Journal of Science and Medicine in Sport 22 (2019) 580–585

Contents lists available at ScienceDirect

Journal of Science and Medicine in Sport

journal homepage: www.elsevier.com/locate/jsams

Original research

Cognition in breast cancer survivors: A pilot study of interval and continuous exercise

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ARTICLE INFO

Article history:
Received 14 August 2018
Received in revised form
23 November 2018
Accepted 29 November 2018
Available online 6 December 2018

Keywords:
High-intensity interval training
Cerebrovascular circulation
Cognitive function
Cardiorespiratory fitness

ABSTRACT

Objectives: The current study investigated the effects of two exercise interventions on cognitive function amongst breast cancer survivors.
Design: Pilot randomised-controlled trial.
Methods: Seventeen female cancer survivors (mean: 62.9 ± 7.8 years) were randomised into three groups: high-intensity interval training (HIIT, n = 6); moderate-intensity continuous training (MOD, n = 5); or wait-list control (CON, n = 6). The HIIT and MOD groups exercised on a cycle ergometer 3 days/week for 12-weeks. Primary outcomes were cognitive function assessments utilising CogState. Secondary outcomes were resting middle cerebral artery blood flow velocity, cerebrovascular reactivity and aerobic fitness (VO_{2peak}). Data were analysed with General Linear Mixed Models and Cohen's d effect sizes were calculated.
Results: All 17 participants who were randomised were available for follow-up analysis and adherence was similar for HIIT and MOD (78.7 ± 13.2% vs 79.4 ± 12.0%; p = 0.93). Although there were no significant differences in the cognitive and cerebrovascular outcomes, HIIT produced moderate to large positive effects in comparison to MOD and CON for outcomes including episodic memory, working memory, executive function, cerebral blood flow and cerebrovascular reactivity. HIIT significantly increased VO_{2peak} by 19.3% (d = 1.28) and MOD had a non-significant 5.6% (d = 0.72) increase, compared to CON which had a 2.6% decrease.
Conclusions: This study provides preliminary evidence that HIIT may be an effective exercise intervention to improve cognitive performance, cerebrovascular function and aerobic fitness in breast cancer survivors. Considering the sample size is small, these results should be confirmed through larger clinical trials.

Practical implications

- High-intensity interval training may be an effective intervention to improve cognitive function in survivors of breast cancer.
- To increase aerobic fitness in breast cancer survivors, high-intensity interval training may be a more efficient method of prescribing exercise than moderate-intensity continuous exercise.
- High-intensity interval training appears to be a safe and effective method of prescribing exercise to breast cancer survivors which has a similarly high rate of adherence to a traditional moderate intensity continuous exercise protocol.

1. Introduction

Breast cancer is the most commonly diagnosed cancer in Australian women over the age of 50.[1] Although the prevalence of breast cancer is increasing in this age group, the prognosis for cancer patients has improved. As 5-year survival rates for breast cancer rise to just over 90%,[1] attention is being paid to how interventions, such as physical exercise, can address the long-term chronic health effects of cancer treatment. In particular, as many as 75% of cancer survivors report cognitive impairments during and after treatment, particularly in the domains of working memory, executive function and memory performance.[2,3] The exact mechanisms by which cancer and associated treatments may impact cognition are unclear but may relate to increased atrophy of grey matter, metabolic disturbances, cardiovascular impairments, inflammatory pathways or socioemotional factors including sleep and fatigue.[3–5] These pro-

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https://doi.org/10.1016/j.jsams.2018.11.026
1440-2440/

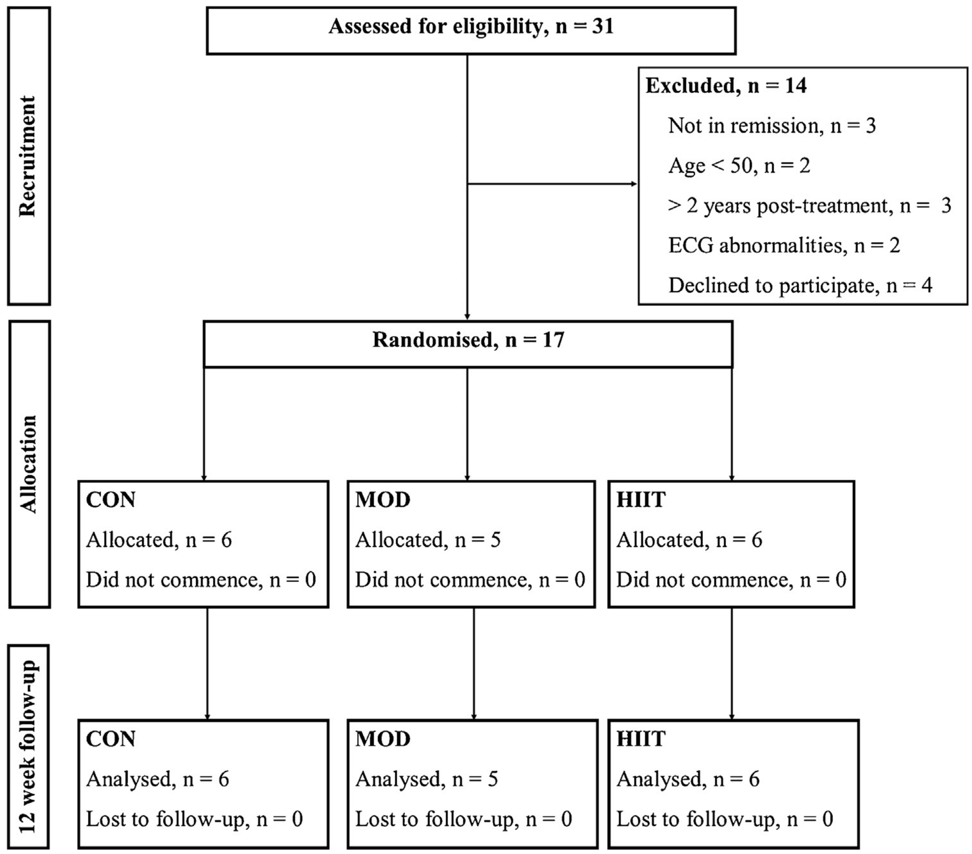

Fig. 1. CONSORT diagram depicting the flow of participants through the study.

cesses are similar to many age-related effects on the brain, although cancer survivors tend to exhibit more rapid and earlier declines.[6]

Whilst physical exercise shows promise as a treatment for age-related cognitive decline,[7] few studies have investigated this in breast cancer survivors.[8,9] Initial evidence from observational research suggests that cognitive function is preserved with higher levels of physical activity in cancer patients.[10,11] Similarly, cognitive performance in breast cancer survivors is improved when the duration of moderate to vigorous intensity physical activity levels are increased through a 12-week behavioural change program.[8] Recently, Peterson et al.[9] observed improved executive function and memory performance in cancer survivors, including from breast cancer, following a 12-week aerobic exercise intervention at moderate intensity. Although preliminary, these intervention studies suggest that cancer survivors' cognitive function may be improved through relatively short duration, moderate intensity exercise interventions. However, to improve clinical guidelines within the exercise oncology field, an improved understanding of the effects of exercise dose on cognition as well as potential mechanisms is required.

A growing body of evidence is emerging for the benefits of high-intensity interval training (HIIT), particularly for aerobic fitness (i.e. VO_{2peak}) and cardiovascular disease risk factors in clinical populations.[12] Research on HIIT in cancer survivors is an emerging area, and although effects on cognition have not been investigated, these initial studies may provide direction for its potential benefits. For instance, in research on healthy brain ageing, interventions incorporating aerobic exercise to improve VO_{2peak} have demonstrated increases in cognitive function.[13] In breast cancer survivors, Dolan et al.[14] showed a 6-week HIIT intervention elicited similar improvements to VO_{2peak} as a moderate intensity continuous group, with no adverse events recorded despite the increased intensity. Adams et al.[15] similarly showed a 12-week HIIT intervention improved VO_{2peak} alongside improvements in several cardiovascular risk factors including reduced arterial stiffness and inflammation in testicular cancer survivors. Higher arterial stiffness and inflammation negatively impact the brain, partly through damage to the cerebral microvessels and the endothelium.[16] Poor cerebrovascular health is associated with impaired cognitive function,[17] potentially due to decreased cerebral blood flow[18] or endothelial dysfunction.[19] Whilst there is evidence that exercise, and particularly HIIT, is effective at improving the function of the peripheral vasculature in cancer survivors, it is not clear if these effects extend to the cerebrovascular system. As cerebrovascular function is associated with aerobic fitness[20] and can be improved with exercise[21,22] in healthy populations, it presents a further mechanistic pathway to investigate the effects of HIIT on cognition.

Due to the limited understanding regarding the effect of exercise on cognition in breast cancer survivors over the age of 50, there is a need for preliminary investigations to inform subsequent large-scale clinical trials.[6] Therefore, the purpose of the current study was to investigate the effects of a 12-week aerobic exercise intervention of either HIIT or moderate intensity continuous exercise (MOD) on cognitive performance in breast cancer survivors in comparison to a wait-list control (CON). Secondly, the effects of these interventions on aerobic fitness and cerebrovascular function were examined as a potential mechanism to explain exercise-induced changes in cognitive performance.

2. Methods

The study piloted a three-arm, 12-week randomised controlled trial with pre- and post-intervention outcome assessments. Participants were recruited over a 15-month period from Canberra, Australia.

Table 1
Baseline characteristics of the study sample by group allocation.

	CON n = 6	HIIT n = 6	MOD n = 5	P
Age, years (SD)	61.5 (7.8)	60.3 (8.1)	67.8 (7.0)	0.83
Height, cm (SD)	163.5 (5.5)	165.6 (5.8)	165.6 (5.6)	0.77
Weight, kg (SD)	75.6 (7.7)	69.5 (16.1)	68.8 (11.5)	0.59
Cancer stage, n				0.45
I	3	2	1	
II	3	2	4	
III	0	2	0	
Treatment, n				0.30
Surgery	0	0	1	
	1	0	0	
Surgery + chemotherapy				
Surgery + radiation	2	3	4	
	3	3	0	
Surgery + chemotherapy + radiation				
Hormonal therapy				
Aromatase inhibitor	3	3	2	0.87

Data are presented as mean (SD) or number of participants.

Eligible participants were female breast cancer survivors ≤24 months post-diagnosis and aged 50–75 years of age. We additionally excluded participants with a history of central nervous system or bone metastatic cancers, any secondary cancers, using anti-hypertensive medication, diagnosed cardiovascular or cerebrovascular diseases, were participating in ≥30 min of moderate to vigorous intensity physical activity on more than 5 days per week or currently undertaking HIIT exercise. All eligible and consenting participants were required to obtain physician clearance and subsequently complete an exercise stress test with a 12-lead electrocardiogram (ECG) to be enrolled in the study. The flow of eligible and consenting participants through the study is shown in Fig. 1. The three groups were similar at baseline ($p > 0.05$) for all descriptive variables (Table 1). All participants provided written informed consent, and the study was approved by the University of Canberra Human Research Ethics Committee (project number 13-153).

Participants attended the laboratory on two separate days to complete the pre- and post- intervention outcome assessments. On day 1, participants completed the cognitive performance assessments (primary outcomes) and on day 2 participants completed the cerebrovascular and aerobic fitness assessments (secondary outcomes), in that order. All participants were instructed to avoid caffeine in the 12 h prior and strenuous physical activity and alcohol in the 24 h prior to each testing session. All testing took place in the morning and participants were asked to consume their normal breakfast 2 h prior to reporting to the laboratory. All post-intervention testing took place 2–4 days following the final exercise session.

Participants were randomised to either HIIT, MOD or CON using a computer-generated sequence of numbers in blocks of variable sizes in a 1:1:1 ratio, stratified by age. After baseline testing, a sealed, opaque envelope with the group allocation was delivered to the participant.

The two intervention groups (HIIT and MOD) exercised 3 times per week for 12 weeks (up to 36 sessions). Each session was conducted on a cycle ergometer (Monark 828E Ergometer), lasted 20–30 min and was fully supervised. Attendance was recorded to assess adherence. Participant's heart rate (Polar FT40 Monitor, Finland) and rating of perceived exertion (RPE; Borg 6–20 scale) were monitored to record the response to each session.

The MOD cycling group completed a 5-min warm-up and cool-down at 50% of peak power divided by a 20-min conditioning period completed at 55–65% of their peak power. The participant's peak power was determined from the maximal incremental cycle test completed pre-intervention. The workload began at 55% of peak power and was adjusted within this range over 12 weeks to ensure their RPE remained between 9 and 13 on a modified Borg scale (6–20) during each session. Heart rate and RPE was measured at 5-min intervals to monitor the participant's response to the exercise.

The HIIT group also completed a 5-min warm-up and cool-down at 50% of their peak power achieved in the pre-intervention maximal incremental cycle test. Following the warm-up, participants initially (week 1) completed four intervals lasting 30 s with 2 min of active recovery between each. The number of intervals was increased by one each week until the target of seven intervals was achieved in week 4. The number of intervals were maintained at seven for the remainder of the intervention. Participants in HIIT were instructed to increase their pedalling rate to between 95 and 115 revolutions per minute (RPM) to ensure a consistent and maximal effort across each interval. The resistance was adjusted by the supervisor over the intervention for each participant to ensure they remained within the 95–115 RPM range and reached a heart rate above 90% of their maximum by the fourth interval. The active recovery was performed with a light resistance at a self-selected pedalling rate. Heart rate and RPE was measured at the end of each interval and recovery period to monitor the participant's response to the exercise. From unpublished work within our laboratory in this population, this HIIT protocol elicits an average work rate of ∼105% of peak power during the 30 s intervals, although participants power output was unable to be measured across the entire intervention in the current study.

Participants in the CON group were asked to maintain their current lifestyle, including their level of physical activity, for 12 weeks following their baseline assessment. These participants were offered a 12 week fully supervised exercise intervention with aspects of HIIT and MOD at the completion of their follow-up testing.

The primary outcome of cognitive performance was assessed using tasks from the CogState battery, which has good construct validity and strong correlations with neuropsychological tests.[23] The following tests were selected based on the cognitive domains identified as being affected by cancer and are explained in detail elsewhere.[23] Briefly, the total number of words recalled in the three learning trials of the *International Shopping List* was used to assess verbal learning. The number of words recalled in the *International Shopping List Delayed Recall* was used to assess episodic memory. The *Groton Maze Learning Task* was used to assess executive function, scored by the total number of errors made across the five trials. The *One-Back Test* was used to test working memory, assessed by the proportion of correct responses.

The secondary outcome of cerebrovascular function was assessed by resting cerebral blood flow and reactivity to CO_2 (an index of endothelial function) of mean flow velocity in the right middle cerebral artery (MCA_{Vmean}) using 2 MHz transcranial Doppler ultrasonography (DWL Doppler, Compumedics Ltd., Germany) by a single trained operator. The middle cerebral artery was identified through the right temporal window using search techniques described previously.[24] Blood pressure was monitored noninvasively by finger photoplethysmography (Human NIBP, ADInstruments, Australia). The partial pressure of end-tidal CO_2 ($P_{ET}CO_2$) was assessed via a sampling tube connected to a Hans Rudolph mask and an online gas analyser (ML206; ADInstruments, Australia). All raw analogue signals were sampled at 1000 Hz via PowerLab (LabChart 7, ADInstruments, Australia). Following participant setup, a seated 5-min baseline measurement was taken. Resting MCA_{Vmean} indices were calculated from the final 60 s of the baseline. Participants then performed a modified rebreathing protocol to assess cerebrovascular reactivity to CO_2, in a seated position, as described previously.[25] The rebreathing protocol consisted of three phases. First, the participants completed a

Table 2
Outcome data for cognitive performance, cerebrovascular function and aerobic fitness.

	CON		HIIT		MOD		HIIT vs CON	MOD vs CON	HIIT vs MOD
	Pre	Post	Pre	Post	Pre	Post	*d*	*d*	*d*
Cognitive performance									
Verbal learning, words	26.0 (2.9)	27.6 (2.8)	27.8 (1.5)	28.3 (2.1)	26.0 (3.4)	26.6 (4.8)	−0.39	−0.36	−0.23
Episodic memory, words	9.7 (0.8)	9.3 (1.8)	10.3 (0.8)	10.7 (0.5)	9.8 (1.3)	10.0 (2.1)	**0.76**	**0.66**	−0.05
Executive function, errors	56.2 (12.8)	53.2 (19.0)	46.5 (11.4)	36.2 (9.1)	57.8 (6.1)	52.6 (7.7)	**0.75**	0.20	**0.55**
Working memory, acc	1.4 (0.1)	1.4 (0.1)	1.2 (0.1)	1.3 (0.1)	1.4 (0.2)	1.3 (0.1)	**0.81**	−0.34	**1.41**
Resting cerebrovascular function									
MCA_{Vmean}, $cm\,s^{-1}$	52.8 (10.0)	52.6 (10.0)	55.4 (8.2)	58.9 (9.8)	52.5 (12.1)	54.4 (11.7)	**0.86**	0.31	0.24
Reactivity, $\%\,mmHg^{-1}$	5.9 (2.1)	5.1 (0.8)	4.6 (1.5)	4.8 (2.0)	4.8 (2.4)	4.6 (1.4)	**0.72**	0.38	**0.54**
Resting blood pressure									
MAP, mmHg	78.3 (12.5)	73.9 (7.7)	86.4 (6.4)	82.7 (13.0)	82.0 (12.5)	80.7 (9.2)	−0.17	−0.45	0.13
Resting respiratory variables									
$P_{ET}O_2$, mmHg	103.8 (1.5)	103.7 (5.0)	103.0 (4.0)	101.9 (4.7)	101.5 (4.3)	101.9 (5.3)	−0.24	0.11	−0.44
$P_{ET}CO_2$, mmHg	33.8 (1.4)	33.5 (2.1)	35.5 (3.3)	35.8 (3.5)	34.5 (1.6)	34.7 (2.5)	0.31	0.23	0.01
Aerobic fitness									
VO_{2Peak}, $mL\,kg^{-1}\,min^{-1}$	20.9 (3.1)	20.3 (2.9)	18.5 (3.9)	22.0 (3.5)	21.8 (3.4)	23.1 (4.3)	**1.28**	**0.72**	0.19

Pre and post data are mean (SD). *d*: standardised change score expressed as Cohen's *d*.
Abbreviations: CON: wait-list control; HIIT; high-intensity interval training; MOD; moderate intensity continuous training; MCA_{vmean}: middle cerebral artery mean blood flow velocity; MAP: mean arterial pressure; $P_{ET}O_2$: partial pressure end-tidal oxygen; $P_{ET}CO_2$: partial pressure of end-tidal carbon dioxide.
Bold values signify moderate or large effect sizes.

second baseline measurement breathing room air. Secondly, the participants hyperventilated for 1 min to achieve a target $P_{ET}CO_2$ of 20–25 mmHg. Finally, the participants were switched to the rebreathing Douglas bag which contained 93% O_2 and 7% CO_2 and breathed normally until $P_{ET}CO_2 \geq 60$ mmHg, ventilation exceeded $100\,L\,min^{-1}$, or participants experienced discomfort. The coefficient from the linear regression between relative ΔMCA_{Vmean} and $P_{ET}CO_2$ was used to assess cerebrovascular reactivity to CO_2.

Aerobic fitness was assessed with a maximal incremental exercise test conducted on a cycle ergometer (High-Performance Ergometer, Schoberer Rad MeBtechnik, Germany). The exercise protocol began at 20 W and was increased by a further 20 W every minute until participants reached their peak load. Participants self-selected their pedalling cadence >60 revolutions per minute. Expired gases were analysed through a Hans-Rudolph face mask and averaged over 30 s to calculate VO_{2peak} (Vyntus CPX Metabolic Cart, Jaeger, Germany).

Statistical analysis were conducted with R version 3.4.2.[26] The mean and standard deviation of the outcome measures at baseline and follow up were calculated for each group. Group differences in baseline characteristics were assessed with one-way ANOVA or Kruskal–Wallis test. Data were analysed by General Linear Mixed Models with a random intercept fitted for subjects to take into account the repeated measures nature of the data and interindividual variability using the lme4 package.[27] Visual inspection of QQ-plots generated for each model showed no obvious deviations from normality. For each model, p-values were obtained using Type II Wald F tests with the car package[28] and underwent a Simes–Benjamini–Hochberg false discovery rate adjustment[29] to account for multiple comparisons. Statistical significance was accepted at adjusted $p < 0.05$.

Traditional hypothesis testing from pilot studies should be interpreted with caution as the small sample sizes can result in imprecise estimates and are unlikely to reach statistical significance. Therefore, we additionally calculated effect sizes for the pairwise changes in cognitive, cerebrovascular and aerobic fitness variables between the three experimental conditions. Effect sizes were calculated as Cohen's *d* using the pooled standard deviation of the random effects to account for the structure of the Linear Mixed Model. A positive effect size indicated a favourable effect towards the relevant intervention and was interpreted as small, moderate, and large based on cut-off points of 0.2, 0.5 and 0.8, respectively.

3. Results

Exercise adherence was similar between the HIIT and MOD groups (proportion of sessions attended: 78.7 ± 13.2% vs 79.4 ± 12.0%; $p = 0.93$), and there were no adverse events recorded during the intervention. On average, HIIT had a significantly higher relative heart rate (93.9 ± 5.7% vs 84.1 ± 5.2; $p < 0.01$) and RPE (14.5 ± 2.7 vs 12.3 ± 1.6; $p < 0.01$) compared to MOD immediately prior to the warm-down during the intervention.

The pre- and post-intervention group means and effect sizes for the primary outcome of cognitive performance are presented in Table 2. There were no statistically significant group × time interaction effects for verbal learning ($F_{14,2} = 0.1$; $p = 0.95$), episodic memory ($F_{14,2} = 0.6$; $p = 0.71$), executive function ($F_{14,2} = 0.9$; $p = 0.45$), or working memory ($F_{14,2} = 1.3$; $p = 0.44$). However, both HIIT and MOD had moderate-sized effects for episodic memory in comparison to CON. In comparison to CON and MOD, the HIIT group had moderate and large effect sizes for executive function and working memory, respectively (Table 2).

For the secondary outcome of cerebrovascular function (Table 2), there were no statistically significant group × time interactions for resting MCA_{Vmean} ($F_{13,2} = 0.6$; $p = 0.73$) or cerebrovascular reactivity ($F_{13,2} = 0.2$; $p = 0.80$). Similarly, mean arterial pressure ($F_{13,2} = 0.2$; $p = 0.84$), end-tidal CO_2 ($F_{13,2} = 0.3$; $p = 0.72$), and end tidal O_2 ($F_{13,2} = 0.2$; $p = 0.82$) did not have significant changes. However, there was a large-sized effect for HIIT in comparison to CON for resting MCA_{vmean}. In comparison to both CON and MOD, the HIIT group showed moderate-sized effects for CRV.

For VO_{2peak} there was a significant group × time interaction (Table 2; $F_{12,2} = 6.5$; $p = 0.02$). Examination of fixed effects showed a significantly greater increase in VO_{2peak} for HIIT compared to CON (b = 4.0 [1.9–6.0]). There were no significant differences in VO_{2peak} for MOD in comparison to CON or HIIT. The calculated effect sizes for VO_{2peak} showed HIIT and MOD elicited a large and moderate-sized effect in comparison to CON, respectively.

4. Discussion

This pilot randomised controlled trial is the first to investigate the feasibility of HIIT or MOD on both cognitive performance and cerebrovascular function in breast cancer survivors. As the proportion of breast cancer survivors over the age of 50 increases, the development of interventions to negate the effects of the illness and treatments will become crucial to the ongoing care and rehabilitation of this population. The HIIT intervention elicited positive moderate-to-large effects in comparison to both MOD and CON for aspects of cognitive performance including episodic memory, working memory and executive function. These effects extend to the secondary outcomes, where HIIT resulted in a moderate-sized improvement to MCA_{vmean} and a large effect on cerebrovascular reactivity in comparison to CON. In addition, there was a statistically significant effect of HIIT on aerobic fitness in comparison to the control group. Given there was a high adherence and no adverse events during the intervention, these novel results provide preliminary evidence that exercise interventions, particularly at higher intensities, are a safe and efficacious method to improve cognitive function and brain health in this population.

These findings for cognitive function are consistent with meta-analyses demonstrating the effects of exercise on cognition in older adults without cancer[7] and recent studies in cancer survivors.[8,9] Peterson et al.[9] showed within-group improvements to working memory, executive function and verbal memory following 12-weeks of a moderate intensity stationary cycling intervention, which overlap directly with the cognitive tests that appeared sensitive to HIIT in the current study. Although we did not show the same effects for MOD in comparison to CON, the MOD group improved performance for all four cognitive assessments. In addition to differences in the statistical analysis, the previous study included both male and female survivors of several types of cancer and a different cognitive assessment tool. In agreement with our findings, Hartman et al.[8] found a dose-response effect on executive function with a 12-month intervention to increase lifestyle moderate to vigorous intensity PA in breast cancer survivors. This effect concurs with the tendency towards larger effect sizes on cognition for HIIT in the current study.

This study adds to the evidence supporting the positive effects of exercise training on resting cerebrovascular function[21] and is the first to do so in a cancer population. Previously, a 12-week moderate-intensity aerobic exercise intervention in older adults improved cerebrovascular reactivity and resulted in an average increase in resting MCA_{Vmean} of $4.0\,cm\,s^{-1}$, which is similar to the $3.5\,cm\,s^{-1}$ increase observed in the current study's HIIT group.[21] The exact cause of the increase in resting cerebral blood flow in the HIIT group is unclear but could be related to higher aerobic fitness post-intervention,[20] changes in $P_{ET}CO_2$, cerebral angiogenesis, or increased pre-frontal cortex volume. Whilst larger participant numbers would allow some of these factors to be investigated, the addition of neuroimaging to future studies would be beneficial in providing a further mechanistic explanation. Interestingly, previous work by Adams et al.[15] investigating HIIT in cancer survivors found significant benefits to plaque burden and arterial stiffness in the carotid artery[15] which corresponds with the increase in cerebral blood flow and improved cerebral endothelial function shown here. Given vascular risk factors contribute to cognitive decline and an increased risk of Alzheimer's disease,[17] these initial effects on the cerebrovascular system present an important mechanistic target for future research.

In addition to the changes in cerebrovascular function, the participants in the exercise interventions displayed improvements in aerobic fitness. The mean improvement in VO_{2peak} over the 12 weeks (HIIT: +19.3%; and MOD +5.6%) is consistent with a previous meta-analysis comparing HIIT and MOD interventions for cardiovascular disease risk factors.[12] This finding demonstrates that the two exercise interventions provided a sufficient training stimulus for positive physiological adaptation to occur and that the HIIT stimulus was greater. Moreover, whilst the exercise groups increased their fitness, participants in the control group experienced a slight decline (−2.6%) in VO_{2peak} over the 12-week duration. Breast cancer patients have been observed to have lower aerobic fitness than their age-matched counterparts which, in turn, may contribute to an increased risk of breast cancer mortality and chronic health conditions including cardiovascular disease.[30] Given prior longitudinal research has shown lower baseline VO_{2peak} also to be associated with cognitive decline,[31] this study provides further evidence that exercise may be beneficial in improving health outcomes for breast cancer survivors.

The methodology presented here provides a framework to guide and inform future large-scale clinical trials in cancer survivors that, with modification, will enable evidence-based exercise recommendations to be provided to this population. A key limitation which arose during the current study was recruiting participants who met the inclusion criteria. When considering the inclusion criteria of the pilot study it was considered a priority to restrict the age of participants (50–75 years), to recruit from a single type of cancer (breast cancer), and to exclude participants on blood pressure medication due to the known effects on the cerebrovascular assessments. Initial discussions with clinicians working with these patients indicated a high availability of participants, however, the number of people who met the inclusion criteria within the time-frame over which the study was conducted was limited. In addition, due to the substantial heterogeneity within this population, there are several other inclusion criteria which could be considered in future research, including the cancer treatment type and the presence of depressive symptoms. Whilst excluding participants with depression may be considered for future studies with cognitive function outcomes, it may not be representative of a cancer survivor population and will further limit the number of eligible participants. These controls may also further limit the number of eligible participants, and as such a multi-site approach to maximise the eligible participant pool is suggested.

5. Conclusions

The initial findings suggest that exercise, particularly HIIT, may be an effective intervention in breast cancer survivors to reduce cognitive impairment and improve aerobic fitness. As the effects observed may be beneficial to future health outcomes in breast cancer survivors, future randomised controlled trials are required to confirm these findings and to investigate potential mechanisms to enable evidence-based exercise recommendations to this population.

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