.63, 14.29±3.86; STC: 11.67±3.43, 12.00±2.74; p = .261). It is standard to also scale the sum of scaled scores from all three conditions. Results from this calculation were also insignificant (FSA: 12.63±3.70, 14.13±2.53; TMW: 12.00±2.52, 13.43±3.74; STC: 12.11±3.33, 12.67±3.32; p = .624). This is shown in Figure 3.

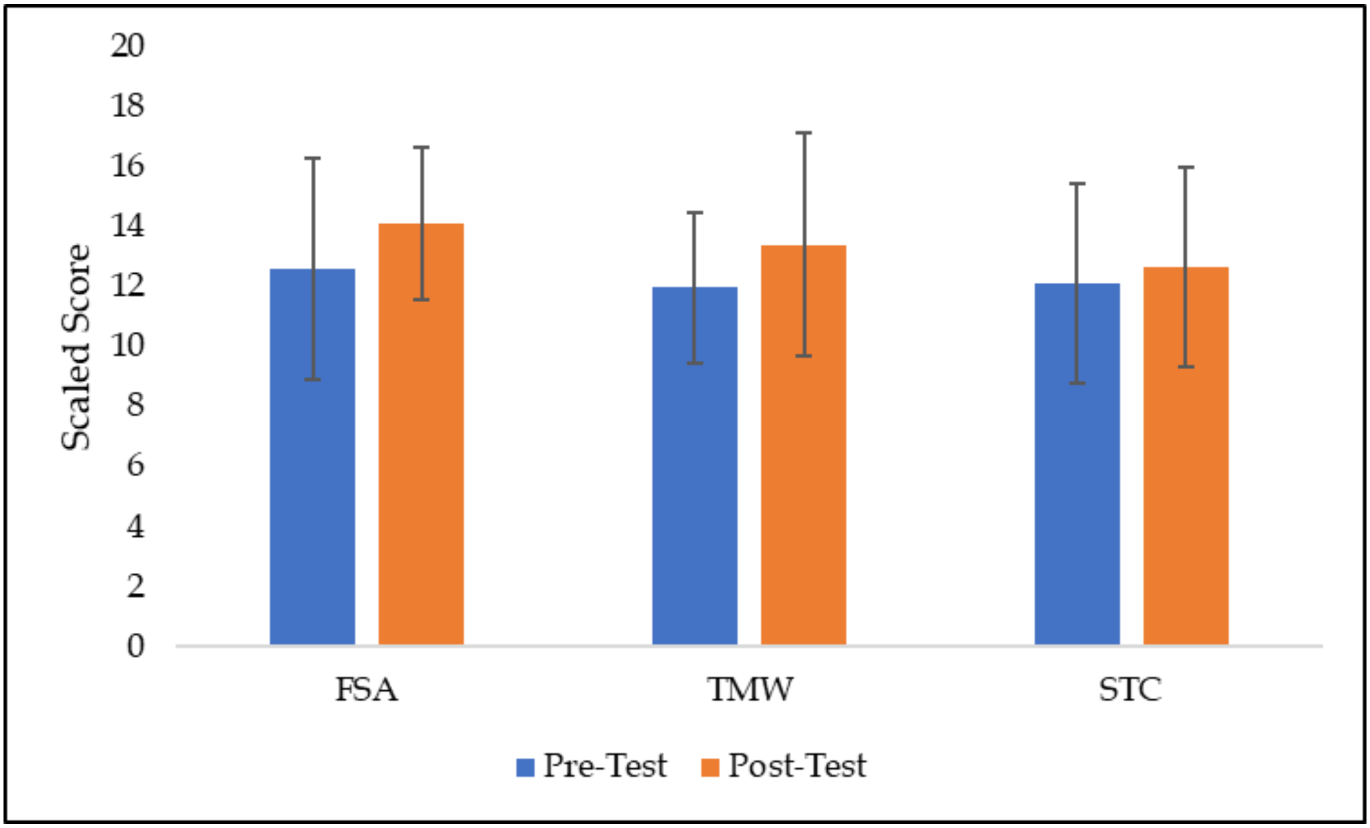

Figure 3. Effect of exercise modality over time on design fluency.

Grooved Pegboard: There was very little change in scores, and no interaction between group and time on the speed of test completion for the dominant hand (FSA: 77.07±13.29, 77.58±9.94; TMW: 62.88±8.05, 61.10±9.78; STC: 73.61±15.60, 70.02±11.51; p = .602) or the non-dominant hand (FSA: 76.02±9.36, 78.26±12.52; TMW: 78.72±7.01, 78.90±16.03; STC: 76.34±17.15, 79.79±20.39; p = .863), indicating that exercise modality has little to no impact on psychomotor function.

Fitness: Exercising heart rate decreased slightly following participation in the FSA and TMW interventions, whereas 12-weeks of STC resulted in an increased exercising heart rate. However, this did not result in a significant interaction between group and time (FSA: 113.94±20.76, 108.25±22.94; TMW: 113.33±9.84, 102.58±10.81; STC: 105.36±12.84, 109.21±14.65; p = .101), indicating that intervention group assignment did not have a statistically significant effect on exercising heart rate, but demonstrating a potentially clinically important improvement in cardiorespiratory fitness with either type of exercise. The percent of change in these results is shown in Figure 4 (p = .093).

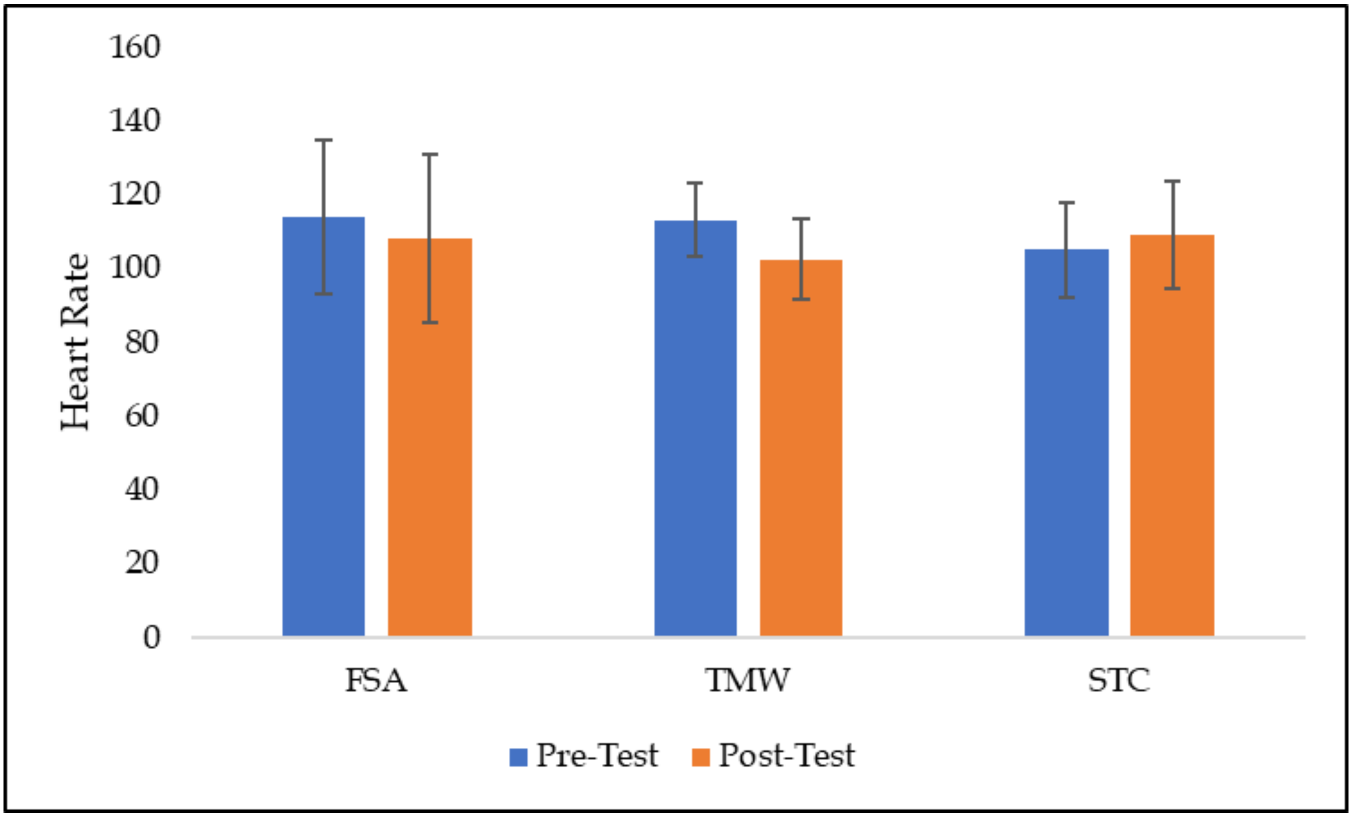

Figure 4. Effect of exercise modality on exercising heart rate at a constant intensity.

DISCUSSION

There was a significant interaction between group and time on TMT-A results (p = .011) in our similarly designed previous study of healthy women (13), indicating that FSA can be more effective than TMW at improving attention and processing speed in healthy women. Among breast cancer survivors, both FSA and TMW improved TMT-A results to a slightly greater, though not significant extent, compared to STC. It is possible that the small sample size prevented significant findings. It is also possible that the intervention was not rigorous enough to result in significant improvements.

Researchers have shown that verbal fluency can be diminished in breast cancer survivors following treatment (10, 18). Our intervention did not result in significant improvements in verbal fluency using COWAT assessments. While exercise was expected to improve brain function, it is possible that physical movement does not improve verbal abilities.

It was expected that executive function would increase to the greatest extent in FSA participants due to the nature of this modality, which requires multi-tasking processes in the brain. However, there was no indication of improvement in any group on the TMT-B or switching trial of verbal fluency, which were the two assessments of executive function. This indicates that 12 weeks of structured aerobic exercise might not be sufficient to significantly improve executive function in recent breast cancer survivors. Rehabilitating executive function might also require more complex cognitive tasks than can be provided from an exercise modality. Interestingly, however, Ehlers et al. recently reported that breast cancer survivors who were more physically active, as measured by minutes of moderate-to-vigorous activity per day, had higher executive function than those who were less active, indicating that an active lifestyle might be as important as a structured exercise program (6).

Similar to executive function, the interventions did not appear to have any impact on assessments of psychomotor function. Since psychomotor function was not directly challenged during the interventions, this was expected.

Both exercise intervention groups had a decreased average exercising heart rate, with intensity held constant, during post-testing as compared to pre-testing. While this change was not statistically significant, it could be clinically significant if it was correlated with improvements in cardiorespiratory fitness. A decreased exercising heart rate with aerobic training is consistent with the literature (17) and demonstrates that the women assigned to FSA did not significantly reduce their fitness benefits, compared to those using a treadmill, by adding multi-directional, cognitively stimulating movements.

The greatest limitation to this study was that it took more than 2 years to enroll 25 recent breast cancer survivors who completed the intervention and post-testing. Due to the extreme difficulty in recruitment, it was recommended that the study be closed before the target sample size of 30 was obtained, which increases the risk of type II errors. Directly correlated with the inadequate sample size was the inability to fully randomize participants. In an effort to get enough women who could participate in the study, consideration was given to class time preference, but not modality preference, when determining group assignment. Even so, classes did not have the recommended number of eight women for group dynamics (19).

Future studies should focus on determining an exercise intervention to improve each domain of cognitive function among breast cancer survivors. Manipulation of intensity, duration, and frequency of each session could result in greater cognitive effects than were shown in this study. Strategies addressing muscular strength, endurance, and flexibility in a well-controlled cognitive intervention are also warranted. Additionally, research with cancer survivors should be conducted in collaboration with local oncologists who can refer all eligible patients and encourage participation. Finally, screening for subjective or objective cognitive dysfunction prior to enrollment would allow for greater benefits to be seen from an intervention.

Although results were inconclusive, this study still provides some of the most specific information available regarding aerobic exercise modality for cognitive improvement among recent breast cancer survivors. In conjunction with previous research demonstrating the health benefits of exercise for cancer survivors and past studies showing cognitive improvement with exercise, this study demonstrates the need for more research in this area.

Participation in aerobic exercise has long been encouraged for health promotion and chronic disease prevention. It has previously been shown to be a safe and effective means for cancer survivors to reduce various cancer-related side effects. Until new studies provide further evidence, healthcare providers should encourage recent breast cancer survivors who suffer from CICD to participate in 150 minutes per week of a moderately intense aerobic exercise program.

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